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**ARAŞTIRMA MAKALESİ /** *RESEARCH ARTICLE*

# Histopathological and Biochemical Investigation of Silymarin's Inhibitory Effect on the Formation of Obesity Induced by High Fat Diet in Rats

## *Ratlarda Yüksek Yağlı Diyetle İndüklenen Obeziteye Karşı Silymarin'in Önleyici Etkisinin Histopatolojik ve Biyokimyasal Olarak İncelenmesi*

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**ABSTRACT**

***Aim:*** *Obesity is a health problem caused by excessive fat accumulation in the body and can lead to many health complications. Nurses play an important role in managing the care of patients struggling with obesity. This study investigated the restorative effect of silymarin on obesity induced by a high-fat diet (HFD).*

***Materials and Methods:*** *In this study, 32 rats were randomly divided into four groups (n=8). Control: no action. Obesity: was fed with HFD. Silymarin: 3 mg/kg silymarin was given by orogastric gavage daily. Obesity+silymarin: 3 mg/kg silymarin daily was given in addition to HFD. Liver function tests and lipid profile values were measured in serum samples, and the liver was examined histopathologically.*

***Results:*** *Macro-microvesicular fatty changes and coagulation necrosis were observed in centrilobular hepatocytes in livers of the obesity group, while a normal histological appearance of the liver was viewed in the obesity+silymarin group. In the obesity group, ALP and LDH activities in addition to triglyceride levels were significantly higher than control, while these values in the obesity+silymarin group were similar to control.*

***Conclusions:*** *Silymarin largely prevented fatty liver changes and significantly restored impaired lipid profile and liver function tests in rats fed with HFD.*

**Key words:** *liver function tests; lipid profile; histopathology; nurse care; obesity; silymarin*

**ÖZET**

***Amaç:*** *Obezite vücutta aşırı yağ birikmesinden kaynaklanan ve birçok sağlık komplikasyonuna yol açabilen bir sağlık sorunudur. Hemşireler obezite ile mücadele eden hastaların bakımının yönetilmesinde önemli bir rol oynamaktadır. Bu çalışmada, silimarinin yüksek yağlı diyet (HFD) ile indüklenen obezite üzerindeki onarıcı etkisi araştırılmıştır.*

***Materyal ve Metot:*** *Bu çalışmada 32 rat rastgele dört gruba ayrılmıştır (n=8). Kontrol: hiçbir işlem yapılmadı. Obezite: HFD ile beslendi. Silimarin: 3 mg/kg silimarin orogastrik gavaj yoluyla günlük olarak verildi. Obezite+silymarin: Günlük 3 mg/kg silimarin HFD'ye ek olarak verildi. Serum örneklerinde karaciğer fonksiyon testleri ve lipit profili değerleri ölçüldü ve karaciğer histopatolojik olarak incelendi.*

***Bulgular:*** *Obezite grubunun karaciğerlerinde sentrilobüler hepatositlerde makro-mikroveziküler yağ değişiklikleri ve koagülasyon nekrozu gözlenirken, obezite+silimarin grubunda karaciğerin normal histolojik görünümü izlendi. Obezite grubunda ALP ve LDH aktiviteleri ile trigliserid düzeyleri kontrole göre anlamlı derecede yüksekken, obezite+silimarin grubunda bu değerler kontrole benzerdi.*

***Sonuçlar:*** *Silimarin, yağlı karaciğer değişikliklerini büyük ölçüde önlemiş ve HFD ile beslenen sıçanlarda bozulmuş lipit profili ve karaciğer fonksiyon testlerini önemli ölçüde düzeltmiştir.*

**Anahtar kelimeler:** *karaciğer fonksiyon testleri; lipit profili; histopatoloji; hemşirelik bakımı; obezite; silimarin*

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## Introduction

Obesity is defined by the World Health Organization as abnormal or excessive fat accumulation in adipose tissues. This abnormality is one of the most common global health problems for all age groups[1,2]. The prevalence of obesity is increasing worldwide and is becoming one of the important health problems among children and adolescents as well as the adult population[3]. Industrialization and urbanization are indicated as the major changes in people's lifestyle that may predispose to obesity. In addition, the fact that food items contain high amounts of fat and sugar and are abundant and cheap, increased ready-eat, and rapid eating habits, and decreased physical activity, and excessive calorie intake contributes to the increase in obesity[4]. Nurses can provide both preventive and therapeutic care related to obesity. The role of nurses in obesity treatment begins with informing and directing patients about options such as diet, exercise, medication, and surgical treatment. Additionally, nurses are an important part of the multidisciplinary team by assessing patients' nutrition habits and physical activity levels, ensuring correct use of medications, and collaborating with other healthcare professionals[5]. According to the data of the World Health Organization, obesity has been reported to be one of the most important factors in the occurrence of chronic diseases such as diabetes, heart disease, chronic respiratory diseases, stroke and cancer, which are responsible for approximately 60% of all deaths in the World[6,7]. Recently, the search for preventive measures and treatments to reduce the risk of obesity, hypertension, type 2 diabetes mellitus, hypercholesterolemia, hyperlipidemia, and thrombosis has increased. In line with these searches, nurses have an important role in the management of obesity-related health problems. Methods such as diet and medical applications (statins) are frequently used to prevent high blood cholesterol and related pathologies. Accordingly, two different medicines named as orlistat and sibutramine, are recommended by the American Food and Drug Administration (FDA). Of these two drugs, orlistat reduces the absorption of fat in intestinal by suppressing the pancreatic lipase enzyme, and sibutramine also reduces appetite by suppressing the deactivation of neurotransmitters such as dopamine, serotonin and neurosephrine in brain. However, these two different drugs can reduced whole body weight moderately[8–11]. Today, pharmacotherapy is recommended as a second-line therapy for weight management after the lifestyle change. In fact, for the long-term management of obesity have been developed a large number of drugs that can provide a positive energy balance, target various pathways through various different mechanisms, and affect various factors. Especially in recent years, some anti-obesity medications have been used to treat morbid obesity; however, most of these drugs have been removed from the market due to their serious cardiovascular side effects[12]. For this reason, as in many diseases, herbal and preventive medicine is among the methods used for the prevention and treatment of obesity and they are very popular[13]. Herbal products in Türkiye and in the world is the most popular form of complementary and alternative Medicine[14]. International studies have perceived herbal and traditional therapies such as the consumption of "organic" and "unprocessed" foods that do not contain toxins or additives as harmless, while for their drugs they are "chemicals" that should be avoided[15]. Silymarin that is a natural flavonoid, is a thistle (*Silybum marianum*) component. It is a metabolic regulator known to have anti-oxidant, anti-inflammatory, anti-cancer, anti-mutagenic, anti-bacterial and anti-virus effects. In addition, silymarin has more than one pharmacological activity and its components include silibinin, silenanine and silistristin. Silymarin metabolically stimulates liver cells and activates ribosomal RNA synthesis to stimulate protein Formation[16]. Non-alcoholic fatty liver disease that is a chronic liver disease, is found mostly in obese people who are fed high-fat diets and have sedentary lifestyles[17]. Silymarin is used in the treatment of many liver disorders characterized by functional impairment or degenerative necrosis. Also, it has preventive and curative effects on prevention of various diseases such as Alzheimer, and insulin resistance especially in cirrhotic patients, cancer and cardiovascular diseases. In addition, silymarin has many of activities such as delaying aging, increasing life time, increasing movement speed and stimulation, renal protection, hypolipidemic and anti-atherosclerosis activities[18]. Silymarin can play an important role as an antioxidant as it prevents their absorption and biological activation by increasing the metabolism and excretion of polyunsaturated fatty acids and mycotoxins[19]. Silymarin is a well tolerated active ingredient and no drug interaction has been reported. The most common problems as a side effect are digestive system disorders. However, the incidence of these disorders is the same as placebo[20]. In this study, the protective effect of silymarin on liver tissue, was investigated by liver function tests, lipid profile values and histopathologically in rats with experimental obesity induced with a high-fat diet.

## Material and Methods

### *Experiments*

Ethical approval was obtained for the study from the Van Yüzüncü Yıl University Experimental Research Local Ethics Committee (Ethics committee Decision No: 2018/02). In the study, 32 male Wistar Albino rats were used at 3 months old and weighing 200–280 g. The rats were fed with tap water and standard pellet rat food (for the control and slymarin groups) at a temperature of 22±2° C, at a rhythm of 12 hours light and 12 hours dark in rooms with 60% humidity. Feed and water intake was left free (adlibitum) for all groups. The rats were weighed at the beginning of the study and randonmly assigned into groups to be as evenly distributed in weight as possible.

### *Preparation of High Fat Diet (HFD)*

After the standard pellet feed from a private commercial feed manufacturer was milled, 300 g/kg of butter was melted and added to the feed. With this method, a fatty diet pellet feed with a high energy value (over 4000 kcal / kg) consisting of 60% saturated fat was obtained. The average amount of feed that the rats could eat for a week was calculated, and high-fat diets were prepared fresh weekly[21]. Also, silymarin was purchased commercially and was administered to rats at a daily dose of 3 mg/kg by orogastric gavage.

### *Creating Groups*

Thirty-two rats were divided equally and randomly into four groups (n=8). Groups were created as follows.

*Control Group:* The rats were fed with standard pellet feed.

*Obesity Group:* The rats were fed with high-energy dietary pellet feed.

*Obesity+Silymarin Group:* The rats were fed with dietary pellet feed with high energy value, and 3 mg/kg of silymarin daily was given by orogastric gavage.

*Silymarin Group:* The rats were fed with a daily 3 mg/kg silymarin orogastric gavage in addition to the standard pellet feed.

The study was continued for 8 weeks. The weight changes were determined by weighing the rats in all groups on the 0, 15, 30, 45 and 60 days of the experiment. At the end of the study, after the rats anesthetized with a mixture of 0.5 mg/kg Ketamine + 0.1 mg/kg Xylazine, intracardiac blood and other tissue samples were taken for histopathological and biochemical examinations.

### *Biochemical Analysis*

After the blood taken into yellow capped biochemistry tubes was centrifuged at 3000 *xg* for 10 minutes, the serum samples in upper phase were transferred to another tube and stored at -80° C until they were studied. Measurement of AST, ALT, GGT, LDH, alkaline phosphatase, HDL, LDL, cholesterol, triglyceride and glucose values in serum samples were measured using the chemiluminescence immunoparticle method by the Architect SystemAbbott Plus CI 16200® (AbbottDiagnostic Plus CI 16200, USA) analyzer.

### *Histopathological Examination*

At the end of the experimental application, all animals were anesthesied and tissue samples were taken from the livers. Macroscopic findings observed in internal organs including the liver, were recorded. After the liver tissue samples were fixedin 10% buffered formalin, 4 μm sections were taken with a microtome (Leica RM2235), embedded in paraffin blocks, stained with hematoxylin-eosin (HE) and Oil Red O (for fatty changes) for histopathological examination and examined under a light microscope (Nikon Eclipse 80*i, DS-Ri2*). Liver tissues; it was examined in terms of inflammation, steatosis, degeneration, and fibrosis.

### *Statistical Analysis*

Results are expressed as mean and standard deviation. IBM Statistical Package for Social Sciences (SPSS) program (version 20) was used for analysis. The Shapiro Wilks test was used to check whether the data were normally distributed or not. Since the data were distributed normally, whether there was any difference between the groups, was determined by the Kruskal-Wallis test. Posthoc was performed to determine from which group the differences originated. Averages with a p value of 0.05 or less were considered significant relative to each other. In addition, correlation analysis between parameters was also performed.

## Results

### *Biochemical Findings*

During the study, the results of the increase in the average weight of the animals by groups and days were shown in detail in Table 1. There were no significant differences between the weight averages of the groups at the beginning and 15th day of the study, and all the group values were similar (p>0.05). However, it was observed that the weight averages of other groups other than the control group increased considerably from the 30th day (p<0.009). But there was no significant difference between the obesity and obesity + silymarin groups of the 60th day (p>0.05). Also, comparing the time-dependent group weight averages within the same group depending on the age increase in the control group from the starting day until the 60th day, the other groups showed increases due to age and diet.

### *Results of Liver Function Tests*

Results of AST, ALT and LDH values from liver function tests are shown in detail in Table 2 and Fig. 1. In the obesity group, LDH values increased significantly compared to the control group (p<0.05), while ALT values decreased (p<0.05). There was no significant difference in AST values (p>0.05). Also, LDH values in the obesity+silymarin and silymarin groups were quite low compared to the obesity group (p<0.05). In addition, ALT values in the control and silymarin group were higher than in the obesity group (p<0.05). There was no significant change in GGT values and the values of all groups were similar (p>0.05).

When lipid profile values were examined in Table 2 and Fig. 2, interestingly, total cholesterol values in the obesity group were not significant, but were low compared to the control group (p>0.05), while obesity+silymarin and silymarin were high (p<0.05). Also, HDL values were lower in the obesity group compared to the control and obesity+silymarin groups, while the highest LDL and HDL values were observed in the obesity+silymarin group (p<0.05). There was no significant difference between the LDL values of the other groups. Also, triglyceride values were highest in the obesity group, while the lowest was in the silymarin group (p<0.05). There was no significant difference between the obesity+silymarin and silymarin groups (p>0.05).

***Table 1.*** *Live weight average and standard deviation values according to groups and days*

| | Control | Obesity | Obesity+Silymarin | Silymarin | P value (time) |
|---|---|---|---|---|---|
| **Baseline** | 155.17±17.46 | 162.86±9.99 | 174.00±9.17 | 168.29±19.85 | 0.155 |
| **15 thday** | 187.67±12.48$^{\neq}$ | 199.43±11.65$^{\neq}$ | 209.71±11.40$^{\neq}$ | 204.57±21.09$^{\neq}$ | 0.077 |
| **30th day** | 196.17±13.03$^{*\neq}$ | 218.57±11.18$^{\neq}$ | 219.43±13.45$^{\neq}$ | 218.29±13.24$^{\neq}$ | 0.009 |
| **45th day** | 212.67±13.84$^{\neq}$ | 223.14±11.25$^{\neq\phi}$ | 237.43±18.17$^{*\neq\varphi}$ | 223.14±10.06$^{\neq}$ | 0.028 |
| **60 thday** | 216.67±17.47$^{\neq\phi}$ | 250.86±19.18$^{\theta\neq\varphi}$ | 250.00±20.07$^{\theta\neq\varphi}$ | 238.71±15.01$^{\neq\phi}$ | 0.009 |
| **Pvalue (group)** | 0.011 | 0.020 | 0.001 | 0.001 | |

*p: Significant compared to the other groups on the 30th or 45th days (p <0.05), †p: significant compared to control and Silymarin groups on the 60th day (p <0.05), ≠p: significant according to the starting day in the same group (p <0.05), ϕp: significant according to day 15th in the same group (p <0.05), φp: significant according to the 15th and 30th days within the same group (p <0.05).

***Table 2.*** *Mean and standard deviation values of some liver function tests and lipid profile values at the end of study*

| | Control | Obesity | Obesity+Silymarin | Silymarin | P values |
|---|---|---|---|---|---|
| **AST** | 107±11 | 104±9 | 104±9 | 115±10 | 0.076 |
| **ALT** | 45±5 | 27±3$^{\neq}$ | 28±4$^{\neq}$ | 37±2 | 0.001 |
| **LDH** | 295±21 | 1084±83$^{*}$ | 601±36$^{\theta}$ | 596±42$^{\theta}$ | 0.001 |
| **GGT** | 2.92±0.12 | 3.10±0.12 | 3.08±0.15 | 2.98±0.14 | 0.109 |
| **Alk-P** | 186±20 | 203±13 | 177±14 | 235±43$^{*}$ | 0.004 |
| **Cholesterol** | 53±4 | 48±4 | 67±3$^{*}$ | 55±8$^{\phi}$ | 0.001 |
| **HDL** | 37.3±3.6 | 30.9±2.8$^{*}$ | 48.5±2.4$^{*}$ | 40.1±6.6 | 0.001 |
| **LDL** | 10.2±0.9 | 9.6±0.9 | 13.5±1.7$^{*}$ | 10.4±1.8 | 0.009 |
| **Triglyceride** | 111±9$^{*}$ | 128±8$^{*}$ | 84±6$^{*}$ | 69±5$^{*}$ | 0.001 |
| **Glucose** | 126.5±9.5 | 116±18 | 87.5±7$^{\theta}$ | 88±6$^{\theta}$ | 0.002 |

AST: aspartattransaminase, ALT: alanintransaminase, LDH: lactatedehydrogenesis, GGT: gammaglutamyltransferase, AlkP: alkalenfosfataz, HDL: high-density lipoprotein, LDL: low-density lipoprotein, *p: Significant according to other groups (p<0.05), ϕp: Significant according to control and Silymarin groups (p <0.05), θp: significant according to obesity and obesity + Silymarin groups (p <0.05), θp: significant according to control and obesity groups (p <0.05).

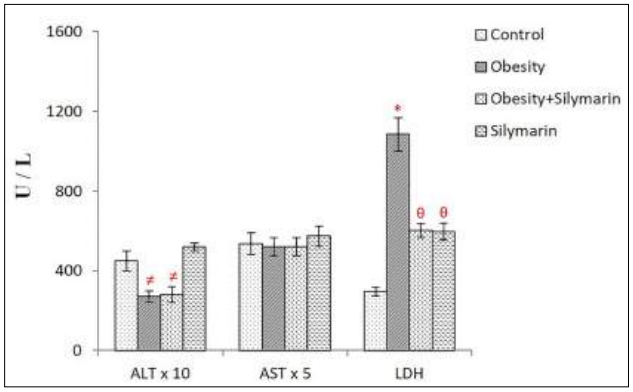


***Figure 1.*** *Comparison of AST, ALT and LDH values from liver function tests *p: Significant compared to other groups (p <0.05), ≠p: Significant compared to other groups (p <0.05), θp: Significant compared to control and obesity groups (p <0.05).*

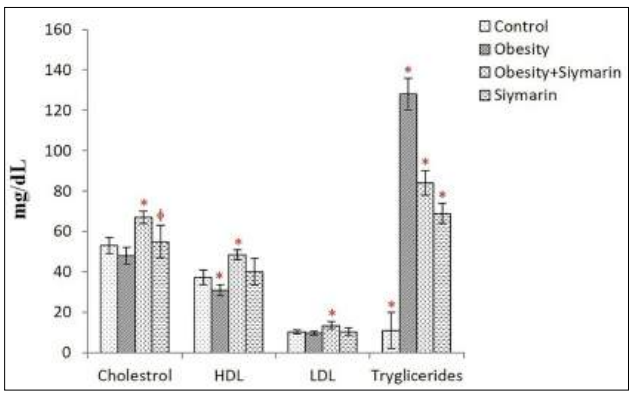


***Figure 2.*** *Collective comparison of lipid profile values.*p: Significant compared to other groups (p<0.05), ≠p: Significant compared to control and Silymarin groups (p <0.05), θp: Significant compared to obesity and obesity + Silymarin groups (p <0.05).*

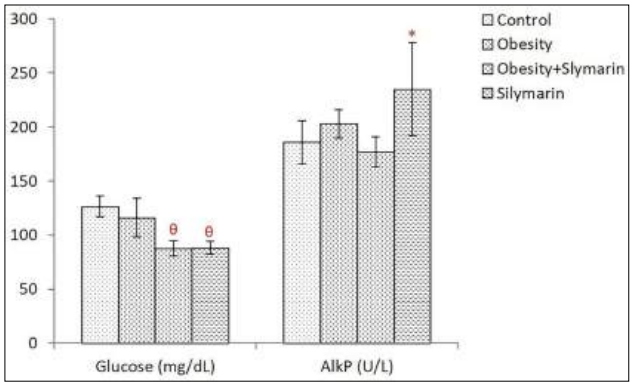


***Figure 3.*** *Comparison of glucose and AlkP values *p: Significant compared to other groups (p <0.05),θp: Significant compared to control and obesity groups (p <0.05).*

Alkaline phosphatase values from parameters associated with bone development during development were higher in the silymarin group than in other groups (p<0.05). There was no significant difference between the other groups (p>0.05). Also, glucose values of silymarin and obesity + silymarin groups were lower than control and obesity groups (p <0.05, Table 1 and Fig. 3). Also, the Pearson-correlation coefficients and degrees of importance of the groups according to the parameters and between the parameters are given in detail in Table 3. A positive value indicates that the parameters are positively correlated and the negative value parameters are negatively correlated. Correlations are expressed as percentages. The results showed a positive correlation between ALT and AST values, while there was a significantly negative correlation between LDH and ALT and HDL values. When cholesterol values were examined, there

***Table 3.*** *Collective display of values for correlation between groups and parameters*

| Correlations | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Groups | AlkP (U/L) | ALT (U/L) | AST (U/L) | Cholesterol (mg/dL) | HDL (mg/dL) | LDL (mg/dL) | Glucose (mg/dL) | LDH (U/L) | Triglyceride (mg/dL) |
| **Gruplar** | 1 | | | | | | | | | |
| **AlkP (U/L)** | 0.415* | 1 | | | | | | | | |
| **ALT (U/L)** | 0.205 | 0.302 | 1 | | | | | | | |
| **AST (U/L)** | 0.464* | 0.286 | 0.85** | 1 | | | | | | |
| **Cholesterol (mg/dL)** | 0.341 | -0.084 | -0.237 | -0.204 | 1 | | | | | |
| **HDL (mg/dL)** | 0.392* | -0.086 | -0.118 | -0.135 | 0.927** | 1 | | | | |
| **LDL (mg/dL)** | 0.248 | -0.144 | -0.348 | -0.301 | 0.862** | 0.825** | 1 | | | |
| **Glucose (mg/dL)** | -0.797** | -0.200 | -0.117 | -0.310 | -0.511** | -0.551** | -0.453* | 1 | | |
| **LDH (U/L)** | 0.111 | 0.144 | -0.428* | -0.077 | -0.337 | -0.430* | -0.240 | 0.045 | 1 | |
| **Triglyceride (mg/dL)** | -0.801** | -0.250 | -0.335 | -0.359 | -0.528** | -0.610** | -0.387* | 0.701** | 0.443** | 1 |

*p: The correlation is significant to the 0.05 value (2-tailed), **p: The correlation is significant to the 0.01 value (2-tailed),

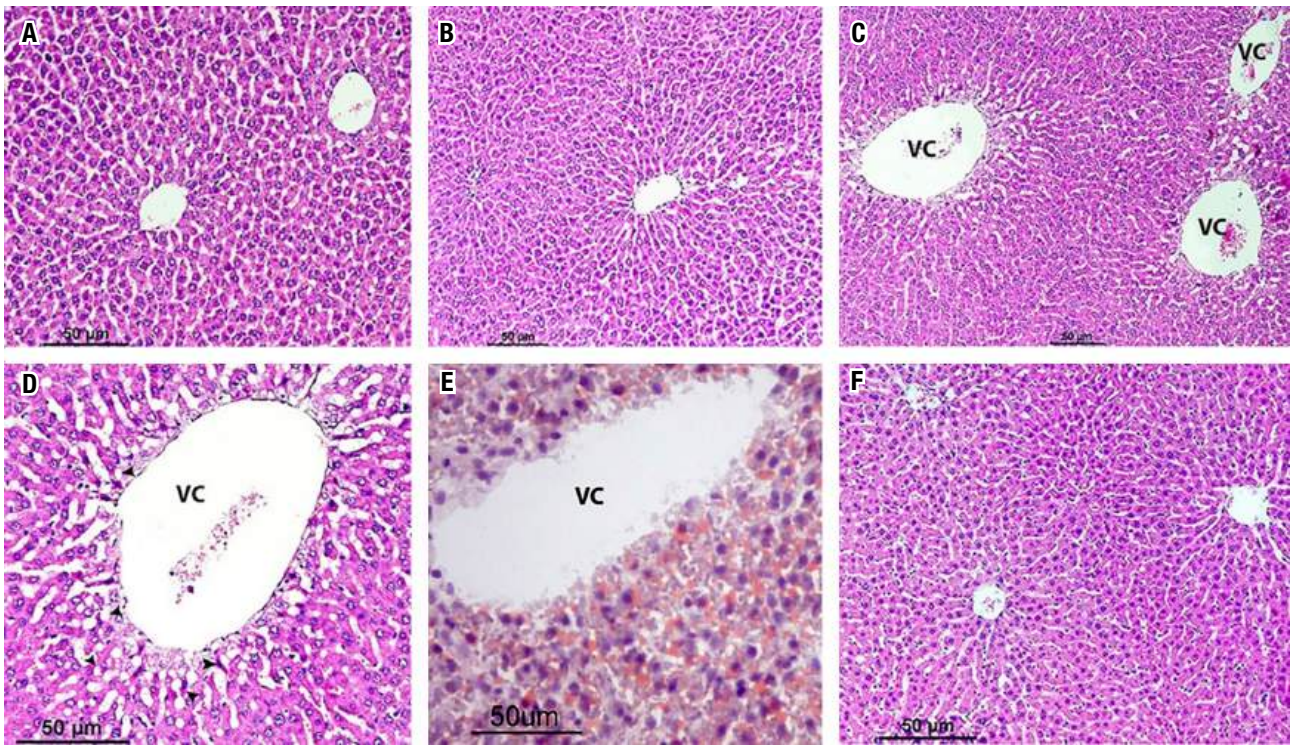


***Figure 4.*** *Collective demonstration of histopathological images for all groups. A: Control group, the normal microscopic view of liver tissue is observed (H.E.). B: Silymarin group, the normal microscopic view of liver tissue is observed (H.E.). C: Obesity group; vacuoles degeneration is observed in centrilobular hepatocytes (VC) in liver tissue (H.E.). D: Obesity group; in the liver tissue, sharp limited vacuoles of different sizes in centrilobuler hepatocytes (VC) and coagulation necrosis (arrowheads) are observed in some of these hepatocytes (H.E.). E: Obesity group; fat deposits in orange color are observed in centrilobular hepatocytes (Oil Red O satining). F: Obesity + Silymarin group; the normal histological appearance is observed in the liver tissue (H.E.) (Bar: 50 µM).*

was a positive correlation between cholesterol and HDL and LDL values, while there was a negative correlation between glucose and triglyceride values. Also, there was a positive correlation between HDL values and LDL values, while there was a negative correlation between glucose, LDH, and triglyceride values. Also, there was a negative correlation between LDL values and glucose and triglyceride values, while there was a positive correlation between glucose and LDH values and triglyceride values.

### *Macroscopic Findings*

No morphological changes were detected in the macroscopic examination of the organs in the necropsies of the control and experimental group rats.

### *Histopathological Findings*

***Control:*** Microscopically, it was observed that the liver had a normal histological appearance. The structures of the hepatocytes and portal areas appeared normal. The hepatocytes formed regular remark cords around the vena centralis and the sinusoids between the remark cords were normal (Fig. 4A).

***Obesity:*** Almost similar morphological changes were observed in the livers of all rats in this group. These changes were especially localized in hepatocytes in the periacinar and intermediary regions of the lobules. It was determined that the cytoplasm of hepatocytes in these regions had sharp limited vacuoles of different sizes and it was determined in Oil Red O staining that these vacuoles were related to fatty changes (Fig. 4E). This **steatosis** (macrovesicular or microvesicular) was one of the commonest morphological of hepatocytes. Macrovesicular steatosis, in which the nucleus of the hepatocyte is displaced by one or more fat vacuoles easily visible by light microscopy. Also, coagulation necrosis was observed in some of these hepatocytes. The nucleus of necrotic hepatocytes were generally the dark stained, picnotic and flattened in appearance (Fig. 4C-D). Inflammatory reactions consisting of focal mononuclear cell infiltrations were seen in the portal regions. However, there was no increase in connective tissue in these areas. The congestion and dilatation were observed in sinusoids around of some vena centralis (Fig. 4C-D).

***Obesity+Silymarin and Silymarin groups:*** In the livers of all rats in these groupswere observed to have the normal histological appearances as in the control group (Obesity+Silymarin: Figures 4F; Silymarin: Figures 4B).

## Discussion

Current treatments for obesity include dietary changes, psychotherapy and various pharmaceutical interventions for people with eating disorders, surgical interventions for patients with complications, and nursing care is required for this condition[5,8]. Also, current anti-obesity treatments are limited due to the high cost and numerous side effects[22]. Current medications and toxic chemicals have been reported to cause liver damage and may even cause liver cirrhosis and cancer[19]. Anti-obesity drugs such as rimonabant, fenfluramine and sibutramine have been withdrawn from the market for serious adverse effects such as increased cardiovascular risks, mood disorders and even suicidal sensitivity[23]. These drug treatments can cause numerous side effects such as depression, anxiety, headache, dizziness, nausea, and fatigue[8]. Therefore, the development of new types of anti-obesity drugs is an urgent need[24]. Natural anti-obesity products are gaining popularity in recent years[25]. Natural products are promising alternatives due to their effective biological activity and potentially less serious side effects[24]. Since current anti-obesity drugs have strong side effects, it is necessary to develop functional foods as adjuvant therapies[22]. Recently, algae are recognized as a good source of anti-obesity substances[26]. Supportive therapies such as herbal remedies may be required for individuals who do not respond to lifestyle changes[27]. Therefore, herbal prescriptions with relatively few side effects, which offer the advantage of being useful for a variety of indications, have been recently re-investigated[8]. As an alternative approach, many researchers have focused on the anti-obesity effects of natural ingredients consumed daily. Because these ingredients are generally considered less toxic than synthetic drugs[28]. Dietary supplements based on thistle (silymarin) are among the most common preparations used by the EU and US adult population[18]. Thistle is one of the oldest medicinal plants and has been used for centuries to treat many diseases[29]. Silymarin, the effective ingredient of thistle seeds, is one of the medicinal plants specific to chemotypes used in drug production for liver diseases[30]. In a study investigating the effect of silybum marianum extract on obesity, it was reported that silymarin prevented liver damage by regulating lipid metabolism, leptin and insulin levels and parameters related to obesity in the blood in rats fed with HFD[31]. Another study showed that silymarin increased hepatocyte membrane permeability to glucose in streptozotocin-induced diabetes. It has also shown that silymarin not only reduces hyperglycemia but also acts as a protector against the stresses associated with high glucose to increase insulin resistance[32]. A study by Sung-Hyun Kim et al., Showed that silymarin is highly promising for the development of gastric cancer drugs, as it inhibits cell growth and tumor formation by inducing apoptosis in human gastric cancer cells both in vitro and in vivo[33]. In a study conducted to determine whether long-term treatment with silymarin is effective in reducing lipoperoxidation and insulin resistance in diabetic patients with liver cirrhosis, it was shown that silymarin effectively neutralizes superoxide radicals and reduces systemic signs of inflammation. In addition to reducing membrane peroxidation, silymarin also significantly reduced glycosylated hemoglobin and insulin requirements[34]. In a study, it was reported that silymarin has a protective effect depending on the dose in the indomethacin-induced ulcer model and that silymarin at a dose of 100 mg/kg accelerates the healing process. In addition, it has been determined that silymarin, indomethacin or other Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) may have beneficial effects in preventing gastric damage[35]. Hepatic steatosis induced by excessive lipid deposition in the liver is highly associated with obesity and associated complications[24]. Obesity leads to metabolic stress resulting in liver damage, including nonalcoholic fatty liver disease (NAFLD)[22]. It has been proven that silymarin has a healthy effect on the liver and prevents liver damage histopathologically when given with a drug that causes hepatotoxicity such as isoniazid[36]. In this study, there were no macroscopic differences between the control group and the experimental groups in the liver of rats, but microscopically, the liver was in normal histological appearance in the control group and the silymarin group, and but there were sharply limited vacuoles of different sizes (fatty changes) in the centrilobular hepatocytes of the liver in the obesity group fed with HFD. In addition, it was determined that some of these hepatocytes had coagulation necrosis. However, in the group fed with silymarin together with HFD, despite HFD, it was observed that silymarin prevented the fatty changes of liver and degenerative necrotic changes.

Plasma or serum levels of ALT, AST, GGT and ALP enzymes, key biomarkers in the diagnosis of liver diseases, are crucial indicators of liver damage or injury. The increase in serum levels of these enzymes is caused by the damage to the structural integrity of the hepatocytes and their mixing into the bloodstream. It was reported that silymarin and naringin reduce liver damage caused by methotrexate with antioxidant effects[37]. Another study reported that silymarin, which is given for treatment against ethanol-induced liver toxicity in mice, increases antioxidant enzyme activity and GSH levels[37,38]. In another study, it was reported that in rats treated with CCl4 at a dose of 50 and 200 mg/kg milk thistle, increased liver ALT and AST levels with CCl4 were significantly reduced and brought closer to control group values[39,40]. Previous studies reported that milk thistle significantly decreased ALT and AST values, which were increased compared to the control group, in rats treated with 0.5 mL/kg CCl4 twice a week for eight weeks[40,41] reported that the increased serum ALT, AST, and ALP values in rats with liver damage with anti-tuberculosis decreased with the administration of 200 mg/kg of milk thistle and approached the control group values. In this study, no significant difference was found between the groups in serum GGT and AST levels. However, LDH, triglyceride and serum glucose values were found to be low, and total cholesterol and HDL values were found to be high in the experimental groups receiving silymarin. These results are also in keeping with the previous studies mentioned above. However, we think that the reason why silymarin increased total cholesterol levels as an unexpected effect in the group given slymarin may be related to the dose and duration of treatment used in our study.

## Conclusion

In the obesity group, it was noted that fat degeneration and necrotic changes occurs in hepatocytes around the vena centralis, while in the obesity + silymarin group, an almost normal appearance of liver is observed. It is thought that this hepatoprotective effect is due to the positive effects of silymarin on the antioxidant and circulatory system, as well as the regulating effects of blood triglyceride levels. The likely cause of fat degeneration, especially in hepatocytes around vena centralis; due to the histological structure of the liver, hepatocytes in these regions are thought to be most susceptible to hypoxia and are related to the circulatory disorder, which can be caused by feeding on a high-fat diet. As a result, it has been determined that silymarin significantly prevents liver fatty changes and damage, at the same time significantly regulates blood glucose and triglyceride levels, and also increasing HDL levels, called good cholesterol. Moreover, nurses play a crucial role in combating obesity and liver diseases by providing education and counseling to patients on the use of herbal products, diet, exercise, and lifestyle habits, as well as ensuring the proper use of medications and managing health problems associated with obesity. In this regard, it is known that silymarin has beneficial effects against fatty liver and obesity, however we believe that more studies high-quality value are needed to apply it in clinics.

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### *Declaration of Interest*

The authors have no conflicts of interest associated with publication of this article.

### *Data Availability Statement*

Data available on request due to privacy/ethical restrictions (The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions)

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**ARAŞTIRMA MAKALESİ /** *RESEARCH ARTICLE*

# The Effect of Gender Role Attitudes on Multidimensional Leadership Orientations Among Pre-hospital Emergency Medical Services Worker

*Cinsiyet Rolü Tutumlarının Hastane Öncesi Acil Sağlık Hizmeti Çalışanları Arasında Çok Boyutlu Liderlik Yönelimlerine Etkisi*

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## ABSTRACT

***Aim:*** *This study aims to examine the effects of gender roles on multidimensional leadership orientations of employees working in pre-hospital emergency medical services.*

***Material and Method:*** *The research was planned as a cross-sectional study. The sample consisted of 350 emergency health service workers. Data were collected using a socio-demographic information form, the Gender Role Attitude Scale, and the Multidimensional Leadership Orientations Scale. Data analysis was performed using IBM Statistical Package for Social Sciences (SPSS) program version 22.0, with statistical significance set at p<0.05.*

***Results:*** *The mean age of the participants was found to be 24.21±6.39. Gender showed a significant difference in terms of the Gender Roles Attitude Scale; male participants had higher scale scores than female participants. In terms of the Multidimensional Leadership Orientations Scale, both gender and profession showed significant differences. While the human leadership sub-dimension scores of female participants were found to be higher than males, the total scale scores of doctors and paramedics were found to be higher compared to emergency medical technicians (p<0.05). No significant relationship was found between the Gender Roles Attitude Scale and the Multidimensional Leadership Orientations Scale (p>0.05).*

***Conclusion:*** *In this study, which was conducted to examine the effect of gender roles on multi-dimensional leadership orientations of pre-hospital emergency medical services employees, it is striking that although male personnel received high scores in Gender Role Attitude Scale and female personnel received high scores in the Multidimensional Leadership Orientations Scale human resources sub-dimension, both genders received lower scores in the Multidimensional Leadership Orientations Scale total and sub-dimensions.*

**Key words:** *emergency medical service; gender roles; leadership*

## ÖZET

***Amaç:*** *Bu çalışma, hastane öncesi acil sağlık hizmetlerinde görev alan çalışanların, toplumsal cinsiyet rollerinin çok yönlü liderlik yönelimlerine olan etkisini incelemeyi amaçlamaktadır.*

***Materyal ve Metot:*** *Araştırma kesitsel bir çalışma olarak planlanmıştır. Çalışmaya 350 acil sağlık hizmetleri çalışanı katılmıştır. Veri toplama aracı olarak; sosyo-demografik bilgi formu, Toplumsal Cinsiyet Rolleri Tutum Ölçeği ve Çok Yönlü Liderlik Yönelimleri Ölçeği kullanılmıştır. Verilerin değerlendirilmesinde IBM Sosyal Bilimlerde İstatistik Paket Programı (SPSS) sürüm 22.0 paket programı kullanılmış ve istatistiksel anlamlılık düzeyi p<0,05 olarak kabul edilmiştir.*

***Bulgular:*** *Katılımcıların yaş ortalaması 24,21±6,39 olarak bulunmuştur. Toplumsal Cinsiyet Rolleri Tutum Ölçeği açısından cinsiyet anlamlı bir fark göstermiştir; erkek katılımcıların ölçek puanları kadın katılımcılardan daha yüksek bulunmuştur. Çok Yönlü Liderlik Yönelimleri Ölçeği açısından ise hem cinsiyet hem de meslek anlamlı farklılık göstermiştir. Kadın katılımcıların insan kaynaklı liderlik alt boyut puanları erkeklerden daha yüksek bulunurken, doktor ve paramediklerin toplam ölçek puanları, acil tıp teknisyenlerine kıyasla daha yüksek saptanmıştır (p<0,05). Toplumsal Cinsiyet Rolleri Tutum Ölçeği ile Çok Yönlü Liderlik Yönelimleri Ölçeği arasında anlamlı bir ilişki saptanmamıştır (p>0,05).*

***Sonuç:*** *Hastane öncesi acil sağlık hizmetleri çalışanlarının çok boyutlu liderlik yönelimleri üzerinde cinsiyet rollerinin etkisini incelemek amacıyla yürütülen bu çalışmada, erkek personelin Toplumsal Cinsiyet Rolleri Tutum Ölçeği'nden yüksek puanlar almasına ve kadın personelin Çok Yönlü Liderlik Yönelimleri Ölçeği insan kaynakları alt boyutunda yüksek puanlar almasına rağmen, her iki cinsiyetin de Çok Yönlü Liderlik Yönelimleri Ölçeği toplamında ve alt boyutlarında daha düşük puanlar alması dikkat çekicidir.*

**Anahtar kelimeler:** *acil sağlık hizmetleri; toplumsal cinsiyet rolleri; liderlik*

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## Introduction

Pre-Hospital Emergency Medical Services (EMS) play a critical role in the healthcare system as the initial phase of emergency care and treatment provided outside of hospital settings[1]. EMS include comprehensive health services delivered from the scene of an injury or emergency, through the transportation process, and within healthcare facilities, using medically equipped vehicles managed by specialized teams[2]. EMS aim to minimize time spent on scene and quickly transport patients to fully equipped emergency facilities[3]. In order to provide these services, emergency medical technicians, paramedics and doctors, depending on the equipment of the ambulances, take part in the care of patients reached by air, land or sea ambulances[4].

While the term sex refers to biological characteristics, gender represents a cultural construct that shapes individuals' social roles, behaviors, and identities[5]. Gender roles determine the expected behavior patterns for individuals based on their gender according to societal values and beliefs. These roles are based not only on biological differences but also on cultural norms and social expectations. Individuals internalize these roles through social interactions and environmental factors, acquiring societal cues about which behaviors are appropriate or acceptable for each gender[6–9]. Gender roles imposed by society lead to gender inequality. Gender inequality is seen in many areas, especially in the society we live in. One of the areas where gender inequality is most clearly manifested is the health sector[10]. Gender roles have a significant impact on leadership and supportive roles in the workplace. Men are often placed in more leadership positions, while women tend to remain in more supportive roles[11]. Studies indicate that traditional gender roles have a significant impact on perceptions of leadership positions, with men typically viewed as leaders and women assigned to supportive roles. This situation shows that leadership perceptions are shaped based on gender[12,13]. Additionally, it has been noted that leadership selections in pre-hospital EMS are based on factors such as experience and clinical role, but these selections are also influenced by gender perceptions[13]. However, in critical service delivery areas such as EMS, the leadership role is of critical importance and gender perception should not be a limiting factor.

To the best of our knowledge, there are no studies in the literature examining the relationship between gender roles and multidimensional leadership orientations among employees in pre-hospital EMS. Therefore, this study aims to explore the relationship between gender roles and multidimensional leadership orientations among employees working in pre-hospital EMS.

## Material and Method

***Type of Study:*** The research was planned as a cross-sectional study.

### *Research Questions*

What is the Gender Role Attitudes Scale (GRAS) Score of pre-hospital EMS workers?

What is the Multidimensional Leadership Orientation Scale (MLOS) Score of pre-hospital EMS workers?

Is there a relationship between GRAS and MLOS in pre-hospital EMS workers?

***Study Setting and Characteristics:*** This study was conducted with physicians, Emergency Medical Technicians (EMTs), and paramedics working in pre-hospital EMS in Türkiye.

### *Population and Sample*

The population of the study consists of doctors, EMTs, and paramedics working in pre-hospital EMS in Türkiye who are members of the Association of Emergency Medical Technicians and Technicians (ATTDER). The sample size was calculated based on the total number of doctors, EMTs, and paramedics (N: 3000) who are members of ATTDER in Türkiye, with a confidence level of 95% and 5% margin of error. Using a sample size calculation program for known populations, the sample size was determined to be 341[14]. It was determined that all participants in the study filled out the survey forms completely and the study was completed with 350 participants. Random sampling method was used in the study.

This study included participants on a voluntary basis, specifically those who work in pre-hospital EMS in Türkiye and are members of the ATTDER and who voluntarily agreed to participate in the study. Individuals were excluded from the study if they did not consent to participate, did not work in pre-hospital EMS in Türkiye, were not members of ATTDER, or decided to discontinue the survey at any point or failed to complete it.

### *Data Collection Instruments*

The data of the study were collected using the Sociodemographic Information Form, the Gender Roles Attitude Scale and the Multidimensional Leadership Orientation Scale.

**Socio-demographic Information Form:** This form consists of 8 questions created by the researchers through a literature review. It gathers information on age, gender, marital status, educational level, profession, years of experience, and whether the participant has received training in multidimensional leadership orientation[15–18].

**Gender Role Attitudes Scale (GRAS):** The GRAS, developed by García-Cuetoet al. (2015) and validated in Turkish by Bakioğlu and Türküm (2019), is used to measure individuals' egalitarian attitudes towards gender roles[17,19]. The scale includes 20 items and is formatted in a 5-point Likert scale (1=Strongly Disagree, 5=Strongly Agree). It is unidimensional, with the first six items coded directly and the last 14 items reverse coded. The total score is obtained by summing the responses, ranging from 20 to 100. A higher score indicates more egalitarian attitudes towards gender roles. The reliability of the scale, measured by Cronbach's alpha internal consistency coefficient, was calculated as 0.99[17]. In this study, the Cronbach α internal consistency level was found to be 0.808.

**Multidimensional Leadership Orientation Scale (MLOS):** The MLOS, developed by Dursun et al. (2019), comprises 19 items and four main sub-dimensions: charismatic leadership (items 13, 15, 16, 18, 19), political leadership (items 3, 6, 9, 10, 11), structural leadership (items 1, 4, 5, 7), and human resources leadership (items 2, 8, 12, 14, 17)[18]. The scale is designed in a 5-point Likert format, ranging from "1=Strongly Disagree" to "5=Strongly Agree." The total score of the scale is between 19–95, and higher scores indicate higher leadership orientation skills of individuals. The internal consistency coefficients are as follows: human resources leadership $\alpha$=0.73, charismatic leadership $\alpha$=0.74, political leadership $\alpha$=0.80, and structural leadership $\alpha$=0.72. The overall internal consistency coefficient is $\alpha$=0.85[16,18]. Additionally, in this study, the Cronbach α internal consistency level was found to be 0.972, with sub-dimension Cronbach α values being: human resources leadership $\alpha$=0.926, charismatic leadership $\alpha$=0.909, political leadership $\alpha$=0.918, and structural leadership $\alpha$=0.910.

**Data Analysis:** Data were analyzed using the IBM SPSS program version 22.0 software package. The analysis included descriptive statistics such as frequencies, percentages, minimum and maximum values, mean, and standard deviations. Statistical tests used in the analysis:

– In cases where the data were parametrically distributed, it included the Independent Sample t-Test, Sperman Correlation Analysis, One-Way Analysis of Variance (ANOVA), and in cases where variances were homogeneous, it included the LSD Post-Hoc, and in cases where variances were not homogeneous, it included the Dunnet-C Post-Hoc analysis.

– In cases where the data were not parametrically distributed, it included the Mann-Whitney U test and the Kruskal-Wallis H analysis. The normality assumption of the data was assessed using Kurtosis and Skewness coefficients (±2)[20]. Statistical significance levels were accepted as $p<0.05$ and $p<0.001$.

### *Ethical Consideration*

The study was conducted in accordance with the Helsinki Declaration and relevant ethical principles. Participant confidentiality and anonymity were maintained, and the data were stored in a secure environment. The collected data were used solely for scientific purposes and were not shared with third parties. Ethical approval for the study was obtained from the Ethics Committee for Medical Research at Ege University with the decision number 24–2.1T/17 dated 22.02.2024.

## Results

A total of 76.9% of the participants were female, 78.3% were single and 69.7% were associate degree graduates. A total of 83.7% of the participants were paramedics, 82.9% had no children, 73.4% had 1–5 years of professional experience, and 81.1% had not received training in multifaceted leadership orientations. The average age of the participants was found to be 24.21±6.39 (Table 1).

Participants scored an average of 41.11±9.81 on the GRAS. On the Political Leadership subscale they scored 18.71±4.59, on the Human Resource Leadership subscale 20.66±4.38, on the Charismatic Leadership subscale 19.14±4, on the Structural Leadership subscale 16.23±3.57 and a total score of 74.74±16.01 on the Multi-Faceted Leadership Orientations Scale.

There is a statistically significant difference between the participants' gender and the total score average of the GRAS ($p<0.001$). The average score of men was found to be higher than that of women. However, the

***Table 1.*** *Demographic characteristics of the participants (N=350)*

| | | | | n | % |
|---|---|---|---|---|---|
| **Gender** | Female | | | 269 | 76.9 |
| | Male | | | 81 | 23.1 |
| **Marital status** | Married | | | 76 | 21.7 |
| | Single | | | 274 | 78.3 |
| **Educational level** | High school | | | 21 | 6.0 |
| | Associate degree | | | 244 | 69.7 |
| | Bachelor's degree | | | 71 | 20.3 |
| | Master's degree | | | 14 | 4.0 |
| **Profession** | Emergency medical technician | | | 47 | 13.4 |
| | Paramedic | | | 293 | 83.7 |
| | Doctor | | | 10 | 2.9 |
| **Status of having children** | Yes | | | 60 | 17.1 |
| | No | | | 290 | 82.9 |
| **Years of professional experience** | 1–5 years | | | 257 | 73.4 |
| | 5–10 years | | | 44 | 12.6 |
| | 10–15 years | | | 29 | 8.3 |
| | More than 15 years | | | 20 | 5.7 |
| **Received training on multifaceted leadership orientations** | Yes | | | 66 | 18.9 |
| | No | | | 284 | 81.1 |
| **Numeric variables** | **N** | **Min.** | **Max.** | **Mean** | **Standard deviation** |
| Age | 350 | 18.00 | 50.00 | 24.21 | 6.39 |

***Table 2.*** *Comparison of GRAS scores by demographic characteristics (N=350)*

| | | | GRAS Total | | |
|---|---|---|---|---|---|
| | | n | Ort. ± SD | Test | p |
| **Gender** | Female | 269 | 39.71±8.58 | t=-4.220 | **<0.001** |
| | Male | 81 | 45.77±12.03 | | |
| **Marital status** | Married | 76 | 40.29±8.81 | t=-0.822 | 0.412 |
| | Single | 274 | 41.34±10.08 | | |
| **Educational level** | High school | 21 | 37.14±9.71 | F=1.431 | 0.234 |
| | Associate degree | 244 | 41.31±9.91 | | |
| | Bachelor's degree | 71 | 41.87±9.49 | | |
| | Master's degree | 14 | 39.64±9.33 | | |
| **Profession** | Emergency medical technician | 47 | 41.66±9.24 | F=0.482 | 0.618 |
| | Paramedic | 293 | 41.12±9.81 | | |
| | Doctor | 10 | 38.30±12.82 | | |
| **Status of having children** | Yes | 60 | 40.35±9.57 | t=-0.657 | 0.511 |
| | No | 290 | 41.27±9.87 | | |
| **Years of professional experience** | 1–5 years | 257 | 41.12±9.84 | F=0.217 | 0.885 |
| | 5–10 years | 44 | 40.43±9.86 | | |
| | 10–15 years | 29 | 42.28±10.22 | | |
| | More than 15 years | 20 | 40.70±9.35 | | |
| **Received training on multifaceted leadership orientations** | Yes | 66 | 42.02±11.01 | t=0.833 | 0.406 |
| | No | 284 | 40.90±9.52 | | |

t: t test was conducted in independent groups, F: ANOVA test was applied.

total score average of the GRAS does not show a statistically significant difference based on marital status, profession, education level, years of work experience, having children, or receiving training on multi-faceted leadership orientations (p>0.05; Table 2).

The MLOS score for the Human Resources Leadership sub-dimension was found to be statistically significant in relation to gender (p=0.004). The average score for women was higher than that of men. Additionally, the difference in the average scores of the Human Resources Leadership sub-dimension based on profession was statistically significant (p=0.003). In post-hoc analysis to determine the source of the difference by profession, it was found that the scores of EMTs were lower than those of Paramedics and Doctors (Table 3).

***Table 3.*** *Difference between of MLOS and its sub-dimensions scores by demographic characteristics (N=350)*

| | | | Political leadership | Human resources leadership | Charismatic leadership | Structural leadership | MLOS total |
|---|---|---|---|---|---|---|---|
| | | n | Mean ± SD | Mean rank (1. -3. Quartile) | Mean ± SD | Mean rank (1. -3. Quartile) | Mean rank (1. -3. Quartile) |
| **Gender** | Female | 269 | 18.75±4.47 | 184.00 (20–24)- | 19.30±4.46 | 178.09(15–19)- | 178.74(69–87)- |
| | Male | 81 | 18.57±4.98 | 147.27 (20–24)- | 18.62±4.75 | 166.91(15–19)- | 164.73(69–87)- |
| | **Test / significance** | | t=0.321 p=0.749 | U=86.080 **p=0.004** | t=1.184 p=0.237 | U=10198.500 p=0.377 | U=10022.500 p=0.274 |
| **Marital status** | Married | 76 | 18.17±5.09 | 165.98 (20–24)- | 18.72±5.06 | 171.88(15–19)- | 168.55(69–87)- |
| | Single | 274 | 18.86±4.44 | 178.14 (20–24)- | 19.26±4.38 | 176.80(15–19)- | 177.43(69–87)- |
| | **Test / significance** | | t=-1.161 p=0.247 | U=9688.500 p=0.349 | t=-0.904 p=0.366 | U=10137.000 p=0.721 | U=9883.500 p=0.498 |
| **Educational level** | High school | 21 | 17.67±5.27 | 148.67(20–24)- | 17.90±5.57 | 175.67(15–19)- | 157.24(69–87)- |
| | Associate degree | 244 | 18.84±4.56 | 178.88(20–24)- | 19.14±4.58 | 175.32(15–19)- | 176.42(69–87)- |
| | Bachelor's degree | 71 | 18.68±4.25 | 167.89(20–24)- | 19.54±3.96 | 175.02(15–19)- | 175.68(69–87)- |
| | Master's degree | 14 | 18.21±5.81 | 195.46(20–24)- | 19.07±4.98 | 180.89(15–19)- | 185.96(69–87)- |
| | **Test / significance** | | F=0.481 p=0.696 | $x^2_{KW}$=2.753 p=0.431 | F=0.699 p=0.553 | $x^2_{KW}$=0.043 p=0.998 | $x^2_{KW}$=0.855 p=0.836 |
| **Profession** | Emergency medical technician | 47 | 17.40±4.91 | 134.36(20–24)- | 17.36±4.89 | 150.71(15–19)- | 136.66(69–87)- |
| | Paramedic | 293 | 18.81±4.53 | 180.32(20–24)- | 19.32±4.44 | 177.73(15–19)- | 179.25(69–87)- |
| | Doctor | 10 | 21.90±2.73 | 227.70(20–24)- | 22.10±3.00 | 226.55(15–19)- | 248.20(69–87)- |
| | **Test / significance** | | F=4.479 **p=0.012*** | $x^2_{KW}$=11.332 **p=0.003** | F=6.165 **p=0.002**** | $x^2_{KW}$=5.661 p=0.059 | $x^2_{KW}$=12.507 **p=0.002** |
| **Status of having children** | Yes | 60 | 17.83±5.23 | 161.89 (20–24)- | 18.65±5.31 | 162.55(15–19)- | 162.93(69–87)- |
| | No | 290 | 18.89±4.43 | 178.32 (20–24)- | 19.24±4.36 | 178.18(15–19)- | 178.10(69–87)- |
| | **Test / Significance** | | t=-1.632 p=0.104 | U=7883.500 p=0.247 | t=-0.919 p=0.358 | U=7923.000 p=0.270 | U=7945.500 p=0.290 |
| **Years of professional experience** | 1–5 years | 257 | 18.86±4.48 | 177.74(20–24)- | 19.19±4.49 | 176.05(15–19)- | 177.25(69–87)- |
| | 5–10 years | 44 | 18.75±4.56 | 182.30(20–24)- | 19.45±4.04 | 190.45(15–19)- | 180.69(69–87)- |
| | 10–15 years | 29 | 17.17±5.56 | 151.78(20–24)- | 17.69±5.43 | 146.10(15–19)- | 145.74(69–87)- |
| | More than 15 years | 20 | 19.00±4.52 | 166.23(20–24)- | 19.95±4.67 | 178.20(15–19)- | 184.80(69–87)- |
| | **Test / significance** | | F=1.202 p=0.309 | $x^2_{KW}$=2.131 p=0.546 | F=1.285 p=0.279 | $x^2_{KW}$=3.525 p=0.317 | $x^2_{KW}$=2.874 p=0.412 |
| **Received training on multifaceted leadership orientations** | Yes | 66 | 19.06±4.94 | 167.48(20–24)- | 19.45±4.92 | 180.01(15–19)- | 183.02 (69–87)- |
| | No | 284 | 18.63±4.51 | 177.36(20–24)- | 19.07±4.45 | 174.45(15–19)- | 173.75 (69–87)- |
| | **Test / significance** | | t=0.686 p=0.493 | U=8842.500 p=0.470 | t=0.625 p=0.532 | U=9074.500 p=0.684 | U=8875.500 p=0.502 |

U: Mann-Whitney U test was performed. t: t test was conducted in independent groups.
F: ANOVA test was applied. $x^2$KW: Kruskal-Wallis test was applied.
*LSD Post-Hoc test was applied **Dunnet-C Post-Hoc test was applied

***Table 4.*** *Examination of the relationship between the gender roles attitudes scale and the MLOS (N=350)*

| | | GRAS Total |
|---|---|---|
| Political leadership | r | 0.074 |
| | p | 0.170 |
| Human resources leadership* | r | -0.096 |
| | p | 0.072 |
| Charismatic leadership | r | 0.089 |
| | p | 0.098 |
| Structural leadership* | r | -0.075 |
| | p | 0.164 |
| Total MLOS* | r | -0.071 |
| | p | 0.188 |

* Spearman correlation analysis

Among the participants, Doctors scored higher than EMTs and Paramedics in the Political Leadership, Human Resources Leadership, Charismatic Leadership sub-dimensions, and in the overall MLOS score. Additionally, Paramedics had higher scores than EMTs ($p<0.05$; Table 3).

There is no statistically significant relationship between the Political Leadership sub-dimension score, Human Resources Leadership sub-dimension score, Charismatic Leadership sub-dimension score, Structural Leadership sub-dimension score, and the overall Multi-Dimensional Leadership Orientations Scale score and the total score of the GRAS ($p>0.05$; Table 4).

## Discussion

The aim of this study is to examine the relationship between the gender role attitudes and multi-dimensional leadership orientations of healthcare professionals working in pre-hospital EMS. The findings of this study provide various results that help us understand the connection between gender roles and leadership orientations. This research was completed with 350 healthcare personnel (EMTs, doctors, and paramedics) working in pre-hospital EMS.

The knowledge and awareness of healthcare professionals regarding gender contribute to their recognition of gender inequality issues and ensure that these issues are taken into account in the delivery of healthcare services. This understanding supports the promotion of gender equality and the provision of inclusive healthcare, thereby contributing to a more just and effective healthcare system[15].

In this study, the participants scored an average of 41.11±9.81 on the GRAS. In a study conducted with students from the School of Health Services, the average GRAS score was found to be 54.31±8.93.[21] Another study with university students also found the scale score to be at a moderate level[22]. Additionally, a different study identified that the participants held an egalitarian attitude[23]. The findings of this study align with previous research. Pre-hospital EMS operate under unstable conditions by nature, and it is crucial that healthcare workers exhibit an egalitarian attitude in terms of gender roles to ensure the quality of service, making this an important finding.

The study results also indicate a statistically significant difference in gender roles attitude based on gender. Male participants scored higher on the GRAS compared to female participants. Similarly, a study by Önder et al. (2013) found that men had higher GRAS scores[24]. However, in a study by Özden and Gölbaşi (2018), conducted to assess the gender role attitudes of healthcare workers, female participants had higher scores on the scale[15]. In another study by Palas and Aksu (2020), examining the relationship between gender role attitudes and psychological well-being among healthcare students, women also scored higher on the scale[21,24]. However, in this study, the higher gender roles attitude scores among men may be explained by the working conditions of pre-hospital EMS. Ambulance teams typically consist of three personnel, with two healthcare workers in the patient cabin who must perform interventions together and work in a coordinated manner. The need for equal participation in ensuring service efficiency may contribute to greater awareness of gender equality among male workers in this field. It is also thought that another reason why the results differ may be due to individual and cultural differences.

Participants in this study scored an average of 74.74±16.01 on the MLOS, indicating that the participants' scale score was above the mean. Similarly, in a study conducted with nursing students using a different scale on leadership orientations, it was found that the student nurses' leadership orientation scale score was above the mean[25]. The score for the Human Resource Leadership sub-dimension of the MLOS was found to be higher among female participants compared to males. In a study conducted by Ünlü and Hasirci (2023) on the leadership orientations of kickboxing athletes, it was revealed that female athletes scored statistically higher than male athletes in the sub-dimensions of political

leadership, human resource leadership, charismatic leadership, and structural leadership[26]. Similarly, in a study investigating the impact of gender roles on multifaceted leadership orientations among sports science students, it was found that women scored higher than men in the Human Resource Leadership sub-dimension[27]. Another study conducted by Özdemir Özkan et al. (2015) on nursing students' leadership orientations and motivation levels also found that student nurses had higher human resource leadership orientations[28]. Comparable results were obtained in a study examining the influence of personality traits and leadership orientations on the career adaptability of nursing students[25]. Similar findings have been reported in various studies, where the score for human-centered leadership was found to be higher[28–30]. However, no other studies investigating multifaceted leadership orientations among pre-hospital EMS workers were found. The higher scores of female participants in the Human Resource Leadership sub-dimension may be related to the fact that women generally have more developed social skills compared to men. The characteristics of human resource leadership are associated with solving interpersonal problems, helping others, being a good listener, and leading in the resolution of issues. Human resource-oriented leaders value relationships and emotions[18]. Contrary to the findings of this study, there are also studies indicating that there is no statistically significant difference between leadership orientations and gender[31–33]. It is believed that the variation in research results may be due to the differences in sample groups and professions being studied. In addition, the differences in the measurement tools used and the different educational or socio-cultural levels depending on the sample size may also be effective.

The average score for the Human Resource Leadership sub-dimension of the MLOS was found to be statistically lower among EMTs compared to Doctors and Paramedics. Additionally, Doctors and Paramedics had statistically higher scores than EMTs on the total MLOS score as well as on the Political Leadership, Human Resource Leadership, and Charismatic Leadership sub-dimensions. Existing literature has investigated leadership orientations among sports science students, athletes, and students of midwifery and nursing. However, no studies have been found that specifically examine the leadership orientations of personnel working in pre-hospital EMS, highlighting the uniqueness of this study. In pre-hospital emergency health services, Paramedics serve as team leaders. Within the emergency health system, Doctors primarily work as consulting physicians at command control centers, with the number of medical stations varying based on the size of the region but usually ranging from one to two. Teams are organized with combinations such as Paramedic-EMT or Doctor-EMT. The role of Doctors or Paramedics as team leaders is thought to positively contribute to the leadership orientations of individuals in this profession due to their responsibilities.

In this study, no statistically significant relationship was found between the total scores and sub-dimensions of the GRAS and the Multifaceted Leadership Orientation Scale. However, a study examining the relationship between gender role perceptions and leadership behaviors among students in a Faculty of Sports Sciences found that as individuals' levels of egalitarian gender roles increased, so did their levels of human resource leadership orientation[27]. Similarly, literature reviews have identified studies indicating a relationship between gender roles and leadership orientations[34–36]. The discrepancy in results may be attributed to the fact that these studies were conducted within the field of sports sciences, which may differ from the context of pre-hospital EMS. Therefore, further research is needed to explore the impact of gender roles on leadership orientations specifically within the pre-hospital emergency health services sector.

### *Limitations*

This study was completed with the participation of 350 EMS workers. In addition, the participants were employees who were members of ATTDER. These factors constitute the limitations of the study. Future studies can be conducted with a larger sample group covering the entire population and at different times.

## Conclusion

In this study, which was conducted to examine the effect of gender roles on multi-dimensional leadership orientations of pre-hospital EMS employees, it is striking that although male personnel received high scores in GRAS and female personnel received high scores in the MLOS human resources sub-dimension, both genders received lower scores in the MLOS total and sub-dimensions.

In this study, it was found that male personnel working in pre-hospital EMS had higher scores on the GRAS. An egalitarian approach to gender roles is a crucial criterion for both employees and patients receiving services. It is recommended that training programs be implemented to promote egalitarian attitudes among all employees.

The MLOS revealed higher scores in the human resource leadership sub-dimension among female employees. The higher social skills, problem-solving approaches, and communication abilities of women are believed to positively contribute to the human resource leadership dimension. However, it is also necessary to enhance the average scores of female employees in the political leadership sub-dimension. Political leadership is crucial for problem-solving, conflict management, collaboration, and effective resource use. Additionally, the finding that EMTs scored lower on the total and sub-dimensions of the MLOS Scale is significant. It is suggested that training programs be established to improve multifaceted leadership orientations among all employees, promoting collaboration and participation. Finally, there is a need for further academic research on gender roles and multifaceted leadership orientations among pre-hospital EMS personnel.

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**ARAŞTIRMA MAKALESİ /** *RESEARCH ARTICLE*

# The Effect of Medical Malpractice Fear and Defensive Medicine Practices on the Professional Well-being of Emergency Medicine Residents: A Survey Study

## *Acil Servis Asistanlarında Medikal Malpraktis Korkusu ve Defansif Tıp Uygulamalarının Mesleki İyilik Hali Üzerine Etkisi: Bir Anket Çalışması*

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### ABSTRACT

***Aim:*** *This study aimed to explore the relationship between the fear of malpractice, defensive medicine practices, and professional burnout among emergency medicine residents in Türkiye.*

***Material and Method:*** *The study was designed as a prospective, cross-sectional survey. Emergency medicine residents working in Türkiye who had no ongoing or concluded legal malpractice cases and had not received any psychiatric or psychological treatment within the past year were evaluated. Participation was voluntary. The participants were administered electronic surveys containing sociodemographic information, the Malpractice Fear Scale, the Maslach Burnout Inventory, and the Defensive Medicine Behavior Scale. The collected data were analyzed using IBM Statistical Package for Social Sciences (SPSS) program version 20.*

***Results:*** *A total of 309 emergency medicine residents participated in the study, and 40.1% were female. Of the participants, 60.8% were in the 20–29 age group. The mean score on the Malpractice Fear Scale was 25.35, indicating a high level of fear. Concerning the Maslach Burnout Inventory, the scores for emotional exhaustion, depersonalization, and personal accomplishment were 21.30 (moderate), 10.52 (moderate), and 12.95 (low), respectively. A positive correlation was observed between MF, professional burnout, and defensive medicine practices. However, there was a negative correlation between defensive medicine tendencies and burnout levels*

***Conclusion:*** *In current conditions, emergency medicine residents are driven toward professional burnout due to the fear of malpractice; however, they attempt to mitigate this burnout by adopting defensive medicine practices.*

**Key words:** *burnout; emergency residents; defensive medicine; malpractice*

### ÖZET

***Amaç:*** *Çalışmamızın amacı ülkemizde çalışan acil tıp asistanlarının malpraktis korkusu, defansif tıp uygulama eğilimleri ve mesleki tükenmişlikleri arasındaki ilişkinin araştırılmasıdır.*

***Materyal ve Metot:*** *Çalışmamız prospektif, kesitsel bir çalışma olarak yapılmıştır. Çalışmamızda Türkiye'de görev yapan acil tıp asistanlarından son bir yılda aktif adli-idari soruşturma geçirmeyen, psikiyatrik-psikolojik tedavi veya destek almayan, çalışmaya katılmaya gönüllü olanlar değerlendirildi. Katılımcılara sosyodemografik verilerini ve malpraktis korku ölçeği, Maslack tükenmişlik ölçeği ve defansif tıp uygulaması ölçeğini içeren anketler elektronik yolla ulaştırıldı. Elde edilen veriler elektronik ortama aktarıldı ve IBM Sosyal Bilimlerde İstatistik Paket Programı (SPSS) sürüm 20 ile istatistiksel analizi yapıldı.*

***Bulgular:*** *Çalışmaya 309 acil tıp asistanı dâhil edildi. Bunlardan %40,1'i kadınlardan oluşmakta idi. Katılımcıların %60,8'i 20–29 yaş aralığında idi. Katılımcıların ortalama medikal malpraktis skoru 25,35 (yüksek korku düzeyi) idi. Katılımcıların duygusal tükenmişlik skoru 21,30 (orta düzeyde), duyarsızlaşma skoru 10,52 (orta düzeyde), kişisel başarısızlık skoru 12,95 (düşük) olarak gözlendi. Katılımcıların malpraktis korku durumları ile mesleki tükenmişlik durumları ve defansif tıp uygulama eğilimleri arasında pozitif bir ilişki gözlendi. Ancak defansif tıp uygulama eğilimleri ile tükenmişlik düzeyleri arasında negatif bir ilişki gözlendi.*

***Sonuç:*** *Günümüz koşullarında acil tıp asistanları malpraktis korkusu nedeni ile mesleki tükenmişliğe doğru itilirken geliştirdikleri defansif tıp uygulama eğilimleri ile tükenmişliklerini azaltmaya çalışmaktadır.*

**Anahtar kelimeler:** *acil uzmanı; defansif tıp; malpraktis; tükenmişlik*

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## Introduction

The pressures physicians face due to malpractice risks have driven them to adopt defensive behaviors. Defensive medicine (DM) refers to a behavioral pattern physicians often develop to safeguard themselves from malpractice claims. Defensive medicine can be defined as either the ordering of unnecessary tests and procedures or the avoidance of treatment in patients perceived as high-risk[1]. Defensive medicine practices are divided into two main categories: negative DM (the avoidance of procedures in high-risk patients due to concerns over complications or survival) and positive DM (the excessive ordering of procedures, imaging, tests, or consultations that offer little to no benefit to the patient's medical condition)[2].

Emergency medicine is a specialty characterized by a high-intensity working environment, long hours, and constant variability in clinical cases, requiring physicians to make rapid, accurate, and definitive decisions. Emergency medicine residents and specialists must often make "life-or-death decisions" with minimal clinical information while also functioning as effective team members[3]. While this high-pressure environment can be stimulating, it also imposes significant emotional stress, contributing to professional burnout[4]. Of the various instruments available to measure professional burnout, the Maslach Burnout Inventory (MBI) is one of the most important[5].

This study aimed to investigate, for the first time in Türkiye, the levels of professional burnout, malpractice fear (MF), and defensive medicine practices among emergency medicine residents and to evaluate the relationships among these factors. The findings are expected to provide a deeper understanding of the effects of MF and defensive medicine practices on the professional well-being of emergency medicine practitioners.

## Material and Method

### *Study Design and Participant Selection*

This study was approved by the Clinical Research Ethics Committee of xxx University (decision number: 2/98, date: March 29, 2024) and conducted as a prospective, cross-sectional study between April 1, 2024, and August 1, 2024. Survey forms prepared for the study were distributed to participants electronically.

The study targeted emergency medicine residents actively working in public or private universities throughout Türkiye. Emergency medicine residents who voluntarily completed the survey were included, while those who did not respond were excluded. Further exclusions applied to emergency medicine residents who had received psychiatric or psychological treatment or support within the past year, were involved in ongoing or concluded legal malpractice cases, or had faced disciplinary or criminal investigations, as these factors could potentially affect the study's results. The survey was distributed to a total of 1,259 emergency medicine residents, and 519 responded. Among these respondents, 19 residents had ongoing legal malpractice cases, 108 had received psychiatric or psychological treatment or support within the past year, 22 had been subject to workplace investigations, and 61 left the survey incomplete. After excluding these residents, the final sample consisted of 309 emergency medicine residents (Fig. 1).

### *Scales Used in the Study*

***1. Sociodemographic information form:*** A descriptive form was created to collect information about participants' age, gender, duration of residency in emergency medicine, marital status, whether they had children, smoking and alcohol use, whether they had received psychiatric-psychological support or treatment, whether they had been subject to disciplinary or criminal investigations, and whether they had any ongoing or concluded legal malpractice cases.

***2. Medical malpractice fear scale (MMFS):*** First developed by Katz et al.[6] in 2005 to assess MF among emergency physicians evaluating patients with symptoms suggestive of acute coronary syndrome, the Turkish adaptation and validation of the MMFS were undertaken by Uğrak et al.[7] in 2005. The Cronbach's alpha value of the scale was reported to be 0.860 in the adaptation study[7]. The scale consists of six Likert-type questions, each scored from 1 (strongly disagree) to 5 (strongly agree). Based on the total score, MF levels are categorized as low (less than 15 points), medium (15 to <20 points), or high (20 points and above)[6,7].

***3. The defensive medicine practices attitude scale (DMBPAS):*** This scale, developed by Başer et al.[8] was used to measure participants' tendencies toward DM. The Cronbach's alpha value for the scale was reported to be 0.853[8]. The scale consists of 18 questions. The first nine questions assess positive DM practices, the next five questions evaluate negative DM practices, and the last four questions measure physicians' knowledge about DM. The first 14 questions are scored on a five-point Likert scale ranging from 1 (strongly disagree) to 5 (strongly agree), while the last four questions are closed-ended with 'yes' or 'no' responses[9].

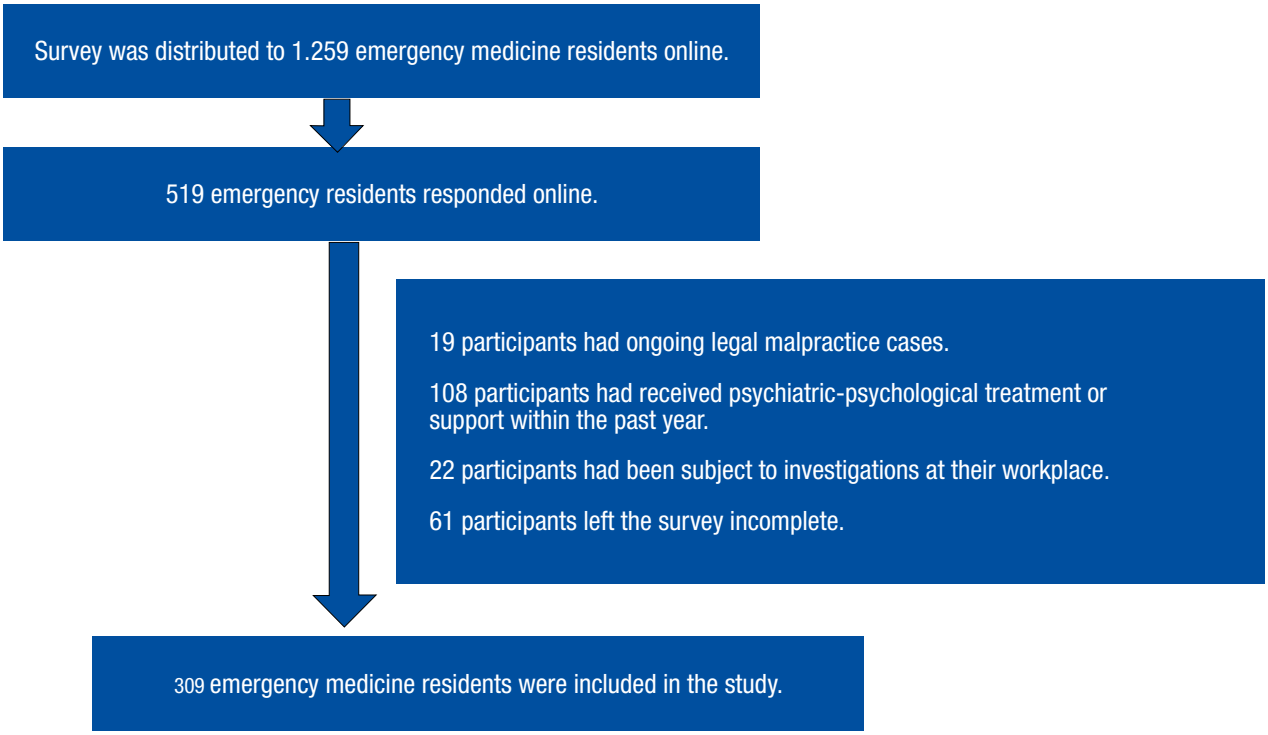


***Figure 1.*** *Flowchart of participants included in the study.*

***4. Maslach burnout inventory (MBI):*** To evaluate professional burnout, the MBI was used. Developed by Maslach and Jackson[10], this Likert-type self-report inventory provides a multidimensional assessment of burnout and is divided into three subscales: emotional exhaustion, depersonalization, and personal accomplishment. The Turkish adaptation and validation of the scale were conducted by Ergin et al., who determined Cronbach's alpha value to be 0.83[11]. The inventory contains 22 items: five for emotional exhaustion, five for depersonalization, and eight for personal accomplishment. High burnout levels are indicated by high scores in emotional exhaustion and depersonalization and low scores in personal accomplishment. Scores range from 0 to 36 for emotional exhaustion, from 0 to 20 for depersonalization, and from 0 to 32 for personal accomplishment. The emotional exhaustion subscale score is determined based on responses to items 1, 2, 3, 6, 8, 13, 14, 16, and 20 in the MBI. When the scores from these items are calculated, a total score of less than 16 indicates a low level of emotional exhaustion, scores between 16 and 27 indicate a moderate level of exhaustion, and scores above 27 indicate a high level of emotional exhaustion. The level of depersonalization is assessed using responses to items 5, 10, 11, 15, and 22. Based on the scores from these items, a total score of less than 6 indicates low depersonalization, scores between 7 and 12 indicate moderate depersonalization, and scores above 13 indicate high depersonalization. Personal accomplishment is evaluated through responses to items 4, 7, 9, 12, 17, 18, 19, and 21. When these items are scored, a total score of less than 31 reflects a low level, scores between 32 and 38 indicate a moderate level, and scores above 39 suggest a high level of personal accomplishment[12].

### *Statistical Analysis*

Based on Liang et al.[13], G*Power 3.1 software estimated that 305 participants were needed to detect a correlation of 0.46 between MMFS and MBI scores with 80% power and a 95% confidence level. Data were analyzed using IBM Statistical Package for Social Sciences (SPSS) program version 20. Descriptive statistics were used, and normality was assessed through the Shapiro-Wilk and Kolmogorov-Smirnov tests, QQ plots, skewness, and kurtosis. Independent-samples t-tests or Mann-Whitney U tests were used depending on normality. Categorical variables were compared using the chi-square test. Pearson's correlation coefficients examined relationships between variables, and Cronbach's alpha assessed reliability. Construct validity was tested using the KMO and Bartlett's tests. The mediating role of decision-making attitudes in the relationship between mental fatigue and burnout was analyzed using structural equation modeling (SEM) in IBM AMOS, with the Bootstrap method applied. A significance level of $p < 0.05$ was used.

## Results

When examining the gender distribution of the participants, 40.1% (n=124) were female, and 59.9% (n=185) were male. In terms of age groups, 60.8% (n=188) of the participants were aged 20 to 29 years. In addition, 29.4% (n=91) had been working as emergency medicine residents for two to three years. The sociodemographic characteristics of the participants are summarized in Table 1.

The reliability analysis for the scales used in the study yielded Cronbach's alpha values of 0.875 for the MMFS, 0.898 for the DMPAS, and 0.867 for the MBI. The participants' emotional exhaustion levels on the MBI showed a mean score of 21.30, a standard deviation (SD) of 6.82, and a median score of 22. For depersonalization, the mean value was 10.52, the SD was 3.95, and the median score was 11. Regarding the sense of personal accomplishment, the mean, SD, and median scores were 12.95, 4.17, and 13, respectively. Table 2 presents the mean, SD, and median values for participants' attitudes toward positive and negative DM practices, overall DM score, and MF levels.

***Table 1.*** *Sociodemographic characteristics of participants*

| Variable | Groups | n | % |
|---|---|---|---|
| **Gender** | Female | 124 | 40.1% |
| | Male | 185 | 59.9% |
| **Marital status** | Single | 164 | 53.1% |
| | Married | 145 | 46.9% |
| **Age** | 20–29 years | 188 | 60.8% |
| | 30–39 years | 121 | 39.2% |
| **Having children** | Yes | 59 | 19.1% |
| | No | 250 | 80.9% |
| **Type of healthcare institution** | Training and research hospital | 128 | 41.4% |
| | Public university hospital | 139 | 45% |
| | State hospital | 42 | 13.6% |
| **Duration of emergency medicine residency** | <1 year | 53 | 17.2% |
| | 1–2 years | 84 | 27.2% |
| | 2–3 years | 91 | 29.4% |
| | 3–4 years | 47 | 15.2% |
| | >4 years | 34 | 11% |
| **Alcohol consumption** | Absent | 132 | 45% |
| | Present | 177 | 55% |
| **Smoking status** | Non-smoker | 135 | 43.7% |
| | Smoker | 174 | 56.3% |

### *Analyses on the Mediating Role of Medical DM Practices in the Relationship Between MF and Burnout*

The mediating role of attitudes toward DM practices in the relationship between medical MF and burnout was tested using SEM. The model was validated based on goodness-of-fit statistics and hypotheses demonstrating statistically significant relationships between variables. Fig. 2 presents the SEM model showing the mediating role of DM practices in the effect of medical MF on healthcare workers' burnout levels. According to the model, MF directly affects the burnout levels of healthcare professionals, and this effect largely occurs through attitudes toward DM practices.

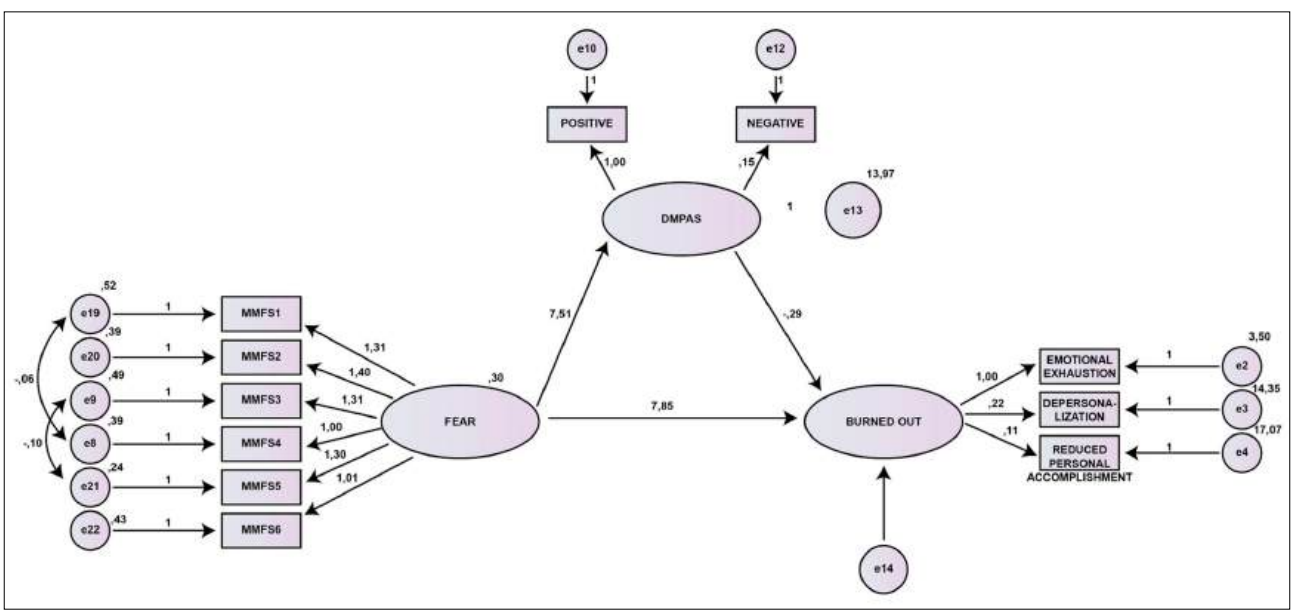


***Figure 2.*** *Structural equation model illustrating the mediating role of attitudes toward defensive medicine practices in the relationship between medical malpractice fear and burnout.*

MF had a strong and positive effect on attitudes toward DM practices, with a critical ratio (CR) value of 10.496, indicating a very strong level of significant relationship. In addition, MF had a direct and positive effect on the burnout levels of healthcare professionals, as indicated by the CR value (5.558), which was notably high and suggested that the relationship was significant. In contrast, attitudes toward DM practices appeared to negatively affect burnout levels. The CR value (-2.103) exceeded the threshold for significance, demonstrating that this relationship was also statistically significant. The relationship between MF, the tendency to engage in MF practices, and burnout levels is summarized in Table 3.

The MMFS showed a moderate positive correlation with the emotional exhaustion subscale of the MBI (r=0.419, p=0.000), a low positive correlation with the depersonalization subscale (r=0.156, p=0.006), a low positive correlation with the personal accomplishment (r=0.135, p=0.018), and a moderate positive correlation with the total MBI score (r=0.381, p=0.000). The correlations between the MMFS scale, MBI, and DMPAS are summarized in Table 4.

***Table 2.*** *Participants' scores on the evaluated scales*

| Variable | n | Mean | SD | Median | Skewness | Kurtosis | Min | Max |
|---|---|---|---|---|---|---|---|---|
| MBI-emotional exhaustion | 309 | 21.30 | 6.82 | 22 | -0.458 | 0.264 | 4 | 36 |
| MBI-depersonalization | 309 | 10.52 | 3.95 | 11 | 0.049 | -0.123 | 2 | 20 |
| MBI-personal accomplishment | 309 | 12.95 | 4.17 | 13 | 0.84 | 1.319 | 3 | 27 |
| DMPAS total | 309 | 50.76 | 9.64 | 50 | -0.024 | -0.182 | 28 | 69 |
| Positive DM | 309 | 34.63 | 5.99 | 35 | -0.321 | 0.028 | 18 | 45 |
| Negative DM | 309 | 16.14 | 4.94 | 16 | 0.151 | -0.675 | 5 | 25 |
| MMFS | 309 | 25.35 | 4.11 | 26 | -1.126 | 1.247 | 12 | 30 |

MBI: Maslach burnout inventory, DMPAS: defensive medicine altitude scale, DM: defensive medicine, MMFS: medical malpractice fear scale. SD: standard deviation.

***Table 3.*** *Results of the model on the mediating role of attitudes toward defensive medicine practices in the relationship between medical malpractice fear and burnout*

| | | | | Bootstrap | | 95% CI | | |
|---|---|---|---|---|---|---|---|---|
| Hypotheses | Direct effect | SE | CR | Indirect effect | p | LL | UL | Hypothesis test result |
| MF → DM | 7.611 | 0.725 | 10.496 | | 0.000** | | | Supported |
| MF → Burnout | 7.946 | 1.430 | 5.558 | | 0.000** | | | Supported |
| DM → Burnout | -0.294 | 0.140 | -2.103 | | 0.036* | | | Supported |
| MF → DM → Burnout | | | | -0.178 | 0.000** | -0.478 | -0.011 | Supported |

**p <0.01, *p <0.05, MF: malpractice fear, DM: defensive medicine, SE: standard error, CR: critical ratio, LL: lower level, UL: upper limit, Bootstrap resampling=5.000.

***Table 4.*** *Correlation between the scales*

| | | MMFS | MBI | Emotional exhaustion | Depersonalization | Personal accomplishment | DMPAS |
|---|---|---|---|---|---|---|---|
| MMFS | r | 1 | | | | | |
| | p | | | | | | |
| MBI | r | 0.381** | 1 | | | | |
| | p | 0.000 | | | | | |
| Emotional exhaustion | r | 0.419** | 0.856** | 1 | | | |
| | p | 0.000 | 0.000 | | | | |
| Depersonalization | r | 0.156** | 0.659** | 0.390** | 1 | | |
| | p | 0.006 | 0.000 | 0.000 | | | |
| Personal accomplishment | r | 0.135* | 0.523** | 0.165** | 0.088 | 1 | |
| | p | 0.018 | 0.000 | 0.004 | 0.123 | | |
| DMPAS | r | 0.585** | 0.167** | 0.159** | 0.033 | 0.135* | 1 |
| | p | 0.000 | 0.003 | 0.005 | 0.569 | 0.017 | |

MMFS: malpractice fear scale, MBI: Maslach burnout inventory, DMPAS: defensive medicine behavior scale.

## Discussion

This study revealed that MF increased both the tendency toward DM practices and the levels of burnout among emergency medicine residents. Furthermore, it was found that emergency medicine residents with a higher tendency to practice DM had lower levels of burnout. This study is significant as it is the first in Türkiye to evaluate MF and DM practices among emergency medicine residents and explore their relationship with professional burnout.

In modern healthcare settings, MF is widely prevalent among physicians. Naturally, this fear emotionally affects doctors, leading to an increase in professional burnout. A study conducted on orthopedic and trauma surgeons in Türkiye revealed that physicians who experienced malpractice-related professional problems had higher levels of burnout compared to their colleagues[14]. The necessity to make quick and critical decisions and crowded emergency room environments are among the reasons why burnout is higher among emergency medicine doctors[15]. When combined with MF, the increase in burnout becomes inevitable. Our study also showed that as MF increased, so did the level of burnout among emergency medicine residents. Increased MF can lead to more significant issues, such as higher job turnover rates among emergency physicians, reduced quality of care, and an increase in DM practices. These outcomes are only a few of the potential future challenges.

Globally, efforts are being made to address the rising burnout levels among healthcare professionals. A previous study examining burnout and stress among healthcare workers in operating rooms suggested that listening to music during work might be a solution to burnout[16]. Although other attempts have been made to reduce burnout and stress levels among emergency department workers, it has been reported that while some methods have partial positive effects, no definitive solution has been achieved[17]. In Türkiye, no routine interventions have been established to reduce burnout among emergency service doctors, leaving them to fight burnout on their own. In our study, we observed that the fear of malpractise increased the tendency to practice DM. Emergency medicine doctors likely lean toward DM to avoid malpractice. As a result, they may feel a temporary sense of relief, using DM practices as a mechanism to reduce their feelings of burnout. However, an increase in DM practices will bring its own set of challenges. A study found that although emergency physicians were aware that DM tendencies led to prolonged patient stays in emergency rooms, they continued to practice DM to avoid medico-legal issues[18]. In addition to lengthening patient stays, the tendency toward DM results in an excessive number of unnecessary tests being ordered, which is another significant issue in emergency departments. This not only increases healthcare costs but also contributes to overcrowding[19]. Another study revealed that DM practices reduced the sense of job satisfaction among emergency medicine residents[20]. However, practicing DM does not reduce the rate of medical errors[21]. Despite the potential for DM practices to reduce burnout, new approaches should be developed to decrease reliance on DM and promote the well-being of emergency medicine residents. One such method could be implementing state-supported professional liability insurance for doctors to protect physicians from malpractice concerns. In addition, providing continuous stress management training for emergency medicine residents, improving the safety of those working in emergency departments, and introducing new measures to reduce medico-legal fears could help address these challenges.

### *Limitations*

Our study has several limitations. First, we were unable to reach all emergency medicine residents working in Türkiye; therefore, the participants represent only a portion of the target population. In addition, as this was a survey-based study, the results rely on self-reporting, which may not accurately reflect the true feelings and attitudes of the residents. Lastly, the sensitive nature of the survey topics (malpractice and DM) may have caused frustration and/or anxiety in some participants, potentially leading to extreme responses.

## Conclusion

Our study demonstrated that MF increased burnout levels among emergency medicine residents, but this relationship was partially mitigated by attitudes toward DM practices. The tendency to engage in DM practices may have a protective effect on burnout. These findings offer important insights into how health policies and management strategies should address MF and attitudes toward DM to reduce the burnout levels of healthcare workers.

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**ARAŞTIRMA MAKALESİ /** *RESEARCH ARTICLE*

# Relationship between Caregiver Burden and Depression among Primary Caregivers of Stroke Patients: A Descriptive Study

## *İnme Hastalarına Birincil Bakım Verenlerde Bakım Yükü ile Depresyon Arasındaki İlişkinin İncelenmesi: Tanımlayıcı Bir Araştırma*

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## ABSTRACT

***Aim:*** *This research investigates the levels of burden and depression experienced by primary caregivers of stroke survivors and analyzes their association.*

***Material and Method:*** *This descriptive investigation enrolled 92 primary caregivers of stroke patients receiving care in a university hospital setting, specifically its neurology intensive care unit (ICU), stroke center, and outpatient clinic, between March 2021 and September 2022. Participant data was gathered using a Sociodemographic Data Form, the Zarit Caregiver Burden Interview (ZCBI), and the Beck Depression Inventory (BDI).*

***Results:*** *Caregivers' mean ZCBI and BDI scores were 41.02±10.12 and 25.59±10.32, respectively. Statistical analysis revealed no significant correlation between Zarit Caregiver Burden Interview (ZCBI) and Beck Depression Inventory (BDI) scores. Sociodemographic factors (excluding kinship) showed no significant association with burden or depression (p>0.05). However, kinship degree influenced ZCBI and BDI scores (p<0.05): non-family caregivers reported lower burden. Caregivers exhibiting minimal depressive symptoms reported significantly lower burden scores (ZCBI) than those with higher levels of depression. (p<0.05).*

***Conclusion:*** *Primary caregivers exhibited moderate burden and depression levels, but no causal connection between these phenomena was identified. However, lower depression levels were correlated with reduced caregiving burden. Notably, kinship –rather than other sociodemographic factors– significantly influenced outcomes, highlighting the critical role of emotional and relational dynamics in caregiving. These findings underscore the need for psychosocial support programs that address relationship-specific challenges and integrate routine depression screenings. By advancing the understanding of how caregiver burden and depression interact –and emphasizing kinship's unique impact– this study calls for further exploration of relational factors to tailor interventions effectively.*

**Key words:** *caregiving; care burden; depression; stroke*

## ÖZET

***Amaç:*** *Bu çalışmanın amacı, inmeli hastaların birincil bakım verenlerinin bakım yükü ve depresyon düzeylerini ölçmek ve aralarındaki ilişkiyi araştırmaktır.*

***Materyal ve Metot:*** *Bu tanımlayıcı çalışma, Mart 2021 – Eylül 2022 tarihleri arasında bir üniversite hastanesindeki nöroloji yoğun bakım ünitesi, inme merkezi ve nöroloji kliniğinde yatan, inme tanısı almış 92 hastanın birincil bakım verenleri ile yürütülmüştür. Sosyodemografik Veri Formu, Bakım Verme Yükü Ölçeği ve Beck Depresyon Envanteri ile veri toplanmıştır.*

***Bulgular:*** *Bakım vericilerin ZCBI (Zarit Bakım Verici Yükü Ölçeği) ve BDI (Beck Depresyon Envanteri) puan ortalamaları sırasıyla 41,02±10,12 ve 25,59±10,32 olarak bulunmuştur. Yapılan istatistiksel analizlerde, ZCBI ve BDI puanları arasında anlamlı bir korelasyon saptanmamıştır. Akrabalık ilişkisi dışındaki sosyodemografik faktörler ile bakım yükü ve depresyon düzeyleri arasında anlamlı bir ilişki bulunmamıştır (p>0,05). Ancak, akrabalık derecesi ZCBI ve BDI puanlarını etkilemiştir (p<0,05); aile bireyi olmayan bakım vericiler daha düşük bakım yükü bildirmiştir. Ayrıca, minimal düzeyde depresif semptomlar gösteren bakım vericilerin ZCBI puanları, daha yüksek depresyon düzeyine sahip olanlara göre anlamlı düzeyde daha düşük bulunmuştur (p<0,05).*

***Sonuç:*** *Bu çalışma, birincil bakım verenler, orta düzeyde bakım yükü ve depresyon deneyimlemiş olsa da, ikisi arasında doğrudan bir nedensel ilişki bulunamamıştır. Bununla birlikte, düşük depresyon düzeylerinin azalmış bakım yükü ile ilişkili olduğu gözlemlenmiştir. Özellikle, diğer sosyodemografik faktörlerden ziyade akrabalık ilişkisinin sonuçları önemli ölçüde etkilediği ve bakım sürecindeki duygusal/ilişkisel dinamiklerin kritik önemini vurgulamaktadır. Bu bulgular, ilişkiye özgü zorlukları ele alan ve rutin depresyon taramalarını entegre eden psikososyal destek programlarının gerekliliğini ortaya koymaktadır. Bakım verenin yükü ile depresyon arasındaki etkileşimi anlama noktasında ilerleme sağlayan ve akrabalığın benzersiz rolünü vurgulayan bu çalışma, müdahalelerin etkinliğini artırmak için ilişkisel faktörlerin derinlemesine incelenmesi önermektedir.*

**Anahtar kelimeler:** *bakım; bakım yükü; depresyon; inme*

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## Introduction

The WHO (World Health Organization) predicts that fifteen million people have a stroke annually, of whom five million become permanently incapacitated and five million pass away[1]. In Türkiye, 96,778 individuals died due to cerebrovascular diseases in 2019[2]. Stroke is the second leading cause of death globally and the third leading cause of disability-adjusted life years[3]. Stroke causes individuals to experience deficiencies in physical, psychological, and social areas[4]. Stroke has significant socioeconomic and emotional impacts on both patients and their families[3].

Caregiving is an experience that is perceived by caregivers and encompasses different dimensions. Caregiving isn't limited to just assistance, but also includes physical, financial, or emotional support[5]. In the Turkish Language Association dictionary, care is defined as "the act of meeting and providing for someone's needs, such as dressing and feeding"[6]. Care is a concept that relies on mutual relationships and trust, has moral and emotional dimensions, and requires scientific knowledge and special psychomotor skills[7]. During the care process, caregivers may face emotional, physical, and economic difficulties that can negatively affect their health. Caregivers may experience feelings of inadequacy and loss of control, leading to depression[8–11]. The literature indicates that the caregiving burden is lower in the early stages of stroke, but increases in later stages. As the caregiving duration increases, factors such as fatigue and loss of physical strength can result in a high level of physical burden for caregivers[12]. Both the characteristics of the caregiver and the caregiving situation can affect the caregiving burden[13]. The presence of chronic illnesses, such as stroke, in family members can lead to a burden on family members and disruptions in family relationships. This burden can result in social and financial problems for caregivers, psychological and physical health issues, and disruptions in family communication[10]. The post-stroke caregiving process imposes a significant physical and psychological burden not only on patients but also on caregivers. Research indicates a correlation between increased caregiving burden and a decline in caregivers' quality of life; this effect is often intensified by insufficient social support[14]. A stroke can create a crisis for relatives, and if not addressed, it can lead to anxiety, depression, and burnout syndrome in caregivers. The incidence of depression is high among caregivers, and as the caregiving burden increases, so does the level of depression[9,15,16].

The primary objective of this research is to assess the burden of care and depression among individuals who are the main caregivers for stroke patients. There are not enough studies examining the relationship between caregiving burden and depression in primary caregivers of stroke patients. This study is designed to fill the gap in the literature. The purpose of this study is to investigate how the caregiving burden correlates with depression levels in primary caregivers of stroke patients. The following research questions will guide this investigation:

1. What is the current level of caregiving burden among primary caregivers of stroke patients?

2. What are the depression levels observed in primary caregivers of stroke patients?

3. Is there an association between the caregiving burden and the depression levels of primary caregivers of stroke patients?

## Materials and Methods

### *Study Design*

This is a descriptive study research design.

### *Setting and Participants*

The study included primary caregivers of stroke patients admitted to the hospital in the **neurology intensive care unit (ICU), stroke center, and outpatient clinic** of Süleyman Demirel University Research and Application Hospital between March 2021 and September 2022. The required sample size was determined using the **G*Power 3.1.9.7 program**. A power analysis, anticipating a potentially **lower effect size** (r=0.3), indicated that a minimum of **82 participants** would be necessary to achieve a **95% confidence level** and **80% power.** This study employed a **convenience sampling method.** A hundred and thirty patients applied during the research period. Of these, relatives of 130 patients met the study's inclusion criteria and consented to participate. However, due to incomplete completion of 38 questionnaire forms, the sample of the study consisted of 92 patients. The inclusion criteria for the study were: being the primary caregiver of stroke patients, having no communication barrier, being able to speak Turkish, being over 18 years old, and being willing to participate in the study. "The post-hoc power analysis conducted in this study highlighted that while some analyzes had sufficient power, the

results should be interpreted with caution, particularly due to the low power in the correlation analysis. It was recommended that future studies aim for larger sample sizes, balanced groups, and effect sizes consistent with the literature. A post-hoc power analysis was also conducted to assess the adequacy of statistical power in the main tests used."

### *Data Collection*

Data was collected through survey questionnaires. Participants received information regarding the study's purpose and content. After obtaining written and verbal consent from volunteers, data collection forms were distributed and then gathered. Participants completed these forms independently, a process that took approximately 10 minutes per form.

### *Data Collection Tools*

**Sociodemographic data form:** It includes information such as gender, age, education level, occupation, marital status, social security, income level, degree of kindship, and presence of chronic illness[10,17,18].

**Zarit Caregiver Burden Interview (ZCBI):** The Zarit Caregiver Burden Interview was first developed by Zarit and colleagues in 1990 to assess the caregiving burden of individuals caring for patients with dementia (Zarit and Zarit, 1990)[19]. The scale evaluates the problems and caregiving burden experienced by individuals providing care to those in need. The scale consists of 22 items, each rated on a 0–4 (never, rarely, sometimes, often, or almost always) Likert-type and unidimensional scale. There are no reverse scored items. A total score on this instrument, ranging from 0 to 88, indicates caregiving burden, with higher scores reflecting a heavier burden. The Turkish version of the Zarit Caregiver Burden Interview was validated and its reliability assessed by Inci and Erdem in 2008[17]. They reported an internal consistency coefficient of 0.95, whereas for this study, the coefficient was determined to be 0.81.

**Beck Depression Inventory (BDI):** Created by Beck and colleagues in 1961, the Beck Depression Inventory is comprised of 21 items, each rated on a 4-point Likert scale (0–3). The overall score, from 0 to 63, serves as an indicator of depression levels, with higher scores denoting increased severity[20]. Classification of scores is as follows: 0–9 for minimal depression, 10–16 for mild, 17–29 for moderate, and 30–63 for severe depression. The scale does not include any reverse-scored items. The Turkish version's validity and reliability were established by Hisli (1989), who determined an internal consistency coefficient of 0.80[21]. For this study, the calculated coefficient was 0.76.

### *Data Analysis*

For numerical variables, descriptive statistics are presented as mean and standard deviation, while categorical variables are described using frequencies and percentages. The Shapiro-Wilk test assessed the normality of scale score distributions, confirming a normal distribution ($p<0.05$). To compare scale scores across demographic characteristics, an independent samples t-test was employed for categorical variables with two groups, and Analysis of Variance (ANOVA) for those with three or more groups. Tukey's multiple comparison test identified specific group differences. Furthermore, Pearson correlation analysis explored the relationship between scale scores. All analyses were conducted using IBM Statistical Package for Social Sciences (SPSS) program version 22.0, with statistical significance set at $p<0.05$.

### *Ethical Considerations*

The Non-Interventional Clinical Research Ethics Committee of Pamukkale University granted ethical clearance for the study (dated 05.02.2021, with number E-60116787-020-14428), and the study's conducting institution provided written consent. The Helsinki Declaration was followed when conducting the study. Participants gave their written and verbal consent, and the authors gave their approval for the use of data collecting instruments.

## Results

This study examines the relationship between the depression levels and caregiving burden of primary caregivers of stroke patients. Post-hoc power analysis for this study showed that the risk of Type II error was high due to the low power of the relationship between ZCBI and BDI in the correlation analysis (17.6%), meaning that even if there was a relationship, there was a high probability of not detecting it. In the ANOVA analysis, the power to detect differences between depression classes was found to be sufficient (88.1%), but the sample imbalance between the groups limited generalizability. In the t-Test analysis, the power remained at a moderate level (63.2%) due to the small sample size of the "caregiver/other" group, which affected statistical reliability.

***Table 1.*** *Sociodemographic characteristics of caregivers (n=92)*

| Variables | | n | % |
|---|---|---|---|
| **Age (mean ± SD)** | | | 44.25±15.70 |
| **Gender** | Female | 68 | 73.91 |
| | Male | 24 | 26.09 |
| **Marital status** | Single | 25 | 27.17 |
| | Married | 67 | 72.83 |
| **Education level** | Illiterate | 4 | 4.35 |
| | Primary school | 16 | 17.39 |
| | Middle school | 7 | 7.61 |
| | High school | 27 | 29.35 |
| | University | 38 | 41.30 |
| **Occupation** | Worker | 15 | 16.30 |
| | Civil servant | 33 | 35.87 |
| | Retired | 14 | 15.22 |
| | Freelancer | 6 | 6.52 |
| | Housewife | 21 | 22.83 |
| | Other | 3 | 3.26 |
| **Social security** | Yes | 81 | 88.04 |
| | No | 11 | 11.96 |
| **Income** | Less than expenses | 31 | 33.70 |
| | Equal to expenses | 44 | 47.82 |
| | More than expenses | 17 | 18.48 |
| **Degree of kindship** | Spouse | 19 | 20.65 |
| | Child | 13 | 14.13 |
| | Father | 17 | 18.48 |
| | Mother | 14 | 15.22 |
| | Relative | 22 | 23.91 |
| | Caregiver/other | 7 | 7.61 |
| **Chronic illness** | Yes | 22 | 23.91 |
| | No | 70 | 76.09 |

The sociodemographic characteristics of participants are presented in Table 1: the average age is 44.25±15.70 years, 73.91% are female, 72.83% are married, and 41.30% are university graduates.

The average depression and caregiving burden scores of the caregivers are 25.59±10.32 and 41.02±10.12, independently. According to the score orders of the BDI, 3.26 of the actors have minimum depression, 18.48 have mild depression, 31.52 have severe depression, and 46.74 have moderate depression. According to the BDI, there's a statistically significant correlation between the average caring burden score and the caregivers' depression classes ($p<0.05$). Caregivers with minimum depression situations have lower average caregiving burden scores compared to those in other depression scores (Table 2).

There were no significant differences between caregiving burden and depression scores according to chronic illness, gender, education level, occupation, social security or income status, and marital status ($p>0.05$). However, according to the kinship degree, there was a significantly lower average caregiving burden score in caregivers/caregivers-other ($p<0.05$). There was no significant association between caregiving burden and depression. This result implies that the impact of caregiving burden on depression level is not direct and that other factors (such as factors related to the individual and environment) may exert a stronger influence on depression (Table 3).

## Discussion

The objective of this research was to determine the extent of **caregiving burden** and **depression** among primary caregivers of stroke patients, as well as to evaluate the association between these two factors. The mean caregiving burden score for participants was 41.02±10.12, with nearly 50% of the caregivers reporting moderate depression. The post-hoc power analysis conducted in this study highlighted that while some

***Table 2.*** *The caregiving burden and depression score averages for caregivers (n=92)*

| Scales | N | % | x ± SS | Min-Max | F and p value |
|---|---|---|---|---|---|
| **ZCBI** | 92 | 100 | 41.02±10.12 | 14–59 | **4.096** |
| **BDI** | 92 | 100 | 25.59±10.32 | 1–49 | **0.009*** |
| Minimal | 3 | 3.26 | 4.67±4.04 | 1–8 | |
| Mild | 17 | 18.48 | 13.76±2.08 | 11–15 | |
| Moderate | 43 | 46.74 | 23.47±3.84 | 19–27 | |
| Severe | 29 | 31.52 | 37.83±5.13 | 32–49 | |

* $p<0.05$: analysis of variance (ANOVA).

***Table 3.*** *Comparison of caregiver burden and depression score averages based on the sociodemographic characteristics of caregivers*

| Variables | | ZCBI | Statistic | BDI | Statistic |
|---|---|---|---|---|---|
| **Gender** | Female | 41.21±9.74 | t -0.292<br>p 0.771 | 25.54±10.53 | t 0.067<br>p 0.947 |
| | Male | 40.50±11.36 | | 25.71±9.91 | |
| **Marital status** | Single | 39.96±12.34 | t -0.612<br>p 0.542 | 26.64±9.82 | t 0.596<br>p 0.553 |
| | Married | 41.42±9.24 | | 25.19±10.54 | |
| **Education level** | Illiterate | 48.00±3.37 | F 0.849<br>p 0.498 | 30.25±3.95 | F 0.744<br>p 0.565 |
| | Primary school | 39.75±12.04 | | 22.31±8.90 | |
| | Middle school | 40.43±10.28 | | 24.00±12.70 | |
| | High school | 42.63±10.05 | | 25.74±8.57 | |
| | University | 39.79±9.73 | | 26.66±11.91 | |
| **Occupation** | Worker | 43.27±11.29 | F 0.525<br>p 0.757 | 26.47±10.05 | F 1.780<br>p 0.125 |
| | Civil servant | 41.33±9.16 | | 27.33±12.39 | |
| | Retired | 38.50±8.57 | | 26.93±7.89 | |
| | Freelancer | 39.67±12.91 | | 30.33±7.39 | |
| | Housewife | 40.24±11.55 | | 20.10±7.50 | |
| | Other | 46.33±8.08 | | 24.67±11.06 | |
| **Social security** | Yes | 41.57±9.74 | t -1.412<br>p 0.161 | 25.83±10.37 | t 0.604<br>p 0.547 |
| | No | 37.00±12.37 | | 23.82±10.23 | |
| **Income** | Less than expenses | 43.77±10.79 | F 2.079<br>p 0.131 | 27.19±9.11 | F 0.592<br>p 0.555 |
| | Equal to expenses | 40.25±9.67 | | 24.57±10.67 | |
| | More than expenses | 38.00±9.34 | | 25.29±11.66 | |
| **Degree of kinship** | Spouse | 40.79±9.94[a] | F 2.446<br>p 0.040* | 26.32±8.88 | F 1.116<br>p 0.358 |
| | Child | 42.15±9.02[a] | | 21.46±8.98 | |
| | Father | 42.35±9.97[a] | | 26.82±10.86 | |
| | Mother | 43.64±10.26[a] | | 24.14±10.62 | |
| | Relative | 41.59±8.91[a] | | 28.59±10.95 | |
| | Caregiver/other | 29.29±11.80[b] | | 21.71±11.80 | |
| **Chronic illness** | Yes | 40.09±11.95 | t test 0.492 p 0.624 | 22.64±8.05 | t test 1.550 p 0.125 |
| | No | 41.31±9.56 | | 26.51±10.82 | |
| **Scales** | | 41.02±10.12 | r 0.104<br>p 0.326 | 25.59±10.32 | r 0.104<br>p 0.326 |

T: t test, F: analysis of variance (ANOVA), *p<0.05: analysis of variance (ANOVA), [a,b]: different letters signify the difference between groups (Tukey test).

analyzes had sufficient power, the results should be interpreted with caution, particularly due to the low power in the correlation analysis. It was recommended that future studies aim for larger sample sizes, balanced groups, and effect sizes consistent with the literature. In a study, 3.8 % of caregivers exhibited severe depression symptoms, 13.5% moderate, 34.6% minimal, and 48.1% showed no signs of depression[22].

In a study conducted in 2018, it was found that psychologically healthy caregivers had minimal levels of caregiving burden[23]. Stroke is a disease that limits individuals' physical abilities, negatively impacting their quality of life and restricting their level of physical activity. This situation brings various responsibilities and burdens to those who care for the individual at home or in the hospital. These responsibilities can negatively

affect the caregiver's mental state and lead to caregiving burden due to the physical and emotional changes experienced from providing care.

The study's results demonstrated no significant relationship between overall depression scores and caregiving burden. Nevertheless, it was observed that caregivers experiencing mild depression reported a lesser caregiving burden than those in more elevated depression groups. This finding differs from Hu's (2018) research, which concluded there was a significant association between caregiving burden and depression scores in caregivers of stroke patients. Their study indicated that increased duration of caregiving and caregiving burden are associated with higher depression scores[24]; Similarly, Denno (2013) found that greater caregiving burden elevates the risk of experiencing anxiety and depression[25]. Loh (2016) concluded from their meta-analysis that caregivers had a significant global prevalence of depression and anxiety symptoms. They proposed that mental health screenings be undertaken for both stroke sufferers and their caregivers[26]. The results of this study may be related to the sample size and diversity. No significant association was found between the sociodemographic characteristics of primary caregivers of stroke patients –such as gender, age, presence of chronic illness, education level, occupation, social security, and income status– and their average caregiving burden or depression scores. However, when examining the degree of kinship, it was found that caregivers classified as caregiver/other had lower caregiving burden score averages, yet there was a significant difference in terms of depression score averages. In the 2017 study by Yilmaz and Ata, it was found that 76.6 % of caregivers were family members, while 23.4% were caregivers/other health personnel. The study also determined that the caregiving burden for family members was at a moderate level[27].

Dağdeviren and colleagues conducted a study that found no statistically significant relationship among caregivers' degree of kinship to the patient, their caregiving duration, and the burden they experienced[28]. It is thought that the lack of a special social or blood bond between caregivers and the person they care for may lead to this situation. A study found that the caregiving burden is influenced by the caregiver's employment status and profession, increases as the patient's level of dependency increases, and is affected by the caregiver's health perception[29].

Similar studies in the literature have generally found that female caregivers have a higher caregiving burden[27,30]. However, this study found no difference in caregiving burden between female and male caregivers. Additionally, it has been judged that individuals with lower education levels have higher depression levels, while income level does not affect caregiving burden or depression levels[15,31–33]. A systematic review indicated that 46.2%-92.5% of caregivers for stroke patients are women, and 20%-83% of caregivers are either a spouse or partner of the patient[30]. Caregivers of individuals with neurological diseases showed a gender disparity, with a study determining that women reported a higher caregiving burden than men. This could be due to the belief that women see caregiving as their duty and feel the need to meet societal expectations regarding this role[24].

In the study by Arca and Ceylan (2020), it was found that the depression experienced by relatives of patients did not vary with age, marital status, gender, occupation, or degree of kinship; However, individuals with a primary school education had higher levels of depression. This could be due to the characteristics of the sample. Relatives of patients with higher education levels may be more knowledgeable about managing the stress they experience. When examined in terms of income level, there are differences in the findings of various studies[22]. In the study by Azizi (2020), it was concluded that a low income level could increase the caregiving burden by raising unmet treatment and care expenses. However, in this study, it was found that income level did not affect caregiving burden and depression scores[34].

Stroke is a disease that restricts individuals' physical abilities, diminishes their quality of life, reduces physical activity levels, and imposes significant responsibilities and burdens on caregivers in home or hospital settings[35]. Caregivers primarily function to identify and fulfill the care needs of the patient precisely. This role can lead to a caregiving burden that directly affects the quality of life of both the individual receiving care and the caregiver themselves[35]. Research from 2019 highlighted a significant association between a heavier caregiving burden and elevated rates of depression and anxiety[36]. Thus, impartially evaluating the caregiving burden is an essential prerequisite for crafting interventions that improve the psychosocial health of both patients and caregivers.

According to a 2019 study that looked at the connection between anxiety, depression, and caregiving load, depression levels climb in tandem with caring stress[36].

In another study examining the depression levels of caregivers for patients, it was found that 3.8 % of caregivers exhibited severe depression symptoms, 13.5%

moderate, 34.6% mild, and 48.1% showed no signs of depression[37]. In our research, it was concluded that 3.26% of participants had minimal depression, 18.48% mild, 31.52% severe, and 46.74% moderate levels of depression. This is most likely due to sample differences, and this study found no significant relationship between caregiving burden and the average depression scores. A notable finding from Imarhiagbe's (2017) study was that around one-fifth of caregivers expressed a desire to be free of their caregiving responsibilities, and about one-third reported a negative impact of the caregiving burden on their health. Interestingly, for those who felt caregiving affected their health, no statistically significant differences in caregiving burden were observed based on gender, age, education level, or duration of caregiving, when compared to caregivers who reported no such health impact[32]. In their study, Zhu and Jiang (2018) stated that caregivers with good mental health experience less caregiving burden[23].

Caregivers are frequently viewed as the second victims of any disease, having taken on this role under unexpected and difficult conditions, with little preparation and little counsel or assistance from the healthcare system. In a qualitative study involving caregivers of patients with stroke, it was noted that the caregiver's distress began almost immediately after assuming their caregiving role and lasted for more than a year post-stroke. Additionally, caregivers reported 2.5 times more psychological distress compared to non-caregivers[38].

Findings from a different study indicated that while the caregiving burden intensified as the care recipient moved towards the end of life, many family members in caregiving roles **failed to recognize this heightened burden as a concern.** They expressed that caring for a family member who had previously taken care of them felt like a rewarding experience[13].

### *Study Limitations and Strengths*

This study examined the levels of caregiver burden and depression experienced by caregivers and found no significant relationship between them. The findings indicate the need to evaluate the burden felt by caregivers and implement interventions to reduce this burden. Such interventions are critical for the prevention and treatment of depression. The findings of the study can be used to guide programs to improve the quality of life of caregivers.

The study had some limitations. One of them was that the study was conducted in only one hospital. Additionally, the data was based on self-reporting from participants. Since the study was conducted as part of a master's thesis, there was a time limit. The results of the study were sample-based and cannot be generalized. Another one is that the factors that may affect the caregiver burden of individuals caring for stroke patients (caregiver care duration, level of ability to meet the physical needs of the stroke patient, number of time the patient has lived with this condition, use of invasive devices necessary to meet the patient's needs, etc.) were not examined in this study. Researchers may be advised to conduct studies examining the effects of these factors on caregiver burden and the effects of interventions aimed at improving this situation.

## Conclusion

This study revealed that caregivers of stroke patients exhibited a moderate level of caregiver burden and variable levels of depression. No statistically significant relationship was found between caregiver burden and depression; however, individuals with moderate and severe depression levels perceived a higher caregiver burden. A significant difference was found between caregiver burden and depression levels based on the degree of kinship, with those classified as "caregiver/other" experiencing a lower caregiver burden.

These findings highlight the critical importance of evaluating stroke patients and their caregivers through a holistic approach, determining caregiver burden and depression levels, and referring them to relevant professionals based on the results to preserve their quality of life. Furthermore, studies examining the long-term effects of caregiver burden and depression could provide valuable insights for future research and clinical practice.

Based on these findings, support programs should be developed and implemented for caregivers of stroke patients. In particular, regular monitoring of caregivers' depression levels and providing psychological support when necessary may help reduce the caregiving burden. Furthermore, identifying the varying needs of caregivers based on their degree of kinship and offering personalized support is of great importance.

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**ARAŞTIRMA MAKALESİ /** *RESEARCH ARTICLE*

# The Relationship Between Obstructive Sleep Apnea Severity and Right Heart Cavities Echocardiographic Features

*Obstrüktif Uyku Apne Şiddeti ile Sağ Kalp Kavitelerinin Ekokardiyografik Özellikleri Arasındaki İlişki*

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## ABSTRACT

***Aim:*** *Obstructive sleep apnea (OSA) has been attributed to an increased risk of cardiovascular disease and death from all causes. It has been demonstrated that OSA affects the right ventricle's (RV) diastolic and systolic functioning, with diastolic dysfunction usually appearing before systolic failure. Delaying the progression of right ventricular failure may be clinically beneficial if RV diastolic insufficiency is accurately assessed and treated early. This study aimed to investigate right ventricular diastolic function in patients with OSA and its relationship with disease severity.*

***Material and Method:*** *The study comprised 88 participants with an OSA diagnosis who had transthoracic echocardiography. Based on their apnea and hypopnea index, the individuals were split into two groups as mild-moderate OSA (mild; apnea and hypopnea index 5–14 events/hour, moderate; apnea and hypopnea index 15–29 events/hour) and severe OSA (apnea and hypopnea index ≥30 events/hour).*

***Results:*** *The severe group consisted of forty-three people, whereas the mild-to-moderate group had forty-five. The right atrial volume index (RAVI) (13.26±4.81 mL/m² vs. 24.24±10.75 mL/m2; p <0.001) and E/Em tricuspid ratio (5.70±2.32 vs. 7.21±3.83; p=0.046) of the severe group were substantially higher than those of the mild-moderate group.*

***Conclusion:*** *The severity of OSA can be accurately predicted using the echocardiographic measures RAVI and tricuspid E/Em, which are practical, affordable, and easily available.*

**Key words:** *obstructive sleep apnea; right ventricular diastolic dysfunction; right atrial volume index*

## ÖZET

***Amaç:*** *Obstrüktif uyku apne sendromu (OUAS) kardiyovasküler riskte artış ve tüm ölüm nedenli ölümler ile ilişkilidir. Obstrüktif uyku apne sendromu sağ ventrikülün (SğV) hem sistolik hem de diyastolik fonksiyonlarını bozar. SğV'nin diyastolik fonksiyonları sistolik fonksiyonlardan önce bozulur. SğV diyastolik fonksiyon bozukluğunun doğru değerlendirilmesi ve erken müdahale sağ kalp yetmezliğinin ilerlemesini geciktirmede klinik olarak faydalı olabilir. Bu çalışmada OUAS hastalarında SğV diyastolik fonksiyon bozukluğunu tespit etmeyi amaçladık.*

***Materyal ve Metot:*** *88 OUAS tanısı alan hastanın transtorasik ekokardiyografi kayıtları incelendi. Çalışmaya alınan tüm hastalar apne-hipopne endeksi'ne göre hafif-orta (hafif; apne-hipopne endeksi 5–14/saat, orta; apne-hipopne endeksi 15–29/saat) ile şiddetli (apne-hipopne endeksi ≥30/saat) olmak üzere iki gruba ayrıldı.*

***Bulgular:*** *Hafif-orta grupta 45, ağır grupta 43 OUAS hastası vardı. Triküspit E/Em oranı (5,70±2,32 vs. 7,21±3,83 p=0,046) ve sağ atriyal volüm endeksi (13,26±4,81 mL/m2 vs. 24,24±10,75 mL/m2; p <0,001) değeri şiddetli grupta, hafif-orta gruba göre anlamlı derecede daha yüksek bulundu.*

***Sonuç:*** *Ekokardiyografik parametrelerden sağ atriyal volüm endeksi ve triküspit E/Em, obstrüktif uyku apne şiddetini predikte edebilen, kolay ulaşılabilir ve uygulanabilir ölçümlerdir.*

**Anahtar kelimeler:** *obstrüktif uyku apne sendromu; sağ ventrikül diyastolik disfonksiyonu; sağ atriyal volüm indeksi*

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## Introduction

Obstructive sleep apnea (OSA) is a common disorder characterized by intermittent cessation of breathing during sleep, and it represents a significant public health concern[1]. Obstructive sleep apnea has been associated with an increased risk of cardiovascular events, stroke, all-cause mortality, and the development of diabetes mellitus[2].

Obstructive sleep apnea can contribute to the development of multiorgan dysfunction and cause both systolic and diastolic dysfunction of the right ventricle[3]. Right ventricle (RV) diastolic dysfunction usually occurs before RV systolic dysfunction and dilation[4]. Prompt intervention and early detection of RV diastolic dysfunction may be essential in preventing the progression to right heart failure[5,6]. There is little data on how OSA affects RV diastolic function, despite its clinical significance.

Echocardiography is a widely used non-invasive diagnostic technique for assessing heart function. The purpose of this research is to identify early indicators of RV diastolic dysfunction in OSA patients.

## Material and Method

### *Population Study*

This study comprised 88 individuals over the age of 18, 58 of whom were male (64.9%) and had been diagnosed with OSA. Patients who underwent both polysomnography and transthoracic echocardiography (TTE) between January 2023 and May 2024 were scanned from hospital records. Those diagnosed with OSA on polysomnography were included in the study. The TTE of the patients included in the study was evaluated in June 2024 by a cardiologist blinded to the apnea and hypopnea index. Apnea and hypopnea index (AHI) index scores of patients were recorded from the hospital records. The classification was based on the AHI, which is the total number of apnea and hypopnea events per hour of sleep. Obstructive sleep apnea was diagnosed using the criteria defined by the American Academy of Sleep Medicine. Patients were divided into two groups according to AHI values: mild-moderate OSA (mild; AHI 5–14 events/hour, moderate; AHI 15–29 events/hour) and severe OSA (AHI ≥30 events/hour)[7].

The study excluded patients with obstructive lung disease, a history of smoking, or pre-existing cardiovascular problems (such as congenital heart disease, atrial fibrillation, or coronary artery disease (CAD)). Furthermore, those with a left ventricular ejection fraction (LVEF) below 50% or poor-quality echocardiograms were not eligible to participate. The local ethics committee approved this study.

### *Imaging Procedure*

The Philips Epic 7c echocardiography device was used to perform the TTE evaluation. Every measurement was carried out in compliance with the American Society of Echocardiography's recommendations[8].

Using the biplane method of discs, the LVEF was computed to evaluate left ventricular function. The biplane approach was used to measure the maximal left atrial volume from apical two- and four-chamber views. The left atrial volume index (LAVI) was subsequently computed by indexing these volumes to body surface area. In order to assess diastolic function, transmitral inflow parameters, such as peak early (E) and late (A) diastolic velocities, were measured using pulsed-wave Doppler echocardiography. The E/A ratio was then calculated. Tissue Doppler imaging was used to measure the diastolic velocities (Em and Am) at the septal and lateral mitral annular regions. To gain a better knowledge of diastolic function, E/Em ratios for the lateral and then septal walls have been established.

The tricuspid annular plane systolic excursion (TAPSE) and RV end-diastolic diameter (RVDD), two essential echocardiographic measures for assessing right ventricular (RV) function, were acquired using 2D mode. Pulsed-wave Doppler imaging was used to quantify the early (E) and late (A) diastolic peak flow velocities from the apical four-chamber view. E′, A′, and S′ cardiac velocities were measured using tissue Doppler imaging at the tricuspid annular plane, which was also acquired from the same point of view. The right atrial volume index (RAVI) has been determined using the adjusted Simpson's method and then normalized to the body surface area. Additional data, including tricuspid E/A and E/Em ratios, right ventricular fractional area change (RVFAC), TAPSE / tricuspid regurgitation velocity (TRV), and TAPSE / pulmonary artery systolic pressure (PASP) ratios, were obtained from recorded measurements.

***Table 1.*** *Demographic, clinical, and laboratory characteristics of all patients with mild to moderate and severe OSA, with p value*

| Variable | Mild to moderate OSA (n=45) | Severe OSA (n=43) | Total patients (n=88) | p-value |
|---|---|---|---|---|
| Age (years) | 48±14 | 56±12 | 52±14 | 0.009 |
| Female gender, n (%) | 17 (37.8) | 13 (30.2) | 30 (34.1) | 0.458 |
| BMI (kg/cm²) | 30.27±6.19 | 35.13±5.75 | 32.64±6.42 | **<0.001** |
| HT, n (%) | 13 (28.9) | 30 (69.8) | 43 (48.9) | **<0.001** |
| DM, n (%) | 6 (13.3) | 7 (16.3) | 13 (14.8) | 0.699 |
| CAD, n (%) | 5 (11.1) | 11 (25.6) | 16 (18.2) | 0.080 |
| WBC (10^3/uL) | 7.55±1.29 | 7.95±2.21 | 7.75±1.80 | 0.960 |
| Neutrophil (10^3/uL) | 4.34±1.20 | 4.59±1.42 | 4.47±1.31 | 0.542 |
| Hgb (g/dL) | 14.10±1.67 | 14.81±2.29 | 14.45±2.02 | 0.093 |
| Platelet (10^3/uL) | 238±57 | 227±62 | 233±59 | 0.318 |
| ALT (mg/dL) | 19 (14–33) | 24 (16–35) | 21 (15–35) | 0.197 |
| CRP, mg/dL | 3.2 (1.8–6.0) | 4.8 (2.1–9.0) | 3.6 (2.1–8.0) | 0.222 |
| Creatinine (mg/dL) | 0.94±0.43 | 0.94±0.15 | 0.94±0.32 | 0.133 |
| MAX apnea time | 23.0 (17.0–33.7) | 51.6±18.6 | 37.6 (21.3–60.0) | **<0.001** |
| AHI (events/h) | 13.8±6.1 | 69.8±28.6 | 41.2±34.7 | **<0.001** |
| **OSA severity (%)** | | | | |
| 1 | 26 (57.8) | 0 (0.0) | 26 (29.5) | |
| 2 | 19 (42.2) | 0 (0.0) | 19 (21.6) | **<0.001** |
| 3 | 0 (0.0) | 43 (100.0) | 43 (48.9) | |
| HR (bpm) | 72±11 | 74±15 | 73±13 | 0.792 |

OSA: obstructive sleep apnea, BMI: body mass index, HT: hypertension, DM: diabetes mellitus, CAD: coronary artery disease, WBC: white blood cell, Hgb: hemoglobin, ALT: alanine aminotransferase, CPR: C-reactive protein, AHI: Apnea-Hypopnea index, HR: heart rate.

### *Statistical Analysis*

Statistical Package for Social Sciences (SPSS) program version 22.0 (IBM Inc., Chicago, IL) was used to analyze the research data. The descriptive continuous variables which have the normal distribution were described as mean and standard deviation, as median and interquartile ranges for continuous variables which do not have the normal distribution, and as percentage values for categorical variables. Kolmogorov-Smirnov test was used to analyze the normal distribution characteristics of continuous variables. To determine the differences between the groups for continuous variables, the Mann-Whitney U test or the two-sample student's *t*-test was used. Variables that were significant in univariate analysis were included in multivariate logistic regression to identify independent predictors of severe OSA. The optimal cut-off values of the significant variables in the multivariate analysis in predicting the development of severe OSA were determined by calculating ROC (receiver operating characteristic curves) and their AUC (area under the curve) values. The p-value <0.05 was taken for statistical significance.

## Results

A total of 88 patients diagnosed with obstructive sleep apnea syndrome and evaluated at the cardiology echocardiography laboratory of Kafkas University Hospital between January 2023 and May 2024 were included in the study. Of them, forty-three patients were allocated to the severe OSA group and forty-five patients to the mild-to-moderate OSA group.

The body mass index (BMI) of the severe OSA group was higher than that of the mild-to-moderate group. The severe group was older and had a higher prevalence of hypertension (HT). No significant differences were observed between the two groups regarding sex, diabetes mellitus (DM), heart rate (HR), coronary artery disease (CAD), or laboratory parameters. The classification of baseline demographic information and lab results by group is shown in Table 1.

***Table 2.*** *Echocardiographic parameters of all patients with mild to moderate and severe OSA, with p value*

| Variable | Mild to moderate OSA (n=45) | Severe OSA (n=43) | Total patients (n=88) | p-value |
|---|---|---|---|---|
| E wave, (cm/s) | 68±17 | 68±18 | 68±17 | 0.967 |
| A wave (cm/s) | 76±16 | 78±20 | 77±18 | 0.767 |
| E/A, mitral | 0.93±0.31 | 0.98±0.67 | 0.95±0.52 | 0.323 |
| Em lateral, mitral (cm/s) | 10.1±4.1 | 10±3.3 | 10.1±3.7 | 0.822 |
| Em septal, mitral (cm/s) | 7.4±2.1 | 7.2±1.9 | 7.3±2.0 | 0.333 |
| Em mean, mitral | 8.75±2.64 | 8.58±2.22 | 8.67±2.43 | 0.723 |
| E/Em septal, mitral | 10.09±4.1 | 10.22±4.36 | 10.16±4.20 | 0.844 |
| E/Em lateral, mitral | 7.61(5.13–9.67) | 6.45(5.39–8.63) | 6.93(5.32–8.90) | 0.679 |
| E/Em mean, mitral | 8.48±3.28 | 8.50±3.96 | 8.49±3.61 | 0.686 |
| LVEF, (%) | 58±5 | 57±7 | 58±6 | 0.314 |
| E, tricuspid (cm/s) | 53.4±13.9 | 59.3±25.1 | 56.3±20.2 | 0.304 |
| A, tricuspid (cm/s) | 60.1±18.3 | 59.0±20.6 | 59.6±19.3 | 0.793 |
| E/A, tricuspid | 0.95±0.32 | 1.04±0.37 | 0.99±0.35 | 0.155 |
| RV Em (cm/s) | 10.4±3.6 | 9.1±2.9 | 9.8±3.3 | 0.123 |
| RV Am (cm/s) | 13.5±4.1 | 14.1±4.8 | 13.8±4.4 | 0.628 |
| RV S'(cm/s) | 12.5±2.8 | 12.7±3.2 | 12.6±3 | 0.825 |
| LAVI (mL/m²) | 17.05±8.82 | 24.45±13.35 | 20.67±11.8 | **0.001** |
| E/Em, tricuspid | 5.70±2.32 | 7.21±3.83 | 6.44±3.22 | **0.046** |
| TRV, m/s | 1.5±0.6 | 1.9±0.8 | 1.7±0.7 | 0.050 |
| TAPSE, mm | 2.4±0.5 | 2.3±0.5 | 2.4±0.5 | 0.703 |
| IVC, mm | 1.4±0.4 | 1.4±0.5 | 1.4±0.4 | 0.927 |
| sPAP, mmHg | 14.86±8.03 | 20.62±12.14 | 17.68±10.59 | 0.044 |
| TAPSE/TRV, mmx $(m/s)^{-1}$ | 1.87±1.09 | 1.58±0.93 | 1.73±1.02 | 0.071 |
| TAPSE/sPAP | 0.17 (0.13–0.27) | 0.13(0.07–0.27) | 0.16(0.09–0.27) | 0.072 |
| RVDD (mm) | 3.8±0.7 | 4.2±0.6 | 4.0±0.7 | 0.008 |
| MPAd, mm | 2.1±0.4 | 2.2±0.3 | 2.1±0.4 | 0.016 |
| RAVI, mL/m² | 13.26±4.81 | 24.24±10.75 | 18.63±9.90 | **< 0.001** |
| RVFAC (%) | 0.48±0.15 | 0.50±0.16 | 0.49±0.15 | 0.861 |

E: peak early inflow velocity, A: peak late inflow velocity, Em: early diastolic tissue Doppler velocity, LAVI: left atrial volume index, LVEF: left ventricle ejection fraction, RV Em, RV Am, and RV S'; right ventricle peak early (Em), Late (Am) and systolic (S') tissue Doppler velocities, LAVI: left atrial volume index, TRV: tricuspid regurgitation velocity, TAPSE: tricuspid annular plane systolic excursion, IVC: inferior vena cava, sPAP: systolic pulmonary artery pressure, RVDD: right ventricular end-diastolic diameter; MPAd: main pulmonary artery diameter at diastole, RAVI: right atrial volume index, RVFAC: right ventricle fractional area change.

A summary of the echocardiographic results, broken down by group, is shown in Table 2. The severe group's LAVI was substantially greater than that of the mild-to-moderate group (17.05±8.82 mL/m² vs. 24.45±13.35 mL/m²; p=0.001) in terms of left-sided characteristics. The groups' LVEFs did not differ significantly. The severe group had considerably higher right-sided measures, including the right atrial volume index (RAVI) (13.26±4.81 mL/m² vs. 24.24±10.75 mL/m²; p <0.001) and the E/Em tricuspid ratio (5.70±2.32 vs. 7.21±3.83; p=0.046).

According to Table 3's multivariate analysis, severe OSA was independently predicted by HT, BMI, and RAVI (HR: 1.231, 95% CI: 1.120–1.353; p <0.001). A RAVI cutoff value of 17.3 predicts severe OSA with 72.1% sensitivity and 86.7% specificity, according to the ROC curve analysis shown in Fig. 1 (AUC=0.822, 95% CI: 0.726–0.895; p <0.001).

## Discussion

This study searched the subclinical effects of severe OSA on cardiac structure and function using two-dimensional echocardiography. The main findings revealed that patients with severe OSA had significantly higher values of LAVI, tricuspid E/Em ratio,

***Table 3.*** *Univariate and multivariate logistic regression analysis of demographic, biochemical, and echocardiographic parameters for diagnosis of severely OSA*

| | Univariate | | | Multivariate | | |
|---|---|---|---|---|---|---|
| Variable | Odds ratio | 95% CI | p-value | Odds ratio | 95% CI | p-value |
| Age | 1.049 | 1.013–1.085 | 0.007 | | | |
| HT | 5.680 | 2.273–14.197 | <0.001 | 4.928 | 1.383–17.558 | **0.014** |
| BMI | 1.153 | 1.059–1.255 | 0.001 | 1.128 | 1.009–1.261 | **0.034** |
| LAVI | 1.073 | 1.019–1.131 | 0.008 | | | |
| E/Em Tricuspid | 1.181 | 1.010–1.380 | 0.036 | | | |
| TRV, m/s | 2.011 | 1.067–3.792 | 0.031 | | | |
| sPAP | 1.056 | 1.012–1.103 | 0.013 | | | |
| RV basal diameter | 2.323 | 1.155–4.674 | 0.018 | | | |
| MPAd | 4.475 | 1.222–16.383 | 0.024 | | | |
| RAVI | 1.231 | 1.120–1.353 | <0.001 | 1.256 | 1.120–1.410 | **<0.001** |

HT: hypertension, BMI: body mass index, LAVI: left atrial volume index, E: peak early inflow velocity, Em: early diastolic tissue Doppler velocity, TRV: tricuspid regurgitation velocity, sPAP: systolic pulmonary artery pressure, RV: right ventricle, MPAd: main pulmonary artery diameter at diastole, RAVI: right atrial volume index.

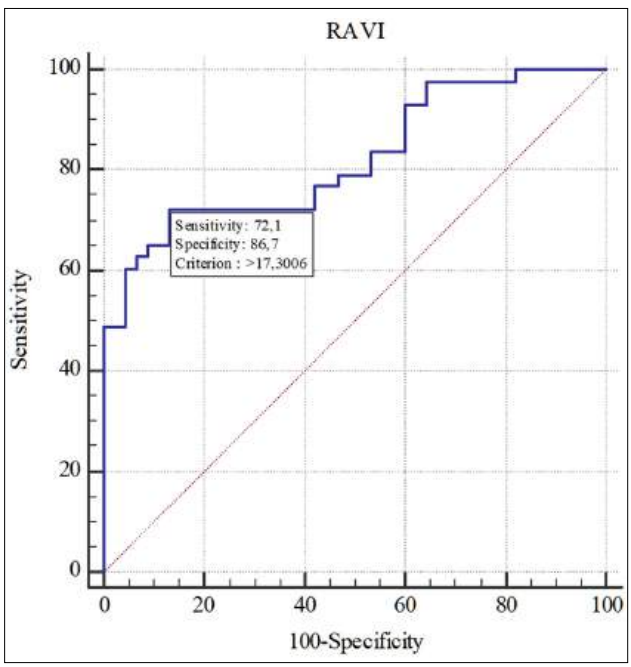


***Figure 1.*** *Receiver operating characteristic (ROC) curve analysis for RAVI for severe OSA group.*

and RAVI compared to those with mild-to-moderate OSA. Furthermore, severe OSA was independently linked to RAVI.

The literature currently in publication emphasizes the difficulties in precisely evaluating RV morphology and function in clinical settings, with studies frequently presenting contradictory results. Patients with OSA exhibit functional and structural dysfunction in their RV, and the severity of the illness is connected with these changes, according to studies employing both conventional and tissue Doppler imaging techniques[9]. Accurate measurement of RV function in OSA is crucial for prompt management, monitoring therapy effects, predicting prognosis, and reducing deleterious cardiovascular events. Myocardial performance index, RVFAC, TAPSE, and other 2D echocardiographic parameters can be used to evaluate global right ventricular function. Another important and sensitive early sign for assessing RV impairment is RV diastolic insufficiency[10]. In conventional echocardiography, the metrics used to assess the right ventricle's diastolic function are similar to those used to assess the left. RAVI, tissue Doppler imaging parameters like Em, Am, and the E/Em ratio, and pulse Doppler imaging parameters like E, A, and the E/A ratio are among them[11]. For the detection of subclinical RV dysfunction, tissue Doppler imaging is more sensitive than 2D echocardiography[10]. The TAPSE and RVFAC groups did not differ in the current investigation; however, in line with earlier research[10,12], we demonstrated that patients with severe OSA had greater RAVI and E/Em ratios than patients in the mild-to-moderate OSA group. Furthermore, RAVI was discovered to be an independent predictor of severe OSA in the current investigation. There aren't many studies assessing E/A and E/Em among those assessing right ventricular diastolic dysfunction in the literature. We discovered that patients with severe OSA had higher E/Em values, which is in line with the work of Li et al.[12]. Among other techniques, including strain calculation, this is the most useful and appropriate way to assess the RV's diastolic dysfunction. In patients with OSA, right ventricular dysfunction may result from a number of processes.

During apnea episodes, inspiratory efforts against the constricted pharynx cause the right ventricle to distend, increase venous return, and cause volume overload[13]. Additionally, the increased myocardial oxygen demand brought on by right ventricular (RV) structural remodeling, in conjunction with decreased coronary artery perfusion from vasoconstriction and vascular endothelial remodeling, may exacerbate RV dysfunction[14] and cause RV ischemia. This syndrome may also be caused by a number of other conditions, including CAD, obesity, and systemic HT.

Left atrial volume index was considerably higher in the patients with the severe OSA group than in the patients with the mild-to-moderate OSA group, which is consistent with evidence from the literature[15]. Left atrial volume index may have been higher in the severe OSA group due to increased rates of HT, DM, and CAD, which are predictors of LV dysfunction, albeit this effect was not statistically significant. Furthermore, blood pressure might rise due to sympathetic hyperactivity and nocturnal hypoxia, and transmural pressure can rise as a result of significant negative intrathoracic pressure brought on by respiratory effort during apnea. Over time, these events cause the left and right ventricles to experience increasing afterload, which causes ventricular hypertrophy and cardiac malfunction in both the diastolic and systolic phases, ultimately leading to heart failure (HF)[16]. Similar to HF, the development of HT as a result of OSA is a normal occurrence. Heart failure is a significant predictor of the severity of OSA, and our study demonstrated that the prevalence of HT was elevated in individuals with severe OSA, aligning with existing literature.

Numerous studies have shown a correlation between severe OSA and BMI. According to Young T. et al., a 5.3 BMI gain increases the likelihood of getting OSA by four times[17]. Indeed, BMI severity and apnea severity were both numerically examined and associated in a recent study by Fattal D. et al.[18]. In line with these, our study found that individuals with severe OSA had higher BMI values than those with mild to moderate OSA. Additionally, our research revealed that BMI is a reliable indicator of the existence of severe OSA. This condition can be explained by a variety of variables. Because fat deposits, especially around the upper airways, can result in a smaller airway lumen and higher collapsibility, weight gain is believed to exacerbate apnea. Moreover, the accumulation of fat around the chest decreases resting lung volume and chest compliance. Such decreases in lung volume promote pharyngeal collapsibility by decreasing tracheal traction[19].

Knowing that OSA exhibits structural and functional alterations of right heart chambers, detecting the changes using imaging methods seems to be reasonable. Right atrial volume index and E/Em are a part of the 2D echocardiography imaging method and are easily measurable. Because of being user-friendly and accessible, echocardiography may be used in the first stage, although there are more advanced imaging methods.

## Conclusion

Given the high prevalence of OSA and its association with cardiovascular complications, routine assessment of disease severity is crucial. Our findings suggest that echocardiographic parameters such as RAVI and tricuspid E/Em ratio are effective, affordable, and practical markers for predicting OSA severity, and may aid in early identification of patients at risk for cardiac involvement.

### *Limitations*

This study has several limitations. First, the lack of a non-OSA control group limits our ability to evaluate the absolute contribution of OSA to echocardiographic changes. Second, the sample size was relatively small, which may affect statistical power. Third, although comorbid conditions such as CAD, hypertension, and diabetes were included due to their frequent association with OSA, they may have confounded the relationship between OSA severity and echocardiographic parameters.

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**ARAŞTIRMA MAKALESİ /** *RESEARCH ARTICLE*

# Problems Experienced by Health Personnel on Duty and Solution Suggestions

*Nöbetli Çalışan Sağlık Personelinin Yaşadığı Sorunlar ve Çözüm Önerileri*

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## ABSTRACT

***Aim:*** *The aim of this study is to investigate the difficulties encountered by healthcare personnel working with a shift system in training and research hospitals and to suggest solution-oriented approaches.*

***Material and Method:*** *Designed as a qualitative case study, the study was conducted with 28 healthcare personnel working in research hospitals in Istanbul. Data were collected using a semi-structured interview form and analyzed with MAXQDA 2020.*

***Results:*** *The effects of the shift system and the proposed solutions were categorized under 10 main codes. Sleep Problems and Positive Feedback were the most emphasized subcodes for daily routines (28%). While Impact on Family Relationships (38%) was emphasized regarding family and social life, Resentment and Criticism (44%) were prominent in the perspectives of family and friends. Participants emphasized Positive Feedback in career development and job satisfaction. Health effects were dominated by Physical Health Problems such as insomnia and headache (56%). Lack of Time and Other subcodes were equally prominent problems regarding educational opportunities (32%). The difficulties experienced during shifts were mostly attributed to Relationships with Patients and Their Relatives (33%), while Self-Motivation (50%) was the most frequently mentioned coping strategy. Solution suggestions were highlighted as Shift Arrangements and Staff Increase (52%). These findings underline the extensive impact of on-call systems on healthcare professionals.*

***Conclusion:*** *On-call systems affect healthcare professionals' daily lives, family dynamics, careers and health. Improvements are essential, especially in managing physical health issues, improving patient relationships and optimizing shift arrangements.*

**Key words:** *on-call system; healthcare management; healthcare business management; strategic management*

## ÖZET

***Amaç:*** *Bu çalışmanın amacı, eğitim ve araştırma hastanelerinde nöbet sistemi ile çalışan sağlık personelinin karşılaştığı zorlukları araştırmak ve çözüm odaklı yaklaşımlar önermektir.*

***Materyal ve Metod:*** *Nitel bir vaka çalışması olarak tasarlanan araştırma, İstanbul'daki araştırma hastanelerinde çalışan 28 sağlık personeli ile yürütülmüştür. Veriler yarı yapılandırılmış görüşme formu kullanılarak toplanmış ve MAXQDA 2020 ile analiz edilmiştir.*

***Bulgular:*** *Nöbet sisteminin etkileri ve önerilen çözümler 10 ana kod altında kategorize edilmiştir. Günlük rutinler için Uyku Sorunları ve Olumlu Geri Bildirimler en çok vurgulanan alt kodlardır (%28). Aile ve sosyal yaşamla ilgili olarak Aile İlişkileri Üzerindeki Etki (%38) vurgulanırken, aile ve arkadaşların bakış açılarında Kınama ve Eleştiri (%44) öne çıkmıştır. Kariyer gelişimi ve mesleki memnuniyette katılımcılar Olumlu Geri Bildirimleri vurgulamıştır. Sağlık etkilerine uykusuzluk ve baş ağrısı gibi Fiziksel Sağlık Sorunları (%56) hâkimdir. Eğitim fırsatları konusunda Zaman Eksikliği ve Diğer alt kodlar eşit derecede belirgin problemlerdir (%32). Vardiyalar sırasında yaşanan zorluklar çoğunlukla Hastalar ve Hasta Yakınlarıyla İlişkiler (%33) olarak atfedilirken, en sık bahsedilen başa çıkma stratejisi Öz Motivasyon (%50) olmuştur. Çözüm önerileri Vardiya Düzenlemeleri ve Personel Artışı (%52) olarak vurgulanmıştır. Bu bulgular, nöbetçi sistemlerinin sağlık profesyonelleri üzerindeki kapsamlı etkilerinin altını çizmektedir.*

***Sonuç:*** *Nöbetçi sistemler sağlık profesyonellerinin günlük yaşamlarını, aile dinamiklerini, kariyerlerini ve sağlıklarını etkiler. Özellikle fiziksel sağlık sorunlarını yönetme, hasta ilişkilerini geliştirme ve vardiya düzenlemelerini optimize etme konusunda iyileştirmeler şarttır.*

**Anahtar kelimeler:** *nöbetçi system; sağlık yönetimi; sağlık işletmeciliği; stratejik yönetim*

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## Introduction

The health sector is the system formed by all institutions and organizations that produce health-related goods and services in order to obtain, protect and ensure sustainability of health so that people can continue their quality lives[1]. According to the regulation published in the Official Gazette No. 29007; *"Medical doctors, dentists, pharmacists, nurses, midwives and opticians and other professionals defined in the additional article 13 of the Law No. 1219"*, *"Other professionals who are not healthcare professionals but have a specific duty within the framework of healthcare service delivery and work in this field"*[2]. Hospitals are organizations that have to provide service 24 hours a day, 7 days a week. The continuity of this service is possible through shift and on-call working[3]. The shift work system is a system that requires employees to perform their duties at different times of the day. This system affects the biological order of individuals, especially sleep disorders, eating habits, family and social relationships, and causes negative effects on their general health[3–5]. Healthcare workers who are subject to shift work encounter various physical, mental and emotional difficulties[6–8]. When these effects are included in the shift work system, the job satisfaction, motivation and professional performance of healthcare personnel are negatively affected[9,10].

Healthcare workers face many difficulties during their shifts, including stress,[11] workload,[11] and sleep problems[12,13]. In addition to these, deficiencies in shift arrangements, lack of personnel consequently increased workload, and deficiencies in physical working conditions increase the sense of burnout of healthcare personnel and reduce their job satisfaction and motivation. Increased levels of burnout also increase the risk of errors in healthcare services and reduce patient satisfaction[14,15].

Understanding the impact of on-call work on health workers and developing solution strategies for problems is vital both to improve the welfare of health workers and to ensure the sustainability of health services. Since healthcare workers address the whole society, the problems they experience are not only individual. Since the problems experienced are not only individual, these problems also have a complex structure that requires systematic solutions. In the process of solving these problems, solution-oriented issues such as reducing the difficulties experienced in the patient-patient relatives relationship, increasing rest opportunities and improving rest conditions, and balancing the workload should be emphasized.

In the literature, there are many studies on health personnel working in shift and on-call shifts. In particular, there are studies investigating the effects of shift or on-call working order on family and social relations,[8,16] sleep and nutrition,[17,18] work stress,[19] work performance,[20] job satisfaction[9,10] etc. in healthcare professionals. This study is important in terms of addressing the health personnel who are included in the on-call working system in research hospitals in Istanbul province and enabling a more in-depth examination of the problems with a semi-structured interview system. In this respect, it is thought that the results obtained from the study will contribute to the literature.

This study aims to identify the problems faced by healthcare personnel working on shifts and to develop solution-oriented approaches to these problems. The study will address the difficulties experienced by healthcare workers during and after shift work, their effects on work-life balance, job satisfaction and general satisfaction levels, and possible consequences on physical and psychological health. In line with the findings, it is aimed to offer applicable solutions to improve the working conditions of healthcare personnel.

## Materials and Methods

In this study, the in-depth interview technique, which is one of the qualitative research designs, was used. In-depth interview emerged as a product of the effort to understand social life and the behaviors of individuals. In-depth interview is a data collection technique based on verbal communication between the researcher and the subject on the subject under investigation. In the in-depth interview technique, data are collected with structured, semi-structured and unstructured interview forms[21]. In this study, data were collected using a semi-structured interview form. In addition, since there are no specific rules and calculations regarding sample size in qualitative research, if the answers given within the scope of the research question were repeated, it was accepted that data saturation was reached and the data collection process was terminated[22]. In the research, the answer to the question "What are the main problems faced by health personnel working with the on-call system, and what solutions can be developed to reduce these problems?" is sought.

This study was found ethically appropriate by the Health Sciences University Hamidiye Scientific Research Ethics Committee with the decision numbered 2024/12 and numbered 12/11 at the meeting dated 17.10.2024.

### Purpose and Importance of the Study

This study aims to identify the problems experienced by healthcare personnel working with the on-call system and to offer solution-oriented approaches in line with these problems. The research aims to present solutions by addressing issues such as the experiences of healthcare personnel during and after the shift, the balance between work and life, job satisfaction and satisfaction, and the effects on physical and psychological health.

It is known that health personnel working with the on-call system experience problems such as irregular working hours, workload and work intensity, and physical and psychological fatigue after the shift. These problems not only affect the work performance of healthcare personnel but also create serious pressure on their physical and psychological health and negatively affect their work-life balance. In this context, it is important to address these problems experienced by health personnel working on duty to increase job performance, job satisfaction, and satisfaction and sustain the quality of health services.

This research will contribute to the literature on the effects of the on-call working system on the work-life balance of health personnel in the health sector. In addition, since the problems experienced by health personnel are listened to first-hand, it will provide a new perspective to the literature by eliminating the current lack of information. On the other hand, it will contribute to taking important steps towards improving the quality of working conditions of health personnel by providing guiding suggestions to policymakers in the field of health management and human resources in solving all these problems.

### Population and Sample

The universe of the study consists of healthcare personnel working on duty in research hospitals. The sample of the study consists of healthcare personnel working on duty in research hospitals located within the borders of Istanbul. While creating the sample, maximum diversity sampling method, which is one of the Purposeful Sampling methods, was preferred. The aim of the maximum diversity sampling method is to define and discover main themes that contain many differences related to the event or phenomenon being examined[23]. In the purposive sampling method, if the sample size is to obtain the maximum amount of information during data collection, that is, when the information saturation point is reached, the data collection process is stopped[22]. In this study, if the answers given were repeated, the data collection process was stopped and the sample size was limited to 28 healthcare personnel.

In order to ensure the external validity of the study, attention was paid to the diversity of characteristics such as age, title, education level, years and number of shift work of the occupational groups. It is also thought that the study will contribute to the literature since it covers healthcare personnel working in research hospitals located in Istanbul.

### Limitations of the Study

This study is limited to volunteer healthcare workers who work in shifts for at least six months in training and research hospitals in Istanbul. Data were collected through a semi-structured interview form developed by the researcher. Istanbul was chosen as the study population due to its easy access, and the maximum working period of healthcare professionals was determined as 6 months, as it was a significant threshold in terms of gaining experience. Factors such as the universe and sample size of this study affect the generalizability of the study results.

### Data Collection

In this study, a semi-structured interview form was used as the data collection method, prepared by the researcher, the first five questions of which were about demographic characteristics (gender, age, education level, marital status, professional position) and the remaining five questions were about shift work arrangements. The content validity of the interview form was ensured by obtaining expert opinion, and the understandability and conceptual appropriateness of the questions were tested through pilot interviews with 5 people. The semi-structured interview form was prepared based on some studies in the literature[11,24–29]. Data were collected between 01.10.2024 – 01.11.2024 by face-to-face (17 people) and telephone (11 people) interviews with healthcare personnel included in the study.

### Data Analysis

The analysis first started with frequency and percentage calculations to determine the demographic characteristics of the participants included in the study. Then, content analysis of the data collected through interviews was carried out and analysis was carried out by coding the data, organizing the codes, and interpreting the findings[30]. MAXQDA 2020 program was used in the analysis. This program is used to classify, code, and

***Table 1.*** *Demographic information of the participants*

| **Age** | **N** | **%** | **Education status** | **N** | **%** |
|---|---|---|---|---|---|
| 20–24 years | 5 | 18 | High school | 4 | 14 |
| 25–29 years | 11 | 39 | Associate degree | 4 | 14 |
| 30–34 years | 4 | 14 | License | 14 | 50 |
| 35 years and over | 8 | 29 | Master's degree | 6 | 22 |
| **Marital status** | **N** | **%** | **Profession** | **N** | **%** |
| Married | 13 | 46 | Nurse | 8 | 29 |
| Single | 14 | 50 | Doctor | 9 | 32 |
| Widow | 1 | 4 | Other health worker | 11 | 39 |
| **Gender** | **N** | **%** | **Number of weekly shifts** | **N** | **%** |
| Male | 13 | 46 | 1 Or 2 times | 14 | 50 |
| Woman | 15 | 54 | 3 Times or more | 14 | 50 |
| **Working time** | **N** | **%** | **On-call working time** | **N** | **%** |
| 1 year and less | 9 | 32 | 1 year less | 10 | 36 |
| 2–6 Years | 5 | 18 | 2–6 Years | 6 | 21 |
| 7–11 Years | 7 | 25 | 7–11 years | 7 | 25 |
| 12 years and over | 7 | 25 | 12 years and over | 5 | 18 |
| **Length of service in the health sector** | **N** | **%** | **Average daily working time** | **N** | **%** |
| 1 Year and less | 6 | 21 | 8 Hours | 7 | 25 |
| 2–6 years | 8 | 29 | More than 8 hours | 21 | 75 |
| 7–11 years | 8 | 29 | | | |
| 12 years and over | 6 | 21 | | | |

analyze text-based data. The data collected within the scope of the research were transcribed and analyzed, then uploaded to the program, and relevant coding was performed. In line with expert opinion and peer confirmation, 10 main codes and 37 sub-codes were created, and a total of 352 codes were performed.

### *Reliability and Validity*

In qualitative research methods, techniques such as participant confirmation, triangulation, and peer verification are preferred to confirm the accuracy of the research questions and the collected data to increase validity and reliability[31]. The research questions were answered and examined by four healthcare professionals from different professional groups and pre-tested. As a result of the feedback, the questionnaire was finalized and applied. The reliability of the research was also determined by evaluating the coding of the answers to the questionnaire by the researcher and colleagues and comparing the "Consensus" and "Disagreement" codes. The calculation was made using the formulation made by Miles and Huberman (1994)[32] and it was concluded that the reliability of the research was 84.090%. Reliability above 0.70% indicates that the research is reliable.

$$\text{Reliability} = \frac{\text{Number of agreed codes (37)}}{\text{Number of agreed codes (37)} + \text{Number of different codes (7)}} * 100 = 84.090$$

## Results

In this study, firstly, the findings on the demographic characteristics of the health personnel who participated in the study are presented. The demographic information of the health personnel participating in the study is given in Table 1.

When the information in Table 1 is evaluated, 54% of the health personnel who participated in the study were female and 46% were male. Participants were predominantly in the 25–29 age group and the majority were single (50%). When the education levels of the participants are evaluated, it is seen that half of the employees (50%) are undergraduate graduates. When the occupational distribution was analyzed, 39% were other healthcare professionals, 32% were physicians, and 29% were nurses. This distribution shows the diversity of professions in the sample.

When the general working time of healthcare personnel in the sector is evaluated, it is determined that 32% of them have been working for 1 year or less, while

25% have been working for 7–11 years and 12 years or more. These rates indicate a balanced distribution of new and experienced employees in the sector. When the working time in the health sector is evaluated, it is seen that more than half of the participants, 58%, have been working in this sector between 2–11 years. 75% of the participants stated that they worked more than eight hours a day and 43% of the participants have been involved in the on-call system for more than 7 years. In terms of the number of shifts per week, 50% of the participants work 1 or 2 shifts per week, while the other 50% work 3 or more shifts per week. This equal distribution indicates that the frequency of shifts is similar among the participants.

The results of the 10 main codes and 37 sub-codes generated in line with the answers given to the research questions are presented in the form of diagrams. In this context, the distribution of the main codes and sub-codes of "Effects on Daily Routine" is shown in Fig. 1.

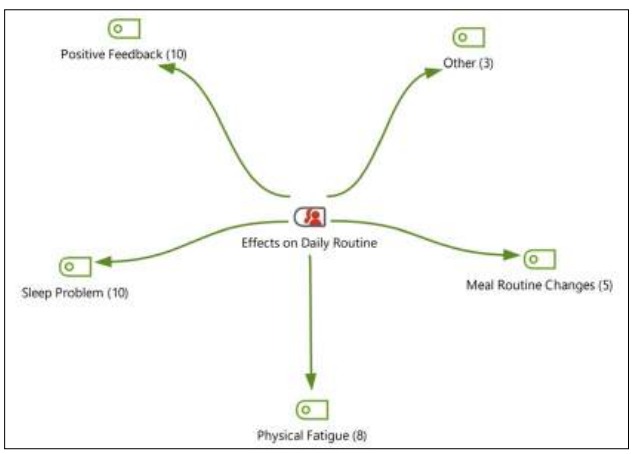


***Figure 1.*** *Classification of participants' answers about the effects of the on-call working system on daily routine according to the number of coded sections –hierarchical code-subcode model (Source: Created by the author according to the program outcomes).*

Fig. 1 shows the classification of the answers regarding the effects of shift work on daily routine according to the number of coded sections. According to this finding, it is seen that the participants mainly emphasized the sub-code Sleep Problem (28%). When the answers given are evaluated; *"Our sleep patterns are disrupted. If our shift was bad, I feel tired and exhausted the day after the shift.", "I think I live a very tired and irregular life, my sleep pattern is disturbed and I cannot spend quality time.", "Because the shift is tiring, the days after the shift are unproductive, usually spent sleeping."* A similar proportion of participants also stated that the on-call working system had positive (28%) effects on daily routine. These examples are as follows: *"It is good in terms of creating free days. The days after the shift can also be spent productively with the right time plan.", "It does not affect me much because I organize my daily routines around my shifts.", "It is good to have free days. I have the opportunity to do the things I could not do during working hours."* When the distribution of the other sub-codes regarding the effects of working on duty on the daily routine is examined, it is seen that 22% of the coded sections are Physical Fatigue, 14% are Changes in Meal Pattern, and 8% are Other.

The distribution of the main code and sub-codes of "Impacts on Family and Social Life" is shown in Fig. 2.

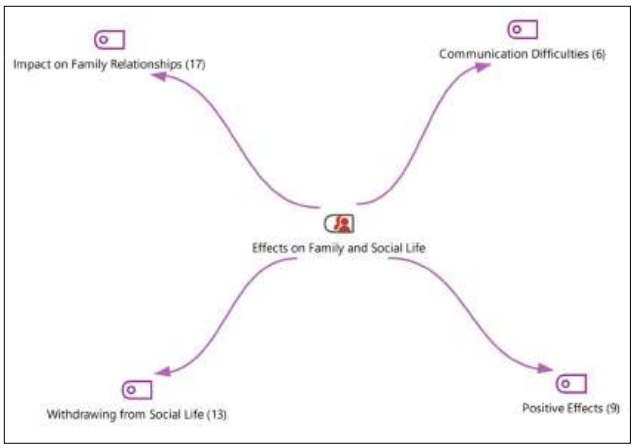


***Figure 2.*** *Classification of the participants' answers regarding the effects of the on-call working system on family and social life according to the number of coded sections –hierarchical code-subcode model (Source: Created by the author according to the program outcomes).*

Fig. 2 shows the classification of the answers regarding the Effects of the shift work organization on Family and Social Life according to the number of coded sections. According to the findings, it is seen that the participants emphasized the sub-code "Impact on Family Relationships (38%)" the most. The participants commented that it harms family relationships as follows: "*I cannot spare enough time because I am tired on the day after my shift. Even if I do, I cannot keep up with their energy.", "Not spending enough time with my loved ones is the biggest problem for me.", "I can spend more time with them when the shifts are not busy.".* The next most emphasized sub-code after family relationships is "Distancing from Social Life (29%)". Some examples of the comments made are as follows: *"Unfortunately, there is no time left for social life. It is difficult to adapt to the family and social environment.", "Unfortunately, on-call work creates an obstacle for my social life.", "I cannot spare enough time for my friends because of my very*

*busy work, and the time I do spare is limited."* When the distribution of other sub-codes regarding the effects of on-call work on family and social life was analyzed, it was seen that 20% of the coded sections emphasized that it had a positive effect (Positive Effects). When the answers related to this sub-code are examined; *"It has a positive effect on me because I have more free days, so I arrange all my meetings according to the extra days left from my shifts.", "I have free days because I am constantly working on duty. This has a positive effect. However, I can be a little nervous the days after the shift."* The remaining emphasis was placed on the "Communication Difficulties" sub-code with a rate of 13%. When the answers in this code are analyzed, it is seen that *"The fact that I work stressfully causes me to be tense in my relationships.", "I have free days because I work on duty all the time. This has a positive effect. However, I can be a little tense on the days after the shift."*

The distribution of the main code and sub-codes of "Views of Family and Friends" is shown in Fig. 3.

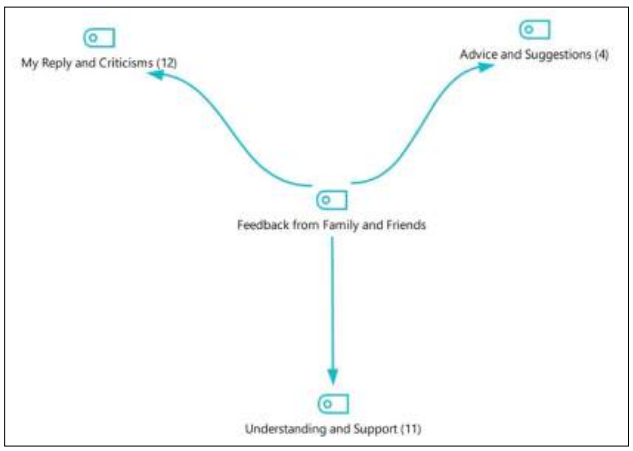


***Figure 3.*** *Classification of participants' answers regarding the views of family and friends on the on-call working system according to the number of coded sections –hierarchical code-subcode model (Source: Created by the author according to the program outcomes).*

Fig. 3 shows the classification of the answers regarding the Family and Friends' Views of the on-call working order according to the number of coded sections. According to the findings, it is seen that the participants emphasized the "Reproaches and Criticisms (44%)" sub-code the most. The participant's family and friends expressed that they reproach and criticize the on-call working order; *"They complain that we do not spend enough time together.", "They think negatively and complain that we cannot spare enough time.", "They may reproach for the time they cannot spare for them."*. Participants emphasized the "Understanding and Support" sub-code by 41%. It is seen that the participant's family and friends support and understand their on-call work; *"My family and friends are aware that I work very hard, they try to support me and sometimes feel sad that I cannot spend time with them.", "They are understanding for now.", "They feel sad and try to support me."*. The last sub-code emphasized with a rate of 15% was "Recommendations and Suggestions". The participants stated that their family and friends gave advice and suggestions as follows: *"They say that I work very hard and that I should switch to a department where there are no shifts.", "They advise me that my salary is good, that every profession is full of difficulties, and that I should be patient."*.

The distribution of the main code and sub-codes of "Impacts on Career Development" is shown in Fig. 4.

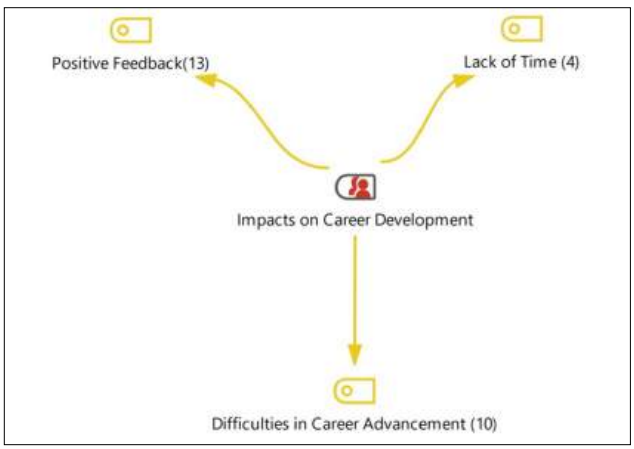


***Figure 4.*** *Classification of participants' answers regarding the effects of the on-call working system on career development according to the number of coded sections –hierarchical code-subcode model (Source: Created by the author according to the program outcomes).*

Fig. 4 shows the classification of the answers regarding the Effects of on-call working on Career Development according to the number of coded sections. According to the findings obtained, the participants emphasized that the on-call working system provided positive feedback on career development the most (48%). The positive feedback is as follows; *"It is good in terms of gaining experience.", "I stay in the hospital for a longer period. Thus, I participate in the follow-up of the patients better. I can have more control over the patients.", "Even if I get tired every hour that the shift is productive, I do not mind because I will see the benefits in the future. The opportunity to learn by reading and seeing on the spot during the time we are in the hospital will take us further."*. Participants emphasized the sub-code "Difficulties in Career Advancement" with a rate of 37%. They stated

that working on duty brings difficulties in advancing in their careers; *"It causes difficulties for me while trying to improve myself.", "Since we cannot allocate a regular time, we do not have time to plan and improve ourselves.", "People sometimes have to attend training after the shift. These trainings are not productive at all.", "I can say it is bad because it affects my Tus study order."* The last sub-code emphasized with a rate of 15% was "Lack of Time". The participants stated that they had insufficient time for career development as follows: *"Since we cannot allocate regular time, we do not have time to plan and improve ourselves.", "Unfortunately, you cannot think of a career because I cannot allocate time for a career."*.

The distribution of the main code and sub-codes of "Effects on Occupational Satisfaction and Motivation" is shown in Fig. 5.

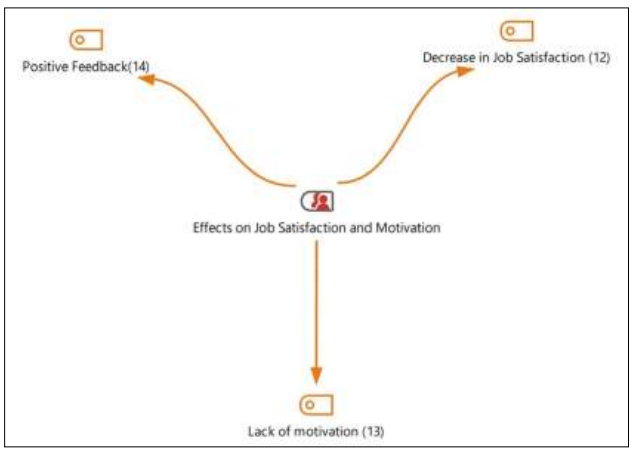


***Figure 5.*** *Classification of participants' answers regarding the effects of the on-call working system on professional satisfaction and motivation according to the number of coded sections –hierarchical code-subcode model (Source: Created by the author according to the program outcomes).*

Fig. 5 shows the classification of the answers regarding the effects of on-call work on professional satisfaction and motivation according to the number of coded sections. According to the findings obtained, the participants emphasized that the on-call working system provided positive feedback (36%) on professional satisfaction and motivation. According to this finding, the participants; *"It contributes to professional satisfaction." "It provides a good motivation because I love my job.", "I chose to work on duty voluntarily because the consciousness of the remaining days after the shifts increases my motivation more."* The second most emphasized sub-code was "Low Motivation (33%)". When the answers given by the participants are examined; *"Unfortunately, it affects me negatively, being tired professionally demotivates me.", "My thoughts about my profession are also negatively affected because it decreases my motivation a lot.", "My motivation decreases immediately because it is exhausting."* The least emphasis with a rate of 31% was on the sub-code "Decrease in Job Satisfaction". The participants stated, *"The fact that there is almost no rest time during shifts caused me to look for an alternative profession from the job I started with enthusiasm.", "It affects negatively. After physical fatigue, there is no professional satisfaction."* The participants stated that their job satisfaction decreased.

The distribution of main codes and sub-codes for "Health Impacts" is shown in Fig. 6.

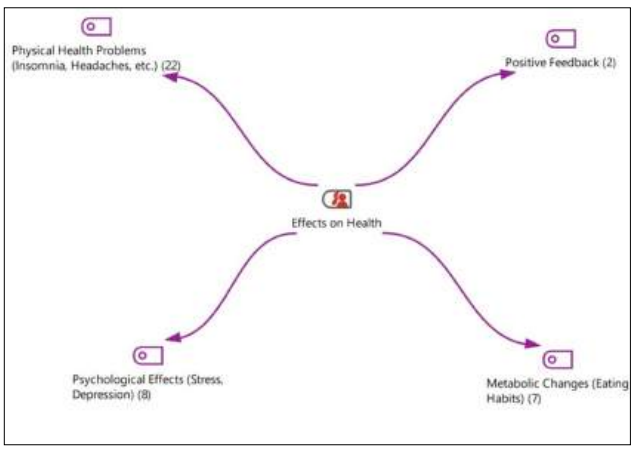


***Figure 6.*** *Classification of participants' answers about the effects of the on-call working system on health according to the number of coded sections –hierarchical code-subcode model (Source: Created by the author according to the program outcomes).*

Fig. 6 shows the classification of the answers regarding the effects of on-call working on health according to the number of coded sections. According to this finding, it is seen that the participants mainly emphasized the sub-code "Physical Health Problems (Insomnia, Headache, etc.) (56%)". When the answers given are evaluated; *"I experience headaches due to disturbance in sleep patterns.", "I experience constant illness, fatigue, weakness, sleep problems, joint pains.", Insomnia, excessive stressors, and cardiac rhythm disorders"*. The participants emphasized the "Psychological Effects (Stress, Depression)" sub-code the second most with a rate of 21%. The participants expressed the effects of working on-call on their psychological health as follows: *"It causes fatigue and psychological depressiveness", "I feel the feeling of burnout intensely", "I feel mentally bad because our social life is poor"*. Participants emphasized the sub-code "Metabolic Changes (Food Habits)" with a rate of 18% and the sub-code "Positive Feedbacks" with a rate of 5%. While

the participants made statements regarding metabolic changes such as *"My most important problem is the disruption in my sleep and eating patterns and this affects me negatively.", "It can be challenging in terms of diet and sleep patterns", "I cannot do sports after and on the day of the shift. I have sleep problems. I do not eat healthy during the shift"*, they also made positive feedback such as *"I do not have any problems in terms of health"*.

The distribution of the main code and sub-codes of "Training and Development Opportunities" is shown in Fig. 7.

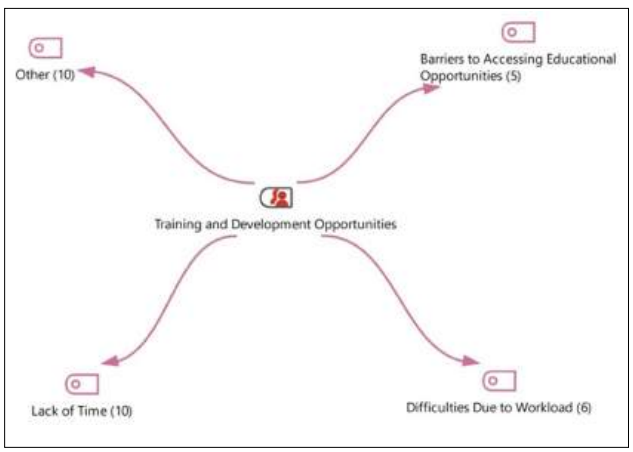


***Figure 7.*** *Classification of participants' answers regarding the training and development opportunities of the on-call working system according to the number of coded sections – hierarchical code-subcode model (Source: Created by the author according to the program outcomes).*

Fig. 7 shows the classification of the answers regarding the training and development opportunities of the on-call working pattern according to the number of coded sections. According to the findings, the participants emphasized the sub-codes "Lack of Time (32%)" and "Other (32%)" the most. Regarding the lack of time; *"Unfortunately, I cannot follow developmental opportunities due to lack of time", "Since I work in shifts, I have difficulty in making arrangements", and "Since we do not have a regular working environment and hours, we cannot participate in activities that will improve ourselves, so we are negatively affected"*. The answers given for the "Other" sub-code are as follows; *"I do not have difficulties", "It is easy to make shift arrangements accordingly", and "I do not have any problems in this regard". The* third highest emphasis with a rate of 19% was placed on the "Difficulties Due to Workload" sub-code. When the answers given by the participants regarding this code are examined; *"I could not go to the certificate program I wanted to go to because there were no nurses working in my unit. The hospital does not allow programs outside the city", "Working intensively affects my motivation to try to improve myself in free time because it is spent resting"*. The least emphasis was placed on the sub-code "Barriers to Access to Educational Opportunities" with a rate of 16%. When the answers given regarding this code are evaluated; *"Since I work on duty, I usually cannot go to the courses regularly and I have problems in accessing education", "We cannot participate in self-improvement activities because we do not have regular working hours, so we are negatively affected", "We have difficulty in accessing educational congresses due to intensive duty hours"*.

The distribution of the main code and sub-codes of "Difficulties Encountered During Watch" is shown in Fig. 8.

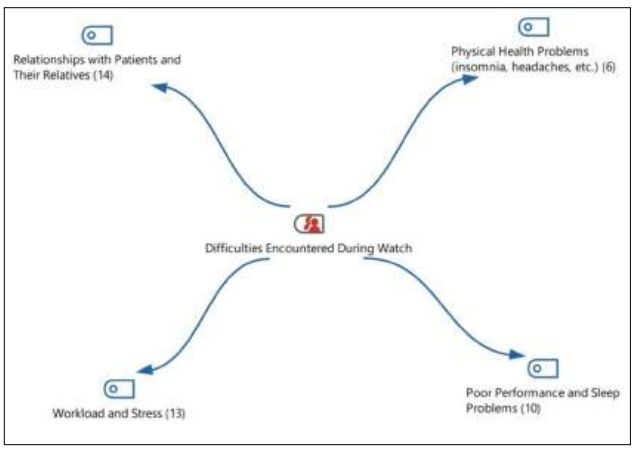


***Figure 8.*** *Classification of the participants' answers about the difficulties they face during the seizure according to the number of coded sections –hierarchical code-subcode model (Source: Created by the author according to the program outcomes).*

Fig. 8 shows the classification of the answers regarding the difficulties encountered during the seizure according to the number of coded sections. According to the findings, the participants emphasized the main code "Relations with Patients and Patient Relatives (33%)" the most. According to this coded section, the participants stated that they encountered problems such as *"Patients and their relatives not being more sensitive to us and not showing enough respect", "Irregular complaints and behaviors of patients' relatives", "Unnecessary discussions with patients' relatives"* and that this situation strained them both mentally and physically. It is seen that the next highest emphasis with a rate of 30% was on the sub-code "Work Intensity and Stress". Participants stated that they encountered difficulties such as *"Excessive workload, work done outside the job description, dealing with the problems of material and technical deficiencies", "I have problems keeping up with the events I will do", And "Excessive workload due to lack of personnel"*. It was also observed that 23% of the participants emphasized the

sub-code of low performance and sleep problems and 14% emphasized the sub-code of physical health problems (insomnia, headache, etc.).

The distribution of the main codes and sub-codes of "Strategies for Coping with Difficulties" is shown in Fig. 9.

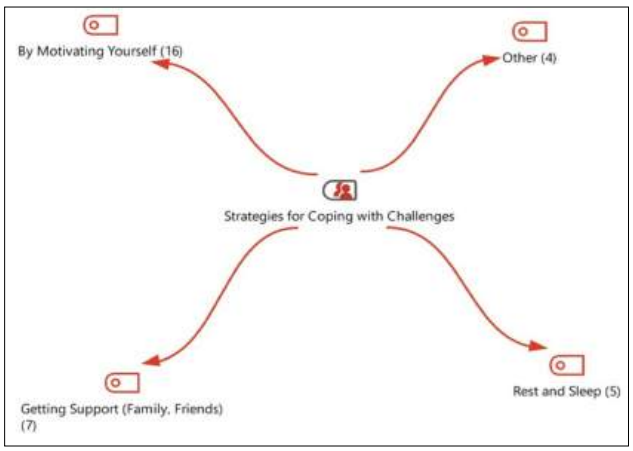


***Figure 9.*** *Classification of participants' responses regarding their coping strategies with the difficulties they encounter during seizures according to the number of coded sections –hierarchical code-subcode model (Source: Created by the author according to the program outcomes).*

Fig. 9 shows the classification of the answers regarding the strategies for coping with the difficulties encountered during the seizure according to the number of coded sections. According to the findings, the participants emphasized the main code "Self-motivation (50%)" the most. The participants stated that they motivated themselves with strategies such as *"Worrying about the problems at the lowest possible level", "Trying to stay calm by not losing myself in the environment", and "Being patient and realizing that the other person is a patient", "thinking that I have a free day after the shift and motivating myself"*. The second emphasis with a rate of 22% was on the sub-code "Getting Support (Family, Friends)". Participants stated that they usually cope with the difficulties they face with the support of their family and friends; *"By sharing the work with friends", "Sometimes I ask my friend to take care of me for 1 hour and I rest and come back more vigorous", "With family support"*. While the participants emphasized the "Rest and Sleep" sub-code with a rate of 16% in terms of coping with difficulties, the least emphasis was placed on the "Other (12%)" sub-code. When the answers given under the other sub-code are examined; *"I cannot cope with the difficulties I experience during the seizure", "Code White", "I usually overcome this job by getting enough sleep after the seizure, taking up a new hobby or spending time with my friends"*.

The distribution of the main code and sub-codes of the last main code "Solution Suggestions and Strategies" is shown in Fig. 10.

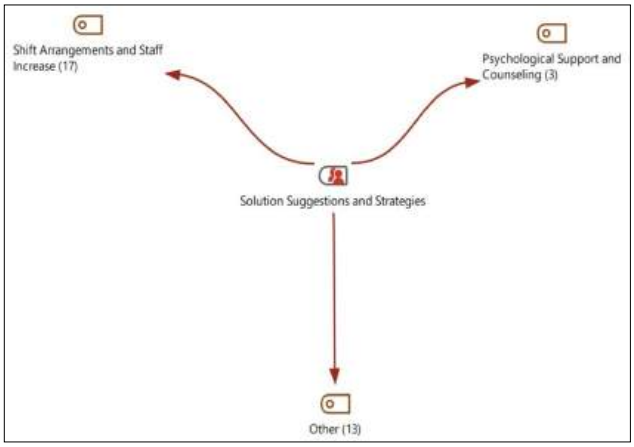


***Figure 10.*** *Classification of participants' answers on solution suggestions and strategies according to the number of coded sections –hierarchical code-subcode model (Source: Created by the author according to the program outcomes).*

Fig. 10 shows the classification of the participants' answers regarding solution suggestions and strategies according to the number of coded sections. Under this main code, the participants emphasized the main code "Shift Arrangements and Staff Increase (52%)" the most. When the answers given by the participants are examined; *"Reducing the number of shifts and having a full-time working order", "We can have more flexible working hours, we can arrange the time when we can organize our lives and increase our quality of life", "Burnout of nurses can be reduced by correcting the insufficiency and poor quality of staff, and the negative effects will decrease"*. The other most emphasized code was the "Other" subcode with 39%. When the answers given regarding this code are examined; *"Human-oriented working conditions and hours that provide motivation should be implemented", "Sports and artistic activities should be organized to discharge", "Shift/shift system working, creation of suitable resting areas", "Separate places should be allocated for male and female employees. to sleep"*. The least emphasized subcode is "Psychological Support and Counseling (9%)". Participants made suggestions such as*; "Effective communication methods should be taught to health personnel, stress management should be taught, better conditions should be provided for basic needs, psychological support, and counseling services should be provided"*.

## Discussion and Conclusion

The results obtained from this study, which aimed to identify the problems of health personnel working with the on-call system and to provide solution-oriented approaches in line with these problems, were included and the results were supported by other studies in the literature.

When the results regarding the general profiles of the health personnel participating in the research are evaluated, it is seen that the participants are predominantly female and between the age groups of 25–29. Considering the marital status of the participants, it was concluded that the predominant group was single. It is seen that the participants are predominantly undergraduate graduates and other health workers. It was concluded that 50% of the participants have been working in the health sector for more than 7 years and 43% of them have been working on call for more than 7 years. While 75% of the participants worked more than 8 hours per day on average, the participants equally stated that they worked 1–2 times or 3 or more weekly shifts.

When the results regarding the effects of the shift work system on the daily routine of healthcare personnel were examined, it was seen that the participants mainly emphasized the sleep problem (27%, 7) and positive effects (27%, 7) categories. The findings of this study are similar to the studies conducted in the literature. In the study conducted by Ozvurmaz and Oncu (2018)[27] on nurses, a statistically significant difference was found between the sleep disorder of nurses working with shift and on-call system. They stated that 56.2% of the nurses working with the shift system and 9% of the nurses working with the on-call system experienced sleep disorders. In this study, it is seen that the participants stated that the on-call working system positively affected their daily routines, that they had the opportunity to do the official work they had to do during working hours, and that they had more free time. There is no study in the literature addressing the positive aspects of on-call work. Therefore, this finding is important in terms of its contribution to the literature. This study is considered to be a pioneer in that it reveals the positive aspects of the shift work system for the first time in the literature.

Under the main code of effects on family and social life, the most emphasized code was family relationships. Participants stated that working on-call negatively affects family relationships and social life. One of the most important effects of the on-call working system is that changing and intense working hours lead to negative relationships due to insufficient and inefficient time for family and social relationships. Similarly, in a study conducted by Yesilcicek Calik et al. (2015)[8] on nurses, 93.8% of nurses working on call (continuous night) and 91.9% of nurses working in shifts (alternating day and night) stated that working hours negatively affected their social/family life. In a study conducted by Ekici and Demirbas (2020)[33] on nurses, similar results were obtained and it was seen that the social isolation sub– dimension was slightly affected negatively as the impairment in role-activity balance increased. Yesilcicek Calik et al. (2015)[8] concluded that working especially on holidays and weekends negatively affected the social lives of nurses. These results support the results of our study. In this study, there are also statements indicating that working on duty has positive effects on family and social life. The participants stated that thanks to the shifts, their days were free and they spent more time with their families and arranged their social gatherings accordingly. There is no study in the literature on the positive effects of on-call work on family relationships. Therefore, this finding is important in terms of its contribution to the literature. In addition, the participants also stated that their family and friends reproached and criticized them for working on duty.

When the answers given regarding the effects of the on-call working system on career development and professional satisfaction and motivation are evaluated, it is seen that the participants mainly stated that working on-call creates free time and that they use this free time to improve themselves, and that this situation increases their motivation. However, the participants also stated that working on-call caused time constraints for career development and difficulties in career advancement, as well as low motivation and decreased job satisfaction. In particular, participants stated that working on-call reduced their motivation and job satisfaction. The decrease in participants' motivation and job satisfaction also has a direct or indirect effect on their career development. In a study conducted by Orhaner and Mutlu (2018)[34] on healthcare personnel working in private hospitals in Ankara, it was observed that job satisfaction positively and significantly affected the motivation levels of employees. In a study conducted by Soyuk et al. (2016)[9] on nurses working in private hospitals in

Istanbul, it was concluded that continuous daytime workers had more job satisfaction than those working alternating day and night shifts. In a study conducted by Koyuturk (2015)[10] on healthcare workers, a significant difference was found in terms of job satisfaction levels of daytime workers and on-call workers. These findings support the findings of this study.

Looking at the answers they gave regarding the effects of the on-call working system on the health of health personnel, the participants stated that they mostly encountered physical health problems (insomnia, headache, etc.). Insomnia, sleep irregularities, and consequently various effects on body systems as a result of shift pattern and on-call work[35]. McDowall et al. (2017)[36] stated that shift work has negative effects on sleep quality. Books et al. (2020)[37] conducted a study on nurses working in hospitals in the USA and reported that working night shifts increased the risk of sleep deprivation, family stressors, and mood changes and that there was a general perception that sleep deprivation leads to negative health outcomes, including obesity. Khan et al. (2020)[38] concluded that shift work and various sleep disorders such as insomnia, obstructive sleep apnea, and insufficient sleep can lead to circadian rhythm disturbances, which may increase the risk of cardiovascular disease. Participants in this study also emphasized the psychological effects of shift work. The study by Genis et al. (2020)[39] supports this finding. Genis et al. (2020)[39] found that depression, anxiety disorder, sleep disturbance, burnout, and stress perception were higher in shift workers. In addition, participants in this study stated that shift work led to metabolic changes (eating habits). Similar findings were obtained in the study conducted by Farais et al. (2020)[40] on Chilean healthcare workers and in the study conducted by Pulat Demir et al. (2017)[41]. In the study conducted by Kesgin et al. (2011)[42] with nurses, it was determined that more than half of the participants mostly preferred junk food for nutrition. In the study conducted by Demirci (2017),[43] it was found that the emotional eating behaviors scores of healthcare workers were higher in shift workers. These findings in the literature support the findings of our study.

Considering the difficulties encountered by the participants during the shift, they stated that they mainly experienced difficulties in patient and patient relations. In the study conducted by Yilmaz and Gunay (2022)[44] on healthcare professionals, the participants stated that the most important factor affecting communication was prejudice, not listening to the other person, and having a self-centered structure were listed as other factors affecting communication. The main factors that are important in effective communication are effective listening, effective speaking and saying an empathic approach, and effective body language[45]. In this research, work intensity and stress, low performance and sleep problems, and physical health problems are other difficulties experienced. Research in the literature supports these findings. In the study conducted by Ferri et al. (2016)[6], cardiovascular symptoms were found to be statistically significant in night shift workers compared to day shift workers. In the study conducted by Gunaydin (2014),[46] a positive relationship was found between mental health status and sleep quality. In the study conducted by Shen et al. (2016)[47] on nurses working in a shift system in Taiwan, it was determined that the anxiety level was higher in the group of nurses working day-night shifts. These results support the results of this study.

Participants stated that they cope with the difficulties they face during the shift mainly by motivating themselves, and the solutions they offered for the problems experienced by health personnel working on duty were mainly shift arrangements and increasing staffing.

As a result, the study concluded that shift work has significant effects on the daily routines, family and social lives, career development, professional satisfaction and health of healthcare personnel. Participants emphasized problems such as sleep disorders, physical fatigue and irregular nutrition; they stated that these situations negatively affect work-life balance and social relationships. It was also stated that shift work makes career advancement difficult and reduces professional motivation. In terms of health, physical disorders and psychological problems have been widely reported. Strategies such as self-motivation, family and friend support and adequate rest are used to cope with these difficulties. Participants suggested solutions such as shift arrangements, staff increase and psychological support services to alleviate these problems.

In line with the findings obtained, it is possible to list the solution suggestions for the problems experienced by health personnel working with the on-call system as follows:

- Due to the intense work tempo and shift/on-call work system, healthcare professionals have limited access to personal and professional development opportunities. In the face of changing technology and social or cultural developments, participation in such trainings is important in order to contribute to the personal and professional development of healthcare professionals. For this reason, flexible working hours can be preferred to solve the problem of lack of time for healthcare professionals to evaluate personal development and training opportunities. A study conducted by Radovan (2024)[48] found that especially in larger companies and those with flexible working hours are more likely to participate in training activities.
- Flexible solutions (such as online training, arrangement of course hours) are recommended to ensure that healthcare professionals can benefit from training opportunities. A study conducted by Chaker et al. (2024)[49] found that continuous training in an online learning environment provides greater learning accessibility for healthcare professionals and is also a solution to temporal and physical constraints.
- The hours and number of shifts can be regulated to reduce the risk of burnout that may occur in health workers due to intensive working hours and a high number of shifts and to facilitate access to rest and development opportunities. In addition, nurses and other health personnel should be encouraged to update their knowledge and skills by supporting the sustainability of their training.
- There should be more open communication with health workers and arrangements should be made in line with the demands and needs of health workers.
- Since the increase in workload due to lack of personnel will increase the rate of burnout, lack of attention, incomplete or incorrect performance of tasks, and burnout, the duties and responsibilities should be alleviated by distributing them fairly by increasing the number of personnel.
- Stress management training can be provided during on-call hours in addition to working hours to help health workers cope with stress and work more calmly and efficiently.
- Physical working conditions can be improved to reduce both physical and psychological health problems of health workers. For example, separate rest areas for male and female workers, regular and productive break times, ergonomic workspaces, etc. can be effective.
- In order to minimize sleep problems during shifts, training on sleep hygiene, including improving sleep quality, creating a suitable sleep environment, and gaining healthy sleep habits can be provided. In addition, opportunities for healthcare workers to rest after the shift can be increased.
- Due to intensive working hours and increased workload, places such as gyms and meditation rooms can be created for both the physical and mental health of health workers.
- It is recommended that healthcare institutions provide strategies for healthcare professionals to motivate themselves to cope with stress during difficult working hours such as shifts[50,51]. Practices such as breathing exercises, time management training, and group support sessions should be developed for these strategies. It is also recommended that psychological support programs structured by experts in the field be implemented once or twice a month, either individually or in groups, and that healthcare professionals be informed about how to cope with stress, burnout, and other psychological difficulties.

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**ARAŞTIRMA MAKALESİ /** *RESEARCH ARTICLE*

# Evaluation of Dermatological Findings in Hemodialysis Patients

*Hemodiyaliz Hastalarında Dermatolojik Bulguların Değerlendirilmesi*

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## ABSTRACT

***Aim:*** *Chronic kidney disease is an increasing global public health concern. Hemodialysis is the most commonly utilized replacement therapy for end-stage renal disease. Common dermatological complications in hemodialysis patients, such as pruritus, xerosis, and nail or mucosal changes, significantly impair quality of life. This study aims to assess the prevalence and characteristics of these dermatological findings in hemodialysis patients.*

***Materials and Methods:*** *This cross-sectional study was carried out between September 20 and November 20, 2020, in a city in Eastern Türkiye. A total of 132 hemodialysis patients underwent a detailed dermatological examination. All pathological dermatological findings were documented, and their associations with comorbidities, duration of hemodialysis, frequency of hemodialysis, and age were evaluated.*

***Results:*** *At least one dermatological finding was detected in all cases among the 132 patients included in the study (mean age: 58.06 years; 48.5% female). Pruritus was observed in 36.4% of the patients, while xerosis was noted in 50%. Nail changes were recorded in 60.6% of the patients. Among oral mucosal findings, the most common were xerostomia (28%) and oral candidiasis (18.2%). Pigmentation disorders were identified in 39.4% of the patients, whereas 38.6% exhibited local complications at the fistula site. Advanced age was significantly associated with a higher prevalence of pruritus (p=0.003), xerosis (p=0.039), and oral candidiasis (p=0.008).*

***Conclusion:*** *Dermatological findings are common and diverse in hemodialysis patients. Pruritus, xerosis, and oral candidiasis significantly increase with aging, highlighting the need for targeted dermatological care. These findings underscore the importance of regular dermatological evaluations to improve patient outcomes and quality of life.*

**Key words:** *skin; dermatologic manifestation; hemodialysis; mucocutaneous*

## ÖZET

***Amaç:*** *Kronik böbrek hastalığı, giderek artan küresel bir halk sağlığı sorunudur. Hemodiyaliz, son dönem böbrek yetmezliği için en sık kullanılan tedavi yöntemidir. Hemodiyaliz hastalarında kaşıntı, kserozis ve tırnak veya mukozal değişiklikler gibi yaygın dermatolojik komplikasyonlar, yaşam kalitesini önemli ölçüde bozabilmektedir. Bu çalışma, hemodiyaliz hastalarındaki bu dermatolojik bulguların prevalansını ve özelliklerini değerlendirmeyi amaçlamaktadır.*

***Materyal ve Metod:*** *Bu kesitsel çalışma, 20 Eylül – 20 Kasım 2020 tarihleri arasında Türkiye'nin doğusunda bir şehirde gerçekleştirilmiştir. Toplam 132 hemodiyaliz hastası detaylı bir dermatolojik muayeneden geçirilmiştir. Tüm patolojik dermatolojik bulgular kaydedilmiş ve bunların eşlik eden hastalıklarla, hemodiyaliz süresi, hemodiyaliz sıklığı ve yaş ile ilişkileri değerlendirilmiştir.*

***Bulgular:*** *Çalışmaya dâhil edilen 132 hastanın tamamında (ortalama yaş: 58,06; %48,5'i kadın) en az bir dermatolojik bulgu saptandı. Hastaların %36,4'ünde kaşıntı, %50'sinde ise kseroz gözlendi. Tırnak değişiklikleri %60,6'sında kaydedildi. Oral mukozal bulgular arasında en sık kserostomi (%28) ve oral kandidiyazis (%18,2) görüldü. Hastaların %39,4'ünde pigmentasyon bozuklukları saptanırken, %38,6'sında fistül bölgesinde lokal komplikasyonlar bulundu. İleri yaş, kaşıntı (p=0,003), kserozis (p=0,039) ve oral kandidiyazis (p=0,008) prevalansının anlamlı şekilde daha yüksek olmasıyla ilişkiliydi.*

***Sonuç:*** *Dermatolojik bulgular, hemodiyaliz hastalarında yaygın ve çeşitlidir. Kaşıntı, kserozis ve oral kandidiyazis yaşla birlikte anlamlı olarak artış göstermekte olup, hedeflenmiş dermatolojik bakım ihtiyacını vurgulamaktadır. Bu bulgular, düzenli dermatolojik değerlendirmelerin hasta sonuçlarını ve yaşam kalitesini iyileştirmedeki önemini ortaya koymaktadır.*

**Anahtar kelimeler:** *deri; dermatolojik bulgu; hemodiyaliz; mukokutanöz*

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## Introduction

Chronic kidney disease is a significant public health concern with an increasing prevalence worldwide, particularly in developed countries[1]. Chronic kidney disease is classified into five stages, with stage 5 characterized by a glomerular filtration rate below 15 ml/min/1.73 $m^2$ or the necessity for renal replacement therapy[2]. Renal replacement therapy is provided through one of three methods: hemodialysis, peritoneal dialysis, or renal transplantation, depending on the patient's clinical condition[3]. Among these methods, hemodialysis is the most commonly preferred treatment. However, hemodialysis therapy is still associated with numerous complications. These complications significantly reduce patients' quality of life and may lead to life-threatening conditions that are challenging to manage[4].

Pruritus, xerosis, and skin infections are among the most commonly encountered dermatological complications in patients undergoing hemodialysis therapy[5]. While some of these issues arise as a result of the natural course of chronic kidney disease, others develop directly due to dialysis treatment[6]. The skin plays a critical role not only in assessing the quality of life of patients but also as an indicator of overall health status[5]. Previous studies report considerable variation in the prevalence and clinical presentation of dermatological findings in hemodialysis patients. These differences reflect variability among populations and the limited number of studies available on the subject[5–8].

In this study, dermatological findings observed in patients undergoing hemodialysis therapy were thoroughly examined, and the data obtained were compared with the existing literature. The primary aim of the study is to identify common and rare dermatological changes in this patient group and to reveal their associations with accompanying comorbidities. The data obtained in this context are intended to provide guiding contributions to clinical practices for the dermatological evaluation of hemodialysis patients.

## Materials and Methods

This study has a descriptive and cross-sectional design, encompassing all patients undergoing hemodialysis therapy in a city located in eastern Türkiye who agreed to participate. The study was conducted between September 20, 2020, and November 20, 2020. The patients included in the study were thoroughly evaluated by a dermatologist during their visits to dialysis centers. A comprehensive dermatological examination was performed on all patients, with suspicious lesions evaluated dermoscopically, microscopic analyses conducted, and histopathological examinations performed when necessary. All pathological findings identified during the study were meticulously documented. Ethical approval for the study was obtained from the ethics committee, and written informed consent forms were collected from all participants.

Statistical analyses were performed using Statistical Package for Social Sciences (SPSS) program version 20.0 software (IBM Corp., Armonk, NY, USA). Descriptive statistics of the data were presented as frequencies and percentages, while the chi-square test was used for pairwise comparisons. A p-value of $<0.05$ was considered statistically significant.

## Results

A total of 132 patients aged 17–90 years (mean: 58.06) were included in the study. Of these, 48.5% (n=64) were female, and 51.5% (n=68) were male. Chronic kidney failure was attributed to hypertension in 35.6% (n=47) and diabetes mellitus (DM) in 28.8% (n=38) of the patients. The mean duration of hemodialysis was calculated as 65.5 months. The sociodemographic characteristics and comorbidities of the patients are presented in Table 1.

All patients included in the study exhibited at least one mucocutaneous finding. Pruritus was reported by 36.4% (n=48) of the patients, with its severity assessed using a visual analog scale (VAS) ranging from 1 to 100. Of these, 13.6% (n=18) rated their pruritus severity as 50 or higher. Nail changes were observed in 60.6% (n=80) of the patients, including conditions such as onychomycosis, half-and-half nails, absent lunula, Terry's nails, leukonychia, Muehrcke's lines, splinter hemorrhages, onycholysis, vertical ridging, yellow nails, and onychogryphosis.

Additionally, oral candidiasis was detected in 18.2% (n=24) of the patients, xerostomia in 28% (n=37), and at least one oral mucosal abnormality other than candidiasis and xerostomia in 17.4% (n=23). The most common mucosal abnormality was a black hairy tongue, observed in 8.3% (n=11) of the patients. Based on biopsy results, two patients were diagnosed with systemic lupus erythematosus (SLE), and three with perforating dermatosis. Local complications such

***Table 1.*** *Sociodemographic characteristics and comorbidities of hemodialysis patients*

| Variable | n | (%) |
|---|---|---|
| **Gender** | | |
| Female | 64 | 48.5 |
| Male | 68 | 51.5 |
| **Age (years)** | | |
| 15–40 | 20 | 15.2 |
| 41–65 | 66 | 50 |
| ≥66 | 56 | 34.8 |
| **Duration of hemodialysis** | | |
| <3 years | 56 | 42.4 |
| >3 years | 76 | 57.6 |
| **Hemodialysis frequency (per week)** | | |
| 1 Session | 5 | 3.8 |
| 2 Session | 127 | 96.2 |
| **Comorbidities** | | |
| Hypertension | 97 | 73.5 |
| Diabetes mellitus | 50 | 37.9 |
| Cerebrovascular disease | 3 | 2.3 |
| Obesity | 11 | 8.3 |
| Coronary artery disease | 29 | 22.0 |

***Table 2.*** *Mucocutaneous changes identified in hemodialysis patients*

| | | n | (%) |
|---|---|---|---|
| **Mucocutaneous condition** | | 48 | 36.4 |
| **Pruritus** | | 66 | 50 |
| **Xerosis** | | 42 | 31.8 |
| **Pallor** | | | |
| | Oral candidiasis | 24 | 18.2 |
| | Herpes zoster | 2 | 1.5 |
| | Pityriasis versicolor | 15 | 11.4 |
| | Tinea cruris | 10 | 7.6 |
| | Folliculitis | 29 | 22.0 |
| **Pigmentation disorders** | | | |
| | Uremic pigmentation | 52 | 39.4 |
| | Melasma | 16 | 12.1 |
| | Vitiligo | 3 | 2.3 |
| | Hypopigmentation | 3 | 2.3 |
| **Oral mucosal disorders** | | | |
| | Black hairy tongue | 11 | 8.3 |
| | Scrotal tongue | 3 | 2.3 |
| | Geographic tongue | 6 | 4.5 |
| | Macroglossia | 1 | 0.8 |
| | Atrophic glossitis | 5 | 3.8 |
| | Xerostomia | 37 | 28.0 |
| | Uremic fetor | 7 | 5.3 |
| | Angular cheilitis | 6 | 4.5 |
| **Nail disorders** | | 80 | 60.6 |
| **Purpura/ecchymosis** | | 43 | 32.6 |
| **Keloid formation** | | 3 | 2.3 |
| **Nephrogenic fibrosing dermopathy** | | 1 | 0.8 |
| **Perforating dermatosis** | | 3 | 2.3 |
| **Systemic lupus erythematosus** | | 2 | 1.5 |
| **Local complications** | | 51 | 38.6 |

as infections or eczematization at the fistula site were identified in 38.6% (n=51) of the patients. Data on mucocutaneous changes are detailed in Table 2.

The relationship between dermatological findings and patients' age, duration of hemodialysis, and weekly frequency of hemodialysis was evaluated. While no significant association was found between the duration or frequency of hemodialysis and dermatological changes, older age was significantly associated with higher frequencies of pruritus (p=0.003), xerosis (p=0.039), and oral candidiasis (p=0.008).

## Discussion

Dermatological changes commonly observed in hemodialysis patients lead to significant issues that adversely affect their quality of life. This study contributes to the literature by providing a detailed analysis of the prevalence and clinical significance of mucocutaneous changes in a large patient cohort. Our findings are generally consistent with the literature while highlighting some unique features.

In 100% of the hemodialysis patients, at least one dermatological issue was identified. In the literature, xerosis has been reported as the most common finding, with prevalence rates reaching up to 96%[5,8–11]. However, Adégbidi et al.[12] (2020) reported this rate as 48%. Similarly, xerosis was observed in 50% of our patients. Disruption of the epidermal barrier and loss of function in sweat glands have been cited as the primary causes of xerosis[13]. Additionally, abnormalities in vitamin A metabolism and malnutrition are also significant contributing factors[8].

Pruritus was identified in 36.4% of our patients. Prevalence rates in the literature range between 21% and 74%[7,8]. Although the exact pathogenesis of pruritus remains unclear, it has been associated with

hyperparathyroidism, xerosis, hypervitaminosis A, anemia, and elevated serum levels of magnesium, calcium, phosphate, and aluminum. Allergic sensitivity to dialysis membranes has also been proposed as a possible cause[14]. Dyachenko et al.[7] reported that pruritus was not correlated with xerosis or excoriations but rather resulted from the accumulation of uremic toxins, which can be improved with effective hemodialysis. Additionally, they observed an increased incidence of neuropathy in these patients[15]. In the study by Dwiyana et al., findings consistent with ours indicated that xerosis and pruritus increased with age in dialysis patients[16].

Pallor in patients is expected due to chronic disease and erythropoietin deficiency, while yellowing of the skin is attributed to the accumulation of fat-soluble pigments such as carotenoids and urobilinogen in the dermis and subcutaneous tissue[14]. In our study, pallor was observed in 31.8% of the patients. Uremic pigmentation is frequently reported in the literature and is characterized by hyperpigmentation in sun-exposed areas, considered a hallmark symptom. This condition has been associated with increased levels of melanocyte-stimulating hormones in tissues[6]. Additionally, increased skin pigmentation has been noted following dialysis initiation, often manifesting as grayish-brown discoloration due to hemosiderin deposition. In the study by Anees et al.,[17] hyperpigmentation was identified as the most common finding, observed in 86% of patients. Similarly, Tajalli et al.[5] reported pigmentation in 89.8% of their study population. However, in our study, the prevalence of pigmentation was lower, at 39.4%.

In patients with end-stage renal disease (ESRD), the immune system is suppressed due to impairments in host defenses. This suppression is characterized by reduced neutrophil function, leukopenia associated with complement activation, diminished phagocytic capacity, weakened T and B lymphocyte functions, and decreased natural killer cell activity[18]. In our study, an increased incidence of mycotic and bacterial infections was observed among the patients. Local complications such as eczematization and infection at the fistula site were reported in 38.6% of the patients. According to the literature, 48–73% of bacteremias are attributed to vascular access sites, and infections are the second most common cause of death in ESRD patients, following coronary artery disease[19]. Therefore, maintaining personal hygiene is essential, and healthcare professionals should exercise maximum caution with antisepsis at vascular access sites during dialysis.

In our study, oral candidiasis was classified as an infectious disease and detected in 18.2% of the patients. The prevalence of oral candidiasis in the literature has been reported to range from 8% to 12%[20,21]. Xerostomia was the most frequently observed oral mucosal complaint in our study, with a prevalence of 28%. However, another study evaluating the oral findings of hemodialysis patients reported a significantly higher prevalence of 70%[21]. The lower prevalence of xerostomia in our patient group may be attributed to the subjective nature of the evaluations. Xerostomia in hemodialysis patients is thought to result from factors such as uremic involvement of the salivary glands, chemical inflammation, mouth breathing, restricted fluid intake, and dehydration[21]. Apart from oral candidiasis and xerostomia, at least one oral mucosal finding was identified in 17.4% of the patients. Ensuring proper oral hygiene in hemodialysis patients is crucial for preventing these pathologies.

Nail changes were observed in 60.6% of the patients in our study, with onychomycosis being among the most frequently identified nail conditions. In Altun's study,[6] onychomycosis was detected in 40.6% of patients, whereas Eftekhari et al.[22] reported a lower prevalence of 12.8%. In the latter study, similar to ours, 37.5% of the patients had diabetes, and among them, 17.9% were diagnosed with onychomycosis. Factors such as age, gender, education level, and dialysis access type are thought to increase the risk of onychomycosis[22]. In our study, a significant association was also observed between older age and a higher frequency of onychomycosis. Since onychomycosis poses a risk for complications such as erysipelas, cellulitis, or more severe infections that can lead to amputations, proper nail care and health are of critical importance in dialysis patients[22].

Ecchymotic lesions were observed in 32.6% of the patients in our study. In the study by Mourad et al.,[23] this rate was reported as 47.3%, while Tajalli et al.[5] reported a lower prevalence of 26.5%. The predisposition to ecchymosis in these patients may be associated with the use of heparin, platelet dysfunction, and increased vascular fragility[23].

Rare findings such as perforating dermatosis (2.3%) and nephrogenic fibrosing dermopathy (0.8%) were identified in our study. Although these conditions are

rarely reported in the literature, their clinical significance is considerable. Nephrogenic fibrosing dermopathy develops as a result of gadolinium, which is used as an alternative to iodinated contrast agents in patients with renal dysfunction. Patients undergoing peritoneal dialysis are at a higher risk for this condition[24]. Perforating dermatoses, on the other hand, are more commonly observed in hemodialysis patients and are associated with oxidative stress, chronic inflammation, and renal dysfunction. Uremic pruritus is thought to contribute to the tearing of collagen fibers and the body's attempt to expel these fibers, a process believed to play a significant role in the pathophysiology of perforating dermatosis[25].

Hypertension was identified as the most common comorbidity in our study, affecting 73.5% of the patients. In a cross-sectional study involving 313 patients, hypertension was reported in 74% of hemodialysis patients, with 97% of these individuals having hypertension before initiating dialysis. Factors associated with hypertension include increased weight gain between dialysis sessions, failure to achieve the target dry weight after dialysis, advanced age, and the presence of diabetes[26]. Diabetes was the second most common comorbidity in our study. Previous studies have noted that dermatological findings such as xerosis, pruritus, nail changes, and onychomycosis are more frequently observed in diabetic patients[6].

Our study has limitations. The inclusion of patients from only a single region and the short data collection period limited the evaluation of rare dermatological findings. Additionally, the heterogeneous nature of the patient population restricts the generalizability of the findings. To address these limitations, future studies with larger sample sizes and longer follow-up periods are needed.

## Conclusion

In conclusion, common mucocutaneous changes in hemodialysis patients significantly impact their quality of life. Pruritus, xerosis, and oral candidiasis are shown to increase significantly with aging. Maintaining personal hygiene, ensuring regular dermatological follow-ups, and implementing early interventions are crucial for preventing these complications, improving quality of life, and reducing morbidity and mortality. To gain a more comprehensive understanding of these findings, large-scale and long-term advanced studies are recommended.

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**ARAŞTIRMA MAKALESİ /** *RESEARCH ARTICLE*

# Comparison of Blood Culture and Multiplex PCR Results in Patients Prediagnosed with Sepsis

*Sepsis Ön Tanısı Alan Hastaların Kan Kültürü ve Multiplex PCR Sonuçlarının Karşılaştırılması*

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## ABSTRACT

***Aim:*** *Sepsis is a life-threatening infection that affects multiple systems, leading to hemodynamic changes, shock, organ dysfunction, and potentially organ failure. Although blood culture is the gold standard for identifying the causative agent, the pathogen cannot be isolated in some cases, posing significant challenges in diagnosis and treatment, affecting mortality and morbidity rates. The aim of this study is to retrospectively and prospectively evaluate the results of blood cultures and the Multiplex PCR sepsis panel sent to Microbiology laboratory.*

***Material and Method:*** *In this study, 100 samples sent to our laboratory for blood culture and sepsis panel between September 1, 2023, and August 31, 2024, were analyzed retrospectively and prospectively. All bottles with a positive signal were subjected to Gram staining, and simultaneous inoculations were made on 5% sheep blood agar, EMB, SDA, and Chocolate agar. After 24–48 hours of incubation at 37°C, the isolated strains were identified using conventional methods (colony morphology, Gram staining, etc.) and biochemical tests (catalase test, oxidase test, tube and slide coagulase tests). For the sepsis panel, nucleic acid extraction was performed on samples received in the laboratory using a total nucleic acid extraction kit based on magnetic bead technology, following the manufacturer's instructions.*

***Results:*** *According to the PCR results of the 100 blood samples included in the study, Candida species were detected in 4 samples. Candida species were also identified in the blood culture. The distribution of strains in the sepsis panel included C.tropicalis, C.albicans, C.glabrata, and C.krusei. Among the blood culture samples, three demonstrated results that were consistent with the sepsis panel findings, while one sample was identified as C.glabrata through conventional methods, in contrast to the result from the sepsis panel. Among bacterial pathogens, Staphylococcus spp. was the most frequently identified (56 cases), followed by Escherichia coli.*

***Conclusion:*** *The results of this study demonstrate that PCR is an effective method for diagnosing sepsis; however, some results need to be confirmed by blood culture. PCR testing provides rapid and accurate information, particularly in situations where quick results are essential, such as in intensive care units and emergency departments. However, it should be noted that PCR can amplify DNA from dead bacteria, so results should be interpreted with caution. In clinical practice, the combined use of both tests will contribute to more effective patient management and treatment.*

**Key words:** *sepsis; blood culture; multiplex PCR*

## ÖZET

***Amaç:*** *Sepsis, birçok sistemi tutan, özellikle hemodinamik değişikliklere yol açabilen, şok, organ fonksiyon bozukluğu ve yetmezliğine kadar gidebilen öldürücü bir enfeksiyondur. Kan kültürü altın standart yöntem olduğu halde bazı durumlarda etken izole edilememekte ve bu durum tanı ve tedavide ciddi zorluklara yol açarak mortalite ve morbidite oranlarına etki etmektedir. Bu çalışmanın amacı, rutin laboratuvarımıza gönderilen kan kültürü ve Multiplex PCR sepsis paneli sonuçlarının retrospektif ve prospektif olarak değerlendirilmesidir.*

***Materyal ve Metod:*** *Bu çalışmada, 1 Eylül 2023 – 31 Ağustos 2024 tarihleri arasında laboratuvarımıza gönderilen kan kültürü ve sepsis panel istemi yapılan 100 örnek prospektif ve retrospektif olarak incelenmiştir. Kan kültür cihazında pozitif üreme sinyali veren tüm şişeler gram boyama yapılmış ve eş zamanlı olarak %5 koyun kanlı kanlı agar, EMB, SDA ve Çikolatamsı agar besiyerlerine ekimleri yapılmıştır. Tüm plaklar 37°C'de 24–48 saat inkübe edildikten sonra izole edilen suşlar konvansiyonel yöntemler (koloni morfolojisi, gram boyama vb.) ve biyokimyasal testler (katalaz testi, oksidaz testi, lam ve tüpte koagülaz) ile tanımlanmıştır. Sepsis paneli için örnekler laboratuvara geldiğinde örneklerin nükleik asit ekstraksiyonu, manyetik boncuk yöntemine dayanan toplam nükleik asit ekstraksiyon kiti kullanılarak, üretici firmanın talimatları doğrultusunda gerçekleştirilmiştir.*

***Bulgular:*** *Çalışmaya dâhil edilen 100 sepsisli hasta örneğinin PCR sonuçlarına göre dört örnekte Candida türleri saptanmıştır. Aynı örneklerden yapılan kan kültürlerinde de Candida türleri saptanmıştır. Suşların dağılımı sepsis panelinde C.tropicalis, C.albicans, C.glabrata ve C.krusei olarak tespit edilmiştir. Kan kültür sonucunda üç örnek sepsis paneli ile aynı sonuçlanırken bir örnek sepsis sonucuna kıyasla konvansiyonel olarak C.glabrata olarak tanımlanmıştır. Bakteriyel etkenler arasında en sık sırasıyla Staphylococcus spp. (56), ikinci sıklıkta E.coli raporlanmıştır.*

***Sonuç:*** *Çalışmanın sonucunda, PCR'nin sepsis tanısı koymada etkin bir yöntem olduğu, ancak bazı sonuçların kan kültürü ile doğrulanması gerektiği ortaya çıkmıştır. PCR testi ile elde edilen sonuçlar, özellikle hızlı ve doğru bilgi sağlanması gerektiği durumlarda (örneğin, yoğun bakım ve acil servisler gibi) faydalıdır. Ancak, testin ölü bakteri DNA'sını çoğaltma özelliği nedeniyle dikkatli bir şekilde yorumlanması gerektiği unutulmamalıdır. Klinik uygulamalarda her iki testin birlikte kullanılması, hastaların daha etkili bir şekilde tedavi edilmesini sağlayacaktır.*

**Anahtar kelimeler:** *sepsis; kan kültürü; multiplex PCR*

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## Introduction

Sepsis is defined as organ dysfunction resulting from dysregulation of the host immune response to infections[1]. Bloodstream infections are significant causes of morbidity and mortality in hospitalized patients. Early diagnosis and the effective use of antibiotics are crucial for improving clinical outcomes in critical medical conditions such as sepsis and septic shock[2,3]. The rapid and accurate identification of bacterial pathogens isolated from blood cultures is important for initiating appropriate treatment at an early stage. This contributes to a reduction in morbidity and mortality, shorter hospital stays, lower healthcare costs, and the prevention of unnecessary antibiotic use[4,5]. Incorrect antibiotic therapy leads to difficulties in identifying the true pathogen, increases antimicrobial resistance, and facilitates the dominance of multidrug-resistant Gram-negative bacteria in the hospital environment[6].

Blood culture is considered the gold standard method for the diagnosis of sepsis. However, pathogens that are difficult or slow to grow may be overlooked in blood cultures from septic patients. Additionally, bacterial isolation from blood cultures may reflect asymptomatic bacteremia or contamination. Variables such as the type of microorganism, the microbial load in the sample, differences in the growth rates of microorganisms, and factors like the duration of sample storage at room temperature can also affect the results. Another disadvantage of blood cultures is their relatively low diagnostic sensitivity, particularly in patients receiving antibiotic treatment[7]. Molecular methods contribute to a reduction in hospital stay duration and mortality rates by enabling the detection of organisms that cannot be cultured, as well as shortening the time required for pathogen identification. Using PCR techniques, bacterial 16S rRNA genes are amplified through nucleic acid amplification. The identification of the pathogen on the same day and the molecular detection of major resistance patterns assist in the formulation of treatment policies[6]. This study aims to compare the results of blood cultures with the sepsis panel tested directly from the blood culture bottles using Multiplex PCR.

## Materials and Methods

In this study, 100 samples of blood cultures and multiplex PCR, requested between September 1, 2023, and August 31, 2024, were prospectively and retrospectively analyzed. The blood culture bottles were incubated in an automated blood culture system (Becton Dickinson, BD BACTEC™ FX40). All bottles that showed a positive growth signal were Gram-stained, and simultaneously, they were cultured on 5% defibrinated sheep blood agar, Eosin Methylene Blue (EMB) agar, Sabouraud Dextrose Agar (SDA), and Chocolate agar. After incubating all samples at 37°C for 24–48 hours, the isolated strains were identified using conventional methods (colony morphology, Gram staining, etc.) and biochemical tests (catalase test, oxidase test, and coagulase test in both tube and slide methods). The antibiotic susceptibility of the strains was determined using the Kirby-Bauer disk diffusion method, and the results were evaluated according to the European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoint table. For coagulase-negative staphylococci, the organism was considered the causative agent if the same bacterium was isolated in at least two blood cultures. If bacterial growth occurred in only one of the two blood cultures but was clinically consistent, or if the same strain was isolated from different infection sites, it was also considered as causative agent.

When the samples for the sepsis panel arrived at the laboratory, nucleic acid extraction was performed using a total nucleic acid extraction kit based on the magnetic bead method (Bioeksen, Istanbul, Türkiye), following the manufacturer's instructions. The extraction was carried out using the Zybio EXM 3000 device (Zybio, Shenzhen, China). The sepsis panel identifies a total of 24 parameters, including *Candida tropicalis, C.albicans, C.parapsilosis, C.krusei, C.glabrata, S.aureus, Staphylococcus spp., E.faecium, E.faecalis, S.pneumoniae, Streptococcus spp., L.monocytogenes, P.aeruginosa, Pseudomonas spp., K.oxytoca, K.pneumoniae, A.baumannii, H.influenzae, Enterobacteriaceae, S.maltophilia, E.coli, N.meningitidis*, as well as Vancomycin-resistant Van and Carbapenem-resistant Oxa strains.

After nucleic acid extraction, the samples were processed for multiplex PCR according to the manufacturer's recommendations shortly as follows;

1. The Sepsis RT-qPCR MX-24L Panel "SY-1 Rxn and SY-2 Rxn" strips were placed on the cooling block, which had been removed from -22°C.
2. 10 µl sample of "Template nucleic acid" was added to each of the "SY-1 Rxn and SY-2 Rxn" strips.
3. The strips were carefully and securely sealed with their caps and placed in the Micro-PCR device for processing. The amplification steps were set according to the settings shown in Table 1.

***Table 1.*** *Amplification steps for multiplex PCR*

| Steps | Cycle | Temperature | Duration |
|---|---|---|---|
| Reverse transcriptase | 1 | 52°C | 3 min. |
| Holding | 1 | 95°C | 10 min. |
| Denaturation | | 95°C | 1 sec. |
| Anneling/extension | 12 Touchdown cycle | 67°C–56°C | 15 sec. |
| Denaturation | 30 | 95°C | 1 sec. |
| Anneling/extension | | 95°C | 15 sec. |
| Read | | (FAM-green) (HEX-yellow) (ROX-orange) (CYS-red) | |

***Table 2.*** *Interpretation of the PCR results*

| Result | IC | Interpretation | |
|---|---|---|---|
| Positive | Positive or negative | Results valid, Pathogen detected | 26<Cq <30 "Low positive"<br>16<Cq <26 "positive"<br>Cq <16 "High positive" |
| Negative | Positive | Results valid, Pathogen not-detected | |

IC: Internal control.

4. The shape of the obtained amplification curves was examined for each reaction well with Cq values. Sigmoidal curves above the threshold value were considered "positive," while non-sigmoidal curves were regarded as "negative."

### *Interpretation of the Results*

For the *Candida krusei, C.glabrata, C.albicans, C.parapsilosis*, and *C.tropicalis* gene targets, a Cq value <26 was reported as positive, while a Cq value >26 was reported as negative. For all other gene targets, a Cq value <23 was reported as positive, and a Cq value >23 was reported as negative. In cases where multiple parameters yielded positive results, the outcome was reported following the evaluation process outlined below (Table 2).

The parameter with the lowest Cq value is identified=Min Cq.

If (the Cq value of the other parameter) –Min Cq <7, a positive result is reported for the other parameter.

If the Cq value of the other parameter –Min Cq >7, a negative result is reported for the other parameter.

### *Ethical Approval*

The study protocol was reviewed and approved by the the non-interventional ethics committee of Kafkas University, with approval number 80576354-050-99/396. As the study involved retrospective and anonymized data and no interventions were performed, the requirement for individual informed consent was waived by the ethics committee.

## Results

Of the blood culture and sepsis panel samples sent to our laboratory with a presumptive diagnosis of sepsis and showing positive growth, 60% came from the Anesthesia and Reanimation Intensive Care Unit, and 13% came from the Palliative Care Unit. The distribution of the samples included in our study according to the clinics is shown in Table 3.

***Table 3.*** *Distribution of sepsis samples according to clinics*

| Clinic | n | % |
|---|---|---|
| Anesthesia and reanimation intensive care unit | 60 | 60 |
| Palliative care unit | 13 | 13 |
| Internal medicine service | 8 | 8 |
| Cardiology service | 7 | 7 |
| Thoracic surgery service | 5 | 5 |
| Urology service | 5 | 5 |
| Neonatal intensive care unit | 1 | 1 |
| Emergency service | 1 | 1 |
| Total | 100 | 100 |

The PCR results of 100 sepsis patients included in the study revealed the presence of Candida species in 4 samples. Candida species were also detected in the blood cultures of the same samples. The distribution of strains in the sepsis panel was identified as *C.tropicalis*, *C.albicans*, *C.glabrata*, and *C.krusei*. In the blood culture results, 3 samples matched the sepsis panel, while one sample was conventionally identified as *C.glabrata* compared to the sepsis result. Among bacterial pathogens, Staphylococcus spp. (56 cases) was the most frequently reported, followed by *E.coli* as the second most common. Of the 100 total samples evaluated, two showed no growth in blood culture but were positive on the Multiplex PCR panel. This accounts for the discrepancy between the total counts of blood culture (n=98) and PCR results (n=100). The distribution of

pathogens detected in the study according to species is shown in Table 4.

***Table 4.*** *Microorganisms detected by blood culture and multiplex PCR sepsis panel*

| Multiplex PCR | n | Blood culture | | n |
|---|---|---|---|---|
| *Staphylococcus aureus* | 4 | *Staphylococcus aureus* | 4 | 56 |
| | | MRKNS* | 40 | |
| *Staphylococcus spp* | 52 | MSKNS** | 12 | |
| | | *Escherichia coli* | | 20 |
| *Enterocuccus faecium* | 5 | *Klebsiella pneumoniae* | | 3 |
| *Enterocuccus faecalis* | 3 | *Enterococcus spp* | | 11 |
| *Streptococcus pneumoniae* | 2 | *Pseudomonas aeruginosa* | | 1 |
| *Streptococcus spp* | 2 | *Acinetobacter spp* | | 3 |
| *Klebsiella pneumoniae* | 2 | Viridans Streptococcus | | 2 |
| *Acinetobacter baumannii* | 5 | *S.pneumoniae* | | 2 |
| *Escherichia coli* | 25 | | | |
| Methicillin resistance mecA | 60 | | | |
| Total | 100 | | | 98 |

* Methicillin resistant coagulase (-) Staphylococcus.
** Methicillin sensitive coagulase (-) Staphylococcus.
Of the 100 total samples evaluated, two showed no growth in blood culture but were positive on the Multiplex PCR panel. This accounts for the discrepancy between the total counts of blood culture (n=98) and PCR results (n=100).

In our study, a concordance rate of 88% was observed between blood culture and PCR results in patients with sepsis. The number of pathogens detected by PCR was found to be higher than that detected by blood culture. Given that the PCR method is capable of amplifying DNA from both viable and non-viable bacteria present in the environment, it was concluded that the interpretation of PCR results in conjunction with blood culture outcomes would yield a more accurate diagnostic approach for sepsis.

## Discussion

Polymerase Chain Reaction (PCR) results provide faster outcomes than blood culture, making it particularly useful in intensive care units or for critically ill patients, where quicker and more accurate information is essential. Moreover, the administration of antimicrobial treatment before blood sampling reduces the sensitivity of blood culture[8]. In a study by Dinç et al, the pathogen detection rate in sepsis patients was found to be 32% with blood culture and 44.9% with PCR[9]. In other studies carried out with SeptiFast, it has been reported that the blood culture positivity ranged from 8–41%, while the PCR positivity ranged from 11–41%[10–12]. However, due to PCR's ability to amplify dead bacterial DNA, positive results must be carefully evaluated. The detection of dead bacterial DNA can lead to false-positive results and may produce outcomes that are not consistent with clinical findings[13]. In our study, when we compared blood culture and PCR results in sepsis patients, an 88% concordance rate was observed between the two methods. In other studies, the concordance between blood culture and PCR has been reported to range from 67–85%[8,10,11,14,15]. It can be concluded from these studies that the PCR method is more successful in pathogen detection. However, it is important to highlight that PCR results should be evaluated alongside blood culture results.

Fungal infections, particularly, have a high mortality rate[16]. In recent years, approximately 5% of sepsis cases are caused by fungi, primarily Candida species. Risk factors contributing to this condition include prolonged use of broad-spectrum antibiotics, parenteral hyperalimentation, the use of intravascular catheters, and corticosteroid therapy[17]. In hospital-acquired fungal infections, *C.albicans* is the most commonly identified pathogen. However, in recent years, the proportion of non-albicans Candida species, which are more difficult to treat with azole antifungals, has been increasing[18]. In a study by Dinç et al., despite the absence of fungal growth in blood cultures, PCR analysis identified two *C.parapsilosis* strains, one *C.albicans* strain, and one *A.fumigatus* strain as the presumed etiological agents[9]. In a study of Yertut et al., the fungal pathogens isolated from blood cultures were *C.albicans* in two samples, *C.krusei* in one sample, and a mold in another. However, using molecular methods, *C.albicans* and *C.krusei* were identified in two samples each[17]. In our study, when comparing the sepsis panel results obtained by PCR with blood culture results, Candida species were detected in four samples (4%). *C.tropicalis, C.albicans, C.glabrata*, and *C.krusei* were all included in the sepsis panel, while one of the strains isolated from the blood cultures was misidentified as *C.glabrata*. This finding suggests that the PCR method may offer an advantage in detecting microorganisms, particularly Candida species, which are difficult to identify using conventional methods.

The distribution of causative agents of sepsis varies between hospitals. Gram-negative bacteria are reported to account for 20–64% of cases, while Gram-positive bacteria are responsible for 27–74% of cases[19]. In other studies, the rate of Gram-positive bacterial growth in blood cultures ranges from 59–70%, while the rate of

Gram-negative bacterial growth ranges from 24–37%[20–22]. In these studies, the most commonly isolated bacteria were *E.coli* and coagulase-negative staphylococci, which are also the predominant pathogens in our study. The detection of these bacteria by blood culture and sepsis panel generally yielded similar results. However, the presence of resistant microorganisms, particularly MRS, is of significant importance for the management of patient treatment processes. The PCR method enables the rapid detection of such resistant organisms, facilitating the prompt initiation of appropriate treatment for patients. For instance, a systematic review and meta-analysis demonstrated that digital PCR offers high sensitivity (94%) and specificity (87%) for detecting pathogenic microorganisms in sepsis patients, outperforming traditional blood cultures in terms of detection time and accuracy[23]. Additionally, a retrospective study found that multiplex digital PCR kits identified a broader range of pathogens, including polymicrobial infections, with a quicker processing time compared to blood cultures[24].

Our study underscores the efficacy of PCR as a diagnostic tool for sepsis; however, it also highlights the necessity of confirming certain results with blood culture. PCR provides valuable insights, particularly in scenarios requiring rapid and accurate information, such as in intensive care units and emergency departments. Nonetheless, given the PCR method's propensity to amplify DNA from dead bacteria, results must be interpreted with caution. False positive results can have significant clinical implications, including unnecessary antibiotic prescriptions, which may contribute to antibiotic resistance. It is crucial for studies to address the potential for false positives in PCR testing and to discuss their impact on clinical decision-making and antibiotic stewardship strategies. The integration of blood culture findings with PCR data can lead to more precise and reliable identification of sepsis pathogens. In conclusion, while PCR offers substantial advantages in sepsis diagnosis, blood culture remains an indispensable diagnostic method. The concurrent application of both tests in clinical practice is likely to enhance the accuracy of diagnosis and improve patient management.

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**ARAŞTIRMA MAKALESİ /** *RESEARCH ARTICLE*

# The Relationship Between the Attitudes of Vocational School of Health Services' Students Towards Elderly People and Their Compassionate Communication Levels

## *Sağlık Hizmetleri Meslek Yüksekokulu Öğrencilerinin Yaşlılara Yönelik Tutumları ile Şefkatli İletişim Düzeyleri Arasındaki İlişki*

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**ABSTRACT**

***Aim:*** *This study was conducted to determine the relationship between the level of compassionate communication and related factors, and to measure the attitudes of students at the Vocational School of Health Services towards older people.*

***Material and Method:*** *A total of 527 students of the Vocational School of Health Services were included in the study. This questionnaire consisted of three sections: a descriptive questionnaire, a Kogan scale of attitudes towards older people and a caring communication scale.*

***Results:*** *Mean age of participants was 20.94±1.98, mean total score of compassionate communication was 90.90±20.70, Kogan's total score of elderly attitude was found 137.16±9.79. Statistically significant relationships were found between the total score of the students on the caring communication scale and gender, willingness to care for older patients, willingness to work in geriatrics, effect of care for older people, and status of supportive and caring contact with older people (p <0.05). Statistically significant relationship was found between Kogan scale of students attitude towards older people and marital status and presence of older relatives (p<0.05).*

***Conclusion:*** *The results of the study show that the level of compassionate communication of the students participating in the study is above the medium level, and the total score of compassionate communication of the female students is higher than that of the male students.*

**Key words:** *attitude; compassion; communication; health student; old age*

**ÖZET**

***Amaç:*** *Bu çalışma, Sağlık Hizmetleri Meslek Yüksekokulu öğrencilerinin şefkatli iletişim düzeyleri ile ilgili faktörler arasındaki ilişkiyi belirlemek ve yaşlılara yönelik tutumlarını ölçmek amacıyla yapılmıştır.*

***Materyal ve Metot:*** *Çalışmaya Sağlık Hizmetleri Meslek Yüksekokulu'nda öğrenim gören toplam 527 öğrenci dâhil edilmiştir. Bu anket üç bölümden oluşmaktadır: tanımlayıcı bir anket, Kogan yaşlılara yönelik tutum ölçeği ve bakım iletişimi ölçeği.*

***Bulgular:*** *Katılımcıların yaş ortalaması 20,94±1,98, şefkatli iletişim toplam puan ortalaması 90,90±20,70, Kogan'ın yaşlı tutum toplam puanı 137,16±9,79 olarak bulundu. Öğrencilerin şefkatli iletişim ölçeği toplam puanı ile cinsiyet, yaşlı hastalara bakım verme isteği, geriatri alanında çalışma isteği, yaşlılara bakım verme etkisi ve yaşlılarla destekleyici ve ilgili iletişim kurma durumu arasında istatistiksel olarak anlamlı ilişki bulunmuştur (p <0,05). Kogan öğrencilerin yaşlılara yönelik tutum ölçeği ile medeni durum ve yaşlı akrabaların varlığı arasında istatistiksel olarak anlamlı bir ilişki bulunmuştur (p<0,05).*

***Sonuç:*** *Çalışmanın sonuçları, çalışmaya katılan öğrencilerin şefkatli iletişim düzeyinin orta düzeyin üzerinde olduğunu ve kız öğrencilerin şefkatli iletişim toplam puanının erkek öğrencilerden daha yüksek olduğunu göstermektedir.*

**Anahtar kelimeler:** *tutum; merhamet; iletişim; sağlık öğrencisi; yaşlılık*

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## Introduction

Old age is a period in which physical and mental differences are experienced in the advanced stage of life as a step after the adulthood period. According to the World Health Organization, this period in which vital functions regress, productivity and the ability to adapt to environmental factors decrease is a duration in which many activities that can be accomplished quickly in youth cannot be performed or are problematic in this period[1]. Populations worldwide are aging faster than in the past, and this demographic shift can affect nearly all aspects of society. Currently, the number and proportion of the population aged 60 and over in the general population is rising. While the number of people aged 60 and over was 1 billion in 2019, it is predicted that this number will grow to 1.4 billion by 2030 and 2.1 billion by 2050. This increase is emerging at an unprecedented rate which is expected to accelerate in the next ten years, particularly in developing countries[2]. There may be intergenerational dissimilarities in manners and attitudes between the elderly and the young. If young and older people are together, they can share each other's emotions and opinions. Emotions are the primary factors that affect thoughts, and thoughts are the main factors that determine attitudes, and this will allow positive emotions and attitudes[3]. With the increase in the life expectancy of individuals, chronic and mental diseases brought on by old age also increase. As a result, the rate of use of health services by elderly individuals and the requirement for health professionals will increase[4]. In this direction, the attitudes of health professionals, who frequently encounter elderly individuals, towards the elderly and aging gain importance[5]. In order to enhance the quality of care for the elderly, it is essential that the healthcare professionals who serve them develop a positive attitude. The most remarkable initiative to accomplish this is to increase awareness of society[6]. Educational institutions have significant responsibilities in issues such as producing policies related to aging and implementing these policies, and organizing training for individuals who will take part in the care of the elderly[6,7].

For this reason, students studying in the health field should receive an education that will best meet the health needs of the aging population and be more competent with training programs such as seminars, courses, and certificate programs[8]. It is crucial to investigate the students' attitudes toward the elderly in the plans to be made for the elderly[3]. Communication can be the transfer of information between the parties and the sharing transfer between the patient and the healthcare professional[9]. While communicating with the patient, healthcare professionals motivate by building trust, which contributes to the patient's recovery[10]. Benevolent communication implies accepting another person's pain, endeavoring to comprehend, showing compassion, avoiding judgment against the other person's faults, and delivering sympathy and empathy[11,12]. In addition, compassionate communication puts the patient's necessities first and provides emotional support by socially sustaining the other individual[12]. It is considered that the use of compassionate communication is vital in the field of health since it is aimed to contribute to the understanding and healing of the patient without judging the patient by communicating with the patient. Those working in the nursing and health field must have the technical knowledge and humane and effective communication skills[13].

This study constructed an analysis measuring health professionals' attitudes and compassionate communication levels toward the elderly before graduation. It was suggested to organize training or seminars in line with the results. In addition, this study is critical because it is the first study on compassionate communication in Health Services Vocational School students known in the literature.

*Research questions:*

- What is the attitude of the students towards older people?
- What are the compassionate communication levels of the students?
- Is there a relationship between students' sociodemographic characteristics and their attitudes towards older people or their compassionate communication?
- Is there a relationship between students' departments and their attitudes towards older people or their compassionate communication?

## Material and Method

### *Purpose of the Stu*

To measure the attitudes of vocational health students towards the elderly and determine the relationship between levels of compassionate communication.

### *Type of Research*

The research was designed as a descriptive relationship-seeking design.

The research was carried out at X University, Y Health Services Vocational School, between March and September 2022.

### *Population and Sample of the Study*

1800 students at Y Health Services Vocational School were included. Five hundred and twenty seven students approved to participate in the study were included without using any sampling method.

### *Data Collection Tools*

The research consists of three parts: Descriptive Characteristics Form, Kogan Attitudes Towards the Elderly Scale and Compassionate Communication Scale.

### *Descriptive Characteristics Form*

The researcher developed this form by scanning the literature. The form includes sociodemographic questions such as the student's gender, age, department, marital status, income level, whether to work or not, family structure, living with an older adult, caring for an elderly patient, and wanting to work in the geriatrics service after graduation[14–16].

### *Kogan's Attitudes Towards Old People Scale*

Created by Nathan Kogan in 1961[17], the Kogan Attitudes Towards Older Persons (KAOPS) is a two-dimensional scale, consisting of 34 items, designed to measure attitudes towards older people. The Likert scale was translated into Turkish in 2011. It has 34 items and six response levels: strongly disagree, disagree, agree, somewhat agree, strongly agree. The categories are scored from 1 to 7. The unanswered item is scored as 4. The scale contains 17 positive and 17 negative statements about older adults. Negative responses are reversed and added to positive responses to calculate the total scale score. Scores on this scale, developed by Kogan, range from 34 to 238. High scores on the scale indicate positive attitudes towards older people, while low scores indicate negative attitudes[18]. For the original study by Kogan (1961)[17], the total item correlation of the scale ranged from 0.1 to 0.717, with a Cronbach alpha value of 0.89 for the Turkish version[17].

### *Compassionate Communication Scale*

The scale was developed by Ramos Salazar[12]. The validity, reliability, and Turkish scale version was conducted in 2020 by Ibrahimoğlu et al.[19] The scale is 23-item and 5-point Likert type (1:Never 2:Rarely 3:Sometimes 4:Mostly 5:Always). There are three sub-dimensions to the scale: compassionate speech, touching, and texting. A minimum of 23 points is obtained from the scale and a maximum of 115. A high mean score indicates a high level of compassionate communication, while a low mean score indicates a low level of compassionate communication. The lowest and highest scores that can be obtained for the sub-dimensions of the scale are 9–45 for compassionate speech, 7–35 for compassionate touching, and 7–35 for compassionate messaging, respectively[19]. In Ramos Salazar's study, the Cronbach $\alpha$ value was found to be 0.80[12], and the Cronbach $\alpha$ value was 0.94 in the Turkish version.

### *Data Collection Process*

After obtaining the ethics committee's approval from the required institution and receiving the necessary permissions from the vocational school of health services, the data were collected online (via Google forms) survey method.

### *Evaluation of Data*

IBM Statistical Package for Social Sciences (SPSS) program version 26.0 was used to analyse the data, using descriptive statistics, parametric tests and correlation.

### *Ethical Principles*

Ethical approval was obtained from the Non-Interventional Research Ethics Committee of a University on 28/02/2022 and decision number 02. Permission was obtained for the measurement tools used in the study. Only participants who agreed to experience the study were included.

### *Limitations and Strengths of the Study*

Since the research was performed in a single center, the results cannot be generalized to all health services vocational school students but to the population. Since the parameters analyzed in this study have not been applied to health services vocational high school students, they construct the basis for descriptive or experimental studies that may be afterward.

## Results

This study was carried out with 527 students at a vocational school for health services. The distribution

of descriptive characteristics of the participants is presented in Table 1.

The mean age of the participants was 20.94±1.98. It was determined that 66.6% of the participants were female, 79.3% were single, and 17.6% were Home Patient Care students. While 93.5% of the participants do not work in any job, 66.2% have a nuclear family, and 70.0% live with an elderly family member. While 78.7% of the participants believe that older adults should live with their children, 62.8% do not demand to care for an elderly patient. It was concluded that 58.1% of the participants wanted to work in the geriatric service. It was determined that 50.1% of them would be challenged to care for the elderly, whereas they would be satisfied with the care, 38.2% of them contacted the older adult once or twice a week, and 97.3% of them were supportive and compassionate (Table 1).

***Table 1.*** *Distribution of students by descriptive characteristics (N=527)*

| **Descriptive features** | X ± SS | Min-Max |
|---|---|---|
| **Average age** | 20.94±1.98 | 18–34 |
| | n | % |
| **Sex** | | |
| Female | 351 | 66.6 |
| Male | 176 | 33.4 |
| **Marital status** | | |
| Single | 513 | 97.3 |
| Married | 14 | 2.7 |
| **Current education status** | | |
| Anesthesia | 75 | 14.2 |
| Home patient care | 93 | 17.6 |
| First and emergency aid | 76 | 14.4 |
| Medical documentation and secretarial | 71 | 13.5 |
| Medical imaging techniques | 67 | 12.7 |
| Medical laboratory techniques | 39 | 7.4 |
| Medical promotion and marketing | 34 | 6.5 |
| Elderly care | 72 | 13.7 |
| **Working condition** | | |
| Employed | 34 | 6.5 |
| Unemployed | 493 | 93.5 |
| **Family structure** | | |
| Nuclear family | 349 | 66.2 |
| Extended family | 166 | 31.5 |
| Broken family | 12 | 2.3 |
| **Elderly family member presence at home** | | |
| Yes | 158 | 30.0 |
| No | 369 | 70.0 |
| **Where should the elderly person live?** | | |
| Own home (alone or with spouse, if available) | 94 | 17.8 |
| With their children | 415 | 78.7 |
| Nursing home or elderly care home | 18 | 3.4 |
| **Willingness to care for the elderly patient** | | |
| Yes | 196 | 37.2 |
| No | 331 | 62.8 |
| **Willingness to work in the geriatrics service** | | |
| Yes | 306 | 58.1 |
| No | 221 | 41.9 |
| **The effect of caring for elderly people** | | |
| It's compelling and it makes me unhappy | 18 | 3.4 |
| It's compelling but i'm happy | 264 | 50.1 |
| I don't have any difficulties and i do it happily | 202 | 38.3 |
| Does not have any effect | 43 | 8.2 |
| **Frequency of communication with elderly individuals** | | |
| I do not contact | 13 | 2.5 |
| Contact once or twice a year | 54 | 10.2 |
| One or two communications per month | 117 | 22.2 |
| One or two communications a week | 201 | 38.1 |
| Communication every day | 142 | 26.9 |
| **Supportive and compassionate communication with the elderly person** | | |
| Yes | 513 | 97.3 |
| No | 14 | 2.7 |

***Table 2.*** *Sub-dimensions of compassionate communication scale, total scale, and KOGAN aged attitude scale scores and averages (N=527)*

| | Min-max | X (SS) |
|---|---|---|
| Compassionate conversation | 9–45 | 38.57±8.08 |
| Compassionate touch | 7–35 | 28.45±6.87 |
| Compassionate messaging | 7–35 | 23.87±8.99 |
| Compassionate communication total score | 23–115 | 90.90±20.70 |
| KOGAN elderly attitude total score | 104–211 | 137.16±9.79 |

In Table 2, the median total score for compassionate communication was 90.90±20.70; the mean total score for Kogan Elderly Attitude was 137.16±9.79.

Statistically significant relationships were found between the students' subscale of compassionate Speech and their gender, willingness to work in geriatrics, the impact of care on the elder, and the status of establishing supportive and compassionate communication with the elder (Table 3; $p<0.05$). Compassionate speaking subscale mean scores were found to be higher among females than males, those who want to work in the geriatric service, those who do not demand to work, those who merrily care for elderly individuals without difficulty, those who have a problem in providing care, those who are unhappy, those who communicate with the older adult in a supportive and compassionate manner and those who cannot communicate with them in a supportive and compassionate way.

Statistically significant relationships were found between the touch subscale and gender, willingness to care for older people, willingness to work in geriatrics, impact of care on older people, and supportive and compassionate communication with older people (Table 3; $p<0.05$).

Statistically significant relationships were found between students' sub-dimension of Compassion Messaging and willingness to work in the geriatric service and the impact of caring for the older people (Table 3; $p<0.05$). Compassionate texting sub-dimension score averages were found to be higher among those who demand to work in the geriatric service, those who do not desire to work, those who care for the elderly happily without difficulty, those who have difficulty in providing care and those who are unhappy.

Statistically significant relationships were found between students' total compassion score and their gender, readiness to care for the elderly, readiness to work in geriatrics, effectiveness of care for older people, and status of developing supportive and compassionate interaction with older people (Table 3; $p<0.05$). Compassionate Communication Scale total score averages are higher for females than males, those who like to care for the elderly patient, those who do not like to work in the geriatric service, those who happily care for the elderly without difficulty, those who have difficulty in providing care, those who are unhappy, those who communicate supportively and compassionately with the older adult, and those who cannot communicate supportively and compassionately.

Statistically significant relationships were found between student attitudes towards old age and marital status and having older relatives (Table 3; $p<0.05$). It was found that the average Kogan Elderly Attitudinal Score was higher for single students than for married students, and that the average Kogan Elderly Attitudinal Score was higher for older family members than for non-married students.

The results of the correlation analysis performed between the subscale and the total scores of the students on the Kogan Attitudinal and Compassionate Communication Scale, did not show a statistically significant relationship between these two factors (Table 4; $p>0.05$).

## Discussion

This study estimated the attitudes, compassionate communication grades, and corresponding characteristics of students researching healthcare departments, including elderly care and home patient care programs. This study has assembled the basis for analyses to guide students' attitudes and empathetic communication levels toward patients, specifically elderly individuals, in their professional lives. In addition, no study has been encountered in the literature researching compassionate communication with healthcare services learners. In this context, our study acquires significance and will form the basis for forthcoming studies.

Examining the total score of compassionate communication in this study indicates that the level of compassionate communication of the students studied is above the medium level. In a study conducted by Öztürk et al. (2022)[14] with nursing students, it is seen that their level of compassionate communication is moderate, with a score of 88.98±14.38[14]. The consequences of the study show equality with our research. In line with these outcomes, it is assumed that the communication skills of the individuals who prefer this specialization may be reasonable because the compassionate communication levels of the health students are moderate and above. Another

***Table 3.*** *Comparison of compassionate communication scale sub-dimensions and KOGAN aged attitude scale according to students' descriptive characteristics*

| | Compassionate conversation | Compassionate touch | Compassionate messaging | Compassionate communication total score | KOGAN elderly attitude total score |
|---|---|---|---|---|---|
| | **X ± SS.** | **X ± SS.** | **X ± SS.** | **X ± SS.** | **X ± SS.** |
| **Sex (n)** | | | | | |
| Female (351) | 39.20±7.86 | 29.16±6.61 | 24.10±8.96 | 92.47±20.09 | 137.72±9.91 |
| Male (176) | 37.31±8.38 | 27.05±7.16 | 23.41±9.05 | 87.78±21.59 | 136.04±9.47 |
| **Significance** | t=2.551 | t=3.349 | t=0.828 | t=2.464 | t=1.859 |
| | p=0.011 | p=0.001 | p=0.408 | p=0.014 | p=0.060 |
| **Marital Status (n)** | | | | | |
| Married (513) | 38.48±8.09 | 28.37±6.86 | 23.77±8.96 | 90.63±20.67 | 137.02±9.46 |
| Single (14) | 41.78±7.46 | 31.64±6.47 | 27.35±9.56 | 100.78±20.26 | 142.35±17.98 |
| **Significance** | t=-1.508 | t=-1.760 | t=-1.471 | t=-1.813 | t=-2.017 |
| | p=0.132 | p=0.079 | p=0.142 | p=0.070 | **p=0.044** |
| **Elderly family member presence at home (n)** | | | | | |
| Yes (158) | 38.74±8.02 | 28.63±6.68 | 24.27±9.01 | 91.65±20.31 | 138.74±10.80 |
| No (369) | 38.50±8.12 | 28.38±6.96 | 23.69±8.99 | 90.58±20.89 | 136.48±9.26 |
| **Significance** | t=0.307 | t=0.379 | t=0.672 | t=0.540 | t=2.430 |
| | **p=0.759** | p=0.705 | **p=0.499** | p=0.589 | **p=0.015** |
| **Willingness to care for the elderly patient (n)** | | | | | |
| Yes (196) | 39.38±7.89 | 29.22±6.80 | 24.75±8.96 | 93.36±20.70 | 137.41±10.16 |
| No (331) | 38.09±8.17 | 28.00±6.88 | 23.35±8.98 | 89.45±20.59 | 137.01±9.58 |
| **Significance** | t=1.768 | t=1.968 | t=1.726 | t=2.101 | t=0.460 |
| | p=0.078 | **p=0.048** | p=0.085 | **p=0.036** | p=0.446 |
| **Willingness to work in the geriatrics service (n)** | | | | | |
| Yes (306) | 40.23±6.34 | 29.83±5.59 | 24.97±8.83 | 95.04±17.16 | 137.03±9.33 |
| No (221) | 36.27±9.55 | 26.55±7.95 | 22.34±9.00 | 85.17±23.65 | 137.33±10.42 |
| **Significance** | t=5.723 | t=5.556 | t=3.339 | t=5.555 | t=-0.351 |
| | **p<0.001** | **p<0.001** | **p=0.001** | **p<0.001** | p=0.726 |
| **The effect of caring for elderly people (n)** | | | | | |
| It's compelling and it makes me unhappy (18) | 30.83±11.73 | 21.61±7.60 | 18.55±9.51 | 71.00±27.04 | 135.72±9.46 |
| It's compelling but I'm happy (264) | 37.81±8.23 | 27.83±6.79 | 22.76±8.49 | 88.41±19.93 | 136.76±9.26 |
| I don't have any difficulties and I do it happily (202) | 40.66±6.27 | 30.11±6.15 | 26.15±8.87 | 96.94±18.26 | 137.25±9.67 |
| Does not have any effect (43) | 36.62±9.79 | 27.37±7.80 | 22.20±9.94 | 86.20±24.11 | 139.76±13.09 |
| **Significance** | F=12.369 | F=11.637 | F=8.621 | F=14.284 | F=1.293 |
| | **p<0.001** | **p<0.001** | **p<0.001** | **p<0.001** | p=0.276 |
| **Supportive and compassionate communication with the elderly person (n)** | | | | | |
| Yes (513) | 38.80±7.86 | 28.61±6.77 | 23.91±8.98 | 91.33±20.33 | 137.19±9.87 |
| No (14) | 30.00±11.36 | 22.78±8.34 | 22.35±9.33 | 75.14±28.06 | 136.07±6.23 |
| **Significance** | t=4.081 | t=3.157 | t=0.639 | t=2.908 | t=0.422 |
| | **p<0.001** | **p=0.002** | p=0.523 | **p=0.004** | p=0.673 |

hypothesis is that students' education in the field of health services influenced their grades in compassionate communication. More detailed research is required in this area.

This study shows that the total score of compassionate communication of female students is higher than male students. Correspondingly, in the study of Öztürk et al.,[14] female students' compassionate communication scores were found to be higher than male students[14]. It is supposed that this situation may be due to the more emotional approach of female students than male students. Due to the limited number of studies on compassionate communication, more data could not be found and compared.

When we look at the factors that influence the overall level of the compassionate speech, touch, message and communication scores, we find that, it is seen that the status of students looking after an elderly patient, their willingness to choose a geriatric service in their working life, students' levels of compassionate communication are influenced by caring for or communicating with older people (Table 3).

It is noticed that the attitudes of healthcare professionals who will work in health institutions in the future toward patients are from a compassionate perspective. It is thought that this circumstance will persist with an empathetic approach and positive care process toward patients and the elderly in their professional lives. It is

***Table 4.*** *Correlation analysis between KOGAN aged attitude and compassionate communication scale sub-dimensions and scale total*

| | | Compassionate conversation | Compassionate touch | Compassionate messaging | Compassionate communication total score |
|---|---|---|---|---|---|
| KOGAN elderly attitude | r | 0.000 | -0.030 | -0.060 | -0.036 |
| | p | 0.993 | 0.489 | 0.166 | 0.408 |

** Correlation is significant at the 0.01 level.

advised to support students with seminars and training in order to maintain and increase compassionate care in students.

In this study, the mean score of the elderly attitude scale was 137.16±9.79. The findings show that students who participated in this study were more than moderately positive towards older people. Considering the results of the studies conducted with students who will work in health services, studies are revealing that students have positive attitudes toward the elderly in parallel with our study[20–28]. In a study conducted with elderly care students on their attitudes towards the elderly, the average score of the attitude scale towards the elderly was found to be 155.62±40.16, which indicates that the students have a positive attitude towards the elderly[29]. In another study examining nursing students' attitudes toward the elderly in Hong Kong, students' attitudes were positive[30]. In a study examining the attitudes of health department students towards the elderly, it was found that they had a positive perspective in contrast to our study[31]. In addition, contrary to our study, there are analyses with students that generate low positive or negative attitudes toward the elderly[7,32–34]. In the results of this research and most studies conducted with health professionals, it is noticed that there is a positive attitude toward the elderly. Our study shows parallelism with the literature. In order to ensure that students have a more positive attitude towards the elderly, practical training and awareness-raising factors such as the guidance of academicians can be provided.

Attitudes towards older people were more positive among the students in this study who lived with an older family member at home. In parallel with our study, Ünsar et al. (2015)[28] and Usta et al. (2012)[35] found a positive attitude between living with the elderly and the attitude towards the elderly[28,35]. López-Hernández et al. (2021)[24], in a study with health students, found that students' previous personal experience with their elderly relatives increased their positive attitudes towards the elderly[24]. On the contrary, some studies state that living with the elderly does not affect their attitude towards the elderly[22,30,33]. In line with the results of this study, it can be discussed that living with an elderly family member positively affects students' attitudes and awareness toward the elderly. On the other hand, it is considered that the differing results may be due to the participants' diverse cultural characteristics or personality features.

This study found no significant difference between gender and attitudes toward the elderly. Parallel to our study, Zehirlioğlu et al. (2015)[7] and Can et al. (2019)[36] studies measuring the attitudes of healthcare students towards the elderly, no significant difference was discovered between gender and attitudes towards the elderly[7,36]. In a study conducted with 139 nursing students in Hong Kong, no significant difference was found between attitudes toward the elderly and gender[30]. On the other hand, in the study of Kavuran and Caner (2021),[29] Pehlivan and Vatansever (2019),[37] and Ayoğlu et al. (2014)[38] with a health care professional students, a statistically significant difference was found between the attitudes and genders of the elderly[29,37,38]. In the study results of López-Hernández (2021)[24], it was found that women are more positive towards the elderly[24]. Also in the study results of Uzuntarla and Ceyhan (2020)[31], it was found that women are more positive towards the elderly[31]. It is thought that this difference may be due to the awareness levels or sociocultural characteristics of the students participating in the research.

A statistically significant relationship was not found between students' attitudinal beliefs about older people and whether they communicated with them with empathy (Table 4). In a study conducted by Öztürk and Kaçan (2022)[14] with health students, the effects of compassionate communication and empathic skills and nursing communication course were examined, and a significant relationship was found[14]. This displays that empathy or communication levels affect compassionate communication. In our study, it was found that the attitude toward the elderly did not affect compassionate communication. More studies are needed in this area.

## Conclusion and Recommendations

In recent years, due to the increase in the elderly population in our country and the whole world, the rate of health professionals spending time and care with the elderly may increase. Therefore, the attitude of health professional candidates toward the elderly is paramount. In addition, caring for the elderly with an empathetic approach and compassionate communication will raise the quality of life of the elderly, and efficient elderly care will be provided.

In our study, the attitudes of healthcare professionals toward the elderly were positive and is higher than the average level. And at the same time the students' levels of compassionate communication are above average.

In line with these results, it is crucial to ensure that students can spend more time with the elderly to increase their positive attitude and compassionate communication levels towards the elderly. For this purpose, it can be suggested to organize social activities with the elderly in nursing homes, provide students with adequate practice opportunities in their fields, improve their relations with the elderly in the family, and organize conferences that will raise awareness about the elderly for the society with the participation of health students. Thus, it is thought that caring for the increasing elderly population can be provided with a more empathetic approach, compassionate care, and a positive attitude toward the elderly.

Additionally, there are very few studies on compassionate communication. It is recommended to increase studies with health students and workers in this field and to support this issue with experimental studies, especially in wider societies.

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### *Conflict of Interests*

Conflicts of interest: none.

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**ARAŞTIRMA MAKALESİ /** *RESEARCH ARTICLE*

# Left Ventricular Diastolic Longitudinal Strain Angle as a Parameter (New Tool) to Predict Left Ventricular Diastolic Function

*Sol Ventriküler Diyastolik Fonksiyonu Tahmin Etmek için bir Parametre Olarak Sol Ventriküler Diyastolik Longitidunal Strain Açısı (Yeni Araç)*

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## ABSTRACT

***Aim:*** *Currently, left ventricular diastolic dysfunction (LVDD) is evaluated using indirect parameters derived from trans-mitral valve inflow velocity (TMIV), pulmonary vein flow, and LV diastolic annular tissue velocity (DATV). None of these parameters is obtained directly from the LV global myocardium. This study aimed to examine the relationship between left ventricular (LV) global longitudinal diastolic strain curve angle (DSCA), which directly assesses myocardial function, and TMIV and DATV parameters, and to determine whether DSCA can serve as a new tool for detecting LVDD.*

***Material and Methods:*** *114 patients with sinus rhythm were included in the study. Conventional pulse wave Doppler parameters [TMIV E and A peak velocity, E/A ratio (E/AR), deceleration time (DT), deceleration slop (DS)], DATV parameters [Septal é (Sé), E/Septal é ratio (E/SéR)], and DSCA parameters, including early (EεA) and late (AεA) diastolic strain angles and their ratio (Eε/AεAR) obtained from apical 2, 4 and 5 apical chamber views (ACV) were compared.*

***Results:*** *A significantly positive strong correlation was found between Eε/AεAR and E/AR, E/SéR on all views (r=0.620, r=0.548, r=0.570, and r=-0.431, r=-0.279, r=-0.255, respectively). Also, a significantly positive correlation was found between the EεA and E velocity, Eε/AεAR, DS on all views, and, except for A4CV, a significantly negative correlation was found between AεA and E velocity, DS on A2CV and A5CV.*

***Conclusion:*** *The EεA, AεA, and Eε/AεAR are a simple, repeatable, useful and new tool for the evaluation of LVDD, and they can be used alone or together with conventional diastolic parameters for the assessment of LVDD.*

**Key words:** *left ventricle; diastolic dysfunction; transmitral inflow velocity; strain; Eε and Aε angle; Eε and Aε angle ratio*

## ÖZET

***Amaç:*** *Günümüzde, sol ventrikül diyastolik disfonksiyonu (LVDD), trans-mitral kapak giriş hızı (TMIV), pulmoner ven akımı ve sol ventrikül (LV) diyastolik anüler doku hızı (DATV) ile elde edilen endirekt parametrelerle değerlendirilir. Bu parametrelerin hiçbiri doğrudan LV global miyokardından elde edilmemektedir. Bu çalışmanın amacı, direkt miyokard fonksiyonunu değerlendiren sol ventrikül global longitudinal diyastolik strain eğri açısı (DSCA) ile TMIV ve DATV parametreleri arasındaki ilişkiyi gözlemlemek ve DSCA'nın yeni bir araç olarak LVDD'yi tespit edip edemeyeceğini belirlemektir.*

***Materyal ve Yöntem:*** *Sinüs ritminde olan 114 hasta çalışmaya dâhil edildi. Konvansiyonel nabız dalgası Doppler parametreleri [TMIV E ve A pik hızı, E/A oranı (E/AR), yavaşlama zamanı (DT), yavaşlama eğimi (DS)], DATV parametreleri [Septal é (Sé), E/Septal é oranı (E/SéR)] ve apikal iki, dört ve beş apikal boşluk görüntülemeden (ACV) elde edilen DSCA parametreleri [(E strain eğri açısı (EεE), A strain eğrisi açısı (AεA), Eε/AεA oranı)] karşılaştırıldı.*

***Bulgular:*** *Tüm görünümlerde Eε/AεAR ile E/AR, E/SéR arasında anlamlı pozitif güçlü bir korelasyon bulundu (sırasıyla r=0,620, r=0,548, r=0,570 ve r=-0,431, r=-0,279, r=-0,255). Ayrıca, EεA ile E hızı, Eε/AεAR, DS arasında tüm görünümlerde anlamlı pozitif korelasyon bulunurken, A4CV hariç, AεA ile E hızı, DS arasında A2CV ve A5CV'de anlamlı negatif korelasyon bulundu.*

***Sonuç:*** *EεA, AεA ve Eε/AεAR, DD'nin değerlendirilmesinde basit, tekrarlanabilir, kullanışlı ve yeni bir araçtır. LVDD'nin değerlendirilmesinde tek başına veya geleneksel diyastolik parametrelerle birlikte kullanılabilir.*

**Anahtar kelimeler:** *sol ventrikül; diyastolik disfonksiyon; transmitral akım hızı; strain; Eε ve Aε açısı, Eε ve Aε açısı oranı*

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## Introduction

The diagnostic classification of heart failure with preserved ejection fraction (HFpEF) requires careful assessment of left ventricular diastolic dysfunction (LVDD), because of its key role in identifying impaired ventricular compliance and hemodynamic mechanisms[1].

Specifically, accurate LVDD diagnosis and management necessitate the capacity to assess regional myocardial function adequately. Early LVDD diagnosis, before the manifestation of global impairment, is desirable for managing myocardial heart disease and related conditions[2].

Although cardiac catheterization is the gold standard for evaluating LVDD, the most commonly used noninvasive method is trans-mitral valve inflow velocity (TMIV) obtained through pulse wave Doppler (PWD) and left ventricular diastolic annular tissue velocity (DATV) measured by tissue Doppler imaging (TDI)[3]. Evaluation of TMIV and DATV offers an indirect assessment of LVDD. Furthermore, it encompasses measurements of various parameters that enable LVDD to be classified[4]. However, it heavily depends on left ventricular end-diastolic pressure, sufficient intravascular fluid volume, and observer experience. Due to the complex nature of LVDD, these noninvasive indices might not show strong correlations with left ventricular (LV) filling pressures[5].

Strain echocardiography is a new imaging technique and has been used for the last 20 years[6]. It is derived from the speckle tracking echocardiography (STE)[7]. It is used to evaluate regional myocardial systolic and diastolic deformation change. Changes in systolic and diastolic strain can discriminate myocardial viability[8]. Also, it can differentiate pathological and physiological hypertrophy from restrictive and constructive cardiomyopathy, without angle-dependent[9]. Currently, STE is used in LVDD assessment. Left ventricular diastolic dysfunction decision is made only with optional peak strain values (e.g., peak S, E, and A) on the diastolic strain curve (DSC)[10]. However, the DSC may provide more information than peak strain values in the evaluation of LVDD[11]. Also, postsystolic strain occurring at the end of systole may cause misinterpretation of LVDD[12]. Therefore, we can obtain more parameters from the left ventricular global longitudinal diastolic strain curve angle (DSCA) than the current evaluation parameters about LVDD[13].

This study aimed to evaluate the relationship between the measurements of DSCA values, TMIV, and DATV diastolic parameters, and to determine whether or not it can be used as a new tool to evaluate LVDD.

This study aimed to evaluate the relationship between DSCA values, TMIV and DATV diastolic parameters, and to investigate the potential utility of DSCA as a novel tool for LVDD assessment.

## Method

### *Study Population*

This retrospective study included 114 participants with preserved left ventricular ejection fraction (≥50%) and varying degrees of left ventricular diastolic dysfunction (LVDD), assessed using pulsed-wave Doppler (PWD) and tissue Doppler imaging (TDI) echocardiography. Data were collected from January 2017 to February 2019 by reviewing digital echocardiographic records stored in the EchoPAC platform. Demographic and clinical information was obtained from electronic health records and institutional medical databases. Exclusion criteria included individuals with a history of coronary artery disease (despite preserved ejection fraction), active systemic infections, malignancies, significant arrhythmias (e.g., atrial fibrillation, atrial flutter, multifocal atrial tachycardia, atrioventricular blocks, or reentrant tachycardias), and severe valvular diseases. The institutional ethics board approved the study protocol by the Declaration of Helsinki (Ethics No: 80576354-050-99-219).

### *Echocardiography*

Echocardiographic examinations were conducted with subjects positioned in the left lateral decubitus position, employing a Vivid 7 ultrasound system (GE Healthcare, Waukesha, WI, USA) equipped with a 3.6 MHz transducer. Two-dimensional echocardiography (2D-Ech), TDI, and STE data were acquired at a frame rate of 60 frames per second by a single, experienced cardiologist. All cardiac measurements adhered to the American Society of Echocardiography guidelines and were obtained at rest in the left lateral decubitus position during breath-hold with stable electrocardiographic monitoring[14]. Three consecutive cardiac cycles were recorded from standard apical 2-chamber (A2CV), 4-chamber (A4CV), and 5-chamber (A5CV) views and subsequently analyzed using EchoPAC Dimension software. Left ventricular ejection fraction (LVEF) was calculated using the

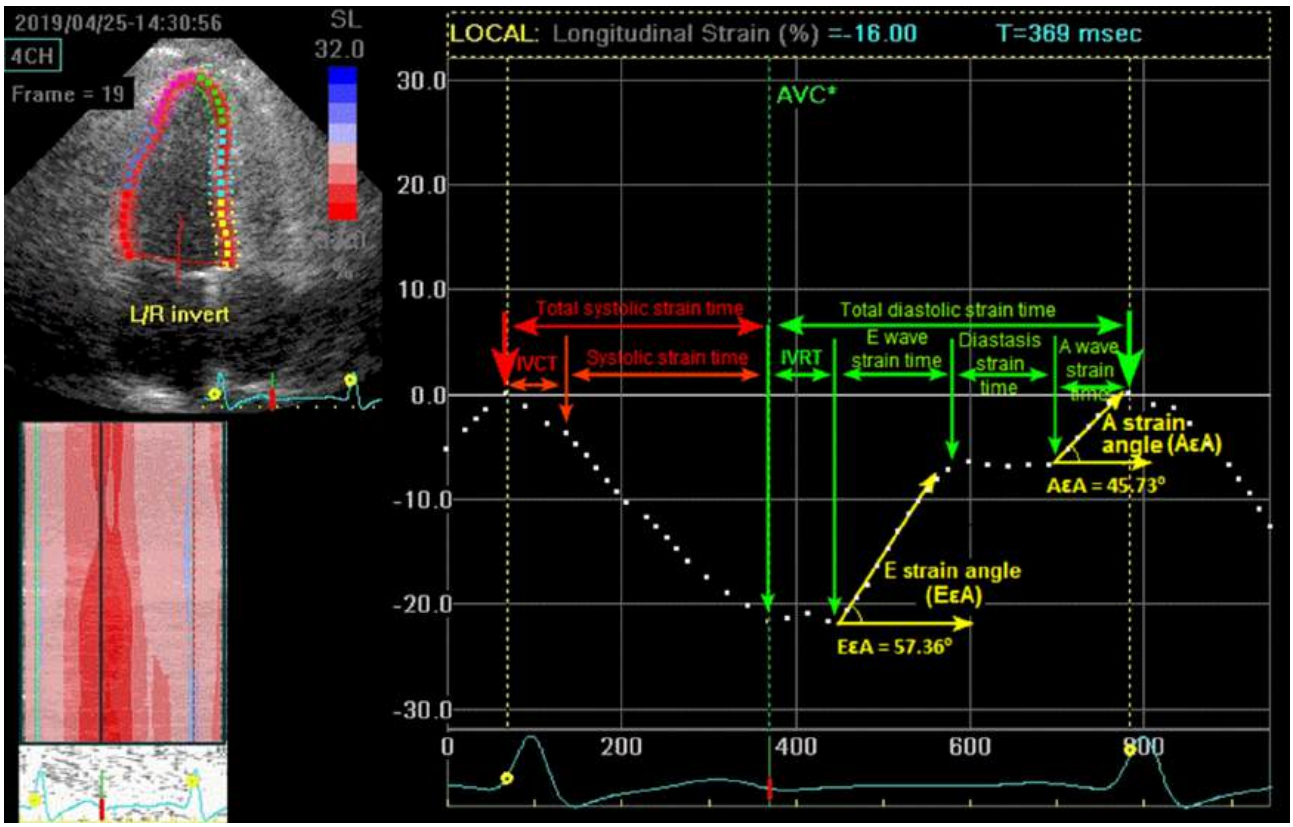


***Figure 1.*** *Schematic demonstration of the E and A strain curve angle (EεA, AεA) on the strain curve formed during a diastolic cardiac cycle.*

modified Simpson's method on the A4CV view, with end-diastolic and end-systolic volumes measured[7].

Transmitral inflow velocity (TMIV) was obtained by PWD echocardiography during breathing hold in an A4CV. Transmitral inflow velocity diastolic parameters assessed included peak velocities during early diastole (E wave) and late diastole (A wave), the E/A ratio (E/AR), E wave deceleration time (DT), and deceleration slope (DS).

Diastolic annular tissue velocity obtained by TDI with the spectral pulse of the septal and lateral mitral annulus was performed, and a peak of the early filling septal and lateral é wave (Sé, Lé) and late filling septal and lateral á wave (Sá, Lá) was measured. Transmitral inflow velocity early E (E velocity) to Lé velocity ratio (E/LéR), E velocity to Sé velocity ratio (E/SéR), Lé velocity to Lá velocity ratio (Lé/LáR), Sé velocity to Sá velocity ratio (Sé/SáR) were calculated automatically.

### *2D-Speckle Tracking Diastolic Strain Curve Analysis*

Offline DSC analysis was performed with EchoPAC Dimension software. The LV systole and diastolic endocardial border were manually traced during the at-end-systole on an end-systolic frame and during the at-end-diastolic on an end-diastolic frame in three views by a point-and-click approach, respectively[15]. After manual tracing of the endocardial contour, the software automatically tracked the motion through the rest of the cardiac cycle, and automatically generated strain curves of every cardiac cycle.

### *Measurement of Diastolic E- and A- Strain Angles*

To measure the strain angle during the early volumetric relaxation period (EεA), the first, start, and end points of the early volumetric phase were identified on the diastolic strain curve. Next, the end of isovolumetric relaxation was used as the starting point of the early volumetric relaxation phase, and the beginning of the diastasis phase was used as the endpoint of this phase. Then, the line segment connecting these two points served as the first line of the early volumetric strain angle. After that, the second line segment was created from a line drawn starting at the point where the "x" axis intersects the first line segment, parallel to the "x" axis. Finally, the angle between these two line segments was measured using J-Image software (Version 1.54 k), and the result was recorded as the early volumetric relaxation angle (Fig. 1).

***Table 1.*** *Patients' demographic, clinical and 2D-Echocardiographic baseline characteristics*

| | | Overall (mean ± SD) n: 114 | Min & max range n: 114 |
|---|---|---|---|
| Age (years) | | 51.86±13.87 | 19–89 |
| Male gender | | 57 (50%) | - |
| Hypertension | | 59 (51.8%) | - |
| Diabetes mellitus | | 3 (2.6%) | - |
| Smoker | | 46 (40.4%) | - |
| Dyslipidemia | | 6 (5.3%) | - |
| Heart rate (bpm) | | 73.15±12.75 | 48–125 |
| **Blood pressure (mmHg)** | SBP | 151.85±34.73 | 100–252 |
| | DBP | 90.51±15.91 | 60–130 |
| | PP | 110.95±21.37 | 80–166.67 |
| **2D – Ech** | IVSd (cm) | 1.26±0.35 | 0.7–2.3 |
| | IVSs (cm) | 1.53±0.37 | 0.9–2.8 |
| | LVEDD (cm) | 4.70±0.61 | 2.4–6.2 |
| | LVESD (cm) | 3.09±0.61 | 1.3–4.5 |
| | PWDd (cm) | 1.01±0.27 | 0.6–1.7 |
| | PWSd (cm) | 1.36±0.48 | 0.7–5.2 |
| | LVEDV ($cm^2$) | 104.94±30.4 | 21–197 |
| | LVESV ($cm^2$) | 39.86±18.80 | 4–94 |
| | LVSV ($cm^2$) | 65.14±19.46 | 17–140 |
| | LVEF (% & $cm^2$) | 65.45±9.85 | 45–88 |
| | LVFS (% & $cm^2$) | 34.62±7.8 | 16–55 |

2D-Ech: two-dimension echocardiography, DBP: diastolic blood pressure, IVSd: interventricular septum diastolic diameter, IVSs: interventricular septum systolic diameter, LVEDD: left ventricular end diastolic diameter, LVEDV: left ventricular end diastolic volume, LVEF: left ventricular ejection fraction, LVESD: left ventricular systolic diameter, LVESV: left ventricular end systolic volume, LVFS: left ventricular fraction stork volume, LVSV: left ventricular stork volume, PP: pulse pressure, PWDd: posterior wall diastolic diameter, PWSd: posterior wall systolic diameter, SBP: systolic blood pressure

To measure the strain angle during the late diastolic filling period (AεA), the endpoints of the diastasis and late diastolic phases were identified on the strain curve. Next, a line segment connecting these two points was drawn to represent the first line segment of the late diastolic filling phase strain angle. Then, a second line segment was created starting from the point where this first line intersects the "x" axis and drawn parallel to the "x" axis, forming the second line segment of the late diastolic filling phase strain angle. Additionally, another line segment parallel to the "x" axis was drawn from the point where it intersects the "x" axis to form an additional line of the late diastolic filling phase strain angle. Finally, the angle between these two line segments was measured using the J-Image software (Version 1.54 k), and the late volumetric filling phase strain angle (AεA) was recorded (Fig. 1). The EεA/AεA ratio (Eε/AεAR) was calculated by dividing the EεA value by the AεA value.

### *Statistics*

Statistical analyses were conducted using IBM Statistical Package for Social Sciences (SPSS) software version 26.0 (IBM Inc., Chicago, IL, USA). The Kolmogorov-Smirnov test was used to check the distribution of continuous variables. Parametric continuous variables are shown as mean ± standard deviation (SD) and were compared with the paired samples t-test. Categorical variables are reported as absolute frequencies (percentages) and compared using Pearson's chi-square test. Pearson's correlation coefficient was used to evaluate correlations between variables. A p-value less than 0.05 was considered statistically significant for all tests.

## Results

The demographic, clinical, and 2D-Echo characteristics of patients are presented in Table 1. 114 patients were included in the study. The mean age in the study population was 51.86±13.87 (min-max: 19–89) years. 50% (n=57) were male. 51.8% (n=59) had hypertension, and 2.6% (n=3) had diabetes mellitus. The average heart rate was 73.15±12.75 beats per minute, with systolic and diastolic arterial blood pressures of 151.85±34.73 mmHg and 90.51±15.91 mmHg, respectively. In the 2D-Echo evaluation; the mean LV) end-diastolic volume was

***Table 2.*** *Comparison of the DSCA obtained on the A2CV, A4CV, A5CV and TMIV values obtained on the A4CV*

| | | TMIV (mean ± Sd) n: 114 | DSCA (mean ± Sd) n: 114 | p |
|---|---|---|---|---|
| E velocity | A2CV EεA | 0.72±0.18 | 50.42±10.23 | <0.001 |
| | A4CV EεA | | 52.46±10.77 | <0.001 |
| | A5CV EεA | | 53.20±10.18 | <0.001 |
| A velocity | A2CV AεA | 0.73±0.17 | 51.77±6.86 | <0.001 |
| | A4CV AεA | | 52.59±7.55 | <0.001 |
| | A5CV AεA | | 50.85±8.59 | <0.001 |
| E/AR | A2CV Eε/AεAR | 1.03±0.36 | 0.99±0.24 | 0.158 |
| | A4CV Eε/AεAR | | 1.02±0.36 | 0.830 |
| | A5CV Eε/AεAR | | 1.06±0.30 | 0.215 |
| DT | A2CV EεA | 192.19±66.95 | 50.42±10.23 | <0.001 |
| | A4CV EεA | | 52.46±10.77 | <0.001 |
| | A5CV EεA | | 53.20±10.18 | <0.001 |
| | A2CV AεA | | 51.77±6.86 | <0.001 |
| | A4CV AεA | | 52.59±7.55 | <0.001 |
| | A5CV AεA | | 50.85±8.59 | <0.001 |
| | A2CV Eε/AεAR | | 0.99±0.24 | <0.001 |
| | A4CV Eε/AεAR | | 1.02±0.36 | <0.001 |
| | A5CV Eε/AεAR | | 1.06±0.30 | <0.001 |
| DS | A2CV EεA | 4.22±1.85 | 50.42±10.23 | <0.001 |
| | A4CV EεA | | 52.46±10.77 | <0.001 |
| | A5CV EεA | | 53.20±10.18 | <0.001 |
| | A2CV AεA | | 51.77±6.86 | <0.001 |
| | A4CV AεA | | 52.59±7.55 | <0.001 |
| | A5CV AεA | | 50.85±8.59 | <0.001 |
| | A2CV Eε/AεAR | | 0.99±0.24 | <0.001 |
| | A4CV Eε/AεAR | | 1.02±0.36 | <0.001 |
| | A5CV Eε/AεAR | | 1.06±0.30 | <0.001 |

A: transmitral late diastolic inflow A velocity, A2CV: apical two-chamber view, A4CV: apical two-chamber view, A5CV: apical two-camber view, AεA: left ventricular global longitudinal A strain angle, DS: deceleration slop, DT: deceleration time, E/AR: transmitral early diastolic inflow E velocity to transmitral inflow A velocity ratio, E: transmitral early diastolic inflow E velocity, Eε/AεAR: left ventricular global longitudinal diastolic strain curve E- and A-strain angle ratio, EεA: left ventricular global longitudinal E strain angle, DSCA: diastolic strain curve angle, TMIV: transmitral inflow velocity, ε: strain

104.94±30.4 $cm^2$, while the end-systolic volume was 39.86±18.80 $cm^2$. LV stroke volume was 65.14±19.46 $cm^2$. In addition, the mean value of LVEF was 65.45±9.85.

Using a statistical analysis of samples, it was determined whether there were differences between the E/AR and Eε/AεAR parameters. As expected, no statistically significant differences were found between the mean of Eε/AεAR and E/AR measured from the left ventricle on the A2CV, A4CV, and A5CV (1.06±0.03 vs 1.03±0.36, p=0.215; 1.02±0.36 vs 1.03±0.36, p=0.830; 0.99±0.24 vs 1.03±0.36, p=0.158; respectively). However, significant differences were found between DSCA values (A2CV Eε, A4CV Eε, A5CV Eε, A2CV Aε, A4CV Aε, A5CV Aε) and TMIV values (E Velocity, A Velocity, DT, DS) on all views (Table 2). Also, significant differences were found between most of the DATV and most of the DSCA values (Table 3).

By correlation analysis, it was determined whether there was a correlation between DSCA values, TMIV values, and DATV values. A significantly strong correlation was found between Eε/AεAR and E/AR, E/SéR on the A2CV A4CV, and A5CV (r=0.620, p <0.001; r=0.548, p <0.001; r=0.570, p <0.001; and r=-0.431, p <0.001; r=-0.279, p=0.003; r=-0.255, p <0.008, respectively) (Table 4, Fig. 2). Also, a significantly positive correlation was found between the EεA and E velocity, E/AR and DS on most ACVs, and, except for A4CV, a significant negative correlation was found between AεA and E velocity,

***Table 3.*** *Diastolic strain curve angle obtained on the A2CV, A4CV, A5CV and DATV obtained on the A4CV values comparison*

| DATV/ DSCA parameters | | DATV values n: 114 | DSCA values n: 114 | p |
|---|---|---|---|---|
| A4CV Lé | A2CV EεA | 0.11±0.09 | 50.42±10.23 | <0.001 |
| | A4CV EεA | | 52.46±10.77 | <0.001 |
| | A5CV EεA | | 53.20±10.18 | <0.001 |
| A4CV Lá | A2CV AεA | 0.12±0.12 | 51.77±6.86 | <0.001 |
| | A4CV AεA | | 52.59±7.55 | <0.001 |
| | A5CV AεA | | 50.85±8.59 | <0.001 |
| A4CV Lé/LáR | A2CV Eε/AεAR | 1.19±0.094 | 0.99±0.24 | 0.028 |
| | A4CV Eε/AεAR | | 1.03±0.27 | 0.070 |
| | A5CV Eε/AεAR | | 1.06±0.30 | 0.170 |
| A4CV Sé | A2CV EεA | 0.094±0.080 | 50.42±10.23 | <0.001 |
| | A4CV EεA | | 52.46±10.77 | <0.001 |
| | A5CV EεA | | 53.20±10.18 | <0.001 |
| A4CV Sá | A2CV AεA | 0.11±0.10 | 51.77±6.86 | <0.001 |
| | A4CV AεA | | 52.59±7.55 | <0.001 |
| | A5CV AεA | | 50.85±8.59 | <0.001 |
| A4CV Sé/Sá R | A2CV Eε/AεAR | 0.95±0.63 | 0.99±0.24 | 0.495 |
| | A4CV Eε/AεAR | | 1.03±0.27 | 0.160 |
| | A5CV Eε/AεAR | | 1.06±0.30 | 0.037 |

DATV: Left ventricular diastolic annular tissue velocity, DSCA: Left ventricular global longitudinal diastolic strain curve angle, E/LéR: Transmitral early diastolic inflow E velocity to lateral annular é velocity ratio, Lá: Lateral annular á velocity, Lé/LáR: Lateral annular é velocity to lateral annular á velocity ratio, Lé: Lateral annular é velocity, Sá: Septal annular á velocity, Sé/Sá R: septal annular é velocity to septal annular á velocity ratio, Sé: Septal annular é velocity

***Table 4.*** *Correlations between DSCA values obtained on the A2CV, A4CV, A5CV and TMIV values obtained on the A4CV.*

| | | | E velocity | A velocity | E/AR | DT | DS |
|---|---|---|---|---|---|---|---|
| A2CV | EεA | r | 0.381 | -0.341 | 0.502 | -0.132 | 0.250 |
| | | p | 0.000 | <0.001 | <0.001 | 0.166 | 0.008 |
| | AεA | r | -0.288 | 0.112 | -0.292 | 0.182 | -0.251 |
| | | p | 0.002 | 0.241 | 0.002 | 0.055 | 0.008 |
| | Eε/AεAR | r | 0.507 | -0.365 | 0.620 | -0.207 | 0.364 |
| | | p | <0.001 | <0.001 | <0.001 | 0.028 | <0.001 |
| A4CV | EεA | r | 0.370 | -0.274 | 0.446 | -0.128 | 0.227 |
| | | p | <0.001 | 0.004 | <0.001 | 0.185 | 0.018 |
| | AεA | r | -0.116 | 0.202 | -0.234 | 0.046 | -0.101 |
| | | p | 0.232 | 0.035 | 0.013 | 0.636 | 0.296 |
| | Eε/AεAR | r | 0.410 | -0.385 | 0.548 | -0.171 | 0.306 |
| | | p | <0.001 | <0.001 | <0.001 | 0.072 | 0.001 |
| A5CV | EεA | r | 0.428 | -0.331 | 0.530 | -0.140 | 0.252 |
| | | p | <0.001 | <0.001 | <0.001 | 0.150 | 0.009 |
| | AεA | r | -0.252 | -0.004 | -0.170 | 0.181 | -0.258 |
| | | p | 0.009 | 0.970 | 0.076 | 0.061 | 0.007 |
| | Eε/AεAR | r | 0.534 | -0.307 | 0.570 | -0.268 | 0.416 |
| | | p | <0.001 | 0.001 | <0.001 | 0.004 | <0.001 |

***Table 5.*** *Correlations between left ventricular DSCA ratio values obtained on the A2CV, A4CV, A5CV and DATV values obtained on the A4CV*

| | | E/LéR | E/SéR | Lé/LáR | Sé/SáR |
|---|---|---|---|---|---|
| A2CV Eε/AεAR | r | -0.260 | -0.431 | 0.314 | 0.554 |
| | p | 0.007 | <0.001 | 0.001 | <0.001 |
| A4CV Eε/AεAR | r | -0.207 | -0.279 | 0.374 | 0.504 |
| | p | 0.033 | 0.003 | <0.001 | <0.001 |
| A5CV Eε/AεAR | r | -0.083 | -0.255 | 0.289 | 0.509 |
| | p | 0.394 | 0.008 | <0.001 | <0.001 |

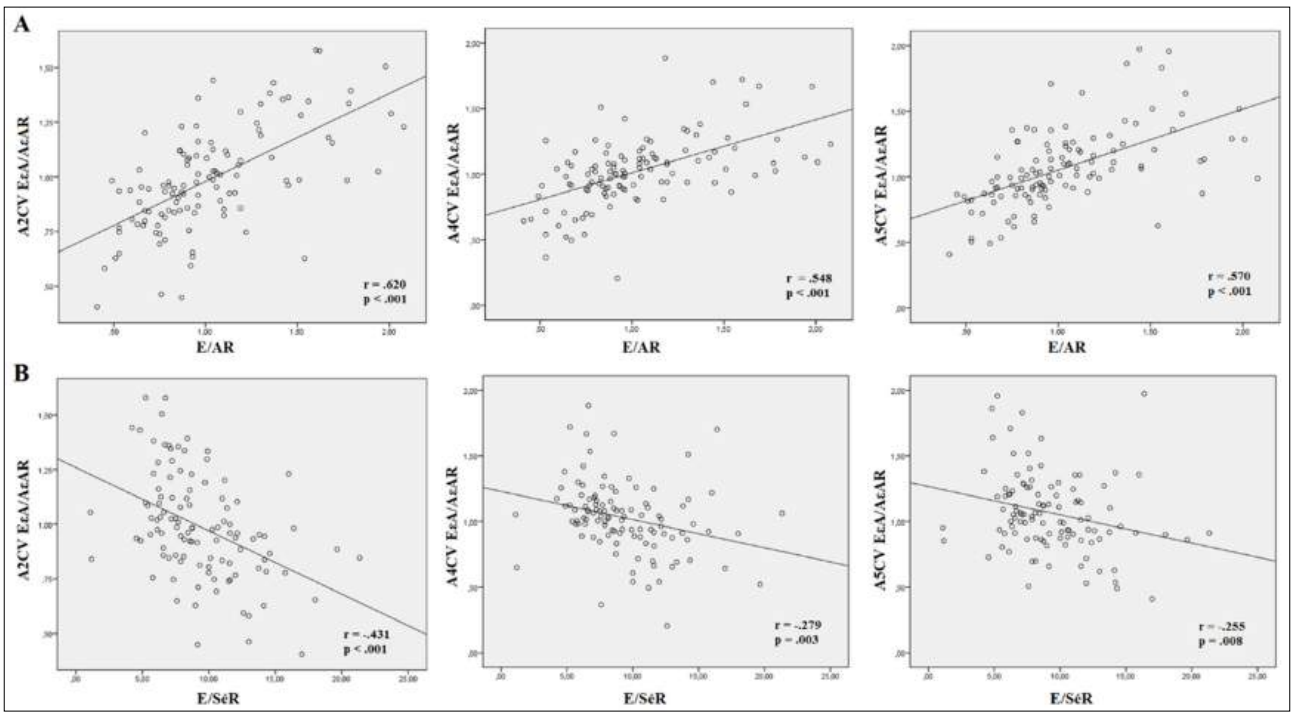


***Figure 2.*** *a, b. Significant correlations between EεA/AεAR obtained on A2CV, A4CV and A5CV, E/AR (a), E/SéR obtained on A4CV during LV diastole (b) (r=correlation coefficient; p=significance level).*

E/AR and DS on A2CV and A5CV (Table 4). Moreover, except for the correlation between Eε/AεAR and E/Lé ratio on the A2CV, a significant correlation was found between Eε/AεAR and E/Lé Ratio, E/ Sé Ratio, Lé/Lá Ratio, Sé /Sá Ratio on all views (r=-0.260, p=.0.007, r=-0.431, p <0.001, r=0.314, r=0.001, r=0.554, p <0.001, on the A2CV), r=-0.207, p=0.033; r=-0.279, p=0.003; r=0.374, p <0.001; r=0.504, p <0.001 on the A4CV and r=-0.255, p=0.008 r=0.289 p <0.001; r=0.509; p <0.001, on the A5CV, respectively) (Table 5).

## Discussion

The main finding in the present study of patients with LVEF >50% was that the DSCA of the early volumetric relaxation period (EεA) to DSCA of the late diastolic filling period (AεA) ratio (EεA/AεAR) is strongly correlated with E/AR, E/LéR, E/SéR, Lé/LáR and Sé/SáR. Also, a positive correlation was found between the EεA and E/AR, E velocity. There was a negative correlation between the EεA and A velocity, DT, and DS. Similarly, there is a negative correlation between the AεA and E/A ratio, E velocity, and DS. To our knowledge, no study has compared these longitudinal diastolic DSCAs and traditional echocardiographic diastolic parameters.

In assessing patients with suspected heart failure or symptoms of shortness of breath, measuring LVDD plays a crucial diagnostic role. The mortality rates linked to heart failure with preserved ejection fraction are similar to those seen in cases of heart failure with reduced ejection fraction[16,17]. Diagnosing heart failure with preserved ejection fraction is more complex than diagnosing heart failure with reduced ejection

fraction. Additionally, it tends to be underdiagnosed when relying solely on ejection fraction[18].

The most frequently employed methods for evaluating and staging LVDD are trans-mitral inflow peak E velocity, late filling A velocity, E/A ratios, and E/é ratio. However, it should be noted that these parameters are indirect, and there are important limitations to evaluating LVDD. The most significant limitation is its susceptibility to loading conditions. Furthermore, for the E- and A-velocities to be reliable, the Doppler velocity records must be referred to at the correct angle. Moreover, the reliability of these measurements may be compromised by factors such as heart rate, presence of heart arrhythmias (notably atrial fibrillation/flutter), PR distance, cardiac output, mitral annulus diameter, and left atrial function and aging, which can lead to erroneous assessments of LVDD. The relationship between changes in left ventricular diastolic and systolic volumes and pressures and their direct impact on mitral annular velocities and time intervals is a crucial consideration.

Left ventricular myocardial longitudinal diastolic strain measured by 2D-STE provides non-invasive and global information about LVDD. Moreover, direct data about left ventricular diastolic function can be obtained with the strain. Although these benefits of strain, diastolic functions cannot be evaluated correctly in the case of the presence of the post-systolic strain, and during the tachycardia onset and end points of the E and A strain curves cannot be distinguished. In these cases, DSCA eliminates the errors arising from the measurements on the diastolic strain curve, and obtains diastolic data from the LV itself. It is also not affected by tachycardia.

Diastolic annular tissue velocity via TDI may inadequately evaluate regional myocardial relaxation due to inherent limitations of Doppler-based methodologies. Key constraints include angle dependence, which introduces significant measurement inaccuracies at interrogation angles exceeding 20°. Furthermore, regional wall motion abnormalities at sampling sites may yield artificially reduced velocities on tissue Doppler, even in the presence of globally preserved relaxation. Early diastolic relaxation, an active energy-dependent process, initiates rapidly in the basal LV segments and propagates apically, generating a base-to-apex strain gradient. This gradient, coupled with myocardial thinning and untwisting mediated by the myocardium's incompressibility, drives chamber dilatation during diastole[19,20]. Consequently, rate-based assessments of early relaxation (e′) at the annular level may overlook localized disturbances in relaxation.

The clinical utility of e′ and derived metrics, such as the E/e′ ratio, remains contentious due to inconsistent evidence. While studies by Kimura et al. and Ersbøll et al. reported that E/e′ ratios derived from STE more accurately predict LV filling pressures than conventional Doppler-based E/e′ measurements[21,22], Kasner et al. found no incremental diagnostic value of STE over TDI in patients with coronary artery disease[23]. Similarly, strain rate imaging failed to demonstrate superiority over TDI for detecting diastolic dysfunction in HFpEF[24]. Such divergent findings underscore the limitations of relying on isolated Doppler or strain-based parameters for LVDD diagnosis.

Emerging evidence in our study suggests that integrating novel speckle-tracking parameters –including EεA, AεA, and Eε/AεA– with conventional TMIV and DATV may enhance diagnostic sensitivity. This multimodal approach, which synthesizes complementary data on myocardial mechanics, could mitigate errors inherent to Doppler-dependent techniques, refine the classification of diastolic dysfunction, and improve diagnostic accuracy in LVDD.

### *Study Limitations*

This research has several constraints. First, the observational, single-center design limits the generalizability of findings, as longitudinal or multi-institutional data were not incorporated. Second, the modest participant pool may restrict the statistical power needed to establish definitive diagnostic thresholds for diastolic parameters such as EεA, AεA, and the EεA/AεA ratio. Larger, population-based studies are essential to validate these metrics as reliable tools for assessing left ventricular diastolic function. Third, the technical demands of speckle-tracking echocardiography pose challenges: accurate myocardial deformation analysis relies heavily on high-quality image acquisition and operator expertise in optimizing 2D echocardiographic windows for precise endocardial border identification. These factors may affect reproducibility in clinical settings with variable imaging resources.

## Conclusions

We documented a significant correlation between the LV diastolic DSCA parameters on the A2CV, A4CV, A5CV, TMIV, and DATV parameters. Diastolic strain

curve angle tool is a diastolic parameter derived from speckle tracking echocardiography that can be used to determine regional myocardial functions quantitatively. It is a new echocardiographic tool that, working with standard 2D-Ech without the limitations of Doppler techniques, provides a comprehensive diastolic analysis of global myocardium. Furthermore, it's a reliable and easy-to-apply noninvasive method for evaluating LV diastolic function. Therefore, in addition to traditional methods, the use of the DSCA tool may be recommended for the evaluation of LV diastolic function.

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**ARAŞTIRMA MAKALESİ /** *RESEARCH ARTICLE*

# Preoperative Risk Scores in Elderly with Gastrointestinal Malignancies: Their Predictive Value for Postoperative Mortality and Morbidity

## *Gastrointestinal Maligniteli Yaşlı Hastaların Preoperatif Risk Skorları: Ameliyat Sonrası Mortalite ve Morbidite Yönünden Prediktif Önemi*

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## ABSTRACT

***Aim:*** *The incidence of gastrointestinal cancers has shifted to older age groups with global population aging. Elderly patients often present with diminished reserves and comorbidities, necessitating individualized risk assessment. This study aimed to evaluate preoperative risk assessment tools, including the Physiological and Operative Severity Score for the Enumeration of Mortality and Morbidity (POSSUM), American Society of Anesthesiologists (ASA) score, and Eastern Cooperative Oncology Group Performance Status (ECOG-PS), in predicting early postoperative outcomes in elderly patients undergoing curative gastrointestinal cancer surgery.*

***Material and Methods:*** *This retrospective study included patients aged ≥75 years (n=65) and 50–65 years (n=60) who underwent curative surgery between 2019 and 2023. Comorbidities, ASA scores, ECOG-PS, POSSUM scores, postoperative complications, and early mortality were analyzed.*

***Results:*** *Elderly patients had significantly higher comorbidity rates, ASA, ECOG-PS, and POSSUM scores. Although early mortality and ICU stays were more frequent in elderly patients, multivariate analysis did not identify age ≥75 as an independent risk factor. The ASA score was significantly associated with postoperative morbidity (OR: 3.2, 95%CI: 1.5–6.7), whereas POSSUM and ECOG-PS scores were not predictive of early mortality.*

***Conclusion:*** *Age alone is not an independent predictor of postoperative outcomes. Higher ASA scores are strongly associated with morbidity, emphasizing the need for comprehensive preoperative assessments.*

**Key words:** *preoperative risk scores; elderly; gastrointestinal cancer*

## ÖZET

***Amaç:*** *Gastrointestinal kanserlerin insidansı, küresel nüfusun yaşlanmasıyla birlikte daha ileri yaş gruplarına kaymıştır. Yaşlı hastalar genellikle azalmış rezervler ve artmış komorbiditelerle başvurduğundan, bireyselleştirilmiş risk değerlendirmesi gerekmektedir. Bu çalışma, küratif amaçlı gastrointestinal kanser cerrahisi geçiren yaşlı hastalarda erken postoperatif sonuçları öngörmede Fizyolojik ve Operatif Şiddet Skoru (POSSUM), Amerikan Anesteziyologlar Derneği (ASA) skoru ve Eastern Cooperative Oncology Group Performance Status (ECOG-PS) gibi preoperatif risk değerlendirme araçlarının kullanımını değerlendirmeyi amaçlamaktadır.*

***Materyal ve Metot:*** *Bu çalışma retrospektif bir çalışma olup 2019–2023 yılları arasında gastrointestinal sistem malignitesi nedeniyle küratif cerrahi geçiren ≥75 yaş (n=65) ve 50–65 yaş (n=60) hastalar çalışmaya dâhil edilmiştir. Hastalara ilişkin komorbiditeler, ASA skorları, ECOG-PS, POSSUM skorları, postoperatif komplikasyonlar ve erken mortalite durumları analiz edilmiştir.*

***Bulgular:*** *Yaşlı hastaların komorbidite oranları; ASA, ECOG-PS ve POSSUM skorları istatistiksel anlamlı olarak daha yüksektir. Erken mortalite ve YBÜ yatışları ileri yaş hastalarda daha sık olsa da multivariant analizlerde yaş ≥75 olması bağımsız bir risk faktörü olarak görülmemiştir. ASA skoru istatistiksel anlamlı olarak postoperatif mortalite ile ilişkili bulunmuştur (OR: 3,2, 95% CI: 1,5–6,7); ancak POSSUM ve ECOG – PS skorları erken mortalite için prediktif görülmemiştir.*

***Sonuç:*** *Yaş, postoperatif takip ve sonuçlar açısından tek başına bağımsız bir risk faktörü değildir. Yüksek ASA skorları morbidite ile güçlü ilişkilidir. Bu durum, kapsamlı bir preoperatif değerlendirmenin ve bu değerlendirme doğrultusunda cerrahiye hazırlık için gerekli olan nütrisyonel destek, hastanın genel kondisyonunun optimize edilmesi vb. müdahalelerin yapılmasının (prehabilitasyon) önemini gösterir.*

**Anahtar kelimeler:** *preoperatif risk skorları; yaşlılık; gastrointestinal kanser*

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## Introduction

The global population's aging has contributed to a rise in the average age of patients diagnosed with gastrointestinal (GI) cancers[1,2]. The peak incidence of GI cancers has shifted to the 6th and 7th decades in men and the 8th and 9th decades in women[1]. Age is recognized as a significant risk factor for many solid tumors. Aging results in a gradual decline in functional reserves across multiple organ systems, though at varying rates[3]. This decline leads to an increased prevalence of comorbidities, a higher incidence of complications, and a worsened prognosis[4]. Due to the variability in functional reserves among elderly individuals, this patient population exhibits high heterogeneity in terms of frailty[3]. As a result, individualized evaluation is crucial, particularly in the treatment of cancer. For instance, up to 70% of elderly patients are unable to receive neoadjuvant or adjuvant chemotherapy due to poor tolerance. The curative treatment for GI cancers remains surgical intervention[5]. However, similar to chemotherapy, surgery in elderly patients is associated with higher morbidity and complication rates[4,5].

This study aims to investigate the prognostic utility of widely used preoperative risk assessment tools (POSSUM, ASA, and ECOG-P scores) in predicting early postoperative outcomes, specifically 30-day morbidity and mortality, in elderly patients (≥75 years) undergoing curative gastrointestinal cancer surgery. The secondary objective is to compare these outcomes with those of middle-aged patients (50–65 years) to evaluate the impact of age-related physiological decline on surgical prognosis.

## Material and Methods

Following approval from the local ethics committee, this retrospective observational study commenced with informed consent obtained from all participants. Patients undergoing elective curative-intent surgeries for gastric, colorectal, or pancreatic cancer at Kafkas University Hospital from 01.01.2019 to 01.11.2023 were included in the study. The study excluded patients with synchronous tumors, gastrointestinal stromal tumors, surgeries performed at external centers, or incomplete data. Data collected included patients' preoperative sociodemographic characteristics, comorbidities, Eastern Cooperative Oncology Group Performance Status (ECOG-PS), American Society of Anesthesiologists (ASA) scores, and Physiological and Operative Severity Score for the enumeration of Mortality and Morbidity (POSSUM) scores, as well as postoperative intensive care unit length of stay, morbidity, and early mortality outcomes. Postoperative morbidity was defined as the presence of complications classified as Grade 2, 3, or 4 according to the Clavien-Dindo classification. All patients' pathology results were staged according to the American Joint Committee on Cancer (AJCC) Tumor-Node-Metastasis (TNM) staging system. Patients were categorized into two groups for outcome analysis: Group 1 (≥75 years) and Group 2 (50–65 years) This grouping allowed for a comparative analysis of surgical outcomes between elderly and middle-aged patients with gastrointestinal cancers.

### *Statistical Analysis*

All statistical analyses were performed using IBM Statistical Package for Social Sciences (SPSS) version 27.0 software. The distribution of continuous variables was assessed using the Kolmogorov-Smirnov test. Normally distributed variables were expressed as mean ± standard deviation (SD), while non-normally distributed variables were presented as median with interquartile range (IQR). For comparisons between two independent groups, the Student's t-test was used for parametric data, and the Mann–Whitney U test was employed for non-parametric data. Categorical variables were compared using the Chi-square test or Fisher's exact test, where appropriate. To identify variables independently associated with early postoperative mortality and morbidity, a binary logistic regression model was constructed, including variables with a p-value <0.10 in univariate analysis. The strength of associations was reported as odds ratios (OR) with 95% confidence intervals (CI). Receiver Operating Characteristic (ROC) curve analysis was used to evaluate the predictive value of the POSSUM score for early postoperative outcomes. The optimal cut-off value was determined using the Youden Index to maximize sensitivity and specificity. A cut-off point of 20.5 yielded the highest diagnostic performance for both morbidity and mortality (sensitivity for mortality: 87.5%, specificity: 53.0%; sensitivity for morbidity: 56.8%, specificity: 53.1%). A two-tailed p-value of less than 0.05 was considered statistically significant in all analyses.

## Results

Present study included 125 patients, comprising 44 female and 81 male participants. The age ≥75 group had significantly higher comorbidities than the 50–65 age group (p=0.001). Of the 11 patients with

***Table 1.*** *Comparison of preoperative demographic data, cancer stages according to TNM classification and risk scores according to age groups*

| Parameters | | Total (n=125) | Age ≥75 (n=66)(52.8%) | Age 50–65 (n=59) (47.2%) | p-value |
|---|---|---|---|---|---|
| Age median (IQR) | | 75.00(21.00) | 80.00 (6.00) | 59.00(8.00) | |
| Male sex n (%) | | 81 (64. 8%) | 44 (66.7%) | 37 (62.7%) | 0.644 |
| Obesity (BMI >30) n (%) | | 39 (31.2%) | 25 (37.9%) | 14 (23.5%) | 0.088 |
| Comorbidities n (%) | | 81 (64.8%) | 58 (87.87%) | 23 (38.98%) | **<0.001** |
| Diabetes mellitus n (%) | | 21 (16.8%) | 11 (20.0%) | 10 (16.9%) | 0.966 |
| Hypertension n (%) | | 46 (36.8%) | 36 (54.54%) | 10 (16.9%) | **<0.001** |
| Coroner artery disease n (%) | | 25 (20%) | 20 (30.30%) | 5 (8.47%) | **0.002** |
| ASA n (%) | 1 | 2 (1.6%) | 1 (1.52%) | 1 (1.69%) | **<0.001** |
| | 2 | 57 (45.6%) | 18 (27.27%) | 39 (66.10%) | |
| | 3 | 65 (52.0%) | 46 (69.69%) | 19 (32.20%) | |
| | 4 | 1 (0.8%) | 1 (1.52%) | 0(0.0%) | |
| ECOG-PS n (%) | 0 | 49 (39.2%) | 17 (25.75%) | 32 (54.25%) | **<0.001** |
| | 1 | 39 (31.2%) | 14 (21.22%) | 25 (42.37%) | |
| | 2 | 22 (17.6%) | 21 (31.82%) | 1 (1.69%) | |
| | 3 | 14 (11.2%) | 13 (19.69%) | 1 (1.69%) | |
| | 4 | 1 (0.8%) | 1 (1.52%) | 0 | |
| POSSUM median (IQR) | | 21.00 (8.00) | 23.00 (5.00) | 16.00 (5.00) | **0.001** |
| AJCC Stage 1 n (%) | | 20 (16%) | 6 (9.09%) | 14 (23.73%) | |
| Stage 2 n (%) | | 47 (37.6%) | 20 (30.31%) | 27 (45.76%) | **0.003** |
| Stage 3 n (%) | | 49 (39.2%) | 32 (48.48%) | 17 (28.81%) | |
| Stage 4 n (%) | | 9 (7.2%) | 8 (12.12%) | 1 (1.69%) | |
| Neoadjuvant treatment | No n, % | 97 (77.6%) | 55 (83.3%) | 42 (71.2%) | 0.104 |
| | Yes n, % | 28 (22.4%) | 11 (16.7%) | 17 (28.8%) | |

ASA: American Society of Anesthesiologists, ECOG-PS: Eastern Cooperative Oncology Group performance status, POSSUM: physiological and operative severity score for the enumeration of mortality and morbidity, IQR: interquartile range, BMI: body mass index.

cerebrovascular events, 10 were in the age ≥75 group (p=0.008). Chronic obstructive pulmonary disease (COPD) was found in 24 patients, including 16 from the age ≥75 group, though not statistically significant (p=0.120). Atrial fibrillation (AF) was observed in 10 patients in total, 9 of whom were in the age ≥75 group (p=0.014) (Table 1). The number of patients with an ASA score of 3 or 4 was 66 (52.8%), of whom 47 (71.2%) were in the age ≥75 group (p<0.001). Among the patients with an ECOG performance score of 0 or 1, 88 (70.4%) were identified, and 57 (64.8%) of these were in the 50–65 age group (p<0.001). The total number of patients with stage 3 or 4 cancer was 58 (46.4%), with 40 (69.0%) belonging to the age ≥75 group (p<0.001). The proportion of patients receiving neoadjuvant therapy showed no significant difference between age groups (p=0.104) (Table 1). Postoperative morbidity did not differ significantly between the age groups (p=0.773). The age ≥75 group had significantly higher ASA, ECOG performance, and POSSUM scores (p=0.001 for all). Cancer-affected organ distribution was similar across both groups (p=0.174). Although early mortality rates and intensive care unit (ICU) stay durations were higher in the age ≥75 group in univariate analysis, multivariate analysis did not identify age as a significant risk factor for ICU stay or early mortality (respectively; p=0.640, p=0.683) (Table 2). Age ≥75 is an independent risk factor for the presence of comorbidities (Odds ratio: 5.001, p=0.047). Similarly, age ≥75 is a risk factor associated with an increase in ASA score, deterioration in performance status, and elevation in POSSUM score (Table 3). Patients were grouped by POSSUM scores (<20.5 and >20.5) for comparison of morbidity and mortality. POSSUM score did not significantly predict morbidity or early mortality (p=0.290 and p=0.062, respectively). Nevertheless, 7 out of 8 patients who developed early mortality had a POSSUM score >20.5 (Table 4). The relationship between risk scores and early mortality and postoperative morbidity was also evaluated specifically in patients over 75 years of age. In this subgroup, an ASA score of 3–4 was found to be associated with postoperative morbidity but not with early mortality in univariate analysis (respectively, p=0.027, p=0.127). However, this association did not reach statistical significance in multivariate analysis (p=0.122).

***Table 2.*** *Comparison of malignancy site and postoperative data of the patients according to age groups*

| Parameters | | Total (n=125) | Age ≥75 (n=66; 52%.8) | Age 50–65 (n=59; 47%.2) | p-value |
|---|---|---|---|---|---|
| Site of malignancy n, % | Stomach | 34 (27.2%) | 22 (33.3%) | 12 (20.3%) | 0.174 |
| | Colon | 58 (46.4%) | 31 (47.0% | 27 (45.8%) | |
| | Rectum | 23 (18.4%) | 8 (12.1%) | 15 (25.4%) | |
| | Pancreas | 10 (8.0%) | 5 (7.6%) | 5 (8.5%) | |
| ICU length of stay median (IQR) | | 1.00(2.00–0.00) | 1.00(2.00) | 0.00(1.00) | **<0.001** |
| Postoperative morbidity n (%) | | 44 (35%.2) | 24 (36%.36) | 20 (33%.89) | 0.773 |
| Early Mortality n (%) | | 8 (6%.4) | 7 (10%.60) | 1 (1%.69) | 0.065 |
| Type of morbidity | | 81 (64.8%) | 42 (63.6%) | 39 (66.1%) | 0.924 |
| | | 11 (8.8%) | 6 (9.1%) | 5 (8.5%) | |
| | | 10 (8.0%) | 6 (9.1%) | 4 (6.8%) | |
| | | 9 (7.2%) | 5 (7.6%) | 4 (6.8%) | |
| | | 1 (0.8%) | 1 (1.5%) | 0 (0.0%) | |
| | | 13 (10.4%) | 6 (9.1%) | 7 (11.9%) | |

ICU: intensive care unit, IQR: interquartile range.

***Table 3.*** *Multivariate analysis of parameters according to age group*

| Parameters | Odds ratio | 95% CI | P value |
|---|---|---|---|
| Comorbidities | 5.001 | 1.020–24.506 | **0.047** |
| ICU length of stay | 1.064 | 0.821–1.379 | 0.640 |
| Cancer Stage 3, 4 | 3.827 | 1.689–8.671 | **0.001** |
| ASA Scores 3, 4 | 5.585 | 2.478–12.586 | **<0.001** |
| ECOG-PS 2, 3, 4 | 32.177 | 7.248–142.856 | **<0.001** |
| POSSUM score | 1.358 | 1.170–1.577 | **<0.001** |
| Early mortality | 3.024 | 0.015–617.089 | 0.683 |

ICU: intensive care unit, ASA: American Society of Anesthesiologists, ECOG-PS: Eastern Cooperative Oncology Group performance status, POSSUM: physiological and operative severity score for the enumeration of mortality and morbidity.

## Discussion

In the present study, age ≥75 was not identified as an independent risk factor for intensive care unit length of stay, early mortality, or morbidity in patients who underwent curative surgery for gastrointestinal malignancies. However, age ≥75 was determined to be an independent risk factor for higher ASA scores, impaired ECOG performance status, and elevated POSSUM scores. In the evaluation of all patients, the ASA score was statistically significant in predicting early mortality and postoperative morbidity, whereas the ECOG-PS and POSSUM scores were not found to be significant.

***Table 4.*** *Comparison of preoperative risk scores in terms of early mortality and morbidity*

| Variables | | Early mortality (n=8) | Univariate analysis P value | Postoperative morbidity (n=44) | Univariate analysis P value |
|---|---|---|---|---|---|
| ECOG-PS age ≥75 | 0, 1 (n=31) | 3 (9.7%) | 1.000 | 8 (25.8%) | 0.093 (0.060*) |
| | 2, 3, 4 (n=37) | 4 (11.4%) | | 16 (45.7%) | |
| ECOG-PS all patients | 0, 1 (n=88) | 4 (4.5%) | 0.222 | 27 (61.4%) | 0.103 |
| | 2, 3, 4 (n=37) | 4 (10.8%) | | 17 (38.6%) | |
| ASA score age ≥75 | 1, 2 (n=19) | 0(0.0%) | 0.179 | 3 (15.8%) | **0.027** (0.122*) |
| | 3, 4 (n=47) | 7(14.9%) | | 21 (44.7%) | |
| ASA score all patients | 1, 2 (n=59) | 0 (0.0%) | 0.007 (0.997*) | 14 (31.8%) | **0.011** (0.029*) |
| | 3, 4 (n=66) | 8 (100.0%) | | 30 (68.2%) | |
| POSSUM score age ≥75 | <20.5 (n=62) | 0 (0.0%) | 0.334 | 1 (8.3%) | **0.043** (0.097*) |
| | >20.5 (n=63) | 7 (13.0%) | | 23 (42.6%) | |
| POSSUM score all patients | <20.5 (n=62) | 1 (12.5%) | 0.062 (0.341*) | 19 (43.2%9 | 0.290 |
| | >20.5 (n=63) | 7 (87.5%) | | 25 (56.8%) | |

ASA: American Society of Anesthesiologists, ECOG-PS: Eastern Cooperative Oncology Group performance status, POSSUM: physiological and operative severity score for the enumeration of mortality and morbidity. *: p-value obtained from multivariate analysis.

Age is a recognized risk factor for malignancies[6]. As the global population continues to age, decision-making in cancer treatment for the geriatric population has become increasingly significant[6,7]. It has been reported that more than half of cancer diagnoses in Europe each year occur in individuals over 70 years of age[6,8]. Advances in perioperative assessment, intraoperative monitoring, and postoperative intensive care management have led to a dramatic reduction in perioperative mortality rates among elderly patients[8–10]. In 1948, Welch et al. reported a perioperative mortality rate of 20.7% in patients over 70 years of age undergoing abdominal surgery[9]. However, with advancements in surgical techniques and perioperative care, this rate has decreased to approximately 5% in recent years[11]. In this study, mortality was observed in 7 (10.6%) patients in the age ≥75 group. However, multivariate analysis revealed no statistically significant difference when compared to the younger patient group, which is consistent with the existing literature. A population-based study on esophageal, gastric, and colorectal cancers reported that curative surgical treatment was significantly less frequently performed in patients over 75 years of age; however, the outcomes of those who underwent surgery were similar to those of other age groups[1]. Although comorbidities increase with chronological age, age alone is insufficient to predict mortality and morbidity following elective curative surgery for gastrointestinal malignancies[7]. In our study, comorbidities increased significantly with age; however, multivariate analysis revealed no association between age and ICU length of stay, early mortality, or postoperative morbidity. Similar to other studies in the literature, the rate of neoadjuvant therapy administration was lower in elderly patients, although this difference was not statistically significant[12].

A study investigating the outcomes of patients over 80 years of age who underwent curative gastrectomy for gastric cancer identified an ASA score of 3/4, involvement of the cardia during gastrectomy, and a pathological stage of 2–4 as independent risk factors for poor prognosis. The same study demonstrated that patients who underwent D0 lymphadenectomy had worse survival compared to those who underwent D2 lymphadenectomy, while POSSUM scores and ECOG performance status were not associated with postoperative mortality[13]. In a study evaluating patients over the age of 85 with gastric cancer, it was found that while the ECOG score was not associated with overall survival, a POSSUM score above 30 significantly increased the risk of mortality[14]. POSSUM score is a surgical risk assessment system which combines both the physiological and surgical status of patients. Qiang Li and Yingjun Lu[15,16] concluded that the POSSUM scoring system can effectively predict postoperative complication rates. However, they suggested that it may overestimate the mortality rate, particularly in elderly patients with colorectal cancer. Matsubara et al. reported that in patients over 80 years of age who underwent surgery for colorectal cancer, there were no difference in mortality or postoperative complications between groups with high (ASA 3–4) and low (ASA 1–2) ASA scores. However, they observed a lower rate of complications in the high ASA score group when laparoscopic surgery was performed compared to open surgery[17]. Rosa F et al. in their study investigated the impact of the preoperative ASA on short term and long term outcomes in patients with gastric cancer. They found that 22.8% of patients, classified as ASA 3–4 preoperatively, had a mean age of 77.5 years. This group showed no significant difference in terms of postoperative surgical and medical complications or mortality rates when compared to patients classified as ASA 1 and 2, whose mean ages were 44.7 and 64.5 years, respectively[18]. In a study evaluating the data of 1.012 patients, ASA score and intraoperative blood transfusion were identified as independent risk factors for postoperative mortality and morbidity in patients over 70 years of age who underwent hepatectomy or pancreaticoduodenectomy. While age itself was not found to be a risk factor for postoperative mortality and morbidity, it was reported that sepsis occurred more frequently in elderly patients[19]. In our study, having an ASA score of 3–4 was also identified as an independent risk factor for postoperative morbidity. In our study, all 7 patients over the age of 75 who experienced mortality were preoperatively classified as ASA 3/4. The lack of statistical significance in the relationship between early mortality and ASA score may be attributed to the small sample size.

Study limitations include its retrospective design and the small sample size of elderly patients. Due to the small number of cancer patients aged over 75 years, patients with inherently different characteristics, such as those with gastric, colorectal, and pancreatic cancers, were analyzed as a single group to enhance statistical power. This approach constrained data harmonization and represented the primary limitation of the study.

## Conclusion

This study highlights that while age ≥75 was associated with increased comorbidities, higher ASA scores, impaired ECOG performance status, and elevated POSSUM scores, it was not an independent risk factor for ICU length of stay, early mortality, or postoperative morbidity in patients undergoing curative surgery for gastrointestinal malignancies. Notably, the ASA score emerged as a significant predictor of postoperative morbidity, whereas ECOG-PS and POSSUM scores did not demonstrate predictive value. These findings underscore the importance of comprehensive preoperative evaluation that goes beyond chronological age when determining surgical risk in elderly patients. An interdisciplinary approach, involving a geriatric specialist prior to surgery, may contribute to improved clinical outcomes. As advancements in perioperative care continue to improve outcomes, this study reinforces the viability of curative surgical treatment in appropriately selected geriatric patients, emphasizing that age alone should not preclude surgical intervention for gastrointestinal cancers.

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**ARAŞTIRMA MAKALESİ /** *RESEARCH ARTICLE*

# Comparison of the Epidemiological Distribution of Pediatric Fractures Requiring Surgical Intervention: Insights from the COVID-19 Pandemic and Beyond

*Cerrahi Uygulanan Çocuk Travmatik Kırıklarının Covid-19 Pandemisi ve Pandemi Öncesindeki Dönemde Dağılımı*

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## ABSTRACT

***Aim:*** *The COVID-19 pandemic and its quarantine and isolation measures led to notable differences in trauma mechanisms and their outcomes. This study aims to compare the epidemiological data, fracture patterns, trauma mechanisms, and surgical interventions of pediatric fractures treated surgically during the pandemic with those treated before the pandemic.*

***Material and Method:*** *In this retrospective study, pediatric patients aged 10 years or younger who underwent surgery for fractures during one year before the pandemic and one year during the pandemic were included. The variables analyzed included gender, age, number of children experiencing fracture at home, fracture patterns, mechanisms of injury, injury location, time of injury, and type of surgery performed. The pre-pandemic period was defined as April 2019 – April 2020, and the pandemic period as April 2020 – April 2021.*

***Results:*** *The mean age of patients presenting with fractures before the pandemic was 6.02±2.62 years, compared to 5.39±2.48 years during the pandemic. Before the pandemic, 57.6% (n=38) of the patients presenting with fractures were male, with the most common fracture site being the distal humerus (56.1%, n=37). Falls were the leading mechanism of injury (95.5%, n=63). 40.9% (n=27) of the injuries occurred indoors, and 40.9% (n=27) of the cases were treated with closed reduction and percutaneous pinning (CRPP). During the pandemic, 71.4% (n=40) of the patients were male, with the most common fracture site being the distal humerus (62.5%, n=35). Falls remained the leading mechanism of injury (92.9%, n=52). 48.2% (n=27) of the injuries occurred indoors, and 50% (n=28) of the cases were treated with CRPP. Compared to the pre-pandemic period, the male-to-female patient ratio was higher during the pandemic (p=0.001). Forearm fractures, which typically require higher-energy trauma, were significantly less common during the pandemic (p=0.003).*

***Conclusion:*** *The findings provide insights into the impact of the COVID-19 pandemic on pediatric fractures.*

**Key words:** *COVID-19 pandemic, pediatric fracture, epidemiology of injury*

## ÖZET

***Amaç:*** *Covid-19 pandemisi ve ardı sıra gelişen karantina ve izolasyon önlemleri, travma mekanizmalarında ve sonuçlarında önemli farklılıklara yol açtı. Bu çalışmanın amacı pandemi sırasında cerrahi olarak tedavi edilen pediatrik kırıkların epidemiyolojik verilerini, kırık tiplerini, travma mekanizmalarını ve cerrahi müdahalelerini pandemiden önce tedavi edilenlerle karşılaştırmaktır.*

***Materyal ve Metot:*** *Bu retrospektif çalışmaya, pandemiden önceki bir yıl ve pandemi sırasında bir yıl boyunca kırık nedeniyle ameliyat edilen 10 ve 10 yaş altı pediatrik hastalar dâhil edildi. Analiz edilen değişkenler arasında cinsiyet, yaş, kırığa maruz kalan çocuğun yaşadığı evdeki çocuk sayısı, kırık tipleri, yaralanma mekanizmaları, yaralanma yeri, yaralanma zamanı ve gerçekleştirilen cerrahi türü yer aldı. Pandemi öncesi dönem Nisan 2019 – Nisan 2020, pandemi dönemi ise Nisan 2020 – Nisan 2021 olarak tanımlandı.*

***Bulgular:*** *Pandemi öncesinde kırık şikâyetiyle gelen hastaların yaş ortalaması 6,02±2,62 yıl iken, pandemi döneminde bu yaş 5,39±2,48 yıldı. Pandemi öncesinde kırık şikâyetiyle gelen hastaların %57,6'sı (n=38) erkekti ve en sık görülen kırık bölgesi distal humerustu (%56,1, n=37). Düşmeler yaralanmanın önde gelen mekanizmasıydı (%95,5, n=63). Yaralanmaların %40,9'u (n=27) iç mekanda meydana geldi ve vakaların %40,9'u (n=27) kapalı redüksiyon ve perkütan pinleme (CRPP) ile tedavi edildi. Pandemi sırasında hastaların %71,4'ü (n=40) erkekti ve en sık görülen kırık bölgesi distal humerustu (%62,5, n=35). Düşmeler yaralanmanın önde gelen mekanizması olmaya devam etti (%92,9, n=52). Yaralanmaların %48,2'si (n=27) iç mekanda meydana geldi ve vakaların %50'si (n=28) CRPP ile tedavi edildi. Pandemi öncesi döneme kıyasla, erkek-kadın hasta oranı pandemi sırasında daha yüksekti (p=0,001). Çoğunlukla daha yüksek enerjili travma sonrası gelişen ön kol kırıkları, pandemi sırasında önemli ölçüde daha az izlendi (p=0,003).*

***Sonuç:*** *Bulgular COVID-19 pandemisinin pediatrik kırıkları üzerindeki etkisine ilişkin fikir vermektedir.*

**Anahtar kelimeler:** *COVID-19 pandemisi, pediatrik kırık, yaralanmanın epidemiyolojisi*

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## Introduction

Pediatric trauma is one of the leading causes of hospital admissions in children across many countries and may result in long-term disabilities[1,2]. Following trauma, children can experience physical limitations, chronic pain, and psychological issues such as post-traumatic stress disorder (PTSD)[3]. These consequences also affect families psychosocially[4]. During pandemic periods, quarantine and isolation measures significantly altered individuals' daily activities[5]. Specifically, home confinement, reduced mobility, and decreased physical activity influenced the types and frequency of orthopedic traumas in both children and adults[5–6]. This led to notable differences in trauma mechanisms and their outcomes[5–6].

The COVID-19 pandemic began in December 2019 and spread worldwide within months. In Türkiye, the first case was reported on March 11, 2020 (Anadolu Agency, 11.03.2020), followed by a period of home quarantine. While mobility restrictions during the pandemic reduced the spread of the virus, domestic traumas persisted and contributed to distinct morbidities[5–6]. Although the COVID-19 pandemic has ended, pandemics remain a recurring reality in human history. The end of the COVID-19 outbreak does not imply the elimination of future health crises. Factors such as globalization, frequent travel, environmental degradation, and zoonoses continue to increase the likelihood of new pandemics. Studies conducted during such periods will contribute valuable insights for managing future pandemics.

This study aims to compare the epidemiological data of pediatric fractures treated surgically during the pandemic with those treated before the pandemic, to identify differences in fracture patterns, trauma mechanisms, and surgical interventions.

## Methods

This retrospective study was conducted in the Department of Orthopedics and Traumatology at our tertiary care hospital. Pediatric patients aged 10 years or younger who underwent surgery for fractures during one year before the pandemic and one year during the pandemic were included. The variables analyzed included gender, age, number of children at home, fracture patterns, mechanisms of injury, injury location, time of injury, and type of surgery performed. The pre-pandemic period was defined as April 11, 2019, to April 10, 2020, and the pandemic period as April 11, 2020, to April 11, 2021, encompassing one year of home confinement.

Administrative approval from the hospital management and ethical approval from the Gülhane Clinical Research Ethics Committee (reference number: 2024-565) were obtained before the study.

### *Statistical Analysis*

Data were presented as numbers, percentages, means, standard deviations, medians, minimum, and maximum values. Statistical analysis was performed using IBM Statistical Package for Social Sciences (SPSS) program version 26. Normality of data distribution was assessed using the Kolmogorov-Smirnov test. The Mann-Whitney U test was used for numerical variables, and the Chi-square test for categorical variables. A p-value of $<0.05$ was considered statistically significant.

## Results

The mean age of patients presenting with fractures before the pandemic was 6.02±2.62 years, compared to 5.39±2.48 years during the pandemic. No significant difference in mean age was found between the groups ($p > 0.05$). The mean number of children at home for patients presenting before the pandemic was 1.83±0.82, compared to 2.45±0.97 during the pandemic. The increase in the number of children at home during the pandemic was statistically significant ($p=0.001$) (Table 1).

Before the pandemic, 57.6% (n=38) of the patients presenting with fractures were male, with the most common fracture site being the distal humerus (56.1%, n=37). Falls were the leading mechanism of injury (95.5%, n=63), with 40.9% (n=27) occurring indoors (e.g., home or school), 68.2% (n=45) happening in the evening, and 40.9% (n=27) treated with closed reduction and percutaneous pinning (CRPP).

During the pandemic, 71.4% (n=40) of the patients were male, with the most common fracture site again being the distal humerus (62.5%, n=35). Falls remained the leading mechanism of injury (92.9%, n=52), with 48.2% (n=27) occurring indoors, 64.3% (n=36) in the evening, and 50% (n=28) treated with CRPP. Compared to the pre-pandemic period, the male-to-female ratio was higher during the pandemic ($p=0.001$). Forearm fractures, which typically require higher-energy trauma, were significantly less common during the pandemic ($p=0.001$) (Table 2). No statistically significant differences were observed in other characteristics or treatment modalities (Fig. 1).

***Table 1.*** *Mean and median ages of the patients having fracture according to the groups*

| | Before Pandemic (n=66) | | During Pandemic (n=56) | | |
|---|---|---|---|---|---|
| | Mean ± SD | Median (Min-Max) | Mean ± SD | Median (Min-Max) | p* |
| Age (Year) | 6.02±2.62 | 6 (0–10) | 5.39±2.48 | 2 (0–4) | 0.14 |
| Number of children at home | 1.83±0.82 | 2 (0–4) | 2.45±0.97 | 2 (1–4) | 0.001 |

* Mann Whitney U test was used

***Table 2.*** *Distribution of patients presenting with fracture complaints according to gender, the fracture pattern, trauma type and location and the treatment applied, according to groups formed with those presenting before and during the pandemic*

| | Before pandemic (n=66) | | During pandemic (n=56) | | |
|---|---|---|---|---|---|
| | n | % | n | % | p |
| **Gender** | | | | | |
| Male | 38 | 57.6 | 40 | 71.4 | 0.001 |
| Female | 28 | 42.4 | 16 | 28.6 | |
| **Fracture pattern** | | | | | |
| Humerus distal | 37 | 56.1 | 35 | 62.5 | 0.46 |
| Femur | 10 | 15.1 | 8 | 14.4 | 0.63 |
| Forearm | 12 | 18.2 | 4 | 7.1 | 0.003 |
| Hand | 4 | 6.1 | 4 | 7.1 | 0.1 |
| Tibia | 3 | 4.5 | 5 | 8.9 | 0.25 |
| **Trauma type** | | | | | |
| Fall | 63 | 95.5 | 52 | 92.9 | 0.7* |
| Impact | 3 | 4.5 | 4 | 7.1 | |
| **Trauma location** | | | | | |
| Indoor (home, school, etc.) | 27 | 40.9 | 27 | 48.2 | 0.42 |
| Outdoor (park, garden etc.) | 39 | 59.1 | 29 | 51.8 | |
| **Trauma time** | | | | | |
| Evening (17:00 – 07.59) | 45 | 68.2 | 36 | 64.3 | 0.65 |
| Morning (08:00 – 16:59) | 21 | 31.8 | 20 | 35.7 | |
| **Operation type** | | | | | |
| CRPP | 27 | 40.9 | 28 | 50.0 | 0.34 |
| ORPP | 22 | 33.3 | 12 | 21.4 | |
| TEN | 17 | 25.7 | 16 | 28.6 | |

* Fisher Test was used, Gray columns: before the pandemic (n=66), Black columns: during the pandemic (n=56), UE: upper extremity, LE: lower extremity.

## Discussion

During the COVID-19 pandemic, significant changes occurred in healthcare practices and patient behaviors[7,8]. Although children's outdoor activities decreased due to restrictions, the number of children at home increased significantly. This resulted in more time spent indoors and a corresponding increase in falls and injuries[9]. This study aimed to analyze these patterns using empirical data.

Key findings revealed notable differences in fracture distributions before and during the pandemic. The most frequent fracture type, distal humerus fractures, was consistent across both periods. These injuries, commonly caused by low-energy trauma such as falls, reflect typical patterns in pediatric populations[9–14]. A notable finding was the decreased incidence of forearm fractures, which usually result from high-energy traumas, during the pandemic[10–13]. This shift likely reflects changes in trauma mechanisms due to reduced outdoor activities and increased time indoors.

Furthermore, the significant rise in the number of children at home during the pandemic was associated with an increased frequency of fractures requiring surgical

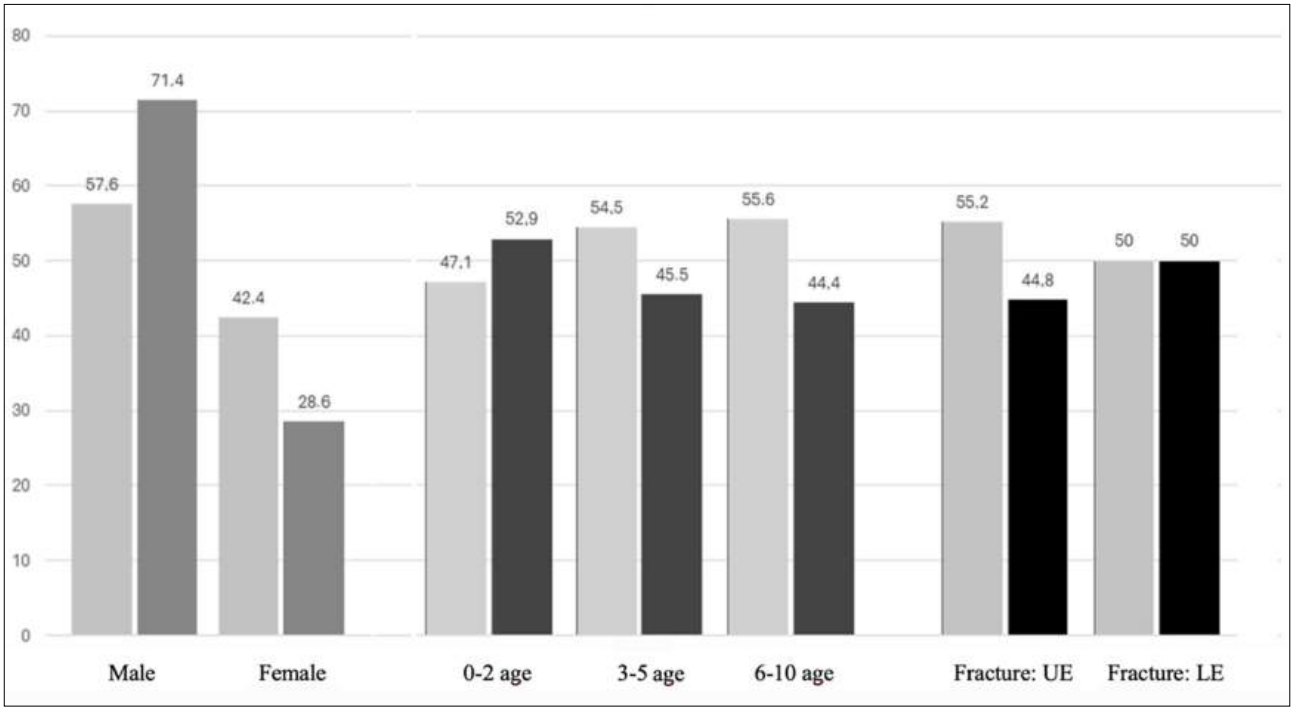


***Figure 1.*** *Evaluation of the patients (in the study groups before and during the pandemic) with fracture complaints according to gender, age ranges, and fracture sites.*

intervention[11]. This may be attributed to heightened interaction and physical activity among children within confined spaces. Crowded living conditions, especially in smaller homes, increase the risk of accidental injuries, such as falls or collisions during play. Additionally, parents may find it more challenging to supervise multiple children simultaneously, making accidents harder to prevent and detect.

Regarding trauma mechanisms, falls were the predominant cause of injuries in both periods[11,14–16]. However, the increase in indoor injuries during the pandemic underscores the need for enhanced safety measures at home. Educating parents on injury prevention and providing safe play areas are essential interventions[17].

In terms of timing, most injuries in both periods occurred in the evening, likely reflecting children's activity patterns and family routines.

The findings of this study also underline the broader implications of the COVID-19 pandemic on pediatric orthopedic care, highlighting not only the shifts in injury patterns but also potential changes in healthcare accessibility and resource allocation. The increased proportion of indoor injuries observed during the pandemic may reflect limited opportunities for outdoor activities and recreational sports, which typically contribute to higher-energy trauma cases such as forearm fractures. This shift emphasizes the importance of targeted injury prevention strategies, particularly within the home environment. Moreover, the rise in male-to-female ratios during the pandemic could be attributed to gender-based differences in activity levels or supervision patterns within households. Future research should explore these sociocultural dynamics further, as understanding such factors could guide public health interventions during future crises. Additionally, while this study focused on surgically treated fractures, it is likely that the pandemic also impacted the prevalence and management of less severe pediatric injuries, which warrants further investigation to capture the pandemic's effect on pediatric trauma care fully.

### *Limitations*

This study's limitations include a relatively small sample size (66 patients pre-pandemic and 56 during the pandemic), which may limit statistical power and generalizability. Additionally, the accuracy of recorded variables such as trauma location and timing could be influenced by recall bias. The lack of long-term follow-up data is another limitation. Future multi-center studies from different geographic regions would enhance the reliability and applicability of these findings.

## Conclusion

The findings of this study provide valuable insights into the impact of the COVID-19 pandemic on pediatric fractures. For pediatric orthopedic practice, these results highlight the importance of developing specific preventive measures for managing indoor injuries during similar crises. Parents should plan indoor activities carefully to ensure safety, while healthcare providers should focus on education and awareness programs.

Future research should explore the long-term effects of pediatric fractures, treatment processes, and effective strategies for injury prevention in the post-pandemic era.

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**ARAŞTIRMA MAKALESİ /** *RESEARCH ARTICLE*

# Investigation of Extended Spectrum Beta Lactamase Frequency in *Escherichia coli* and *Klebsiella pneumoniae* Strains Isolated From Individuals Affected By a Major Earthquake

## *Büyük Depremden Etkilenen Bireylerden İzole Edilen Escherichia coli ve Klebsiella pneumoniae Suşlarında Genişletilmiş Spekturum Beta Laktamaz Sıklığının Araştırılması*

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### ABSTRACT

***Aim:*** *Extended-Spectrum β-Lactamase (ESBL) - producing Escherichia coli (E.coli) and Klebsiella pneumoniae (K.pneumoniae) are threatening pathogens which are more resistant to antibiotics in healthcare settings all around the world. The spread of these pathogens may be triggered by natural disasters such as earthquake and flood.*

***Material and Method:*** *A total of 3129 subjects were included in this study and evaluated retrospectively between January 2023 and July 2024 just before and after a major earthquake. VITEK® 2 compact automatized system was used to identify the strains. Extended-spectrum β-lactamase production was determined by double disc synergy test and combine disc synergy test. VITEK® 2 compact automatized system was used to determine the antibiotic resistance of strains. All statistical analyses were performed using IBM Statistical Package for Social Sciences (SPSS) program. Chi-square test was applied in comparing the variables between the groups. Statistical significance threshold was found to be P value of <0.05.*

***Results:*** *Nine hundred and fifty two E.coli and 355 K.pneumoniae strains were isolated from 3129 clinical samples. The 478 E. coli (50.21%) and 102 K.pneumoniae strains (28.73%) were found to be ESBL-positive. ESBL-producing E.coli strains were mostly resistant to cefuroxime (97.48%), ceftriaxone (84.51%) and 97.05% resistance rate was determined in ESBL-positive K.pneumoniae strains against ceftriaxone.*

***Conclusion:*** *Although ESBL positivity was high in E.coli strains and not significantly different when compared with literature, it was found to be relatively moderate in K.pneumoniae strains. It can be said that despite the major earthquake disaster, these findings are promising.*

**Key words:** *ESBL; E.coli; K.pneumoniae; nosocomials; antibiotic resistance*

### ÖZET

***Amaç:*** *Genişletilmiş spekturum beta laktamaz (GSBL) üreten Escherichia coli (E.coli) ve Klebsiella pneumoniae (K.pneumoniae) türleri dünya genelinde sağlık hizmetleri açısından yüksek oranlarda antibiyotik dirençleri sebebiyle önemli patojenler arasında yer almaktadır. Bu patojenlerin yayılımı deprem ve sel gibi doğal afetler sebebiyle tetiklenebilmektedir.*

***Materyal ve Metod:*** *Bu çalışmaya, büyük depremin hemen öncesi ve sonrasında Ocak 2023 ile Temmuz 2024 tarihleri arasında sağlık kuruluşuna başvuran hastalardan alınan 3129 örnek retrospektif olarak dâhil edilmiştir. Suşların identifikasyonu için VITEK® 2 kompakt otomatize sistem kullanılmıştır. Genişletilmiş spekturum beta laktamaz üretimi çift disk sinerji testi ve kombine disk sinerji testi ile belirlenmiştir. Suşların antibiyotik direnci VITEK® 2 kompakt otomatize sistemle belirlenmiştir. Tüm istatistiksel veriler IBM Sosyal Bilimlerde İstatistik Paket Programı (SPSS) kullanılarak analiz edildi. Gruplar arasındaki değişkenlerin karşılaştırılmasında Ki-kare testi uygulandı. İstatistiksel anlamlılık eşiği P <0,05 olarak belirlendi.*

***Bulgular:*** *Klinik örneklerden izole edilen 3129 mikroorganizmadan 952'sinin E.coli ve 355'inin K.pneumoniae suşu olduğu tespit edilmiştir. E.coli suşlarından 478'i (%50,21) ve K.pneumoniae suşlarından 102'sinin (%28,73) GSBL-pozitif suşlar olduğu belirlenmiştir. GSBL-pozitif E.coli suşlarının çoğunlukla sefuroksim (%97,48), seftriakson (%84,51) dirençli olduğu belirlenirken, GSBL-pozitif K.pneumoniae suşlarının %97,05 oranda seftriakson direnci olduğu bulunmuştur.*

***Sonuç:*** *Genişletilmiş spekturum beta laktamaz pozitifliği E.coli suşlarında yüksek ancak literatürle karşılaştırıldığında anlamlı farklılık göstermemesine rağmen K.pneumoniae suşlarında nispeten orta düzeyde bulundu. Bölgemizde yaşadığımız büyük deprem felaketine rağmen elde edilen bu bulgular, umut vaat edici denilebilir.*

**Anahtar kelimeler:** *GSBL; E.coli; K.pneumoniae; nozokomiyaller; antibiyotik direnci*

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## Introduction

The production of beta-lactamase enzymes in gram-negative bacteria is a major factor contributing to antibiotic resistance. In particular, extended-spectrum beta-lactamases (ESBLs) are enzymes that confer resistance to a wide range of beta-lactam antibiotics and are closely associated with multidrug resistance[1]. ESBL-producing strains of *Escherichia coli* and *Klebsiella pneumoniae* are increasingly implicated in both community-acquired and hospital-acquired infections, significantly diminishing the effectiveness of beta-lactam antibiotics[2]. These pathogens can cause various infections which associated with higher morbidity, increased treatment costs, and prolonged hospital stays[3]. Antimicrobial resistance is a pressing global issue, contributing to an estimated 1.27 million deaths worldwide in 2019[4].

ESBLs were first reported in Germany in 1983[5]. Since then, *E.coli* and *K.pneumoniae* have emerged as prominent ESBL-producing pathogens, especially in healthcare settings[6–8]. While *K.pneumoniae* strains are commonly found in soil, water, and environmental sources, [9] *E.coli* strains are well-known foodborne pathogens[10]. Both are major contributors to community and hospital infections, colonizing mucosal surfaces such as the upper respiratory, gastrointestinal, and urinary tracts[11,12].

These ESBL-producing strains are responsible for a range of infections, including gastroenteritis, urinary tract infections, septicemia, and neonatal meningitis[13,14]. Importantly, the resistance traits can be rapidly transferred to other bacteria via clonal spread and plasmid-mediated conjugation, facilitating outbreaks of resistant strains[15]. Continuous exposure to beta-lactam antibiotics can lead to beta-lactamase overproduction and mutations, resulting in enzymes capable of hydrolyzing penicillins, cephalosporins, and monobactams (e.g., aztreonam), hence the designation "extended-spectrum beta-lactamases"[15,16]. Resistance to oxyimino-cephalosporins and aztreonam in *E.coli* and *K.pneumoniae* due to ESBL production is well documented[17].

Given the increasing resistance rates and the associated clinical challenges, it is essential to monitor the prevalence of ESBL-producing Gram-negative bacteria[18]. This study aims to assess the frequency of ESBL production and resistance profiles of *E.coli* and *K.pneumoniae* strains isolated from various departments of a tertiary care hospital following a major earthquake in our region in February 2023. It was hypothesized that the spread of resistant strains may have increased under the adverse post-disaster conditions.

## Materials and Methods

A total of 3129 clinical samples (blood, urine, wound swab, vaginal swab, sputum, pleural liquid, tracheal aspirate) were collected between the dates Jan 2023 and July 2024 from various departments of a tertiary care hospital and incubated on 5% sheep blood agar and Eosin Methylene Blue (EMB) agar at 35–37°C for 24–48 hours. Conventional methods such as colony morphology, Gram staining, carbohydrate and citrate use, urease test were performed to isolate Enterobacteriaceae. *E.coli* and *K.pneumoniae* strains were identified by Phoenix™ 100 automatized identification system (BD Phoenix System, Beckton Dickinson, USA). Extended-spectrum β-lactamase production was detected by double disc synergy test and combine disc synergy test. Antibiotic resistance profiles of the isolates was tested with VITEK® 2 compact automatized system and the results were evaluated according to European Committee on Antimicrobial Susceptibility Testing (EUCAST) criteria EUCAST 2019[19].

### *Double Disk Synergy Test*

This test was performed on Mueller-Hinton agar (Oxoid) in accordance with the standards of the disk diffusion method. Amoxicillin-clavulanic acid (10+20 μg) disk was placed in the center, and aztreonam (30 μg), ceftazidime (30 μg) and cefotaxime (30 μg) disks were placed on the periphery at a distance of 25 mm from center to center. The results were evaluated after the strains were incubated at 35°C for 18–20 hours. The expansion of the inhibition zones of the antibiotics towards the clavulanic acid disk or the observation of a region where no growth occurred in the area where bacteria grew between the two inhibition zones was interpreted as ESBL-positive.

### *Combine Disc Synergy Test*

Ceftazidime (30 μg) and cefotaxime (30 μg) disks with and without clavulanic acid (10 μg) are placed on Mueller-Hinton medium on which a bacterial suspension of McFarland 0.5 standard density is spread. After incubation at 35°C overnight, the zones of inhibition around the disks with and without clavulanic acid are measured and compared. Strains in which the

zone of inhibition around the combination disks is ≥5 mm wider than the zone of inhibition around the disk without clavulanic acid are considered positive for ESBL production.

This study was approved by Non-invasive Clinical Researches Ethics Committee meeting date 30/10/2024 with the decision number of 11/26. In the study, the relevant provisions of the 1964 Declaration of Helsinki and its later updates and the regulations issued by the Ministry of Health of the Republic of Türkiye were complied with.

### *Statistical Analysis*

All statistical data were analyzed using IBM Statistical Package for Social Sciences (SPSS) program version 23 (IBM Inc., Chicago, IL, USA). Chi-square test was applied in comparing the variables between the groups. Statistical significance threshold was found to be *P* value of <0.05.

## Results

When examined, it was seen that the majority of the isolated pathogens were gram negative bacteria (1954/3129; 62.44%) which followed by gram positive bacteria (923/3129; 29.49%) and *Candida* spp. yeasts (252/3129; 8.05%).

Department of urology was the highest source of isolated microorganisms in total with a number of 753 (24.06%) followed by internal diseases intensive care unit (ICU) (387; 12.36%) and internal diseases various services (381; 12.17%). The distribution of pathogens obtained from various services and ICUs was given in Table 1.

Among the 1954 gram negative bacteria 952 (48.72%) *E.coli* and 355 (18.16%) *K.pneumoniae* strains have been determined. These strains were mostly isolated from urine cultures with a rate of 79.93% for *E.coli* and 58.31% for *K.pneumoniae*. Of the 952 *E.coli* strains, 638 (67.01%) were isolated from female patients and remained 314 (32.99%) from male patients. The number of female patients whom *K.pneumoniae* strains were isolated was 150 (42.25%) and 205 (56.34%) *K.pneuomoniae* strains were isolated from male patients. Four hundred and seventy eight (50.21%) *E.coli* isolates were ESBL-positive and 102 (28.73%) ESBL-producing *K.pneumoniae* strains were determined (Table 2).

***Table 2.*** *The distribution of E.coli and K.pneumoniae strains by clinical specimens*

| Clinical sample | *E.coli* (n) (%) | *K.pneumoniae* (n) (%) |
|---|---|---|
| Urine | 761 (79.93) | 207 (58.31) |
| Wound swab | 121 (12.71) | 48 (13.52) |
| Blood | 51 (5.35) | 35 (9.85) |
| Tracheal aspirate | 7 (0.73) | 42 (11.83) |
| Sputum | 5 (0.52) | 16 (4.51) |
| Other | 7 (0.73) | 7 (1.97) |
| TOTAL | 952 (100) | 355 (100) |

Table 3 presents the distribution of isolated ESBL-positive and ESBL-negative *E.coli* and *K.pneumoniae* strains according to the hospital services and intensive care units from which they were isolated.

A panel of antibiotics has been selected to determine the antibiotic resistance profiles of ESBL (+) and ESBL (-) *E.coli* and *K.pneumoniae* strains by automatized system. Accordingly, ESBL-negative *E.coli* strains

***Table 1.*** *The distribution of pathogens isolated from various departments and ICUs*

| Departments/ICUs | n (%) | Departments/ICUs | n (%) |
|---|---|---|---|
| Department of Urology | 753 (24.06) | Department of General Surgery | 68 (2.17) |
| Internal Diseases ICU | 387 (12.36) | Department of Pediatric Surgery | 68 (2.17) |
| Internal Diseases Various Departments | 381 (12.17) | Department of Plastic, Aesthetic and Reconstructive Surgery | 60 (1.91) |
| Department of Obstetrics and Gynecology | 335 (10.70) | Department of Neurology | 56 (1.78) |
| Department of Orthopedics and Traumatology | 234 (7.47) | Brain and Nerve Surgery ICU | 52 (1.66) |
| Anestesiology and Reanimation ICU | 209 (6.67) | Coronary ICU | 46 (1.47) |
| Department of Infection Diseases | 192 (6.13) | Other (miscellaneous) | 20 (0.63) |
| Surgery ICU | 139 (4.44) | | |
| Department of Dermatology | 129 (4.12) | | |

ICU: intensive care unit.

***Table 3.*** *The distribution of ESBL (+/-) strains isolated from various departments and ICUs*

| Departments / ICUs | ESBL (-) *E.coli* strains. n; % | ESBL (+) *E.coli* strains. n; % | ESBL (-) *K.pneumoniae* strains. n; % | ESBL (+) *K.pneumoniae* strains. n; % |
|---|---|---|---|---|
| Department of Urology | 166; 17.43 | 203; 21.32 | 50; 14.08 | 37; 10.42 |
| Department of Obstetrics and Gynecology | 94; 9.87 | 47; 4.93 | 16; 4.50 | 8; 2.25 |
| Internal Diseases Various Departments | 42; 4.41 | 47; 4.93 | 27; 7.60 | 23; 6.47 |
| Department of Infection Diseases | 32; 3.36 | 40; 4.20 | 15; 4.22 | 8; 2.25 |
| Internal Diseases ICU | 31; 3.25 | 16; 1.68 | 34; 9.57 | 1; 0.28 |
| Department of Pediatric Surgery | 6; 0.63 | 37; 3.88 | – | – |
| Surgery ICU | 10; 1.05 | 13; 1.36 | 20; 5.63 | 3; 0.84 |
| Department of General Surgery | 11; 1.15 | 9; 0.94 | 12; 3.38 | 1; 0.28 |
| Department of Orthopedics and Traumatology | 12; 1.26 | 6; 0.63 | 8; 2.25 | – |
| Anestesiology and Reanimation ICU | 8; 0.84 | 2; 0.21 | 39; 10.98 | – |
| Other | 62; 6.51 | 58; 6.09 | 32; 9.01 | 21; 5.91 |
| p | <0.001 | | <0.001 | |

ICU: intensive care unit.

***Table 4.*** *Antibiotic resistance in ESBL (+/-) E.coli and K.pneumoniae strains*

| ANTIBIOTICS | ESBL (-) *E.coli* (n=474) (%) | ESBL (+) *E.coli* (n=478) (%) | ESBL (-) *K.pneumoniae* (n=253) (%) | ESBL (+) *K.pneumoniae* (n=102) (%) |
|---|---|---|---|---|
| Ampicillin | 248 (52.32) | 476 (99.58) | 253 (100) | 102 (100) |
| AMC | 178 (37.55) | 366 (76.57) | 184 (72.72) | 68 (66.66) |
| Amikacin | 11 (2.3) | 23 (4.81) | 89 (35.17) | 5 (4.9) |
| Ceftazidime | 54 (11.39) | 394 (82.42) | 158 (62.45) | 98 (96.07) |
| Ceftriaxone | 58 (12.23) | 404 (84.51) | 151 (59.68) | 99 (97.05) |
| Cefuroxime | 95 (20.04) | 466 (97.48) | 169 (66.79) | 102 (100) |
| Nitorfurantoin | 25(5.27) | 11 (2.30) | 46 (18.18) | 29 (11.46) |
| SXT | 155 (32.70) | 262 (54.81) | 96 (37.94) | 72 (70.59) |
| TZP | 86 (18.14) | 121 (25.31) | 171 (67.58) | 49 (48.04) |
| Gentamicin | 36 (7.59) | 71 (14.85) | 20 (7.90) | 16 (15.68) |
| Ciprofloxacin | 147 (31.01) | 340 (71.12) | 157 (62.03) | 78 (76.47) |
| Imipenem | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| Meropenem | 0 (0) | 0 (0) | 0 (0) | 0 (0) |

AMC: amoxicillin/clavulanic acid, SXT: trimethoprim/sulfamethoxazol, TZP: piperacillin/tazobactam.

showed the highest resistance to ampicillin, with a rate of 52.32%. These strains were highly susceptible to amikacin (97.2%). The Amoxicillin/clavulanic acid (AMC), Trimethoprim/sulfamethoxazol (SXT), and ciprofloxacin resistance rates of ESBL (-) *E.coli* strains were found to be 37.55%, 32.70%, 31.01%, respectively. On the other hand, the rate of the resistant ESBL (+) *E.coli* strains were higher, as expected, against these antibiotics by 76.57%, 54.81%, and 71.12%, respectively. But higher resistance rates were detected against to ampicillin (99.58%), cefuroxime (97.48%), ceftriaxone (84.51%) and ceftazidime (82.42%). These strains exhibited the highest susceptibility to imipenem and meropenem (100% each), followed by amikacin (95.19%).

Extended-spectrum β-lactamase (-) *K.pneumoniae* strains showed the highest resistance to ampicillin (100%) and amoxicillin-clavulanate (72.72%), followed by piperacillin-tazobactam (67.58%), cefuroxime (66.79%), and ceftazidime (62.45%). Ampicillin

and cefuroxime resistance was 100% in ESBL (+) *K.pneumoniae* isolates. Ceftriaxone and ceftazidime resistance of these isolates were also quite high (97.05% and 96.07, respectively). Extended-spectrum β-lactamase (+) *K.pneumoniae* strains were fully susceptible to carbapenems (100%) and the susceptibility rate was 95.1% against amikacin (Table 4, and Table 5).

***Table 5.*** *Antibiotic resistance in ESBL (+/-) E.coli and K.pneumoniae strains isolated from various ICUs*

| ANTIBIOTICS | ESBL (+) *E.coli* strains isolated from ICUs (n=34) (%) | ESBL (+) *K.pneumoniae* strains isolated from ICUs (n=12) (%) |
|---|---|---|
| Ampicillin | 34 (100) | 12 (100) |
| AMC | 26 (76.47) | 4 (33.33) |
| Amikacin | 2 (5.88) | 0 (0) |
| Ceftazidime | 32 (93.75) | 11 (91.66) |
| Ceftriaxone | 29 (85.29) | 12 (100) |
| Cefuroxime | 34 (100) | 12 (100) |
| Nitrofurantoin | 1 (2.94) | 3 (0.25) |
| SXT | 18 (52.94) | 11 (91.66) |
| TZP | 15 (44.11) | 4 (33.3) |
| Gentamicin | 4 (11.76) | 1 (8.33) |
| Ciprofloxacin | 28 (82.35) | 9 (75) |
| Imipenem | 0 (0) | 0 (0) |
| Meropenem | 0 (0) | 0 (0) |

AMC: amoxicillin/clavulanic acid, SXT: trimethoprim/sulfamethoxazol, TZP: piperacillin/tazobactam.

## Discussion

The treatment of infections caused by Gram-negative enteric bacteria has become increasingly difficult in recent years[20]. ESBL-producing *Escherichia coli* and *K.pneumoniae* are frequently isolated from various infections, particularly in settings with poor healthcare conditions[17,21] and also these strains are more resistant against antibiotics[22].

Gram negative bacteria are leading causes of serious infections with high morbidity and mortality in worldwide[23,24]. These strains can often be isolated from various clinical samples. In a study which conducted by Forouzani and co-workers, it was demonstrated a 64.2% isolation rate for gram negative bacteria[25]. Parmar and co-workers presented a 87.13% isolation rate for gram negative bacteria from clinical specimens in their study. Among these isolates, *E.coli* was the prominent bacterial strain with a 48.4% rate followed by *K.pneumoniae* (13.6%)[26]. In another study conducted in Türkiye, Gürbüz and colleagues analyzed 1.460 clinical samples, of which 69.17% were Gram-negative bacteria. Among these isolates *E.coli* was again the prominent pathogen with a rate of 22.32% followed by *K.pneumoniae* (17.80%)[27]. In our study 3129 subjects were evaluated and the majority of these isolates (1954; 62.44%) were found to be gram negative bacteria in process. The isolation rate was 48.72% for *E.coli* and 18.16% for *K.pneumoniae* strains. *E.coli* strains were most frequently isolated from the urology department, with an isolation rate of 38.76%. Urology service was also the major origin of *K.pneumoniae* strains with an isolation rate of 24.5%. Eighty (8.4%) *E.coli* and 97 (27.32%) *K.pneumoniae* strains were detected in clinical samples obtained from ICUs.

Gram negative bacteria are isolated at different rates from many different clinical samples such as urine, wound, blood, tracheal aspirate and sputum, and etc. However, these pathogens are most commonly isolated from urine specimens, wound swabs and surgical site infections in healthcare settings[28–33]. Ali and co-workers examined the urine specimens and according to their results *E.coli* strains found to be most frequently seen in urine cultures with a rate of 52.6%, they reported. *K.pneumoniae* strains showed an isolation rate of 9.0% in this study[34]. When the results of a study were examined, which conducted in our country, it was reported that 57.61% of the *E.coli* strains were isolated in urine samples taken from ICUs. In the same study, it was stated that 47.15% of *E.coli* and 43.38% of *K.pneumoniae* strains were grown in the urine cultures of patients receiving treatment in inpatient services[35]. In a study in Türkiye performed by Avciküçük and Altin, it was investigated that the gram positive and gram negative bacterial strains isolated from urine cultures and the isolation rates of *E.coli* and *K.pneumoniae* strains were given as 70.4% and 12.4% respectively[36]. In our study it was determined the majority of urinary isolates were *E.coli*, compatible with literature, but with a higher prevalence (79.93%). *K.pneumoniae* was second most common bacterial pathogen isolated from urinary samples with a rate of 58.31%.

Wound and surgical site infections (SSIs) are the important source of gram negative bacterial growth in healthcare settings. SSIs are the second most prevalent nosocomial infections, representing around 25% of all hospital-acquired infections[37]. Wounds provide a suitable environment for pathogens[38]. Gram negative bacteria can easily grow in the wound in suitable

conditions and effect deeper tissues[39]. Various studies have reported that gram-negative bacteria are frequently isolated from wound infections. Watanabe and co-workers have demonstrated 105 gram negative bacteria isolated from 227 blood cultures (46.25%) in their study[40]. In a study it was shown a 62% rate of gram negative bacteria isolated from wound swabs. Among these strains the rate of *K.pneumoniae* isolates was 13.9% and 12.6% for *E.coli* have been determined[41]. The prevalences of *K.penumoniae* and *E.coli* strains isolated from superficial incisional surgical site infections were 39.58% and 29.17%, respectively, have been reported in a study which performed by Ali and Al-Jaff[42]. Tanriverdi Çayci and co-workers determined 65.1% isolation rate for gram negative bacteria isolated from wound swabs between 2015 and 2017[43]. *E.coli* was found to be the dominant microorganism and 20.5% isolation rate for *E.coli* has been given. The rate of isolated *K.pneumoniae* strains was 9.8% and the frequency of *K.pneumoniae* and *E.coli* isolated from wound swabs was found to be 13.52% and 12.71, respectively, in this study[43].

In recent years, both the World Health Organization (WHO) and the United States Centers for Disease Control and Prevention (CDC) have closely monitored antibiotic resistance in Enterobacterales species producing ESBLs. According to the WHO's Global Antimicrobial Resistance and Use Surveillance System (GLASS), as of 2022, 27.4% of bloodstream infections caused by *E.coli* were reported to be resistant against third-generation cephalosporins. This incidence is even higher in low- and middle-income countries. Another comprehensive surveillance initiative established by the WHO, known as the "Tricycle Protocol," adopts a multi-sectoral approach to monitor ESBL-producing organisms in humans, animals, and the environment. Data obtained through this protocol revealed that the carriage rate of ESBL-producing *E.coli* in human fecal samples exceeded 40% in regions such as Southeast Asia and Africa[44].

According to the CDC's *Antibiotic Resistance Threats Report* published in 2019, an estimated 197.400 infections caused by ESBL-producing *E.coli* occur annually in the United States, with approximately 9.100 of these resulting in death. Furthermore, the CDC highlighted the increasing trend of healthcare-associated infections due to ESBL-producing organisms and recommended enhanced active surveillance and stricter infection control measures targeting these pathogens. These findings emphasize the urgent need for continuously updated, strengthened, and globally coordinated strategies for the surveillance and control of antibiotic-resistant bacteria[45].

It is well known that the ESBLs existence in gram negative bacteria lead multi drug resistance against various antibiotics. Dramatical increase in bacterial resistance can easily be detected by time in worldwide and also in Türkiye. Bedzichowska and co-workers investigate the prevalence of ESBL positivity in *K.pneumoniae* and *E.coli* strains in a five year period. Among the pediatric patients, ESBL (+) *E.coli* and *K.pneumoniae* strains were prominent pathogens with 43.5% and 36.9%, respectively in their study[46]. It was reported the ESBL frequency in *E.coli* strains by 8.09% between 1996–2001, 10.61% between 2002–2007, and 28.17% between 2007–2012 in studies performed in Türkiye[47]. One more study performed by Şenol and co-workers, presented the ESBL existence in gram negative bacteria with a rate of 60% in 2021[29]. Bayraktar and co-workers demonstrated a 35% ESBL frequency in *E.coli* and 31% in *K.penumoniae* strains which isolated from blood cultures in a three year period in their study[48]. Extended-spectrum β-lactamase positivity was found to be 48% in *E.coli* and 67% in *K.pneumoniae* strains in another study which performed by Parlak and co-workers[49]. Onuk and co-workers have reported a 66.7% ESBL positivity in *E.coli* strains and 30.0% in *K.pneumoniae* strains isolated from various ICUs in their study[50]. Due to lack of sanitation and hygiene after major earthquake in our region, we aimed to assess the prevalence of ESBL-producing *E.coli* and *K.pneumoniae* strains during the study, even it was monocentric. So, it was determined a 50.21% ESBL positivity in *E.coli* and 28.73% in *K.pneumoniae* isolates. This result is promising despite adverse conditions, although a few studies from our country have reported higher ESBL frequencies in the post-earthquake period. For example, in a recent study which performed by Bursal and co-workers the frequency of ESBL positivity in *E.coli* and *K.pneumoniae* strains isolated from urinary tract infections were presented as 41.4% and 53.2% respectively, by a reflection of a single centric research on post-earthquake period in our country[51]. Akineden and co-workers showed a 47.63% ESBL positivity in *E.coli* strains. They indicated 61.16% rate for ESBL existence in *K.pneumoniae* strains isolated from various clinical specimens in a tertiary care hospital recently[52]. The distribution of

ESBL-positive *E.coli* and *K.pneumoniae* strains by clinics is presented in the Table 3 ($p$= <0.001).

Since ESBL-producing Enterobacteriaceae present multi-drug resistance, it is crucial to well documented the antibiotic resistance profiles of isolated strains. In several studies it was reported various resistance rates for ESBL (+) *E.coli* and *K.pneumoniae*. In this context, Garba and co-workers have demonstrated the resistance patterns of ESBL (+) *E.coli* and *K.pneumoniae* strains isolated from clinical specimens. Accordingly, the higher resistance in these strains was against ciprofloxacin (94.1% and 94.0%, respectively), SXT (83.4% and 89.7%, respectively) and TZP (68.0% and 76.9%, respectively)[53]. Although it is a one of the first line antibiotic choice in empirical treatment option, nitrofurantoin resistance in especially ESBL-producing *K.pneumoniae* strains was alarming with 74.4%[54]. As known the gram negative bacteria isolated from ICUs are more resistant when compared with non-ICU strains, so it would be better to investigate the resistance rates of gram negative bacteria isolated from ICUs and non-ICUs separately. Wani and co-workers showed a high prevalance of nitrofurantoin resistance (71.6%) in gram negative bacteria isolated from ICU patients[55]. Nitrofurantion resistance in inpatient services was 2.09% and 25.49% for ESBL (+) *E.coli* and *K.pneumoniae* strains, respectively. The similar findings were obtained in terms of nitorfurantoin resistance in ESBL (+) *E.coli* and *K.penumoniae* strains isolated from ICUs (2.09% and 25, respectively) in our study. The highest resistant rates for ICUs strains were against ceftazidime (93.75% in ESBL (+) *E.coli* and 91.66% in ESBL (+) *K.pneumonia*), ceftriaxone (85.29% in ESBL (+) *E.coli* and 100% in ESBL (+) *K.pneumonia*), and SXT (52.94% in ESBL (+) *E.coli* and 91.66% in ESBL (+) *K.pneumonia*) we found. In ESBL (+) non-ICUs *E.coli* strains and *K.pneumoniae* strains, the resistance against ceftriaxone was 77.82% and 85.29%, respectively, in our study. Imipenem was the most effective antibiotic agent against both ICUs and non-ICUs ESBL (+/-) *E.coli* and *K.pneumoniae* strains (100% for both) followed by amikacin (between 0% – 5.88% for all ESBL (+) *E.coli* and *K.pneumoniae* strains). The data obtained from various clinical studies performed in Türkiye was compatible with our results. Coşkun and co-workers have demonstrated that ESBL (+) *E.coli* and *K.pneumoniae* isolates were mostly resistant against ampicillin-sulbactam (80.3% and 85.2% respectively). These strains were completely susceptible against amikacin and imipenem[54]. Aydoğmuş and co-workers indicated no resistance against imipenem and meropenem among isolated ESBL (+) *E.coli* and *K.pneumoniae* strains in their study. They have determined that these isolates were completely resistant against ceftriaxone (100%)[56].

The antimicrobial resistance patterns of gram negative bacteria isolated from blood cultures were given in a recent study performed by Öner and co-workers. According to their findings the ceftazidime resistance was 60.3% and 84.2%, ciprofloxacin resistance was 55.7% and 77.1%, SXT resistance was 48.7% and 56.1% for *E.coli* and *K.pneumoniae*, respectively. The most effective antibiotic was found to be amikacin in this study (susceptibility rates were 85.6% for *E.coli* and 68.7% for *K.pneumoniae*)[57].

Keskin and co-workers demonstrated the antibiotic resistance in *E.coli* and *K.pneumoniae* strains isolated from urinary tract infections and the resistance of *E.coli* isolates against imipenem, amikacin, gentamicin, nitrofurantoin, piperacallin/tazobactam (TZP), ciprofloxacin, amoxicillin/clavulanic acid (AMC), cefuroxime, trimethoprim/sulfamethoxazol (SXT), ampicillin was reported as; 0.1% (0.1–1.3), 2.2% (1.9–6.3), 13.1% (12.4–25), 2.3% (2.2–3.8), 13.6% (13.3–18.8), 26.3% (25.3–42.5), 29.4% (28.8–40), 37.2% (35.7–62.5) 34.8% (33.9–49.4), 61.7% (60.9–74.4), respectively. These rates were given as; 10.3% (5.8–43.2) against imipenem, 10.6% against amikacin, 27.9% against gentamicin, 25.3% against TZP, 22.8% against ciprofloxacin, 44.4% against AMC, 46.6% against cefuroxime, and 41.6% against SXT in *K.pneumoniae* strains[58]. In compatibility with the antibiotic panel of this study, to compare our findings were as follows; in ESBL-producing *E.coli* isolates the resistance rate against ampicillin was 99.58%, AMC was 76.57%, amikacin was 4.81%, ceftazidime was 82.42%, ceftriaxone was 84.51%, cefuroxime was 97.48%, nitrofurantoin was 2.30%, SXT was 54.81%, TZP was 25.31%, gentamicin was 14.85%, ciprofloxacin was 71.12%, and imipenem was 0%. The resistance rates in ESBL-producing *K.pneumoniae* isolates were as follows; ampicillin (100%), AMC (66.66%), amikacin (4.9%), ceftazidime (96.07%), ceftriaxone (97.05%), cefuroxime (100%), nitrofurantoin (11.46%), SXT (70.59%), TZP (48.04%), gentamicin (15.68%), ciprofloxacin (76.47%), and imipenem (0%).

## Conclusion

Treatment of infections caused by gram negative bacteria should be based on rational use of antibiotics in healthcare settings. In our study, it was determined high resistance against third generation cephalosporins, ciprofloxacin, and SXT as reported in various studies in Türkiye. Nitrofurantoin serves as an effective antimicrobial choice against ESBL (+) *E.coli* and *K.pneumoniae* strains isolated from both inpatient services and ICUs. Despite the high prevalence of these strains and the lack of sanitation and hygiene following the major earthquake in our region in February 2023, the observed ESBL frequency was consistent with the literature and considered promising. It should be considered that poor living conditions, malnutrition, psychogenic stress factors and change in demographic structure may also trigger these infections in process. Extended-spectrum beta-lactamase production significantly contributes to antimicrobial resistance in *E.coli* and *K.pneumoniae*, leading to limited treatment options and increased morbidity. The frequency of ESBL-producing strains directly influences resistance patterns, making it a critical concern in healthcare settings. To mitigate this issue, several strategies can be implemented in clinical practice. These include strict adherence to infection control measures, routine surveillance of resistance patterns, antimicrobial stewardship programs to reduce inappropriate antibiotic use, and the use of rapid diagnostic tools for early detection. Additionally, clinicians should consider local resistance data when selecting empirical therapies to ensure effective treatment. Ultimately, a multifaceted approach is essential to control the spread of ESBL-producing pathogens and to optimize patient outcomes.

### *Ethical Approvement*

This study was approved by Hatay Mustafa Kemal University Non-invasive Clinical Researches Ethical Committee with a meeting date on 30.10.2024 and decision number of 11–26.

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**ARAŞTIRMA MAKALESİ /** *RESEARCH ARTICLE*

# Hospitalized Recurrent Deep Vein Thrombosis: Demographic, Clinical, and Laboratory Insights from a Single-Center Retrospective Study

*Hastaneye Yatırılan Reküren Derin Ven Trombozlu Hastalarda: Tek Merkezli Retrospektif Bir Çalışmadan Demografik, Klinik ve Laboratuvar Bilgileri*

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## ABSTRACT

***Aim:*** *This study aimed to analyze the demographic, clinical, and laboratory characteristics of hospitalized patients with recurrent deep vein thrombosis (rDVT) and to identify associated risk factors and treatment outcomes.*

***Material and Methods:*** *A retrospective review was conducted on 45 patients hospitalized with rDVT between October 2021 and October 2023. Patients with active cancer, hematological or rheumatological diseases, immunosuppression, or organ failure were excluded. Demographic data, clinical characteristics, venous Doppler imaging, and emergency laboratory results were analyzed. Patients were grouped based on proximal or distal thrombus location, infection burden, and hospital length of stay. Statistical analyses included Student's t-test, Mann-Whitney U test, and Spearman correlation.*

***Results:*** *The median age of the study population was 72 years, with a higher prevalence in males (55.6%). Key risk factors included major surgery within two years (40%), diabetes mellitus (37.8%), and hormone replacement therapy (22.2%). Proximal thrombus was identified in 51% of patients, with males predominantly affected, while females showed higher rates of distal thrombus. Median hospital stay was five days, and longer stays were associated with elevated inflammatory markers, including CRP and uric acid levels. A significant correlation between D-dimer and uric acid was observed (r=0.40, p=0.005). Dual therapy with low molecular weight heparin and rivaroxaban was more common in proximal thrombus cases.*

***Conclusion:*** *This study highlights the distinct clinical and laboratory characteristics of hospitalized rDVT patients, with gender– and location-specific differences influencing management strategies. The positive correlation between D-dimer and uric acid suggests a potential role of uric acid as a biomarker in resource-limited settings. Further research is warranted to address the genetic and hereditary aspects of rDVT.*

**Key words:** *recurrent deep vein thrombosis; risk factors; thrombus location; anticoagulation therapy; laboratory biomarkers*

## ÖZET

***Amaç:*** *Bu çalışmada hastanede yatan tekrarlayan derin ven trombozlu (rDVT) hastaların demografik, klinik ve laboratuvar özelliklerinin analiz edilmesi ve ilişkili risk faktörlerinin ve tedavi sonuçlarının belirlenmesi amaçlanmıştır.*

***Gereç ve Yöntemler:*** *Ekim 2021 ve Ekim 2023 tarihleri arasında rDVT ile hastaneye yatırılan 45 hasta üzerinde retrospektif bir inceleme yapıldı. Aktif kanser, hematolojik veya romatolojik hastalıklar, immünosüpresyon veya organ yetmezliği olan hastalar çalışma dışı bırakıldı. Demografik veriler, klinik özellikler, venöz Doppler görüntüleme ve acil laboratuvar sonuçları analiz edildi. Hastalar proksimal veya distal trombüs yerleşimi, enfeksiyon yükü ve hastanede kalış süresine göre gruplandırıldı. İstatistiksel analizler Student's t-testi, Mann-Whitney U testi ve Spearman korelasyonunu içeriyordu.*

***Sonuçlar:*** *Çalışma popülasyonunun medyan yaşı 72 idi ve erkeklerde daha yüksek bir prevalans vardı (%55,6). Temel risk faktörleri arasında iki yıl içinde geçirilmiş büyük cerrahi (%40), diabetes mellitus (%37,8) ve hormon replasman tedavisi (%22,2) vardı. Hastaların %51'inde proksimal trombüs tespit edilmiş olup, bu durumdan ağırlıklı olarak erkekler etkilenirken, kadınlarda daha yüksek oranda distal trombüs görülmüştür. Medyan hastanede kalış süresi beş gündü ve daha uzun kalış süresi CRP ve ürik asit düzeyleri dâhil olmak üzere yüksek enflamatuvar belirteçlerle ilişkiliydi. D-dimer ile ürik asit arasında anlamlı bir korelasyon gözlenmiştir (r=0,40, p=0,005). Düşük molekül ağırlıklı heparin ve rivaroksaban ile ikili tedavi proksimal trombüs olgularında daha yaygındı.*

***Sonuç:*** *Bu çalışma, hastanede yatan rDVT hastalarının farklı klinik ve laboratuvar özelliklerini vurgulamakta ve cinsiyet ile bölgeye özgü farklılıkların yönetim stratejilerini etkilediğini göstermektedir. D-dimer ve ürik asit arasındaki pozitif korelasyon, ürik asidin kaynakların sınırlı olduğu ortamlarda bir biyobelirteç olarak potansiyel rolüne işaret etmektedir. RDVT'nin genetik ve kalıtsal yönlerini ele almak için daha fazla araştırma yapılması gerekmektedir.*

**Anahtar kelimeler:** *tekrarlayan derin ven trombozu; risk faktörleri; trombüs yerleşimi; antikoagülasyon tedavisi; laboratuvar biyobelirteçleri*

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## Introduction

Deep vein thrombosis (DVT) is a significant global public health concern that can lead to serious complications, particularly pulmonary embolism. When delays in diagnosis and treatment occur, especially in emergency departments, DVT can result in severe outcomes associated with high mortality and morbidity rates[1]. The annual global incidence of DVT is approximately 1.6–1.8 cases per 1000 individuals, varying based on age, sex, and other individual risk factors[2]. Deep vein thrombosis is not only critical in its initial occurrence but also due to its recurrent nature. Recurrent DVT (rDVT) complicates treatment and leads to long-term health issues. Studies have demonstrated that the inability to control underlying risk factors significantly increases the recurrence rates of thromboembolism, thereby substantially elevating mortality risk[1,3].

Deep vein thrombosis is a venous thromboembolic disease that manifests with unilateral leg pain, swelling, redness, edema, increased warmth, and tenderness in the affected extremity[4]. Following an initial DVT episode, rDVT may occur in a provoked or unprovoked manner. Provoking factors include major surgery (operations lasting more than 30 minutes), prolonged immobility or hospitalization for three or more days, hormone replacement therapy, active cancer, chronic inflammatory diseases, chronic cardiac diseases, pregnancy, and genetic predisposition[5]. Despite appropriate and sufficient anticoagulant therapy, approximately one-quarter of primary DVT cases experience recurrent DVT within five years[6]. Early prediction of rDVT risk emphasizes the integration of clinical characteristics such as patient age, sex, and thrombus location with laboratory and imaging findings[7]. The primary challenge in managing recurrent DVT lies in distinguishing whether the current symptoms stem from an exacerbation of post-thrombotic syndrome or a newly developed venous thrombosis[8].

To address this issue, our study aims to evaluate rDVT as an isolated disease, excluding venous thromboembolism-related DVT-pulmonary embolism relationships. This study seeks to generate a comprehensive dataset solely focused on rDVT by analyzing the demographic characteristics, risk factors, clinical follow-up, treatment processes, and emergency department laboratory results of hospitalized rDVT patients, as opposed to those managed with outpatient treatment.

## Materials and Methods

### *Study Design and Patient Selection*

This retrospective study was conducted with the approval of the Nigde Omer Halisdemir University Ethics Committee (approval date and protocol number: 2024/01-29). Patients who presented to the emergency department between October 1, 2021, and October 1, 2023, and were assigned venous thrombosis-related ICD codes (I82, I82.1, I82.8, and I82.9) were identified through the hospital records and automation system (KARMED). The epicrisis files of these patients were reviewed, and those hospitalized with a diagnosis of rDVT were included in the study. Patients with active cancer, those undergoing chemotherapy, individuals with known hematological and/or rheumatological diseases, immunocompromised patients, those with renal or hepatic failure, and individuals with conditions that could adversely affect coagulation and clotting parameters or alter DVT outcomes were excluded from the study. Additionally, patients with missing data or an unconfirmed diagnosis of rDVT were also excluded. Initially, 358 patients were screened based on ICD codes, and after applying inclusion and exclusion criteria, 45 patients were included in the final analysis (Fig. 1).

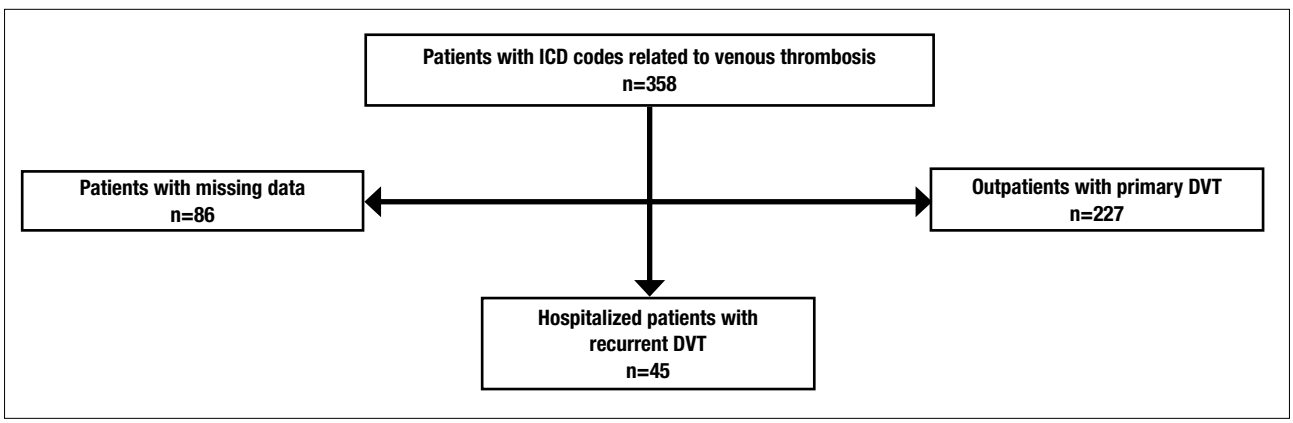


***Figure 1.*** *Distribution of patients diagnosed with deep vein thrombosis (DVT).*

### Variable Selection and Data Collection

***Demographic Characteristics and Risk Factors:*** Data were collected on gender, age, and risk factors for DVT (previous major surgery, diabetes mellitus [DM], coronary artery disease [CAD], and hormone replacement therapy).

***Imaging and Treatments:*** Venous Doppler ultrasonography (USG) results were categorized into proximal (femoral) and distal (popliteal) thrombosis. Treatment approaches were classified as monotherapy (low-molecular-weight heparin) or dual therapy (low-molecular-weight heparin + rivaroxaban).

***Hospitalization:*** Length of hospital stay (in days) was categorized based on the median duration: ≥median as "long stay" and <median as "short stay.

***Infection Burden:*** Patients were grouped based on median C-reactive protein (CRP) levels: ≥median as "high infection burden" and <median as "low infection burden."

***Emergency Department Laboratory Data:*** Hematological and Coagulation Parameters: D-dimer, platelet count (PLT), mean platelet volume (MPV), red cell distribution width (RDW), and international normalized ratio (INR).

Inflammatory and Biochemical Markers: CRP, white blood cell (WBC) count, hemoglobin (Hb), neutrophil count, blood urea nitrogen (BUN), creatinine, alanine aminotransferase (ALT), aspartate aminotransferase (AST), calcium (Ca), sodium (Na), potassium (K), and albumin levels were analyzed.

### Statistical Analysis

Categorical variables were presented as frequency and percentage. Uric acid, MPV, Hb, Ca, and K were presented as mean ± SD, while other continuous variables were expressed as median and interquartile range (IQR 25–75). Student's t-test, Mann-Whitney U test, One-Way ANOVA, and Kruskal-Wallis test were used to examine the relationships between continuous and categorical variables. The relationships between categorical variables were analyzed using Chi-square and/or Fisher's exact test. Spearman correlation analysis was applied to examine the correlation between D-dimer and uric acid, blood urea nitrogen, RDW, age, WBC, and INR. Additionally, linear regression analysis was conducted between uric acid and MPV. Statistical analyses were performed using IBM Statistical Package for Social Sciences (SPSS) program for Windows, version 27.0 (IBM Corp., Armonk, NY, USA). A p-value of <0.05 was considered statistically significant.

## Results

### Demographic and Descriptive

Data A total of 45 patients (25 males, 55.6%; 20 females, 44.4%) were included in the study. The median age of the patients was 72 years (IQR: 58.5–82), with a median age of 74 years in males and 68 years in females. Among the risk factors, 18 patients (40%) had a history of major surgery within the past two years, 17 patients (37.8%) had DM and/or CAD, and 10 patients (22.2%) had a history of hormone replacement therapy. Venous Doppler ultrasonography detected femoral vein thrombosis in 23 patients (51%) and popliteal vein thrombosis in 22 patients (49%). Thirty-three patients (73%) experienced rDVT while on anticoagulant therapy. After hospitalization, 29 patients (64.4%) received dual therapy, whereas 16 patients (35.6%) were treated with monotherapy. The median hospital stay was 5 days, with 26 patients (57.8%) hospitalized for 5 days or longer. A total of 23 patients (51.1%) had a CRP level at or above the median value of 25.2 (Table 1). Emergency laboratory results of the patients are shown in Table 2.

***Table 1.*** *Demographic and descriptive characteristics of patients*

| Variables | | N=45 % |
|---|---|---|
| Age, IQR (25–75) | | 72 (58.5–82) |
| **Gender** | | |
| | Male | 25 (55.6) |
| | Female | 20 (44.4) |
| **Risk factors** | | |
| | Surgical intervention | 18 (40) |
| | Comorbid diseases | 17 (37.8) |
| | Hormone replacement | 10 (22.2) |
| **Location of thrombosis** | | |
| | Femoral | 23 (51) |
| | Popliteal | 22 (49) |
| **Active anticoagulant use** | | |
| | Yes | 33 (73) |
| | No | 12 (27) |
| **Treatment** | | |
| | LMWH | 29 (64.4) |
| | LMWH+Rivaroxaban | 16 (35.6) |
| **Length of hospital stay** | | |
| | Long | 26 (57.8) |
| | Short | 19 (42.2) |
| **Infection burden** | | |
| | High | 23 (51) |
| | Low | 22 (49) |

* shown as median, IQR: inter quartile range, LMWH: low molecular weight heparin.

***Table 2.*** *Emergency department laboratory results of patients*

| Parameters | Results |
|---|---|
| D-dimer, ng/mL (IQR) | 2592 (1213–8075) |
| Uric acid, mg/dl ± SD | 6.19±2.16 |
| INR (IQR) | 1.11 (1.03–1.25) |
| PLT, $10^3$/mcL (IQR) | 215 (173.5–278.5) |
| MPV, fL ± SD | 10.55±1.12 |
| RDW, % (IQR) | 14.8 (13.7–16.55) |
| CRP, mg/L (IQR) | 25.2 (9.2–86.35) |
| WBC, $10^3$/uL (IQR) | 9.83 (7.56–13.42) |
| Hb, g/dL ± SD | 12.66±2.4 |
| Neutrophil, $10^3$/mcL (IQR) | 7.73 (5.35–11) |
| Urea, mg/dl (IQR) | 44 (31.5–64.5) |
| Creatine, mg/dl (IQR) | 0.9 (0.7–1.16) |
| ALT, U/L (IQR) | 15 (11.5–28) |
| AST, U/L (IQR) | 22 (18–32) |
| Ca, mg/dl ± SD | 8.74±0.56 |
| Na, mmol/L (IQR) | 139 (136–141) |
| K, mmol/L ± SD | 4.32±0.63 |
| Albumin, g/L (IQR) | 38 (33–42) |

IQR: inter quartile range, SD: standard deviation, INR: international normalized ratio, PLT: platelet, MPV: mean platelet volume, RDW: red cell distribution width, CRP: C-reactive protein, WBC: white blood cell, Hb: hemoglobin, ALT: alanine aminotransferase, AST: aspartate aminotransferase, Ca: calcium, Na: sodium, K: potassium.

### *Gender*

rDVT due to hormonal therapy was more common in females than in males. In contrast, the presence of DM and/or CAD posed a higher risk for rDVT in males (p<0.001). Femoral vein thrombosis was more frequent in males, whereas popliteal vein thrombosis was more common in females (p=0.002). Females were predominantly treated with LMWH, whereas males received a combination of LMWH and rivaroxaban (p=0.002). The median D-dimer level (p<0.001) and mean uric acid level (p=0.026) were significantly higher in males than in females (Table 3).

***Table 3.*** *Statistically significant results between genders*

| Variables | Female (n=20) | Male (n=25) | p |
|---|---|---|---|
| DM ± CAD | 4 (7.6) | 13 (9.4) | <0.001[a] |
| Hormone replacement | 10 (4.4) | 0 (5.6) | |
| Femoral thrombosis | 5 (10.2) | 18 (12.8) | 0.002[a] |
| Popliteal thrombosis | 15 (9.8) | 7 (12.2) | |
| LMWH | 12 (7.1) | 4 (8.9) | 0.002[a] |
| LMWH+Rivaroxaban | 8 (12.9) | 21 (16.1) | |
| D-dimer Mean Rank | 11.28 | 32.38 | <0.001[b] |
| Uric acid Mean ± SD | 5.4±1.83 | 6.82±2.23 | 0.026[c] |

[a] categorical variables are given as observed (expected) using the Chi-square test, [b] Mann-Whitney U test, [c] Student's t-test, LMWH: low molecular weight heparin, DM: diabetes mellitus, CAD: coronary artery disease, SD: standard deviation.

### *Thrombus Location and Risk Factors*

Patients with femoral vein thrombosis were more frequently treated with dual therapy (p=0.048). These patients were older than those with popliteal vein thrombosis (p=0.024) and had higher median D-dimer levels (p<0.001). Patients with a history of major surgery or DM and/or CAD were older than those who had rDVT due to hormone replacement therapy (p<0.001). Popliteal vein thrombosis was more common in patients undergoing hormone replacement therapy (p=0.012). D-dimer levels were significantly higher in patients with a history of surgery (p=0.014) and DM and/or CAD (p=0.002) compared to those undergoing hormone replacement therapy (Table 4).

***Table 4.*** *Significant results according to thrombus location and risk groups*

| Variables | Femoral (n=23) | Popliteal (n=22) | Hormone (n=10) | Comorbid (n=17) | Surgical (n=18) | p |
|---|---|---|---|---|---|---|
| Monotherapy | 5 (8.2) | 11 (7.8) | | | | 0.048[a] |
| Double therapy | 18 (14.8) | 11 (14.2) | | | | |
| Hormone replacement | 1 (5.1) | 9 (4.9) | | | | 0.012[a] |
| DM ± CAD | 10 (8.7) | 7 (8.3) | | | | |
| Major surgery | 12 (9.2) | 6 (8.8) | | | | |
| Age mean rank | 27.3 | 18.5 | | | | 0.024[b] |
| D-dimer mean rank | 30.33 | 15.34 | | | | <0.001[b] |
| Age average rank | | | 8.4 | 27.18 | 27.17 | 0.001[c] |
| D-dimer average rank | | | 10.30 | 28.41 | 24.94 | 0.014[1]/0.002[2] [c] |

[a] categorical variables are given as observed (expected) using the Chi-square test, [b] Mann-Whitney U test, [c] Kruskal-Wallis test, [1] surgical intervention-hormone replacement, [2] comorbid diseases-hormone replacement, DM: diabetes mellitus, CAD: coronary artery disease.

***Table 5.*** *Relationship of laboratory results with infection burden, length of hospital stay and treatment protocols*

| Parameters | High infection (n=23) | Low infection (n=22) | Long stay (n=26) | Short stay (n=19) | Mono therapy (n=16) | Double therapy (n=29) | p |
|---|---|---|---|---|---|---|---|
| INR Mean Rank | 27.7 | 18.09 | 27.6 | 16.71 | | | 0.014[1]/0.006[2 a] |
| ALT Mean Rank | 27.11 | 18.7 | | | | | 0.032[a] |
| Uric acid Mean ± SD | 6.95±2.33 | 5.4±1.67 | | | 5.37±1.9 | 6.64±2.19 | 0.014[3]/0.049[4 b] |
| Ca Mean ± SD | 8.57±0.59 | 8.91±0.49 | | | | | 0.046[b] |
| Urea Mean Rank | | | 27.4 | 16.97 | | | 0.008[a] |
| D-dimer Mean Rank | | | | | 13.91 | 28.02 | <0.001[a] |

[a] Mann-Whitney U test, [b] Student's t-test, [1] Infection-INR, [2] Hospital stay-INR, [3] Infection-Uric acid, [4] Therapy-Uric acid, INR: international normalized ratio, ALT: alanine aminotransferase, Ca: calcium, SD: standard deviation.

***Table 6.*** *Correlation and lineer regression analysis*

| | | Uric acid | Urea | RDW | Age | WBC | INR |
|---|---|---|---|---|---|---|---|
| D-dimer (N=45) | r* | 0.40 | 0.357 | 0.328 | 0.327 | 0.317 | 0.300 |
| | p | 0.005 | 0.016 | 0.028 | 0.028 | 0.034 | 0.045 |
| Dependent variable | Constant | B | SE | %95 CI | | R | p |
| MPV | Uric acid | 9.53 | 0.49 | 8.54–10.52 | | 0.318 | <0.001 |

* Spearman correlation coefficient, SE: standard error, CI: confidence interval, RDW: red cell distribution width, WBC: white blood cell, INR: international normalized ratio, MPV: mean platelet volume.

### *Infection Load, Hospital Stay, and Treatment Groups*

In patients with a high infection load, INR (p=0.014), ALT (p=0.032), and uric acid levels (p=0.014) were significantly higher, while calcium levels were lower (p=0.046). Patients with a longer hospital stay had significantly higher urea (p=0.008) and INR (p=0.006) levels compared to those with a shorter hospital stay. Patients receiving dual therapy had significantly higher median D-dimer levels (p<0.001) and mean uric acid levels (p=0.049) than those receiving monotherapy (Table 5).

### *Correlation and Regression Analyses*

A moderate positive correlation was observed between D-dimer and uric acid levels (r=0.40, p=0.005). There was a weak positive correlation coefficient in the linear regression analysis between uric acid and MPV levels. Additionally, weak correlations were found between D-dimer and urea (r=0.357, p=0.016), RDW (r=0.328, p=0.028), age (r=0.327, p=0.028), WBC (r=0.317, p=0.034), and INR (r=0.300, p=0.045) (Table 6).

## Discussion

rDVT is a complex clinical entity where the interplay of patient-specific risk factors, thrombus location, laboratory parameters, and tailored treatment strategies plays a pivotal role in guiding effective management and improving prognostic outcomes.

Although the exact cause is unknown, the risk of rDVT is 2 to 4 times higher in men than in women[9]. Similarly, in our study, there was a predominance of male patients. While some literature suggests that the incidence of rDVT increases particularly in patients over the age of 65, another perspective argues that aging has an adverse effect only on the development of DVT and that its impact on rDVT remains unclear[10,11]. According to our results, there is a positive correlation between age and rDVT. The decrease in physical activity and the higher prevalence of comorbid conditions with advancing age may explain this finding.

Individuals with a history of DVT have a 30–40% probability of experiencing rDVT within ten years after the initial diagnosis[12]. Acquired or hereditary risk factors for rDVT include immobilization, genetic conditions such as protein S deficiency, major surgery, estrogen-containing hormone therapies, obesity, chronic inflammatory diseases, atrial fibrillation, CAD, and hypertension[13–15]. Since our study was retrospectively designed, data regarding patients' genetic factors, hereditary risk factors, and body mass index were not accessible. However, our analysis identified hormone replacement therapy as a significant risk factor for rDVT in women, while DM and CAD were significant risk factors in men. This finding may be explained by hormone supplementation in premenopausal or menopausal women, whereas in men, the presence of DM and CAD, which increase in incidence with age, contributes to chronic inflammatory processes.

Additionally, the median age of male patients was higher than that of female patients.

Al Yami et al. found that proximal DVT localization was more common in rDVT patients. They also noted that proximal DVT localization was more frequently observed in men[16]. Hansson et al. identified proximal vein thrombosis localization as an independent risk factor for the development of rDVT[17]. Similarly, we frequently detected proximal DVT localization and observed a predominance of male patients in this group. According to our findings, the increased oxidative stress and inflammatory process due to the presence of DM and CAD –conditions more prevalent in men– along with the higher frequency of dual therapy usage in male patients with proximal DVT, may be associated with this process.

The diagnostic approach for primary acute DVT involves a holistic evaluation that includes clinical suspicion, elevated D-dimer levels, and compression USG[18]. In the context of rDVT, however, there are two differing perspectives regarding the use of D-dimer in the diagnostic process. One perspective suggests that an elevated D-dimer level, along with suspicious physical examination findings for DVT, predicts rDVT[19]. The other perspective argues that since these patients have previously experienced DVT, their baseline D-dimer levels are higher than those of the normal population, and they may be on anticoagulant therapy, making D-dimer evaluation less reliable[20]. Our analysis revealed a median D-dimer measurement of approximately 2600 ng/ml in our patients. Nearly three-quarters of our cases experienced rDVT while on anticoagulant therapy. This finding raised questions about treatment efficacy and/or patient adherence to treatment following primary DVT. However, one clear observation from our data is that male patients exhibited significantly higher D-dimer levels than female patients. We attribute this finding to the older age of male patients and to the fact that major surgery, DM, and/or CAD –recognized as primary risk factors for rDVT in men– were more prevalent in this group. Additionally, the higher D-dimer levels observed in patients receiving dual therapy for proximal vein thrombosis compared to those on monotherapy for distal vein thrombosis suggest an association with this process.

When examining the relationship between emergency department laboratory parameters and rDVT, the most striking result was the moderate positive correlation between D-dimer and uric acid levels. Elevated levels of D-dimer and uric acid have been demonstrated in acute gout attacks, familial Mediterranean fever attacks, and the remodeling process of heart failure patients[21–23].

Similar to our findings, Ren et al.[24] also reported lower uric acid levels in women and in patients with distal vein thrombosis. Furthermore, in the presence of an enhanced thrombotic process and systemic inflammation, uric acid and mean platelet volume (MPV) are correlated[25,26]. We found that approximately 10% of MPV elevation could be explained by elevated uric acid levels. Based on these results, we believe that in emergency departments where D-dimer measurement is unavailable, uric acid –a routine emergency department biochemical parameter– may be utilized in the suspicion of rDVT.

Patients with DVT may experience local or systemic infections due to thrombophlebitis and lymphangitis, presenting with extremity pain, swelling, and erythema. As the infective process progresses, these patients require more healthcare resources[27]. Since all of our patients had rDVT, they were already in a state of chronic inflammation due to their underlying condition. Consequently, more than 50% of our cases exhibited a high infection burden. These patients posed a greater burden on the healthcare system due to prolonged hospitalization.

Endothelial system activation, immune system activation, and increased neutrophil, platelet, and cytokine activity due to thrombosis play significant roles in the pathogenesis of DVT. During this process, protein catabolism leads to elevated blood urea nitrogen levels, and coagulation disorders may develop[28]. In line with the literature, our patients with a high infection burden demonstrated higher blood urea nitrogen and INR levels. Additionally, these patients exhibited elevated uric acid and ALT levels as well as hypocalcemia. This phenomenon may be explained by a systemic inflammatory response secondary to rDVT.

### *Limitations*

The primary limitations of our study include its single-center design and retrospective nature, which precluded access to patients' genetic analyses and hereditary risk factors.

## Conclusion

In this study, valuable insights were obtained regarding rDVT by analyzing the demographic characteristics, clinical follow-up, and treatment processes of hospitalized patients. rDVT was observed more frequently in elderly males. In females, hormone replacement therapy, and in males, the presence of DM and CAD emerged as significant risk factors contributing to recurrence.

Notably, significant laboratory correlations between D-dimer and uric acid levels revealed the potential benefits of uric acid as a biomarker in emergency situations where access to comprehensive diagnostic tools is limited. Additionally, due to the relationship between high infection burden and prolonged hospital stays, we emphasize the need for proactive management of systemic inflammatory responses to optimize healthcare resource utilization.

Current study highlights the importance of classifying rDVT patients based on clinical and laboratory findings to improve treatment strategies. However, further research is needed to explore genetic and hereditary aspects that fall beyond the scope of this single-center retrospective study.

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**ARAŞTIRMA MAKALESİ /** *RESEARCH ARTICLE*

# Comparison of Bifurcation and Trifurcation Anatomy in Distal Left Main Coronary Artery Stenting

## *Distal Sol Ana Koroner Arter Stentlemede Bifürkasyon ve Trifürkasyon Anatominin Karşılaştırılması*

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### ABSTRACT

***Aim:*** *Although there is a lot of data comparing bifurcation and non-bifurcation lesions in left main coronary artery (LMCA) percuteneous coronary intervention (PCI), the specific influence of trifurcation anatomy on procedural outcomes and long-term prognosis is poorly understood. Given the technical complexities and probable disparities in clinical outcomes, a thorough research of these anatomical subgroups is required. This study aimed to compare procedural and clinical outcomes between bifurcation and trifurcation LMCA lesions.*

***Material and Methods:*** *This retrospective study analyzed patients who underwent distal LMCA stenting between January 2019 and June 2024. Patients with stable coronary artery disease (CAD) without prior coronary artery bypass grafting (CABG) and who underwent intravascular ultrasound (IVUS)-guided stenting and who have high surgical risk, as assessed by a heart team, or patient preference for PCI were included. Those with acute coronary syndrome at presentation, prior CABG, or PCI performed without IVUS guidance were excluded. A total of 43 eligible patients were identified from institutional records. Data were collected retrospectively, including procedural details, clinical outcomes, and follow-up findings.*

***Results:*** *There were no significant differences in baseline characteristics, including biochemical parameters and comorbidities, between the two groups (p>0.05). Trifurcation lesions required significantly longer stents (p=0.008). Ischemic events were more common in the trifurcation group (33.3% vs. 4.5%, p=0.015), and major adverse cardiac event (MACE) rates were significantly higher in the trifurcation group compared to the bifurcation group (57.1% vs. 9.1%, p=0.001). Bleeding events and mortality rates did not significantly differ between the groups (p>0.05).*

***Conclusion:*** *Patients with LMCA trifurcation lesions undergoing PCI exhibit higher ischemic event rates and MACE compared to those with bifurcation lesions, despite IVUS guidance. Further prospective studies are warranted to optimize treatment strategies for this high-risk population.*

**Key words:** *angiography; bifurcation; IVUS; LMCA stenting; trifurcation*

### ÖZET

***Amaç:*** *Sol ana koroner arter (LMCA) perkütan koroner girişiminde (PKG) bifurkasyon ve bifurkasyon dışı lezyonları karşılaştıran çok sayıda veri olmasına rağmen, trifurkasyon anatomisinin prosedürel sonuçlar ve uzun vadeli prognoz üzerindeki spesifik etkisi tam olarak anlaşılamamıştır. Teknik karmaşıklıklar ve klinik sonuçlardaki olası farklılıklar göz önüne alındığında, bu anatomik alt grupların kapsamlı bir şekilde araştırılması gerekmektedir. Bu çalışma, bifurkasyon ve trifurkasyon LMCA lezyonları arasındaki prosedürel ve klinik sonuçları karşılaştırmayı amaçlamıştır.*

***Materyal ve Metot:*** *Bu retrospektif çalışmada, Ocak 2019 ile Haziran 2024 tarihleri arasında distal LMCA stentleme yapılan hastalar analiz edildi. Daha önce koroner arter baypas greftleme (KABG) yapılmamış stabil koroner arter hastalığı (KAH) olan ve intravasküler ultrason (IVUS) kılavuzluğunda stent uygulanan ve bir kalp ekibi tarafından değerlendirildiği üzere yüksek cerrahi riski olan veya PKG hasta tercihi olan hastalar dâhil edildi. Başvuru sırasında akut koroner sendromu olanlar, daha önce KABG geçirmiş olanlar veya IVUS kılavuzluğu olmadan PKG uygulanmış olanlar çalışma dışı bırakılmıştır. Kurumsal kayıtlardan toplam 43 uygun hasta tespit edildi. Prosedürel ayrıntılar, klinik sonuçlar ve takip bulguları dâhil olmak üzere veriler retrospektif olarak toplandı.*

***Bulgular:*** *İki grup arasında biyokimyasal parametreler ve komorbiditeler dâhil olmak üzere başlangıç özellikleri açısından anlamlı fark yoktu (p>0,05). Trifurkasyon lezyonları anlamlı olarak daha uzun stent gerektirdi (p=0,008). İskemik olaylar trifurkasyon grubunda daha yaygındı (%33,3'e karşı %4,5, p=0,015) ve majör advers kardiyak olay (MACE) oranları trifurkasyon grubunda bifurkasyon grubuna kıyasla anlamlı derecede yüksekti (%57,1'e karşı %9,1, p=0,001). Kanama olayları ve mortalite oranları gruplar arasında anlamlı farklılık göstermedi (p>0,05).*

***Sonuç:*** *PKG uygulanan LMCA trifurkasyon lezyonlu hastalar, IVUS kılavuzluğuna rağmen, bifurkasyon lezyonlu hastalara kıyasla daha yüksek iskemik olay oranları ve MACE sergilemektedir. Bu yüksek riskli popülasyona yönelik tedavi stratejilerini optimize etmek için daha ileri prospektif çalışmalara ihtiyaç vardır.*

**Anahtar kelimeler:** *koroner anjiyografi, bifürkasyon, trifükasyon, IVUS, LMCA stentleme*

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## Introduction

Although the differences between bifurcation and non-bifurcation lesions in distal left main coronary artery (LMCA) stenting are well documented, the impact of trifurcation anatomy on clinical outcomes remains insufficiently studied. This study compared percutenous coronary intervention (PCI) outcomes in bifurcation and trifurcation LMCA lesions, revealing significantly higher rates of ischemic events and major adverse cardiac events (MACE) in the trifurcation group. Our findings suggest that trifurcation lesions are associated with increased procedural complexity and worse clinical outcomes. Therefore, better patient selection, alternative revascularization strategies, and further research are needed to improve outcomes in this high-risk population.

Percutaneous coronary intervention (PCI) of the left main coronary artery (LMCA) is accepted as one of the most technically challenging and high-risk procedures in interventional cardiology. The LMCA provides an important source of the myocardium by its bifurcation into the left anterior descending (LAD) and left circumflex (LCx) arteries. In some cases, a trifurcation anatomy is present, adding an additional ramus intermedius branch to the distal LMCA, further complicating PCI. These anatomical variances create significant challenges for stent selection, position, and post-procedural results.

Distal LMCA stenting, particularly in the presence of bifurcation or trifurcation, necessitates careful planning and execution. Studies have demonstrated that bifurcation lesions are associated with increased procedural complexity, higher rates of restenosis, and greater risk of major adverse cardiac events (MACE) compared to non-bifurcation lesions[1,2]. Trifurcation anatomy introduces additional complexities, including the need for multiple stents, risk of carina shift, and challenges in achieving optimal flow to all branches[3]. Despite these challenges, PCI of the LMCA remains a critical alternative to coronary artery bypass grafting (CABG) in appropriately selected patients, particularly those who are poor surgical candidates[4].

Although there is a lot of data comparing bifurcation and non-bifurcation lesions in LMCA PCI, the specific influence of trifurcation anatomy on procedural outcomes and long-term prognosis is poorly understood. Given the technical complexities and probable disparities in clinical outcomes, a thorough research of these anatomical subgroups is required.

This study aims to compare the procedural and clinical outcomes of distal LMCA stenting in patients with bifurcation and trifurcation anatomy, hypothesizing that trifurcation anatomy is associated with increased procedural complexity and potentially worse outcomes compared to bifurcation.

## Material and Methods

This retrospective study included patients who underwent distal LMCA stenting between January 2019 and June 2024. Eligible patients were selected based on the following inclusion criteria:

1. Stable coronary artery disease without prior history of coronary artery bypass grafting (CABG).
2. High surgical risk, as assessed by a heart team, or patient preference for percutaneous coronary intervention (PCI).
3. Optimal stent placement guided by intravascular ultrasound (IVUS).

Those with acute coronary syndrome at presentation, prior CABG, or PCI performed without IVUS guidance were excluded. A total of 43 patients meeting the inclusion and exclusion criteria were identified from institutional records. All data were collected retrospectively, including procedural details, clinical outcomes, and follow-up results. As this was a retrospective study, patients who did not want CABG were also included in the study, so surgical risks were not calculated. Xience stents were used in all procedures.The mean follow-up period of the patients was 22 months (min 13 to 61 months).

Ethical approval for the study was obtained from the Bakırçay University Non-Invasive Ethics Committee (no: 1927 date: 18/12/2024).

### *Procedural Technique*

All interventions were performed using standard PCI protocols under fluoroscopic guidance, with adjunctive use of IVUS to optimize stent positioning and expansion. Distal LMCA stenting was performed with either single- or double-stent techniques, depending on lesion complexity and operator discretion. Bifurcation and trifurcation lesions were managed with strategies appropriate for each anatomical subtype, ensuring complete revascularization of all major branches.of 50% in the distal LMCA and its branches were considered severe in accordance with the Medina classification. The distal area of the main coronary

artery below 6 mm² was considered serious in IVUS evaluation. Antiaggregant treatment was continued for 1 year. Trification lesion was accepted as the presence of ramus intermedius wider than 1.5 mm in the distal main coronary artery.

Drug-eluting stents (DES) were used in all patients who underwent single- or double-stent techniques (everolimus-eluting stents [Xience Pro, Abbott Vascular Devices])

### *Study Endpoints*

The primary endpoints included:

1. Bleeding events classified according to the Bleeding Academic Research Consortium (BARC) criteria.
2. Ischemic outcomes, including stent thrombosis and target lesion revascularization.
3. Mortality (all-cause and cardiac-specific).
4. Composite endpoint, defined as a combination of mortality, myocardial infarction,bleeding and target lesion revascularization.

### *Statistical Analysis*

Continuous variables were expressed as mean ± standard deviation or median (interquartile range) based on data distribution and compared using the Student's t-test or Mann-Whitney U-test, as appropriate. Categorical variables were presented as frequencies and percentages and compared using the chi-square test or Fisher's exact test. Kaplan-Meier survival analysis was used to evaluate long-term outcomes, with differences between groups assessed using the log-rank test. Statistical significance was defined as a p-value <0.05.

## Results

A total of 43 patients were retrospectively analyzed, with bifurcation anatomy present in 22 patients (51.2%) and trifurcation anatomy in 21 patients (48.8%).

No significant differences were found in biochemical parameters, including glucose, creatinine, or inflammatory markers such as CRP, between the bifurcation and trifurcation groups (p>0.05). Comorbidities and laboratory characteristics of the patients are given in Table 1.

There was no statistically significant difference in left ventricular ejection fraction between the groups. When we compared the two groups in terms of procedural details, we observed that the number of provisional stenting techniques was higher in both groups. The mean size of the stents used procedurally and the rate of kissing balloon use were similar. The length of the stents used in the trifurcation group was statistically significantly higher. A comparison of procedural details between the two groups is given in Table 2.

Ischemic outcomes were observed in 8 patients (18.6%), with a statistically significant higher prevalence in the trifurcation group compared to the bifurcation group (p = 0.015).Bleeding events occurred in only 1 patient (2.3%), with no significant differences between bifurcation and trifurcation groups (p =

***Table 1.*** *Comparison of laboratory parameters*

| Parameter | Bifurcation (n=22) | Trifurcation (n=21) | P value |
|---|---|---|---|
| Age | 69.1±10.4 | 68.3±9.6 | 0.696 |
| Female (n, %) | 9(41.0%) | 9(43.6%) | 0.511 |
| HT (n, %) | 14 (63.6%) | 17 (81.0%) | 0.186 |
| DM (n, %) | 12 (54.5%) | 15 (71.4%) | 0.113 |
| CKD (n, %) | 5 (22.7%) | 7 (33.3%) | 0.412 |
| COPD (n, %) | 4(18.2%) | 3(14.3%) | 0.323 |
| Glucose (mg/dL) | 134.0±47.2 | 125.7±44.9 | 0.594 |
| Creatinine (mg/dL) | 0.93±0.39 | 1.11±0.37 | 0.145 |
| Hemoglobin (g/dL) | 13.3±2.3 | 12.5±2.8 | 0.381 |
| WBC (×10^3/μL) | 8.6±4.7 | 8.8±5.4 | 0.882 |
| Neutrophil (×10^3/μL) | 5.8±4.6 | 6.0±5.3 | 0.870 |
| Platelets (×10^3/μL) | 251.9±117.3 | 241.7±80.9 | 0.761 |
| Albumin (g/dL) | 42.0±7.9 | 40.7±1.5 | 0.789 |
| LDL (mg/dL) | 163.4±32.5 | 170.0±38.9 | 0.210 |
| HDL (mg/dL) | 41.6±5.4 | 44.2±6.1 | 0.198 |
| Triglycerides (mg/dL) | 125.0±30.2 | 128.0±32.4 | 0.311 |
| LDL (mg/dL) | 163.4±32.5 | 170.0±38.9 | 0.210 |
| LVEF (%) | 49.1±11.5 | 45.2±11.8 | 0.162 |

***Table 2.*** *Comparison of procedural details*

| Parameter | Bifurcation (n=22) | Trifurcation (n=21) | P value |
|---|---|---|---|
| Stent type | Xience | Xience | - |
| Syntax score | 28.72±5.31 | 29.23±7.11 | 0.789 |
| Stenting technique | | | |
| Provisional | 17 (77.3) | 19 (90.5) | 0.412 |
| Double-stent | 5 (22.7) | 2 (9.5) | |
| Stent size (mm) | 3.73±0.30 | 3.67±0.37 | 0.284 |
| Stent length (mm) | 34.5±18.8 | 43.2±21.4 | **0.008** |
| LVEF (%) | 49.1±11.5 | 45.2±11.8 | 0.162 |
| Kissing balloon (n, %) | 16 (72.7%) | 14 (66.7%) | 0.665 |

Bifurcation group; DK Crush: 2, Culotte: 1, TAP: 2, Trifurcation group; DK Crush: 2.

0.300).Mortality was recorded in 5 patients (11.6%), with no statistically significant difference between the two anatomical groups (p = 0.138).Composite major adverse cardiac events (MACE) were significantly higher in the trifurcation group (57.1%) compared to the bifurcation group (9.1%, p = 0.001) (Table 3).

***Table 3.*** *Comparison of clinical outcomes*

| Outcome | Bifurcation (n=22) | Trifurcation (n=21) | P value |
|---|---|---|---|
| Bleeding (n, %) | 0 (0%) | 1 (4.8%) | 0.300 |
| Ischemic events (n, %) | 1 (4.5%) | 7 (33.3%) | **0.015** |
| Mortality (n, %) | 1 (4.5%) | 4 (19.0%) | 0.138 |
| Composite MACE (n, %) | 2 (9.1%) | 12 (57.1%) | **0.001** |

## Discussion

The management of distal left main coronary artery (LMCA) lesions, particularly in the context of bifurcation and trifurcation anatomies, remains a complex and debated area in interventional cardiology. Our study retrospectively analyzed 43 patients who underwent percutaneous coronary intervention (PCI) with intravascular ultrasound (IVUS) guidance, comparing outcomes between bifurcation and trifurcation anatomies. The findings revealed a significantly higher incidence of ischemic events and composite major adverse cardiac events (MACE) in the trifurcation group compared to the bifurcation group.

These results align with existing literature that underscores the increased procedural complexity and risk associated with trifurcation lesions. Although the syntax score determines the procedural complexity of the patients, many other criteria can be used. The presence of trifurcation lesions can be considered as an additional criterion[5,6]. A study by Kovacevic et al.[7] highlighted that trifurcation lesions often require more intricate stenting techniques and are associated with higher rates of adverse events compared to bifurcation lesions. The necessity for multiple stents and the challenge of achieving optimal flow to all branches in trifurcation anatomy may contribute to these outcomes.The study by Kovacevic et al.[8] showed that LMCA trifurcation stenting was feasible, but no comparison was made with bifurcation lesions.

The use of IVUS guidance in our study aimed to optimize stent placement and expansion, which has been shown to improve procedural outcomes. However, despite IVUS guidance, the trifurcation group exhibited higher rates of ischemic events and MACE. This suggests that anatomical complexity may outweigh the benefits conferred by advanced imaging techniques[9,10].

The EXCEL trial reported no significant differences in clinical outcomes between distal LM bifurcation and trifurcation PCI at five-year follow-up[11]. The disparity may be attributed to differences in study populations, procedural strategies, and lesion complexity. Notably, while our study identified a higher need for longer stents in trifurcation cases and a greater incidence of ischemic complications. These differences highlight the need for further prospective studies to refine PCI strategies in complex LMCA lesions and better identify patients who may benefit from alternative revascularization approaches.

In terms of bleeding events, our study observed no significant difference between the bifurcation and trifurcation groups. This finding is consistent with previous research indicating that bleeding complications are more closely related to patient-specific factors and antithrombotic therapy rather than the anatomical complexity of the lesion[12].

Mortality rates did not differ significantly between the two groups in our study. This may be attributed to the relatively small sample size and the short follow-up period. Long-term studies with larger cohorts are necessary to elucidate the impact of lesion complexity on mortality outcomes[13,14].

While dyslipidemia is a known risk factor for coronary artery disease, its direct relationship with lesion anatomy remains unclear. Future studies should explore the interplay between lipid profiles and coronary anatomy to better understand this association[15].

According to the results of this study, CABG should be considered as the first choice in patients with complex LMCA lesions if the risk of surgery is not high, or optimal double stent strategies may be chosen rather than provisional methods. In addition, lifestyle modification should be followed more closely in these patients and more aggressive medical treatment options may be chosen.

This study demonstrates the need for randomized trials specifically in bifurcation and trifurcation LMCA stenting patients. Potent antiaggregant therapies may be selected in patients with trifurcation. It also raises the question, 'Should hemodynamic measurements be performed together with IVUS in the trifurcation patient group?'.

### *Limitation*

Our study has several limitations, including its retrospective design, small sample size, and lack of long-term follow-up. Additionally, the decision to use single or dual stent strategies was left to the operator's discretion, which

may introduce selection bias. Syntax scores were calculated from the coronary angiographies of the patients and found to be similar. Patients who underwent IVUS before PCI and stent control after PCI were included in the study. However, IVUS images have not been analyzed in detail. Plaque and calcification burden of the patients may have differed. Despite these limitations, our findings contribute to the growing body of evidence highlighting the challenges associated with PCI in trifurcation lesions.

## Conclusion

In conclusion, patients with distal LMCA trifurcation lesions undergoing PCI exhibit higher rates of ischemic events and MACE compared to those with bifurcation lesions, even with the use of IVUS guidance. These findings underscore the need for meticulous procedural planning and consideration of alternative revascularization strategies in this high-risk population. Further prospective studies are warranted to develop tailored approaches that can improve outcomes in patients with complex coronary anatomies.

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**ARAŞTIRMA MAKALESİ /** *RESEARCH ARTICLE*

# Iatrogenic Parathyroidectomy and Affecting Factors During Thyroid Surgery

*Tiroid Cerrahisi Sırasında İatrojenik Paratiroidektomi ve Etki Eden Faktörler*

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## ABSTRACT

***Aim:*** *This study aimed to investigate cases of iatrogenic parathyroidectomy following thyroid surgery and to analyze the causes.*

***Material and Methods:*** *A total of 287 patients diagnosed with thyroid-related disorders and surgically treated at various clinics of Private Esencan Hospital between 2019 and 2023 were included in the study. Preoperative ultrasound imaging results and data on patients with multinodular goiter presenting a dominant nodule larger than 4 cm in diameter were recorded, specifically noting the presence of thyroiditis. Thyroid tissues obtained during surgery were examined histopathologically in the pathology laboratory, and the presence of thyroid malignancy and parathyroid tissue was confirmed.*

***Results:*** *The mean age of the patients was 55.6±17.3 years, ranging from 18 to 83 years, and 154 (55.4%) were male. Iatrogenic parathyroidectomy was identified in 26 (9.4%) of the patients. The rate of iatrogenic parathyroidectomy was significantly higher in patients with thyroid malignancy compared to those without (13.9% vs. 5.8%; p=0.02). Patients with thyroiditis also had a higher rate of iatrogenic parathyroidectomy than those without (18.2% vs. 7.2%; p=0.012). Additionally, patients with a dominant nodule diameter showed a significantly increased rate of iatrogenic parathyroidectomy compared to those without (27.0% vs. 6.6%; p<0.001). In the logistic regression analysis, the presence of thyroid malignancy (p=0.024), thyroiditis (p=0.015), and dominant nodule diameter (p<0.001) were identified as independent risk factors for developing iatrogenic parathyroidectomy.*

***Conclusion:*** *Our study shows that the risk of iatrogenic parathyroidectomy is significantly higher, especially in patients with thyroiditis, thyroid malignancy, or large nodules. These patients should be handled more carefully during surgery and should be considered for surgical treatment.*

**Key words:** *thyroid surgery; thyroidectomy; iatrogenic parathyroidectomy; malignancy; thyroiditis; hypocalcemia*

## ÖZET

***Amaç:*** *Bu çalışmada tiroid cerrahisi sonrasında iatrojenik paratiroidektomi görülen olguların irdelenmesi ve buna yol açan faktörlerin analiz edilmesi amaçlanmıştır.*

***Materyal ve Metot:*** *Çalışmaya 2019–2023 tarihleri arasında Özel Esencan Hastanesi hastanemiz çeşitli kliniklerinde tiroidle ilişkili bozukluk tanısı konulan ve tiroid cerrahisi kararı verilere opere edilen toplam 287 hasta dâhil edildi. Hastaların tiroidit varlığı açısından operasyon öncesi yapılan ultrason görüntüleme sonuçlar ve multinödül guatırları olan hastlarda en büyük 4 cm üstünde nodül saptananların nodül olanlar kaydedildi. Operasyon sırasında alınan tiroid dokuları patoloji laboratuvarında histopatolojik olarak incelendi ve tiroit malignitesi varlığı belirlendi. Ayrıca operasyon sonrası süreçte hipokalsemi gelişen hastalar iatrojenik paratiroidektomi olarak kabul edildi.*

***Bulgular:*** *Hastaların ortalama yaşı 55,6±17,3 (Aralık: 18–83) yıl idi ve 154'ü (%55,4) erkekti. Hastaların 26'sında (%9,4) iatrojenik paratiroidektomi saptandı. Tiroid malignitesi olanlarda iatrojenik paratiroidektomi görülme oranı malignitesi olmayanlara göre anlamlı yüksek bulundu (%13,9 vs. %5,8; p=0,02). Tiroidit saptananlarda iatrojenik paratiroidektomi oranı tiroiditi olmayanlara göre anlamlı yüksekti (%18,2 vs. %7,2; p=0,012). Dominant nodül çapı bulunanlarda iatrojenik paratiroidektomi görülme oranı dominant nodül çapı olmayanlara göre anlamlı yüksek bulundu (%27,0 vs. %6,6; p<0,001). Yapılan lojistik regresyon analizlerinde tiroid malignitesi (p=0,024), tiroidit (p=0,015) ve dominant nodül çapı (p<0,001) varlığı iatrojenik paratiroidektomi gelişmesi açısından bağımsız risk faktörleri idi. Buna göre iatrojenik paratiroidektomi görülme riskini tiroid malignitesi varlığı 2,6 kat; tiroidit varlığı 2,9 kat; dominant nodül çapı varlığı ise 5,2 kat artırmaktaydı. Çoklu değişken analizinde ise malignite ile dominant nodül çapının birlikte bulunması iatrojenik paratiroidektomi gelişmesi açısından bağımsız risk faktörü olarak saptandı.*

***Sonuç:*** *Çalışmamızdan elde edilen bulgular tiroid cerrahisinde iatrojenik paratiroidektomi görülme oranının %10 civarında olduğunu, özellikle tiroiditi, tiroid malignitesi ya da dominant nodül çapı olan hastalarda iatrojenik paratiroidektomi görülme riskinin belirgin olarak artmış olduğunu, bu hastalar opere edilirken çok daha dikkatli olunması ve bu hastaların cerrahi sonrasında daha yakından takip edilmesi gerektiğini göstermiştir.*

**Anahtar kelimeler:** *tiroid cerrahisi; tiroidektomi; iatrojenik paratiroidektomi; malignite; tiroidit; hipokalsemi*

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## Introduction

Thyroidectomy is one of the most frequently performed endocrine surgeries. It is considered safe due to its low rates of morbidity and mortality. Overall, complication rates after thyroid surgery are less than 5%. A common complication is damage to the parathyroids, which can decrease parathyroid hormone production and lead to hypoparathyroidism. Often, this damage does not cause noticeable symptoms but results in temporary hypocalcemia lasting several weeks. During this time, patients may experience numbness of varying severity in the extremities and around the mouth. In some cases, this condition worsens or becomes permanent, causing sustained hypocalcemia with clinical symptoms. Typically, this temporary hypocalcemia causes numbness that varies in severity in the extremities and perioral muscles. In some instances, the situation may become more severe or lead to permanent hypocalcemia[1–4].

The parathyroid gland is a delicate structure located very close to the thyroid gland. It receives blood supply from the inferior and superior thyroid arteries. Damage to these structures can cause parathyroid dysfunction and hypocalcemia, as well as damage to the parathyroid tissue. Additionally, parathyroid tissue is often found during histopathological examination after thyroid surgery. It has been reported that parathyroidectomy is more common in thyroid surgery, especially in patients with thyroiditis or thyroid cancer[3–8].

This study aimed to examine the cases of iatrogenic parathyroidectomy after thyroid surgery and analyze the factors that led to this.

## Material and Method

A total of 287 patients diagnosed with thyroid-related disorders and operated on at various clinics of Private Esencan Hospital between 2019 and 2023 were included in the study. Preoperative ultrasound imaging results and patients diagnosed with multinodular goiter featuring a dominant nodule larger than 4 cm in diameter were recorded regarding the presence of thyroiditis. The possible inclusion criteria were defined as follows: patients undergoing total thyroidectomy, those operated on for benign or malignant thyroid conditions, patients with fully documented surgical and pathology reports, individuals who did or did not develop postoperative hypocalcemia, and adult patients (≥18 years of age).

Possible exclusion criteria included patients with a history of previous neck surgery, those with congenital parathyroid anomalies, or a known history of hypoparathyroidism. It also included patients who underwent intraoperative parathyroid autotransplantation or for whom such information was unavailable, individuals with incomplete biochemical data, pregnant women, and pediatric patients.

Thyroid tissues obtained during surgery were examined histopathologically in the pathology laboratory to confirm the presence of thyroid malignancy and parathyroid tissue. Patients with histopathological evidence of parathyroid tissue in the surgical specimen, along with postoperative laboratory-confirmed hypocalcemia, were classified as cases of iatrogenic parathyroidectomy.

### *Statistical Analysis*

All statistical analyses in the study were performed using IBM Statistical Package for Social Sciences (SPSS) program version 25.0 software (IBM, Chicago, IL, USA). Descriptive data are presented as means and standard deviations; distributions of nominal or ordinal variables are given as numbers and percentages. Comparisons between groups for categorical variables were conducted with the Chi Square test. The normality of continuous variables was assessed with the Kolmogorov-Smirnov test. Differences between groups for continuous variables were analyzed using Student's t test. The risk coefficients for variables related to developing iatrogenic parathyroidectomy were determined through logistic regression analysis. Results were evaluated within a 95% confidence interval, and p-values <0.05 were considered statistically significant. Bonferroni correction was applied for the operation type in Table 2.

## Results

The average age of the patients was 55.6±17.3 years (range: 18–83), with 154 patients (55.4%) being male. Iatrogenic parathyroidectomy was identified in 26 patients (9.4%). Histopathological examination confirmed thyroid-related malignancy in 122 patients (43.9%). Most surgeries, 86.7%, involved bilateral total thyroidectomy. Preoperative ultrasonic imaging detected thyroiditis in 55 patients (19.8%). A total of 37 patients (13.3%) had a dominant nodule diameter (see Table 1).

***Table 1.*** *Distributions according to some variables*

| | n | % |
|---|---|---|
| n | 278 | 100.0 |
| **Gender** | | |
| Male | 154 | 55.4 |
| Female | 124 | 44.6 |
| **Paraidectomy** | | |
| Absent | 252 | 90.6 |
| Present | 26 | 9.4 |
| **Malignancy** | | |
| Absent | 156 | 56.1 |
| Present | 122 | 43.9 |
| **Operation type** | | |
| Bilateral total thyroidectomy | 241 | 86.7 |
| Unilateral total thyroidectomy | 29 | 10.4 |
| Completion thyroidectomy | 8 | 2.9 |
| **Thyroiditis on preoperative USG** | | |
| Absent | 223 | 80.2 |
| Present | 55 | 19.8 |
| **Dominant nodule diameter** | | |
| Absent | 241 | 86.7 |
| Present | 37 | 13.3 |
| Age (Mean & SD) (years) | 55.6 | 17.3 |

USG: ultrasound sonography, SD: standard deviation.

***Table 2.*** *Comparison of iatrogenic paraidectomy distributions according to some variables*

| | Paraidectomy none | | Paraidectomy present | | |
|---|---|---|---|---|---|
| | n | % | n | % | p |
| n | 252 | 90.6 | 26 | 9.4 | - |
| **Gender** | | | | | 0.805 |
| Male | 139 | 90.3 | 15 | 9.7 | |
| Female | 113 | 91.1 | 11 | 8.9 | |
| Malignancy | | | | | 0.020 |
| Absent | 147 | 94.2 | 9 | 5.8 | |
| Present | 105 | 86.1 | 17 | 13.9 | |
| **Operation types *** | | | | | 0.643 |
| Bilateral total thyroidectomy | 221 | 91.7 | 21 | 8.7 | |
| Unilateral total thyroidectomy | 24 | 82.8 | 4 | 13.8 | |
| Completion thyroidectomy | 7 | 87.5 | 1 | 12.5 | |
| **Thyroiditis on preoperative USG** | | | | | 0.012 |
| Absent | 207 | 92.8 | 16 | 7.2 | |
| Present | 45 | 81.8 | 10 | 18.2 | |
| **Dominant nodule diameter** | | | | | <0.001 |
| Absent | 225 | 93.4 | 16 | 6.6 | |
| Present | 27 | 73.0 | 10 | 27.0 | |
| Age (mean & SD) (years) | 56.2 | 17.3 | 50.7 | 16.3 | 0.124 |

USG: ultrasound sonography, SD: standard deviation, * Bonferroni correction.

The rate of iatrogenic parathyroidectomy in patients with thyroid malignancy was significantly higher than in those without malignancy (13.9% vs. 5.8%; p=0.02). Similarly, patients with thyroiditis experienced a higher rate of iatrogenic parathyroidectomy compared to those without thyroiditis (18.2% vs. 7.2%; p=0.012). Additionally, patients with a dominant nodule diameter had a significantly increased rate of iatrogenic parathyroidectomy compared to those without a dominant nodule (27.0% vs. 6.6%; p<0.001). The incidence rates of iatrogenic parathyroidectomy were comparable between genders (p=0.805) and operation types (p=0.643) (Table 2).

In the logistic regression analyses, the presence of thyroid malignancy (p=0.024), thyroiditis (p=0.015), and dominant nodule diameter (p<0.001) were independent risk factors for the development of iatrogenic parathyroidectomy. Accordingly, the risk of iatrogenic parathyroidectomy was 2.6 times higher with thyroid malignancy, 2.9 times higher with thyroiditis, and 5.2 times higher with a larger dominant nodule diameter. In multivariate analysis, the coexistence of malignancy and large nodule diameter was identified as an independent risk factor for developing iatrogenic parathyroidectomy (Table 3).

***Table 3.*** *Logistic regression analyzes for iatrogenic paraidectomy*

| | Univariate | | | Multivariate | | |
|---|---|---|---|---|---|---|
| | p | Exp (B) | %95 CI (Lower-upper) | p | Exp (B) | %95 CI (Lower-upper) |
| Malignancy | 0.024 | 2.6 | 1.1–6.2 | 0.002 | 6.1 | 1.9–19.1 |
| Thyroiditis on preoperative USG | 0.015 | 2.9 | 1.2–6.7 | 0.070 | - | - |
| Dominant nodule diameter | <0.001 | 5.2 | 2.1–12.6 | <0.001 | 12.0 | 3.6–40.8 |

Exp (B): exponential B coefficient, odds ratio, CI: confidence interval for Exp (B), USG: ultrasound sonography.

## Discussion

Although thyroid surgery is generally considered a safe procedure, it can often lead to temporary or permanent hypocalcemia due to various factors. One significant cause of hypocalcemia is damage to or removal of the parathyroid tissue during surgery. This condition, known as iatrogenic parathyroidectomy, is commonly seen in thyroid surgeries[1–5]. The study demonstrated that iatrogenic parathyroidectomy is linked to malignancy, size of dominant lymph nodes, and thyroiditis.

Iatrogenic parathyroidectomy rates in patients undergoing thyroid surgery have been reported to range between 7.9% and 31% in studies. In these studies, median values seem to be around 15–17%[6–17]. In our study, iatrogenic parathyroidectomy was identified in 9.4% of patients. This rate is slightly lower than those found in other research. Therefore, about one in ten patients undergoing thyroid surgery experiences iatrogenic parathyroidectomy.

Many studies have shown that iatrogenic parathyroidectomy in thyroid surgery is significantly more common in patients with thyroid malignancy[6–12]. Caulley et al.[13] demonstrated in their large study that not only parathyroidectomy but all complications related to thyroid surgery were higher in patients with thyroid malignancy. However, Sakorafas et al.[6] reported that the presence of thyroiditis did not influence the rate of iatrogenic parathyroidectomy. In our study, the rate of iatrogenic parathyroidectomy was significantly higher in patients with thyroid malignancy, thyroiditis, and larger dominant nodule diameter. Additionally, logistic regression analysis showed that the presence of thyroid malignancy, thyroiditis, and larger nodule diameter were independent risk factors for developing iatrogenic parathyroidectomy. Specifically, the risk increased 2.6 times with thyroid malignancy, 2.9 times with thyroiditis, and 5.2 times with larger nodule diameter. In the multivariate analysis, the coexistence of malignancy and larger nodule size was identified as an independent risk factor for iatrogenic parathyroidectomy. These findings indicate that the likelihood of iatrogenic parathyroidectomy during thyroid surgery is closely associated with thyroid malignancy, thyroiditis, and larger nodule size, and the risk significantly increases in patients presenting these factors.

Sakorafas et al.[6] reported that the rate of iatrogenic parathyroidectomy in women was higher in thyroid surgery. However, Hone et al.,[9] MacGoldrick et al.,[11] and Özoğul et al.[8] found no difference in iatrogenic parathyroidectomy rates between genders and types of surgery in patients undergoing thyroid procedures. Sorgato et al.[7] also reported that gender did not influence iatrogenic parathyroidectomy, but the average age was lower in patients who experienced it, and the rate was higher in those who had lymph node dissection along with total thyroidectomy. Zheng et al.[10] noted that total thyroidectomy carries a greater risk of iatrogenic parathyroidectomy. In our study, the rates of iatrogenic parathyroidectomy were similar across genders and surgical types. Additionally, we found that the average age was comparable in patients who did and did not undergo iatrogenic parathyroidectomy. These findings suggest that factors such as age, gender, and type of operation may not be directly related to the occurrence of iatrogenic parathyroidectomy during thyroid surgery.

### *Study Limitations*

Since the study focuses solely on iatrogenic parathyroidectomy in thyroid surgery and the factors influencing it, the fact that other thyroid surgery complications are not examined in detail can be seen as a limitation. A positive aspect of the study is that the number of patients is sufficient and does not negatively impact the analysis. In recent years, there have been significant advances in surgical techniques designed to preserve the parathyroid glands. One such technique is fluorescence imaging and autotransplantation. The fact that these methods were not used in our patients is a limitation of our study. Integrating these techniques into routine surgical practice is considered an important advancement for patient safety[18–20].

## Conclusion

The findings from our study indicate that the rate of iatrogenic parathyroidectomy in thyroid surgery is about 10%, and the risk of iatrogenic parathyroidectomy is significantly higher, especially in patients with thyroiditis, thyroid malignancy, or larger nodules. Additionally, more caution should be exercised during surgery for these patients, and they should be more vigilant during the postoperative period.

### *Declaration of Interest*

The author declares that there is no conflict of interest regarding the publication of this paper.

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### Authors' Contributions

Study concept and design, Creation of experimental groups and experimental practices, Evaluating the results and writing the manuscript: AÖ

### Ethical Approval

Study approval was obtained from Istanbul Training and Research Hospital, Istanbul, Local Board of Ethics (Decision no: 103 on: 18.10.2024).

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**ARAŞTIRMA MAKALESİ /** *RESEARCH ARTICLE*

# Emotional Burdens and Cognitive Decline: the Role of Anxiety in Mild Cognitive Impairment

*Duygusal ve Bilişsel Gerileme Hafif Bilişsel Bozuklukta Kaygının Rolü*

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## ABSTRACT

***Aim:*** *This study investigates the complex interactions between mild cognitive impairment (MCI), depression, and anxiety, focusing on how these factors affect cognitive function and progression risks. The goal is to inform early diagnostic strategies and targeted therapeutic interventions in individuals with MCI*

***Matherial and Methods:*** *This prospective study included 45 patients diagnosed with MCI (mean age: 66.1±7.7 years; 23 males [51%], 22 females [49%]) at a neurology outpatient clinic. Sociodemographic data, including education level and medical history, were collected. Cognitive and psychiatric assessments were conducted using the Montreal Cognitive Assessment (MoCA), Standardized Mini-Mental State Examination (SMMT), Hamilton Depression Rating Scale (HDRS), and Hamilton Anxiety Scale (HAS). Stratification was done according to anxiety severity, and comparisons were made across these groups on the cognitive performances.*

***Results:*** *Anxiety levels were significantly higher in females than males (p=0.001). While global MoCA and SMMT scores did not differ significantly by gender, males showed significantly better performance in verbal fluency (p=0.025) and a trend in abstract thinking (p=0.057). A significant decline in MoCA total scores was observed with increasing anxiety severity (p=0.024), with verbal fluency (p=0.011), abstract thinking (p=0.005), and attention (p=0.050) notably affected in the severe anxiety group.*

***Conclusions:*** *This study highlights anxiety as a key modifiable risk factor for cognitive impairment in MCI, with domain-specific deficits in executive function. Unlike depression, anxiety showed a stronger correlation with cognitive decline. These findings suggest that early identification and targeted treatment of anxiety in MCI could help delay progression to dementia and improve clinical outcomes.*

**Key words:** *mild cognitive impairment; anxiety; depression; Montreal cognitive assessment; cognitive decline*

## ÖZET

***Amaç:*** *Bu çalışma, hafif bilişsel bozukluğu (HBB) olan bireylerde depresyon ve anksiyetenin bilişsel işlevler ile hastalığın ilerleme riski üzerindeki etkilerini incelemeyi amaçlamaktadır. Bu etkileşimleri anlamak, HBB'li bireylerde erken tanı stratejilerinin ve hedefe yönelik tedavi müdahalelerinin geliştirilmesini sağlayabilir. Hafif Bilişsel Bozukluk (HBB), normal yaşlanma ile demans arasında kilit bir köprü görevi görür ve çoğunlukla depresyon ile anksiyete gibi nöropsikiyatrik semptomlarla kendini gösterir. Bu semptomlar bilişsel gerilemeyi şiddetlendirebilir ve altta yatan nörodejeneratif sürecin en erken göstergeleri olabilir. Bu çalışma, HBB ile depresyon ve anksiyete arasındaki karmaşık ilişkileri araştırmayı, özellikle bu faktörlerin bilişsel sonuçlar ve hastalığın ilerleyişi üzerindeki ortak etkisine odaklanmayı amaçlamaktadır. Elde edilecek bulgular, HBB'li bireylere yönelik tarama yaklaşımlarının ve müdahale stratejilerinin iyileştirilmesine katkıda bulunacaktır.*

***Yöntemler:*** *Hafif Bilişsel Bozukluk tanılı 45 hastadan oluşan (ortalama yaş: 66,1 yıl; %51 erkek) prospektif bir kohorta, şu test protokolleri uygulanmıştır: Montreal Bilişsel Değerlendirme (MoCA), Standartlaştırılmış Mini Mental Durum Testi (SMMT), Hamilton Depresyon Derecelendirme Ölçeği (HDRS) ve Hamilton Anksiyete Ölçeği (HAS). Hastalar anksiyete şiddetine göre sınıflandırılmış ve bu grupların bilişsel performansları karşılaştırılmıştır.*

***Bulgular:*** *Montreal bilişsel değerlendirme ve SMMT puanlarında cinsiyetler arasında anlamlı bir farklılık görülmezken, sözel akıcılık ve soyut düşünme testlerinde erkekler kadınlardan daha yüksek puan almıştır. Anksiyete düzeyleri kadınlarda anlamlı derecede daha yüksek bulundu (p=0,001). Montreal bilişsel değerlendirme skorlarına göre, artan anksiyete şiddetiyle birlikte bilişsel işlevlerde belirgin bir düşüş gözlenmiştir.*

***Sonuç:*** *Anksiyete ve depresyon, HBB hastalarında bilişsel işlevleri belirgin ölçüde etkilemekte ve MoCA alt testlerinde anlamlı etkilere yol açmaktadır. Bu bulgular, bilişsel gerilemeyi azaltmak ve yaşam kalitesini iyileştirmek için psikiyatrik komorbiditeleri ele alan erken tanı ve hedefe yönelik müdahalelerin önemini vurgulamaktadır.*

**Anahtar kelimeler:** *hafif bilişsel bozukluk; anksiyete; depresyon; Montreal bilişsel değerlendirmesi; bilişsel işlevler*

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## Introduction

Mild cognitive impairment (MCI) is the transitional stage between normal cognitive aging and dementia, in which cognitive decline is more pronounced, yet not to a degree that markedly interferes with daily functioning[1,2]. There is growing recognition of the syndrome of MCI as being heterogeneous, including such subtypes as amnestic and non-amnestic forms, with different implications for progression to dementia[3]. The prevalence of MCI is increasing worldwide, underlining its public health importance and the urgent need for targeted interventions. Also MCI was common in older Turkish population especially in those with advanced age and low educational level[4].

Among the many neuropsychiatric symptoms associated with MCI, depression and anxiety are the most prevalent and debilitating conditions. The estimated incidence of depression is 16.9% to 55%, depending on the study design, while anxiety has variously been reported in 9.9% to 52%[5,6]. This not only exacerbates impairments in cognition and daily functioning but also apparently promotes the progression from MCI to dementia[7]. For instance, major depression has been linked with higher amyloid burden and hippocampal atrophy, hallmark pathologies of AD, whereas anxiety might interact with executive dysfunctions to further undermine cognitive resilience[8].

The bidirectional relationships between MCI, depression, and anxiety point to complex underlying mechanisms of neurodegeneration, vascular health, and stress-related pathways. White matter hyperintensities are often found accompanying late-life depression, thereby showing a vascular component in both cognitive and mood disorders[9]. Additionally, these neuropsychiatric conditions could be representing early manifestations of neurodegenerative processes rather than comorbid states per se, and therefore complicate the diagnosis and treatment process[10].

The interplay between MCI, depression, and anxiety is particularly important to understand for the purpose of early diagnosis and intervention, since these disorders together affect disease trajectory and quality of life[11]. The present study investigates cognitive correlates, and progression risks associated with depression and anxiety in MCI to add value to a nuanced understanding of these interactions and to inform evidence-based approaches to care.

## Material and Methods

This prospective study included 45 patients (23 male [51%], and 22 female [49%] participants, with a mean age of 66.1±7.7 years [range: 55–86]). diagnosed with MCI in the neurology outpatient clinic between December 2023 and October 2024. The patients were followed up in the Neurology Department of Alanya Training and Research Hospital. Montreal Cognitive Assessment (MoCA) Test, Standardized Mini-Mental State Test (SMMT), Hamilton Depression Rating Scale (HDRS) and Hamilton Anxiety Scale (HAS) were used in this study. Patients who were examined by neurological physicians and diagnosed with MCI were included and also demographical data which contained age and educational status were recorded. A flowchart illustrating the patient selection process –including inclusion and exclusion criteria– is presented in Fig. 1.

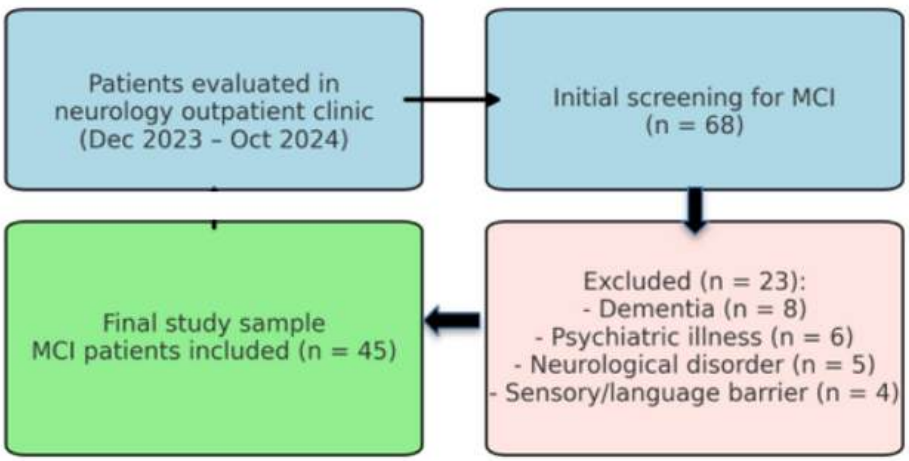


***Figure 1.*** *Patient selection flowchart.*

### Neurocognitive and Psychiatric Assessments

All patients were evaluated by trained neurologists and underwent a battery of standardized cognitive and psychiatric tests:

### Standardized Mini-Mental State Test (SMMT)

Orientation, attention, memory, motor skills and language use were evaluated with the SMMT, which can be easily applied to evaluate the cognitive functions of the patients. A total of 30 points were scored, and it was concluded that the presence of a suspicious cognitive impairment was suspected in individuals with a score of 25 points and a significant cognitive impairment was suspected in individuals with a score of less than 20 points. Mini-mental status examination can be used in both differential diagnosis and treatment follow-up of various disorders. Its ease of application is another advantage. It has also been standardized in Turkish by the Cerrahpaşa Geriatric Psychiatry team and there is a modification for illiterates recommended by the same team[12]. The SMMT, which has a maximum score of 30, consists of items measuring 6-point memory, 5-point attention, 8-point language and 1-point visual-spatial functions, including 10-point time and space orientation, 3-point recording and 3-point recall. This test was administered separately to trained and untrained subjects.

### Montreal Cognitive Assessment (MoCA)

Moca developed for evaluate MCI and cognitive functions. It is a quick and sensitive screening tool designed to detect mild cognitive impairment (MCI) and early dementia. Approximately conduction time is 10 minutes. Moca evaluates a broad range of cognitive domains: Visuospatial/Executive Functions, naming, memory, attention, language, abstraction, orientation. The total score ranges from 0 to 30, with 26 and below indicating anormal cognitive functioning. Its reliability and validity have been established for use by Ozdilek et al.[13].

### Hamilton Depression Rating Scale (HDRS)

Hamilton depression rating scale (HDRS) is carried out using a semi-structured interview, usually 20–30 minutes long. The standardized scoring of its system facilitates consistent scoring of symptoms, which makes it an excellent tool for differential diagnosis and treatment monitoring in manypsychiatric disorders. Hamilton depression rating scale has been transcribed to Turkish and reliability and validity of HDRS have been investigated in Turkish groups[14]. The acceptability of the HDRS in psychiatric practice and the ease of administration hold it to be a dependable instrument for evaluation of depressive severity and treatment response. The total score ranges from 0 to 52, with severity levels typically interpreted as follows: 0–7:Normal (no depression), 8–13:Mild depression, 14–18:Moderate depression, 19–22:Severe depression, ≥23:Very severe depression.

### Hamilton Anxiety Rating Scale (HAS)

This clinician-administered measure is designed to be applied easily in clinical settings and is especially helpful for tracking treatment course in anxiety disorders. Its structured format guarantees consistent evaluation, but the use of it depends on the interviewer's skill. The scale has been standardized inturkish, validated studies showing the reliability and usefulness of the Turkish-speaking population[15]. It has emerged as a practical measure for both clinic use and research, providing clues about the interaction between psychological manifestations and physical manifestations of anxiety. The HAS is generally administered by a semi-structured interview, which usually takes about 10–20 min. The maximum score of the scale is 56 points, with scores interpreted as follows: Mild anxiety (14–17), moderate anxiety (18–24) and severe anxiety (25 and over).

### Ethical Approval

The study was approved by University of Aladdin Keykubat University, Date: 12.09.2023, decision number: 16072023/289. This article was done in accordance with the Declaration of Helsinki with the approval of the ethics committee

### Statistical Analysis

The data were analyzed using Jamovi 2.3.28 software. P value <0.05 was considered statistically significant. Differences between parameter means according to gender and diagnosis were analyzed by independent samples t-test. Normality distribution was determined by normality tests. Moreover, the Kruskal-Wallis test was used to compare the continuous variables of more than two independent groups. Pairwise comparison was performed using the Mann-Whitney U test to determine which groups caused the difference between the variables found to be significant in the Kruskal-Wallis test. Power analysis was performed with G power 3.1 software. With a significance criterion of $\alpha$=0.05 and power=0.798.

## Results

A total of 45 participants were included with a mean age of 66.1 years (SD=7.70, range 55–86 years). Distribution of gender was similar as there were 51% males (n=23) and 49% females (n=22). The level of education of the participants, where most were primary school graduates (68%), followed by middle school (12%), high school (7%) and university graduates (13%), as shown in Table 1.

***Table 1.*** *Demographical characteristics of patients*

| **Age** | | Percentage (%) |
|---|---|---|
| Mean ± SD | 66.1±7.70 | |
| Range | 55–86 years | |
| **Gender** | | |
| Male | 23 | 0.51 |
| Female | 22 | 0.49 |
| **Education status** | | |
| Reader | | |
| Primary school | 31 | 68 |
| Middle school | 5 | 12 |
| High school | 3 | 7 |
| University | 6 | 13 |

### *1. Cognitive Performance by Gender*

Cognitive test scores were compared between males and females using the SMMT and MoCA:

- **SMMT:** No significant difference was found between males (27.7±2.31) and females (27.1±2.01), p=0.429.
- **MoCA:** Both groups had identical mean scores (18.1), with males at 18.1±3.15 and females at 18.1±3.71, p=0.962.

Additional MoCA subdomain comparisons by gender are presented in Table 2.

- **Verbal Fluency:** Males scored significantly higher than females (0.652±0.487 vs. 0.318±0.477), p=0.025.
- **Abstract Thinking:** Males also performed better (1.13±0.757 vs. 0.682±0.780), with borderline significance, p=0.057.
- No significant gender differences were found in trail making, visuospatial ability, naming, attention, sentence repetition, memory, or orientation subdomains.

***Table 2.*** *Cognitive parameters according to the gender*

| Parameter | Male (mean ± SD) | Female (mean ± SD) | p value |
|---|---|---|---|
| SMMT | 27.7±2.31 | 27.1±2.01 | 0.429 |
| MoCA | 18.1±3.15 | 18.1±3.71 | 0.962 |
| Trail making test | 0.391±0.499 | 0.455±0.510 | 0.676 |
| Visuospatial | 2.48±1.41 | 2.36 ±1.29 | 0.778 |
| Naming | 2.35±0.775 | 2.18±0.795 | 0.482 |
| Attention | 4.78±1.35 | 4.95±1.13 | 0.646 |
| Sentence repetition | 0.348±0.647 | 0.545±0.510 | 0.263 |
| Verbal fluency | 0.652±0.487 | 0.318±0.477 | 0.025* |
| Abstract thinking | 1.13±0.757 | 0.682±0.780 | 0.057 |
| Memory | 0.522±1.24 | 0.591±1.10 | 0.844 |
| Orientation | 5.52±0.790 | 5.50 ±0.598 | 0.918 |
| ANXIETY | 9.09±6.69 | 18.50±8.91 | 0.001* |
| DEPRESSION | 6.09±7.71 | 8.32±3.44 | 0.220 |

MoCA: Montreal cognitive assessment scale, SMMT: standartized minimental state examition,
* p value < 0.05 is significant.

### *2. Depression and Anxiety by Gender*

- **HDRS Scores:** Mean depression scores were higher in females (8.32±3.44) than males (6.09±7.71), but the difference was not statistically significant (p=0.220).
- **HAS Scores:** Females exhibited significantly higher anxiety levels (18.50±8.91) compared to males (9.09±6.69), p=0.001.

### *3. Group Comparison Based on Anxiety Severity*

Participants were categorized into four groups based on HAS scores: No anxiety (n=16), Mild anxiety (n=13), Moderate anxiety (n=7), Severe anxiety (n=9). Key findings across these groups are detailed in Table 3:

- **Age:** Significant differences were observed, with the highest mean age in the no-anxiety group (68.6±8.41 years) and lowest in the moderate group (63±3.87 years), p <0.001.
- **Gender:** No significant difference in distribution among anxiety groups, p=0.475.
- **SMMT:** No statistically significant differences among the four anxiety groups, p=0.259.
- **MoCA:** A significant decrease in MoCA scores was found in the severe anxiety group (15.2±3.03) compared to others, p=0.024.
- **HDRS:** Depression severity also increased with anxiety severity. Moderate (12±9.88) and severe (11.6±3.24) anxiety groups had the highest HDRS scores, p <0.001.

***Table 3.*** *Demographic and cognitive characteristics of participants by anxiety groups*

| | No (n=16) | Mild (n=13) | Moderate (n=7) | Severe (n=9) | Total (n=45) | P value |
|---|---|---|---|---|---|---|
| Age (mean ± SD) | 68.6±8.41 | 66.2±9.54 | 63±3.87 | 64.2±4.63 | 66.1±7.70 | <0.001* |
| | (65.5) | (65) | (62) | (64) | (64) | |
| SMMT (mean ± SD) | 27.3±2.54 | 28±1.73 | 28.1±1.35 | 26.2±2.22 | 27.4±2.16 | 0.259** |
| (median) | (28) | (28) | (28) | (26) | (28) | |
| MoCA (mean ± SD) | 19.1±3.58 | 18.2±2.80 | 19.3±2.75 | 15.2±3.03 | 18.1±3.39 | 0.024** |
| (median) | (20) | (20) | (20) | (14) | (19) | |
| Hdt (mean ± SD) | 3.13±2.25 | 6.54±4.68 | 12±9.88 | 11.6±3.24 | 7.18±6.05 | <0.001** |
| (median) | (3) | (5) | (10) | (11) | (6) | |

* Wilcoxon test, ** Kruskal-Wallis, MoCA: Montreal cognitive assessment scale, SMMT: standartized minimental state examition, Hdt: Hamilton depression test, p value < 0.05 is significant.

***Table 4.*** *Comparison of MoCA scores and cognitive subdomains across anxiety levels*

| | No (n=16) | Mild (n=13) | Moderate (n=7) | Severe (n=9) | Total (n=45) | P value |
|---|---|---|---|---|---|---|
| MoCA (mean ± SD) | 19.1±3.58 | 18.2±2.80 | 19.3±2.75 | 15.2±3.03 | 18.1±3.39 | 0.024* |
| (median) | (20) | (20) | (20) | (14) | (9) | |
| Trail making test (mean ± SD) | 0.500±0.516 | 0.462±0.59 | 0.429±0.535 | 0.222±0.441 | 0.422±0.499 | 0.591 |
| (median) | (0.500) | (0) | (0) | (0) | (0) | |
| Visuospatial (mean ± SD) | 2.88±1.50 | 2.38±1.26 | 2.43±1.27 | 1.67±1.00 | 2.42±1.34 | 0.110 |
| (median) | (3.50) | (2) | (3) | (2) | (3) | |
| Naming (mean ± SD) | 2.50±0.516 | 2.15±0.801 | 2.71±0.488 | 1.67±1.00 | 2.27±0.78 | 0.053 |
| (median) | (2.50) | (2) | (3) | (2) | (2) | |
| Attention (mean ± SD) | 4.88±1.50 | 5.23±0.832 | 5.29±1.11 | 4.00±1.00 | 4.87±1.24 | 0.050 |
| (median) | (5) | (5) | (6) | (4) | (5) | |
| Sentence repetition (mean ± SD) | 0.50±0.632 | 0.308±0.40 | 0.714±0.756 | 0.333±0.500 | 0.444±0.586 | 0.556 |
| (median) | (0) | (0) | (1) | (0) | (0) | |
| Verbal fluency (mean ± SD) | 0.688±0.479 | 0.538±0.59 | 0.571±0.535 | 0±0 | 0.489±0.506 | 0.011* |
| (median) | (1) | (1) | (1) | (0) | (0) | |
| Abstract thinking (mean ± SD) | 1.19±0.75 | 1.23±0.599 | 0.571±0.787 | 0.222±0.667 | 0.911±0.793 | 0.005* |
| (median) | (1) | (1) | (0) | (0) | (1) | |
| Memory (mean ± SD) | 0.875±1.45 | 0.538±1.33 | 0.429±0.535 | 0.111±0.333 | 0.556±1.16 | 0.353 |
| (median) | (0) | (0) | (0) | (0) | (0) | |
| Orientation (mean ± SD) | 5.75±0.447 | 5.38±0.870 | 5.29±0.756 | 5.44±0.726 | 5.51±0.695 | 0.386 |
| (median) | (6) | (6) | (5) | (6) | (6) | |

MoCA: Montreal Cognitive Assessment Scale, * p value < 0.05 is significant.

### *4. MoCA Subdomain Performance Across Anxiety Groups*

As presented in Table 4, MoCA subdomains showed significant variation by anxiety severity:

- **Verbal Fluency:** Performance was significantly lower in the severe anxiety group (0±0) compared to all other groups, p=0.011.
- **Abstract Thinking:** Severe anxiety group performed worse (0.222±0.667) than no and mild anxiety groups, p=0.005.
- **Attention:** Lower scores were found in the severe group (4.00±1.00), with marginal significance, p=0.050.
- **Other Domains (Visuospatial, Naming, Sentence Repetition, Memory, Orientation):** No statistically significant differences were observed across anxiety levels.

## Discussion

This study has highlighted the complex inter-relationships between MCI, depression, and anxiety and their interactional effects on cognitive functions. Our findings are in agreement with previous studies that anxiety and depression significantly affect cognitive performance[8].

### *Cognitive Impairment and Utility of MoCA*

The MoCA scores were significantly lower among subjects with severe anxiety and depression, an indication that psychiatric conditions aggravated cognitive decline. This is supported by various reports on the acceleration of cognitive decline and reduction in resilience due to emotional distress. MoCA therefore provides a

better neuropsychological tool because it assesses other domains that include verbal fluency and abstraction compared to the MMT. For example, verbal fluency and abstract thinking were most significantly affected in those subjects who showed severe psychiatric symptoms. This is in line with earlier reports of anxiety and executive dysfunction sharing a common neural basis involving frontal and temporal regions[16,17].

### *Anxiety and Cognitive Function*

Anxiety likely influences cognitive functioning via more than one pathway. Neurobiological mechanisms that have been implicated in anxiety-related deficits in cognition include the hyperactivation of the hypothalamic-pituitary-adrenal axis and disturbances in fronto-limbic connectivity[18]. Chronic anxiety also has been associated with heightened amygdala activity and decreased prefrontal cortex regulation, which may exacerbate deficits in cognition[19,20]. The strong relationship of anxiety severity with cognitive impairment in the present study was further supported by previous reports that anxiety may be not only a causal factor but also an early indicator of neurodegenerative processes[21]. Besides, the participants with severe anxiety had substantial deficits in MoCA scores, mainly in the subdomains of verbal fluency, abstraction, and attention. These findings indicate that increased anxiety has a negative effect on executive functions and general cognitive ability.

### *Depression and Cognitive Outcomes*

In addition, there was a significant difference in gender, where females had a significantly higher anxiety level than males. This concurs with previous literature depicting higher prevalence and severity of anxiety disorders in females, perhaps due to hormonal factors, life stress, or different coping strategies[22,23]. Curiously, though females manifested higher anxiety, males outperformed their female counterparts in cognitive functions like verbal fluency and abstract attitude[24]. These differences must be further elucidated for their underlying mechanisms.

### *Clinical and Research Implications*

These findings underpin the value of MoCA in capturing a broad cognitive consequence of psychiatric disorders and, hence, their suitability as supporting diagnostic tools in identifying MCI. The significant variations found in several subdomains of MoCA, such as verbal fluency and abstract thinking, are an accent on the use of comprehensive neuropsychological diagnostics which capture detailed effects of anxiety. Addressing anxiety early may improve not only cognitive performance but also the quality of life. Pharmacological interventions such as selective serotonin reuptake inhibitors (SSRIs), in combination with the cognitive-behavioral therapy (CBT) have shown some promise in decreasing anxiety symptoms and enhancing cognitive outcomes in older adults with cognitive impairment[25,26]. Personalized care plans that consider the subject's unique interaction between anxiety and cognitive function will optimize the therapeutic outcomes.

The bidirectional relationship between anxiety and cognitive impairment poses a special challenge in managing MCI. Anxiety may act additively to cognitive deterioration by impairing executive functioning, attention, and memory consolidation. On the other hand, cognitive impairment can increase anxiety because the patient has a better awareness of cognitive deficits. This negative cycle may accelerate the transition from MCI to dementia. This reaffirms the need for early intervention.

### *Limitations and Future Directions*

Because this study has a cross-sectional design, it is limited in that no causal inferences can be made, and by a relatively small sample size. These findings have to be extended by future longitudinal studies that explain exactly how anxiety influences the course of MCI and its conversion to dementia. In addition, advanced structural and functional neuroimaging-including functional MRI-could provide further insight into neurobiological pathways underlying this association. Furthermore, the identification of treatments aimed at selective cognitive domains impaired due to psychiatric symptoms may yield specific therapeutic approaches.

## Conclusion

This research addresses a significant gap in the existing literature by demonstrating that anxiety, but not depression, is independently linked to certain cognitive deficits in individuals who experience MCI, specifically in executive functions including verbal fluency, abstract reasoning, and attentional skills. Although earlier research has demonstrated extensive correlations between neuropsychiatric symptoms and cognitive deterioration, our results take the field further by specifying certain impairments within domains and enhancing the diagnostic utility of MoCA subcomponents in early executive dysfunction detection.

Importantly, the findings characterize anxiety not merely as a comorbid symptom but also as a possible early clinical indicator and a modifiable risk factor for cognitive impairment. These findings are particularly applicable to neurologists, geriatricians, and mental health practitioners engaged in the management of elderly individuals. Given the prospect of early diagnosis and intervention, clinicians can look forward to an even better outcome for MCI patients against possibly developing dementia.

In summary, this study adds fresh evidence to the growing body of literature in favor of including psychiatric evaluation in MCI management and underscores the need for personalized interventions toward cognitive and emotional health.

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**ARAŞTIRMA MAKALESİ /** *RESEARCH ARTICLE*

# Cytotoxic Effects of Helichrysum *arenarium* on HepG2 Cells

*Helichrysum arenarium'un HepG2 Hücreleri Üzerindeki Sitotoksik Etkileri*

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## ABSTRACT

***Aim:*** *Hepatocellular carcinoma (HCC) is one of the leading causes of cancer-related mortality worldwide. The search for natural compounds with potential anticancer properties has gained increasing attention. Helichrysum arenarium is a medicinal plant known for its bioactive compounds, but its cytotoxic effects on liver cancer cells remain unexplored. This study aimed to evaluate the cytotoxic effects of Helichrysum arenarium extract on HepG2 liver cancer cells by assessing cell viability and morphological changes.*

***Material and Method:*** *HepG2 cells were treated with different concentrations (0.025–0.1 mg/mL) of Helichrysum arenarium extract for 24 hours. Morphological alterations were observed using phase-contrast microscopy, while cell viability was assessed using the WST-1 assay. Statistical analysis was performed using one-way ANOVA with Tukey's post-hoc test, considering p <0.05 as statistically significant.*

***Results:*** *Helichrysum arenarium exhibited a dose-dependent cytotoxic effect on HepG2 cells. Morphological observations indicated apoptotic-like changes, and the WST-1 assay showed a significant decrease in cell viability, with the highest concentration (0.1 mg/mL) reducing viability to below 30% of the control (p <0.05).*

***Conclusion:*** *These findings suggest that Helichrysum arenarium exhibits potent cytotoxic effects on HepG2 liver cancer cells, likely through potential apoptotic pathways. Further studies are needed to elucidate the molecular pathways involved and to evaluate its potential as a therapeutic agent for hepatocellular carcinoma.*

**Key words:** *Helichrysum arenarium; HepG2 cell line; hepatocellular carcinoma; cytotoxicity; medicinal plants*

## ÖZET

***Amaç:*** *Hepatoselüler karsinom (HCC), dünya genelinde kansere bağlı ölümlerin önde gelen nedenlerinden biridir. Potansiyel antikanser özelliklere sahip doğal bileşiklerin araştırılması giderek artan bir ilgi görmektedir. Helichrysum arenarium, biyoaktif bileşenleri ile bilinen tıbbi bir bitkidir, ancak karaciğer kanseri hücreleri üzerindeki sitotoksik etkileri henüz araştırılmamıştır. Bu çalışmanın amacı, Helichrysum arenarium ekstraktının HepG2 karaciğer kanseri hücreleri üzerindeki sitotoksik etkilerini hücre canlılığı ve morfolojik değişiklikler açısından değerlendirmektir.*

***Materyal ve Metot:*** *HepG2 hücreleri, farklı konsantrasyonlarda (0,025–0,1 mg/mL) Helichrysum arenarium ekstraktı ile 24 saat süreyle muamele edilmiştir. Morfolojik değişiklikler faz-kontrast mikroskobu kullanılarak gözlemlenmiş, hücre canlılığı ise WST-1 testi ile değerlendirilmiştir. İstatistiksel analiz, tek yönlü ANOVA ve Tukey'nin post-hoc testi kullanılarak gerçekleştirilmiş olup, p <0,05 değeri istatistiksel olarak anlamlı kabul edilmiştir.*

***Bulgular:*** *Helichrysum arenarium'un HepG2 hücreleri üzerinde doz-bağımlı sitotoksik bir etkisi olduğu gözlemlenmiştir. Morfolojik gözlemler apoptotik benzeri değişikliklere işaret etmiş ve WST-1 testi hücre canlılığında önemli bir azalma göstermiştir; en yüksek konsantrasyon (0,1 mg/mL) canlılığı kontrolün %30'unun altına düşürmüştür (p <0,05).*

***Sonuç:*** *Bu bulgular, Helichrysum arenarium'un HepG2 karaciğer kanseri hücreleri üzerinde güçlü sitotoksik etkiler gösterdiğini ve bunun muhtemelen apoptozla ilişkili mekanizmalar yoluyla gerçekleştiğini düşündürmektedir. Moleküler yolların aydınlatılması ve hepatoselüler karsinom için potansiyel bir terapötik ajan olarak değerlendirilmesi için ileri çalışmalara ihtiyaç vardır.*

**Anahtar kelimeler:** *Helichrysum arenarium; HepG2 hücre hattı; hepatoselüler karsinom; sitotoksisite; tıbbi bitkiler*

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## Introduction

Hepatocellular carcinoma (HCC) is the most prevalent subtype of liver cancer, accounting for approximately 75% of all cases. It ranks as the fourth leading cause of cancer-related mortality worldwide. Due to its aggressive nature, HCC is often diagnosed at an advanced stage, and prognosis is particularly poor in patients with pre-existing liver dysfunction[1]. Hepatoma cells are widely utilized as models to study both the phenotypic characteristics of liver cancer and the behavior of hepatocytes under healthy and diseased conditions. Among human hepatoma cell lines, HepG2 cells are the most extensively characterized. Their versatility and functional properties make them invaluable for investigating liver functions[2].

*Helichrysum arenarium* (L.) Moench, commonly known as "sandy everlasting", is a perennial plant of the *Asteraceae* family[3]. Native to Europe, it is also found in Türkiye, particularly in the Western Black Sea, Central Anatolia, and Eastern Anatolia regions. Traditionally, the plant has been used in European ethnomedicine for its hepatoprotective, bile-stimulating, and detoxifying properties[4]. Its inflorescences are rich in flavonoids (e.g., chalcone isosalipurposide, naringenin), essential oils, carotenoids, and α-pyrone derivatives[5,6].

Türkiye's diverse climate and rich flora support the growth of various *Helichrysum* species, which are commonly consumed as herbal teas for their bile-regulating and diuretic properties[7]. Due to the documented pharmacological properties of *Helichrysum arenarium*, this study aims to evaluate its cytotoxic effects on HepG2 liver cancer cells in terms of cell viability and morphological alterations. The hypothesis of this study is that *H. arenarium* extract may induce apoptosis-related cytotoxicity in HepG2 cells.

## Materials And Methods

### *Collection and Authentication of Plant Material*

Fresh *Helichrysum arenarium* samples were collected from the Giresun region of Türkiye. The plant material was authenticated by a botanist, and voucher specimens were deposited for future reference. The collected samples were stored under control conditions until further processing.

### *Preparation of Plant Extracts*

The extraction process was performed using dried *Helichrysum arenarium*. A total of 10 mg of dried plant material was weighed and placed into a sterile container. The extraction solution, preheated to 65°C, was added, and the mixture was transferred to a 50 mL Falcon tube. The Falcon tube containing the dried herb was frozen in liquid nitrogen and mechanically crushed while maintaining an air-tight environment. The crushed sample was then incubated at 65°C for 15 minutes. Following incubation, chloroform (Sigma Aldrich, USA) at a 24:1 v/v ratio was added to the Falcon tube and thoroughly mixed. The sample was centrifuged at 2000 × g for 15 minutes at room temperature, after which the upper liquid phase was carefully transferred to a new Falcon tube. The extraction process was repeated with an additional 24:1 v/v chloroform treatment, followed by another 15-minute centrifugation at 2000 × g at room temperature. The resultant liquid phase was combined with 6 mL of isopropanol (Sigma Aldrich, USA) and incubated at -20°C for 5 minutes. The final step involved centrifugation at 8500 × g for 10 minutes, and the supernatant was transferred to a new Falcon tube. The sample was left to rest for three days before being washed twice with 70% ethanol in a water bath maintained at 65°C to ensure purity[8].

### *Cell Culture*

HepG2 cells, obtained from the laboratories of Istanbul University, were maintained under standard culture conditions. Firstly, the liquid nutrient medium was removed, and the cells were washed with 5 mL of phosphate-buffered saline (PBS; Gibco). Following the PBS wash, 1.2 mL of Trypsin (Gibco) was added to facilitate cell detachment, and the cells were incubated at 37°C for 1–2 minutes to activate Trypsin.

Upon confirmation of cell detachment from the culture dish, 5 mL of Dulbecco's Modified Eagle Medium (DMEM; Gibco) supplemented with 10% fetal bovine serum (FBS; Gibco) was added to neutralize Trypsin activity. The cell suspension was then transferred into a 15 mL Falcon tube and centrifuged at 2000 rpm for 5 minutes. Following centrifugation, the supernatant was discarded, and the cell pellet was resuspended in 5 mL of DMEM supplemented with 10% FBS. The centrifugation step was repeated under the same conditions to ensure complete removal of Trypsin.

The cell pellet was resuspended in 2 mL of DMEM, and the viable cell count was determined using a hemocytometer and Trypan Blue staining (Sigma Aldrich). Subsequently, cells were seeded into a 96-well plate at a density of $1\times10^4$ cells per well. The cultures were incubated for 24 hours under standard conditions. Following incubation, cell morphology was observed and documented using a phase-contrast microscope.

In addition to untreated control wells, a solvent control group was included to assess the cytotoxicity of the extraction solvents. The solvent control group received a mixture of chloroform and isopropanol at the same volume and ratio used in the extract preparation. This group was subjected to the same incubation conditions and cell viability was assessed using the WST-1 assay.

### *Detection of Morphological Changes*

HepG2 cells were exposed to different concentrations (0.025–0.1 mg/mL) of *Helichrysum arenarium* extract for 24 h. After the exposure period, cells were observed under an inverted light microscope to detect any morphological changes related to apoptosis.

### *Analysis of Cell Viability*

Cell viability was assessed using the WST-1 colorimetric assay after 24 hours of treatment with different concentrations of *Helichrysum arenarium* extract. Each plate contained blanks, controls, and dilution series with three replicates. The WST-1 assay relies on the cleavage of the tetrazolium salt to formazan by cellular mitochondrial dehydrogenases, with the intensity of the resulting dark yellow formazan dye directly correlating to cell viability. After incubation, a 10 µl aliquot of WST-1 reagent was added to each well (for a total 100 µl solution, maintaining a 9:1 ratio) and further incubated at 37°C for 2 hours. Absorbance was measured at 450 nm using a Multiskan SkyHigh Reader (Thermo Fisher Scientific, USA), with higher absorbance values indicating greater cell viability[9–11].

### *Statistical Analysis*

The data were analyzed using GraphPad Prism software (GraphPad Software, San Diego, CA, USA). The results are presented as mean ± standard deviation (SD). One-way ANOVA was used to assess statistical differences between groups, followed by Tukey's post-hoc test for multiple comparisons. The significance level of $p$ <0.05 was considered statistically significant.

## Results

### *Morphological Changes in HepG2 Cells*

HepG2 cells were treated with *Helichrysum arenarium* extract at concentrations ranging from 0.025 mg/mL to 0.1 mg/mL for 24 hours (Fig. 2). Microscopic analysis revealed distinct morphological changes in a dose-dependent manner. In control conditions, cells maintained a typical epithelial-like morphology with well-defined cell membranes and strong adherence to the culture plate. However, cells exposed to increasing concentrations of the extract exhibited features consistent with cytotoxicity, including reduced cell density, cell shrinkage, membrane blebbing, and detachment from the surface. The most pronounced effects were observed at 0.075 mg/mL and 0.1 mg/mL, where a significant proportion of cells became rounded and detached, indicative of apoptosis. The solvent control group did not show any significant decrease in cell viability compared to the untreated control, indicating that the observed cytotoxic effects were specific to the plant extract.

### *WST-1 Cell Viability Assay*

The WST-1 assay results further confirmed the cytotoxic effect of Helichrysum arenarium on HepG2 cells. A concentration-dependent decrease in cell viability was observed (Fig. 1a). The absorbance values presented in Fig. 1b numerically support this trend, showing a marked decline with increasing extract concentrations. At 0.025 mg/mL, there was a slight but statistically significant reduction in viability ($p$ <0.05). At 0.05 mg/mL and higher, a marked decrease in absorbance values indicated a strong cytotoxic response. The highest tested concentration (0.1 mg/mL) reduced to below 30% of control values. The statistical analysis confirmed that all treatment groups, except the lowest concentration, significantly differed from the control ($p$ <0.05, Tukey's test). These findings suggest that *Helichrysum arenarium* disrupts mitochondrial activity and inhibits cell proliferation in HepG2 cells. The solvent control group exhibited no statistically significant difference in cell viability compared to the untreated control group (p >0.05), indicating that the observed cytotoxic effects were specific to *Helichrysum arenarium* extract and not due to the solvents used in the extraction process. In addition to the graphical data, tabulated absorbance values (Fig. 1b) provide numerical support for the dose-dependent decrease in viability, showing a decline in mitochondrial activity at increasing extract concentrations.

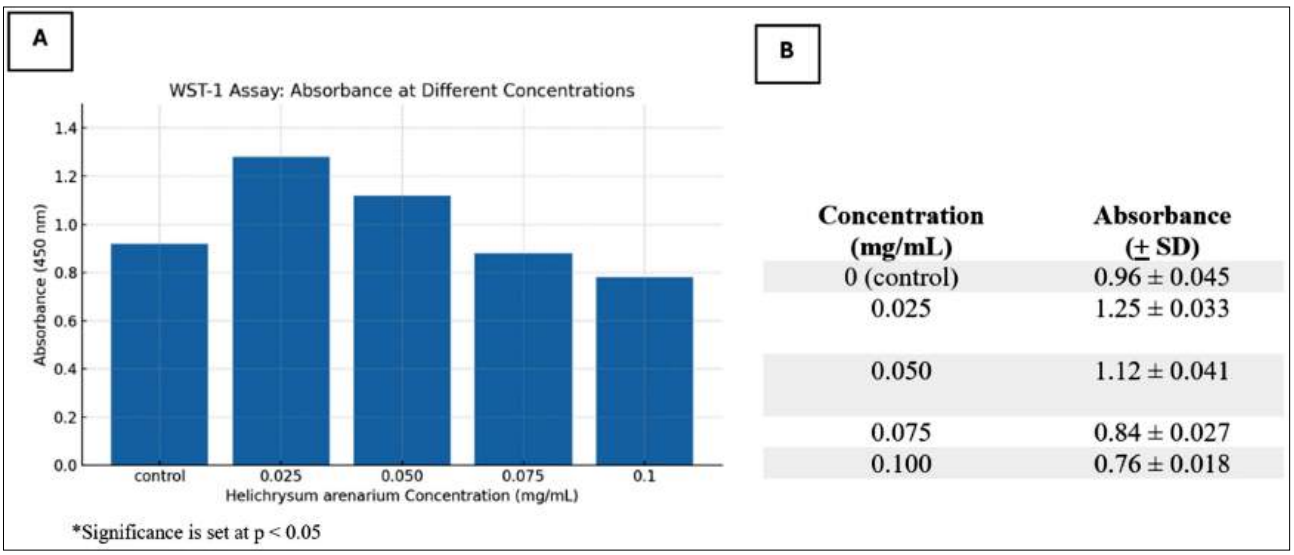


**Figure 1.** *Evaluation of Helichrysum arenarium's effect on HepG2 cells with WST-1 assay.*
*(A) Bar graph showing the absorbance values at 450 nm, indicating mitochondrial activity in HepG2 cells after 24-hour treatment with different concentrations of Helichrysum arenarium extract. Interestingly, a slight increase in absorbance is observed at 0.025 mg/mL, which may suggest a transient proliferative or metabolic activation effect. However, higher concentrations resulted in a marked, dose-dependent decrease in absorbance, reflecting reduced cell viability. (B) Table summarizing the absorbance values (mean ± SD) for each concentration. The consistency between graphical and tabular data supports the conclusion that Helichrysum arenarium exhibits concentration-dependent cytotoxic effects.*

## Discussion

Hepatocellular carcinoma (HCC) poses a growing global health challenge, with its incidence and mortality rates steadily rising[12]. According to estimates from the World Health Organization, liver cancer-related deaths are expected to exceed 1 million by 203012.

The search for natural compounds with anticancer properties has gained attention, with medicinal plants emerging as potential therapeutic agents. This study evaluated the cytotoxic effects of *Helichrysum arenarium* extract on HepG2 liver cancer cells, demonstrating significant dose-dependent inhibition of cell viability and morphological alterations indicative of apoptosis[13–15]. Furthermore, the tabular data in Fig. 1b substantiates the visual evidence from microscopy and WST-1 bar graphs, clearly illustrating the progressive loss of mitochondrial activity with rising extract doses. While such morphological changes are consistent with apoptosis, the observed pattern in this study –particularly the rounded, detached cells at higher concentrations indicates early apoptotic features specific to HepG2 response under Helichrysum arenarium exposure.

The morphological changes observed under phase-contrast microscopy align with typical apoptotic features, including cell shrinkage, detachment, and membrane blebbing. These findings suggest that *Helichrysum arenarium* induces programmed cell death in HepG2 cells, which may be mediated through mitochondrial dysfunction and oxidative stress. Similar effects have been reported for other flavonoid-rich plant extracts, supporting the hypothesis that polyphenols present in *Helichrysum arenarium* contribute to its cytotoxic activity[3]. In this study, however, it should be noted that the apoptosis claim is based solely on morphological observations and WST-1 metabolic activity. No direct biochemical validation (such as caspase-3 activation, Annexin-V staining, or TUNEL assay) was performed, which limits the strength of the mechanistic conclusion.

The WST-1 assay results further corroborate the cytotoxic potential of *Helichrysum arenarium*. The significant reduction in metabolic activity at concentrations above 0.05 mg/mL indicates that the extract interferes with mitochondrial dehydrogenase enzymes, leading to decreased ATP production and cell death. Previous studies have shown that flavonoid-containing plant extracts can modulate apoptosis-related signaling pathways in various cancer cell lines. The active compounds in *Helichrysum arenarium*, including flavonoids and essential oils, may exert their effects through similar mechanisms[16].

While our findings demonstrate promising anticancer activity, there are limitations to this study. The experiments were conducted in an *in vitro* setting, which does

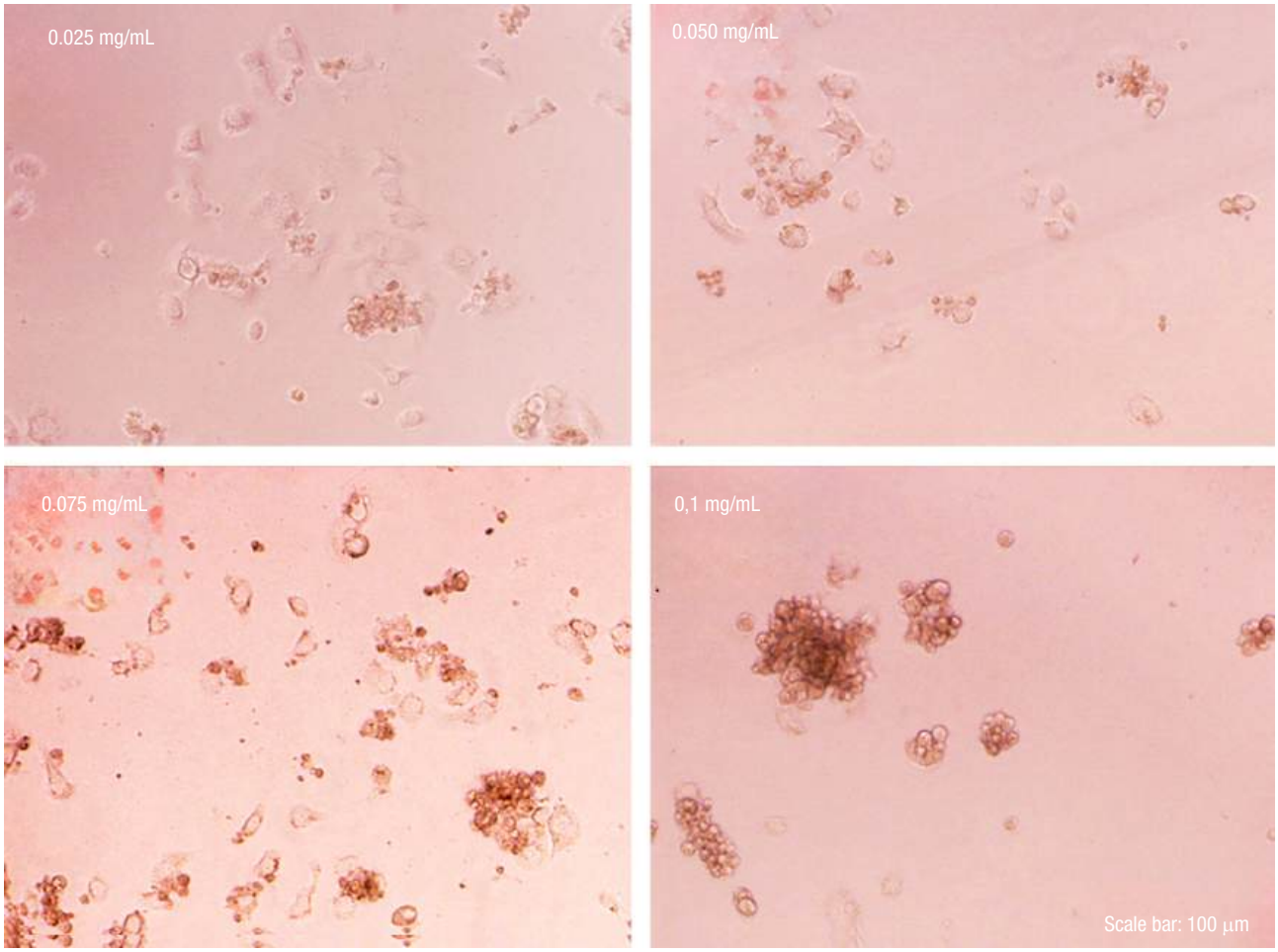


**Figure 2.** *Morphological changes in HepG2 cells after 24-hour treatment with Helichrysum arenarium at different concentrations, showing dose-dependent cytotoxic effects.*

not fully replicate the complexity of tumor microenvironments in vivo. Future studies should focus on elucidating the molecular mechanisms underlying the cytotoxic effects of *Helichrysum arenarium* and assessing its efficacy in animal models. Additionally, identifying the specific bioactive compounds responsible for its anticancer properties could provide valuable insights for the development of novel chemotherapeutic agents. The observed correlation between morphological alterations and WST-1 cell viability results enhances the robustness of the findings and reinforces the hypothesis that *Helichrysum arenarium* exerts its cytotoxic effects through potential apoptotic pathways. To further validate these in vitro results, future studies could incorporate in vivo xenograft models –such as HepG2-derived hepatocellular carcinoma tumors in athymic nude mice– to comprehensively assess the therapeutic potential, pharmacokinetics, and bioavailability of the extract.

## Conclusion

This study demonstrated that Helichrysum arenarium extract exerts significant cytotoxic effects on HepG2 liver cancer cells, reducing cell viability and inducing morphological features associated with apoptosis. While the findings are promising, the study was limited to *in vitro* conditions. Future research should focus on identifying the active constituents responsible for these effects, elucidating the underlying molecular mechanisms, and validating the extract's therapeutic potential through *in vivo* studies. These efforts could contribute to the development of novel plant-based agents for the treatment of hepatocellular carcinoma.

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### *Conflict of Interest*

There is no conflict of interest related to this article.

### *Ethical Approval*

This study was conducted using commercially available ready-to-use cell cultures and, therefore, does not require ethical approval.

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**DERLEME** / *REVIEW*

# Publication Status of Postgraduate Theses Completed in Ankara University's Health Sciences Institute (1984-2023): A Biometric Study

*Ankara Üniversitesi Sağlık Bilimleri Enstitüsü'nde Tamamlanan Lisansüstü Tezlerin Yayın Durumu (1984-2023): Biyometrik Bir Çalışma*

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## ABSTRACT

***Aim:*** *This study determined the publication status and index type of the journals in which the postgraduate theses were published in the Ankara University Institute of Health Sciences between 1984 and 2023.*

***Material and Method:*** *The study was prepared using a bibliometric, retrospective and descriptive design. The data were analyzed using performance analysis, and descriptive statistics were used to calculate the number and percentage distributions of the data.*

***Results:*** *The study determined that 3783 graduate theses (39.2% master's theses and 60.7% doctoral theses) were prepared at Ankara University's Institute of Health Sciences. 25.2% of master's theses and 34.26% of doctoral theses were published, resulting in a total publication rate of 29.8% for graduate theses. Of the publications from master's and doctoral theses, 59.6% were published in international indexes, 22% in national indexes, 16.7% in citation indexes, and 1.5% in national refereed journals.*

***Conclusion:*** *The study revealed that the publication rate of postgraduate theses conducted in the health sciences institute of the relevant university was not high. In this context, the factors affecting the conversion of postgraduate theses into publications should be investigated, and solutions should be produced. Additionally, institutional arrangements should be established to ensure the publication of theses, and effective policies should be implemented to support this process.*

**Key words:** *bibliometrics; doctoral thesis; master's thesis; publication*

## ÖZET

***Amaç:*** *Bu çalışma 1984–2023 yılları arasında, Ankara Üniversitesi Sağlık Bilimleri Enstitüsü'nde yürütülen lisansüstü tezlerin yayın olma durumları ve yayımlandıkları dergilerin endeks türünü belirlemek amacıyla yapıldı.*

***Materyal ve Metot:*** *Çalışma bibliyometrik, retrospektif ve tanımlayıcı desende yürütüldü. Verilerinin analizinde performans analizi yönteminden yararlanıldı. Tanımlayıcı istatistiklerden yararlanılarak verilerin sayı ve yüzde dağılımları hesaplandı.*

***Bulgular:*** *Araştırma sonucunda, Ankara Üniversitesi Sağlık Bilimleri Enstitüsü'nde toplam 3783 lisansüstü tez yürütüldüğü (%39,2'si yüksek lisans tezi, %60,7'si doktora tezi) belirlenmiştir. Yüksek lisans tezlerinin %25,2'si, doktora tezlerinin %34,26'sı yayımlanmıştır. Bu doğrultuda lisansüstü tezlerinin toplam yayımlanma oranı %30,7'dir. Yüksek lisans ve doktora tezlerinden üretilen yayınların %59,6'sı uluslararası endekste, %22'si ulusal endekste, %16,7'si atıf endeksinde, %1,5'i ulusal hakemli dergilerde yayımlanmıştır.*

***Sonuç:*** *Çalışma sonucunda, ilgili üniversitenin sağlık bilimleri enstitüsünde yürütülmüş olan lisansüstü tezlerin yayımlanma oranlarının yüksek olmadığı ortaya konmuştur. Bu kapsamda, lisansüstü tezlerin yayına dönüşmesini etkileyen faktörler araştırılmalı ve çözümler üretilmelidir. Ayrıca, tezlerin yayımlanmasını sağlayacak kurumsal düzenlemeler yapılmalı ve etkili politikalar geliştirilmelidir.*

**Anahtar kelimeler:** *bibliyometrik; doktora tezi; yüksek lisans tezi; yayın*

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## Introduction

The ability of a society to be economically, politically and culturally effective is closely tied to the efficient functioning of its educational institutions. Universities play a crucial role in addressing these needs. Postgraduate education is essential for promoting scientific research and equipping students with the knowledge and skills to evaluate evidence and apply it effectively and critically. It also provides opportunities for those who wish to deepen their professional knowledge. The academic research productivity of postgraduate students is assessed as a measure of universities' ability to prepare the next generation of health scientists[1]. Producing knowledge disseminated through master's and doctoral dissertations contributes to scientific research and practice and prepares qualified and productive master's and doctoral students. Although the higher education system in Türkiye has been offering graduate-level education since 1982, these programs have a long history worldwide[2].

Universities need specific standards to meet changing conditions, expectations and competition. Research universities with high research capacity and significant contributions to science and technology hold a critical place in this context, thanks to their expertise, skilled human resources and knowledge transfer activities[3]. International cooperation and recognition in research are important characteristics of research universities. The performance of these universities is ranked according to various indicators, including the number and rate of publications, the number of citations, the number of national or international awards, the number of patents and the amount of project funding. As expectations from research universities have increased in recent years, many countries have introduced structural regulations and established comprehensive support programs to meet these expectations.

Since 2016, some universities in Türkiye that meet the required criteria have been selected as research universities. These universities collaborate with research universities in various countries to develop specific solutions and create the desired value[4]. International evaluation of research and higher education ensures quality and relies on globally accepted standards for greater assurance. These expectations also apply to doctoral (PhD) programs. Although the PhD is an international degree, the content of these programs is not specified. For this purpose, an international organization called ORPHEUS (Organisation of PhD in Biomedicine and Health Sciences European System) was established in 2005 with the participation of 21 European countries to develop basic standards and good research practices in doctoral education. The first ORPHEUS membership in Türkiye started in 2007 and many universities are at the membership stage. It is known that some of the goals being developed in Europe and enabling our country to reach these ORPHEUS standards will be possible through "research"[5].

The publication performance of universities measures their strength and effectiveness in research activities. In recent years, several criteria have been used to determine the quality of universities. Quantitative evaluation of articles obtained from theses and dissertations, based on specific criteria, is a crucial method for assessing the current state of knowledge in a particular field. The analysis of postgraduate thesis studies provides data on various literature characteristics, allowing a more concrete recognition of the characteristics of the research areas[6]. Although there has been an increase in the productivity of scientific studies by researchers completing graduate programs in our country, the target has not yet been reached[7]. This national and international mission prioritizes academic publication performance, ranking universities according to their quality. Bibliometric studies are widely used to measure and compare the impact and importance of researchers, articles and various journals[8]. Bibliometric studies use statistics to assess research productivity, quality and the overall structure of a discipline[9–11]. It is seen that various bibliometric studies have been conducted on postgraduate theses in our country. However, upon examining the literature, no study has been found on the publication status of postgraduate theses accepted by the Institute of Health Sciences in Türkiye. For this reason, a bibliometric analysis was conducted in this study to provide information about the diversity, publication status and index types of the journals in which theses prepared within the scope of master's and doctoral theses at Ankara University Institute of Health Sciences between 1984 and 2023 were published.

Given these developments, it is essential to evaluate the academic output of universities, particularly in terms of the publication rates and visibility of postgraduate research. Analyzing the extent to which master's and doctoral theses are published, as well as the platforms on which they are made available, provides valuable insights into the quality and impact of academic training. Such evaluations not only help benchmark institutional performance but also identify areas for improvement and the need for supportive policies that foster greater research dissemination.

## Objective

This study determined the publication status of postgraduate theses conducted at Ankara University Institute of Health Sciences between 1984 and 2023, as well as the index type of the journals in which they were published.

### *Research questions*

1. What is the publication rate of graduate theses conducted at the Ankara University Institute of Health Sciences?
2. In which indexes are the journals in which graduate theses are published indexed?

## Material and Method

### *Study Design and Participants*

This study employed a bibliometric, retrospective and descriptive design. The study population consisted of the postgraduate theses conducted at Ankara University Institute of Health Sciences between 1984 and 2023. Ankara University Institute of Health Sciences was established in 1982 under the Rectorate of Ankara University. The Faculties of Medicine, Pharmacy, Dentistry, Veterinary Medicine, Sports Sciences, Health Sciences, Nursing and Interdisciplinary Departments carry out postgraduate education and training activities. In this context, to determine the population, a list of theses conducted between 1984 and 2023 (3889 theses) was received from the institute via email. Of the 3889 theses, 106 were excluded from the study because they were graduation projects from the master's program that did not require a thesis. Then, the information obtained from the theses was classified by thesis type and department and the publication status of the theses in the Thesis Center of the Council of Higher Education was checked. It was determined that 3783 theses were conducted at the Ankara University Institute of Health Sciences.

### *Data Collection*

The data were collected and evaluated from June 1 to November 30, 2023. The publication status of theses was evaluated in four groups: Citation Index, International Index, National Index and National Refereed Journals. Within the scope of the Citation Index, publications published in journals indexed by Science Citation Index (SCI), Science Citation Index Expanded (SCI-exp), Social Science Citation Index (SSCI) and Art and Humanities Index (A&HCI) were considered. Publications in international journals outside these citation indexes were defined as being in an "international index". Publications published in national journals indexed by Ulakbim TR Index and Turkish Citation Index were considered national indexes[12]. Publications published in peer-reviewed national journals that were not indexed in any index were grouped as peer-reviewed journals. In this context, the ISI-Web of Science (WoS) collection, comprising four leading indices (SSCI, SCI-EXP, AHCI, and ESCI), was initially searched to evaluate the citation index status of the thesis. Medline, PubMed, Embase, Science Direct, Ovid and Ebscohost databases were also utilized. Google Scholar and ULAKBIM Turkish Medical Directory were used to identify publications in other indexes.

The databases were searched using the Turkish/English title of the thesis, the author's name, surname and first initial, the advisor's surname and first initial and the thesis keywords. In cases where the thesis could not be found, the author's or consultant's CV was accessed using the Academic Data Management System (AVESIS) and the publication status of the thesis was examined. Since the publication status of theses may change during the scanning period, the data were updated by scanning again between December 1 and 31, 2023.

As a result of the scans made in this context, a total of 1162 published graduate theses were analyzed. The data obtained from the scans, thesis year, thesis type, department, article name, journal name, publication year, number of publications, publication type (national publication, international publication), and index type (national index, international index, citation index, refereed journal) were determined and recorded.

### *Inclusion and Exclusion Criteria*

This study included articles from theses, in any publication stage (such as publication stage, early view), and produced in either Turkish or English. Articles published in books, conference proceedings and languages other than Turkish/English were not included (Fig. 1).

### *Ethical Aspects of the Research*

In this study, postgraduate theses in the Thesis Center of the Council of Higher Education (YÖK-Thesis), which is open to public access, and publications obtained from these theses were included in the sample and conducted retrospectively. For this reason, permission was not obtained from the ethics committee. However, the data obtained from the theses included in the study were presented without including the identities of the authors or advisors.

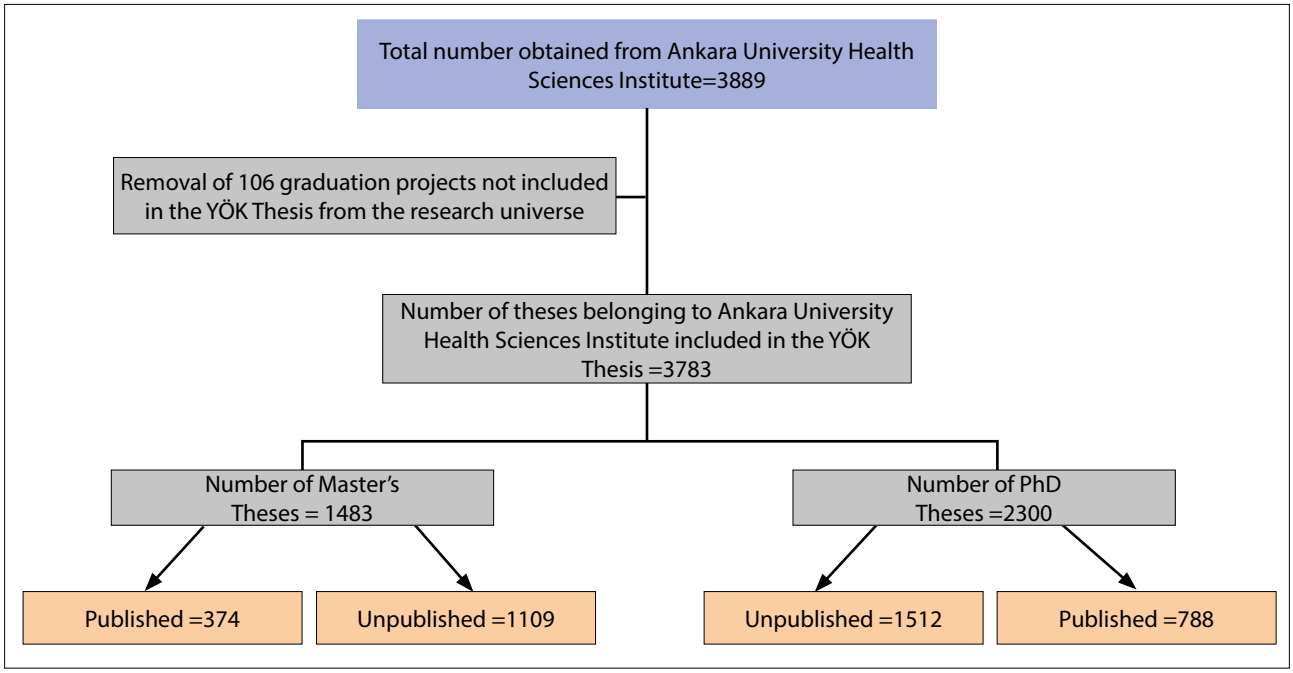


***Figure 1.*** *Publication status of theses conducted at Ankara University Postgraduate School of Health Science.*

### *Data Analysis*

The research data was analyzed using performance analysis, a bibliometric method that examines the contribution of research components to a particular field[13]. In this context, information about the theses was recorded and analyzed using the IBM Statistical Package for Social Sciences (SPSS) program for Windows version 22.0. Data analysis used descriptive statistics, and number and percentage distributions were calculated.

## Results

As a result of the research, it was determined that there was a total of 3783 theses in the main branches of the Ankara University Institute of Health Sciences. Of these theses, 39.2% were master's theses (n=1483) and 60.7% were doctoral theses (n=2300). The total publication rate of master's and doctoral theses is 30.7% (1162/3783). 25.2% (374/1483) of master's theses and 34.26% (788/2300) of doctoral theses were published (Table 1). Descriptive information is given in Table 2.

When the publication status of master's and doctoral theses, categorized by the main branches of science, was examined, 9.38% (109/1162) of the published theses belonged to the Department of Forensic Sciences (Table 3). Of the publications from master's and doctoral theses, 59.6% were published in international

***Table 2.*** *Thesis related baseline characteristics*

| | | MSc | PhD | Total |
|---|---|---|---|---|
| Characteristics | | n | n | n |
| **Gender** | | | | |
| | Male | 549 | 1148 | 1696 |
| | Female | 934 | 1152 | 2082 |
| | Total | 1483 | 2300 | 3783 |
| **Academic title** | | | | |
| | Prof. | 1157 | 2170 | 3327 |
| | Assoc. Prof. | 286 | 113 | 399 |
| | Assist. Prof. | 40 | 17 | 57 |
| | Total | 1483 | 2300 | 3783 |
| **Number_of_advisor** | | | | |
| | Couple counseling | 12 | 9 | 21 |
| **Number of publications obtained from the thesis** | | | | |
| | Single publication | 322 | 648 | 970 |
| | 2 publications | 44 | 93 | 137 |
| | 3 and above publications | 8 | 47 | 55 |
| | Total | 374 | 788 | 1162 |
| | Unpublished | 1109 | 1512 | 2621 |

***Table 1.*** *Distribution of postgraduate theses conducted in the departments of the Ankara University Institute of Health Sciences according to their publication status*

| Publication status of theses | Master theses | | Doctoral theses | | Total | |
|---|---|---|---|---|---|---|
| | n | % | n | % | n | % |
| Published theses | 374 | 25.2 | 788 | 34.26 | 1162 | 30.7 |
| Unpublished theses | 1109 | 74.78 | 1512 | 65.7 | 2621 | 69.28 |
| Total | 1483 | 100 | 2300 | 100 | 3783 | 100 |

***Table 3.*** *Distribution of the publication status of graduate theses conducted at Ankara University Postgraduate School of Health Sciences according to their main branches of science*

| | MASTER'S THESES | | DOCTORAL THESES | | TOTAL | |
|---|---|---|---|---|---|---|
| MAIN SCIENCE | Total number of theses (n) | Number of published thesis (n) | Total number of theses (n) | Number of published thesis (n) | Total number of theses (n) | Number of published thesis (n) |
| Forensic Science | 227 | 53 | 115 | 56 | 342 | 109 |
| Biophysics | 2 | 1 | 2 | 1 | 4 | 2 |
| Biochemistry | 23 | 6 | 24 | 7 | 47 | 13 |
| Public Health | 2 | 1 | 0 | 0 | 2 | 1 |
| Physiology | 2 | 1 | 3 | 1 | 5 | 2 |
| Public Health Nursing | 5 | 2 | 0 | 0 | 5 | 2 |
| Nursing | 34 | 7 | 17 | 8 | 51 | 15 |
| Histology-Embryology | 1 | 0 | 2 | 1 | 3 | 1 |
| Anatomy | 0 | 0 | 3 | 1 | 3 | 1 |
| Stem Cells and Regenerative Medicine | 11 | 1 | 0 | 0 | 11 | 1 |
| Hepatology | 2 | 1 | 0 | 0 | 2 | 1 |
| Medical Biology | 4 | 2 | 0 | 0 | 4 | 2 |
| Medical Education and Informatics | 2 | 1 | 0 | 0 | 2 | 1 |
| History of Medicine and Ethics | 3 | 0 | 2 | 1 | 5 | 1 |
| Internal Medicine | 6 | 1 | 1 | 0 | 7 | 1 |
| Forensic Pharmacy | 1 | 1 | 0 | 0 | 1 | 1 |
| Oral, Dental, and Maxillofacial Radiology | 0 | 0 | 12 | 7 | 12 | 7 |
| Oral, Dental, Maxillofacial Diseases and Surgery | 0 | 0 | 119 | 32 | 119 | 32 |
| Analytical Chemistry | 56 | 34 | 34 | 25 | 90 | 59 |
| Physical Education and Sports | 11 | 5 | 68 | 12 | 79 | 17 |
| Nutrition and Dietetics | 56 | 15 | 20 | 6 | 76 | 21 |
| Pharmacognosy | 66 | 7 | 31 | 8 | 97 | 15 |
| Biostatistics | 5 | 2 | 13 | 4 | 18 | 6 |
| Pharmacology | 39 | 8 | 33 | 10 | 72 | 18 |
| Child Development | 45 | 11 | 21 | 11 | 66 | 22 |
| Dental Diseases and Treatment | 1 | 0 | 57 | 18 | 58 | 18 |
| Fertilization and Artificial Insemination | 7 | 1 | 45 | 2 | 52 | 3 |
| Pharmacy Management | 20 | 6 | 24 | 8 | 44 | 14 |
| Endodontics | 0 | 0 | 45 | 17 | 45 | 17 |
| Pharmaceutical Botany | 11 | 6 | 21 | 16 | 32 | 22 |
| Pharmaceutical Chemistry | 69 | 33 | 39 | 23 | 108 | 56 |
| Pharmaceutical Microbiology | 37 | 14 | 23 | 11 | 60 | 25 |
| Pharmaceutical Technology | 83 | 39 | 43 | 28 | 126 | 67 |
| Pharmaceutical Toxicology | 56 | 11 | 27 | 7 | 83 | 18 |
| Child Health and Diseases | 17 | 4 | 0 | 0 | 17 | 4 |
| Food, Metabolism, and Clinical Nutrition | 13 | 3 | 0 | 0 | 13 | 3 |
| Vision, Artificial Vision, and Rehabilitation of Low Vision | 6 | 4 | 0 | 0 | 6 | 4 |
| Animal Nutrition and Nutritional Diseases | 8 | 0 | 70 | 0 | 78 | 0 |
| Animal Health Economics and Management | 11 | 1 | 43 | 19 | 54 | 20 |
| Ear, Nose, Throat Diseases | 21 | 4 | 0 | 0 | 21 | 4 |
| Orthodontics | 0 | 0 | 107 | 34 | 107 | 34 |
| Pedodontics | 2 | 0 | 76 | 39 | 78 | 39 |
| Periodontology | 0 | 0 | 92 | 32 | 92 | 32 |
| Prosthodontics | 0 | 0 | 136 | 60 | 136 | 60 |
| Health Management | 11 | 1 | 0 | 0 | 11 | 1 |
| Neurosciences | 0 | 0 | 2 | 1 | 2 | 1 |
| Social Service | 76 | 28 | 30 | 10 | 106 | 38 |
| Physical Education and Sports | 28 | 9 | 33 | 3 | 61 | 12 |
| Coaching Education | 72 | 3 | 2 | 2 | 74 | 5 |
| Sport Management | 58 | 29 | 4 | 3 | 62 | 32 |
| Medical Pharmacology | 0 | 0 | 1 | 0 | 1 | 0 |
| Veterinary Anatomy | 3 | 1 | 1 | 1 | 4 | 2 |
| Veterinary Biostatistics | 9 | 0 | 20 | 6 | 29 | 6 |
| Veterinary Biochemistry | 20 | 2 | 44 | 15 | 64 | 17 |
| Veterinary Surgery | 51 | 0 | 60 | 0 | 111 | 0 |
| Veterinary Obstetrics and Gynecology | 16 | 0 | 88 | 0 | 104 | 0 |
| Veterinary Pharmacology and Toxicology | 28 | 1 | 91 | 31 | 119 | 32 |
| Veterinary Physiology | 12 | 2 | 47 | 21 | 59 | 23 |
| Veterinary Genetics | 3 | 0 | 8 | 7 | 11 | 7 |
| Veterinary Food Hygiene and Technology | 69 | 0 | 65 | 0 | 134 | 0 |
| Veterinary Histology-Embryology | 0 | 0 | 28 | 0 | 28 | 0 |
| Veterinary Internal Medicine | 8 | 0 | 58 | 0 | 66 | 0 |
| Veterinary Microbiology | 22 | 5 | 74 | 29 | 96 | 34 |
| Veterinary Parasitology | 8 | 0 | 57 | 33 | 65 | 33 |
| Veterinary Pathology | 1 | 0 | 38 | 26 | 39 | 26 |
| Veterinary Virology | 8 | 2 | 70 | 23 | 78 | 25 |
| Veterinary Medicine Animal Husbandry | 11 | 5 | 93 | 62 | 104 | 67 |
| History of Veterinary Medicine and Deontology | 2 | 0 | 17 | 9 | 19 | 9 |
| Clinical Pharmacy | 0 | 0 | 1 | 1 | 1 | 1 |
| Social Psychiatry | 2 | 0 | 0 | 0 | 2 | 0 |
| Total | 1483 | 374 | 2300 | 788 | 3783 | 1162 |
| Percentile (%) | 100 | 25.2 | 100 | 34.26 | 100 | 30.7 |

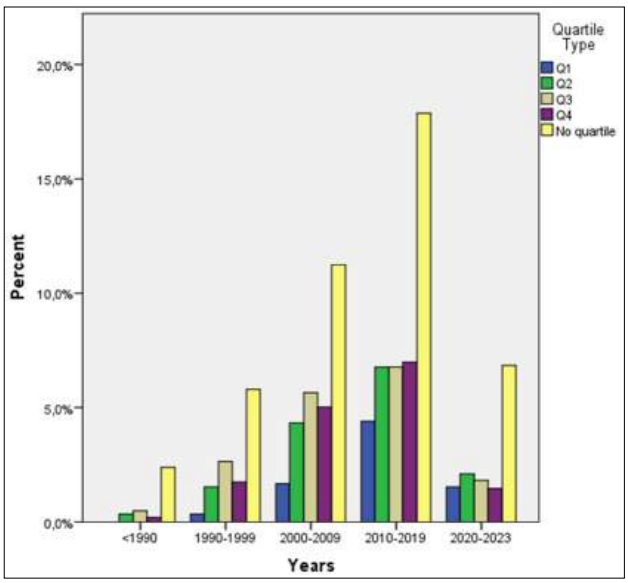


***Figure 2.*** *Distribution of published theses according to journal quartile and years.*

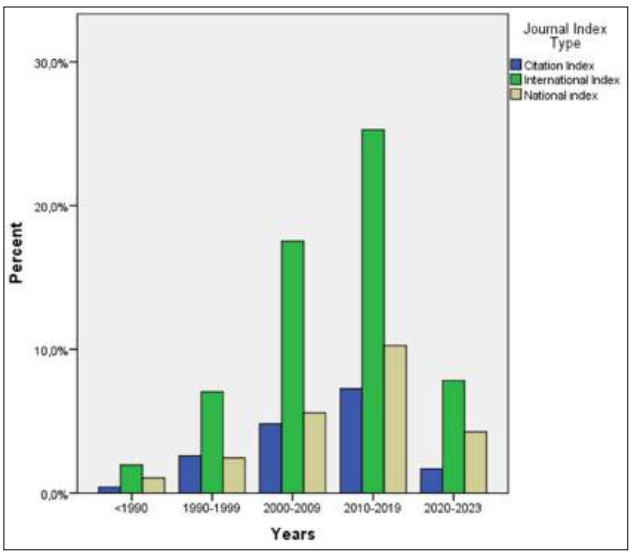


***Figure 3.*** *Distribution of published theses according to journal index types and years.*

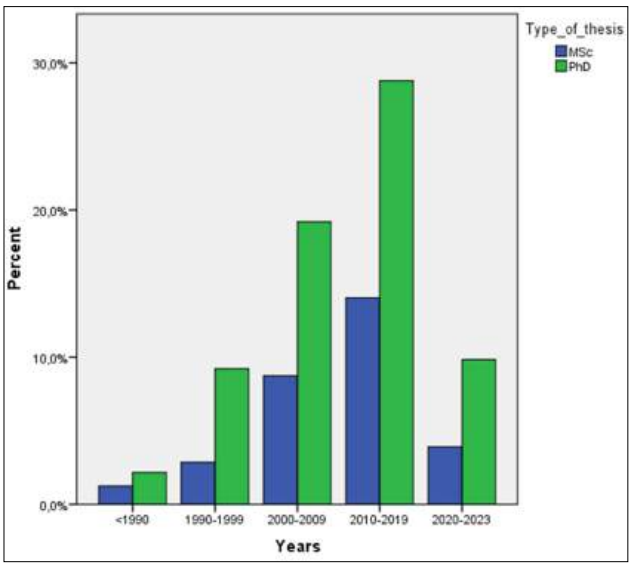


***Figure 4.*** *Distribution of published thesis types by year.*

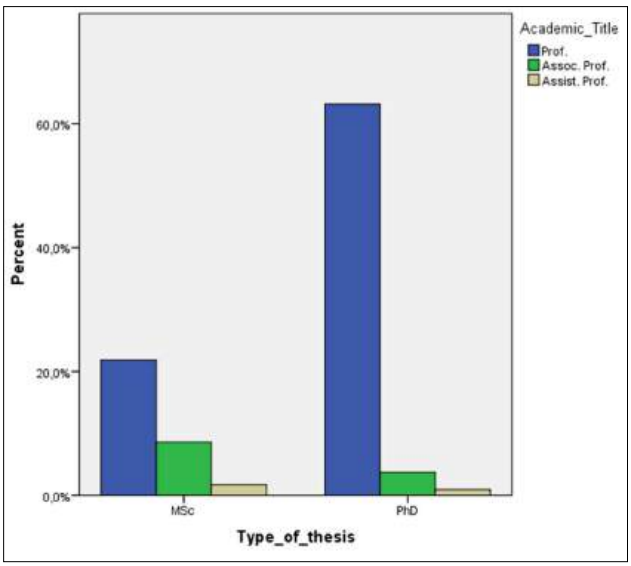


***Figure 5.*** *Distribution of academic titles according to thesis types by year.*

***Table 4.*** *Distribution of publications from master's and doctoral theses according to the type of journal index in which they were published*

| | Master theses | | Doctoral theses | | Total | |
|---|---|---|---|---|---|---|
| Journal index type | n | % | n | % | n | % |
| Citation index | 68 | 15.4 | 172 | 17.35 | 240 | 16.7 |
| International index | 257 | 58.27 | 597 | 60.24 | 854 | 59.6 |
| National index | 113 | 25.6 | 203 | 20.48 | 316 | 22.06 |
| National refereed journals | 3 | 0.68 | 19 | 1.9 | 22 | 1.5 |
| Total | 441* | 100 | 991* | 100 | 1432* | 100 |

*Some theses produced more than one publication

indexes, 22% in national indexes, 16.7% in citation indexes, and 1.5% in national refereed journals (Table 4, Fig.s 2, 3, 4). When the publication status of theses was examined according to the academic titles of the advisors, it was determined that the publication percentages of advisors with the title of professor were higher than those of others. Advisors with the title of professor had 254 (25.7%) publications from master's theses and 734 (74.3%) publications from doctoral theses (Fig. 5).

## Discussion

The primary result obtained in the research is that one-fourth of the master's theses and one-third of the doctoral theses in the main branches of the Ankara University Institute of Health Sciences have been published. In total, approximately one third of the theses (30.7%) were converted into publications. Karaca et al. (2020) found that the conversion rate of health sciences master's and doctoral theses into publications was 40.5% and 57.1%, respectively. Approximately half of the theses were published[14].

In this study, data were collected from participants, whereas in our research, data were obtained by searching databases. At the same time, as stated by the authors in this study, journal articles, books, patents, and oral and poster presentations were also considered as forms of publication. In our study, only articles published in journals were considered as publications. It is believed that the discrepancy in research results is due to methodological differences between the two studies.

Sipahi et al. (2012) examined the rate of publication of public health master's and doctoral theses and found that 29.9% of the theses were published in national and international refereed journals[15]. In the study by Yilmaz et al. (2017), the publication rate of nursing master's and doctoral theses was found to be 14.4% and 7.7%, respectively[16]. Çürük et al. (2021) determined that 40.9% of internal medicine nursing master's theses were published[17]. Kinikoğlu et al. (2020) found that 34% of master's theses on animal rat experiments were published in PubMed-indexed journals[18].

When the publication status of theses in other disciplines was examined, it was found that the publication rate of medical sciences master's theses in refereed journals ranged from 11.4% to 39.1% [19–24]. In the United States, which has the highest rate of scientific publications worldwide, only 25.6% of doctoral dissertations in psychology are converted into publications[25]. In a study analyzing social work theses, the rate of publication of theses was found to be 28.8%[26].

When the results obtained in our study and those of similar studies are evaluated, it becomes apparent that the rate of thesis publication in health sciences and other scientific fields is not at the desired level. Theses are important to graduate education because they require intensive, long-term, and qualified work[15,22]. One of their primary purposes is to contribute to the scientific literature[27]. Indeed, health sciences master's and doctoral theses make significant contributions to the scientific knowledge base and development in the health sciences[28]. It is emphasized that doctoral theses are indispensable in producing new scientific knowledge[29]. However, the way for theses to contribute to the scientific literature is to turn them into articles and publish them in refereed journals[14,30,31]. Turning theses into publications increases the scientific value of the thesis and makes the results more accessible[20,23]. Therefore, the low publication rate of health sciences theses limits their potential contribution to the development of health sciences.

The International Committee of Medical Journal Editors[32] states that one of the roles and responsibilities of authors is to take responsibility for all aspects of the work they have completed and to publish the work they have approved. Accordingly, when master's and doctoral theses are not published, it can be considered that the thesis author has not completed the research process. It also states that authors have ethical obligations to publish their work and disseminate their research findings through publication[33]. For this reason, transforming theses into publications is also important in terms of author responsibilities.

The result is that the publication rates of master's and doctoral theses obtained in our research are not at the desired level, possibly due to many factors. Studies have found that the primary reasons for not publishing theses are lack of time and workload[14,30,31]. Inadequate supervisor guidance and support, negative postgraduate education experiences, difficulty in revising a long document and submitting it to a journal, lack of knowledge and experience in writing articles, search for alternative careers, failure to publish negative and non-significant results, lack of interest and motivation of the thesis author, and family problems were cited as other reasons[25,30,31].

Küpeli et al. (2022) found a significant relationship between the thesis author's career in academia and the publication of his/her thesis. Another study reported that the incentive and motivation to publish a thesis are low when pursuing a non-academic career[21]. Accordingly, the low publication rate of health sciences theses may be due to the fact that some thesis authors continue their professional lives in health centers whose primary purpose is not research but the provision of healthcare services. Horta and Li (2023) stated that the decision to produce publications from the thesis is greatly influenced by the decision whether to continue in academia or not, and that the publication profile is a determining factor in academic placement and promotion at the center of doctoral students' intention to publish their thesis[29]. Our study found that the rate of publication of health sciences doctoral theses was higher than that of master's theses. Similar results were obtained in other studies analyzing health sciences theses[14,30].

In our country, the academic promotion criteria published by the Council of Higher Education are the most important motivation for increasing the number of publications and international publications[24]. The Council of Higher Education sets publication criteria for academic appointments and promotions through Regulations[34]. In addition to these regulations, the Regulation on Academic Incentive Allowance (2018) encourages increasing the quantity and quality of university publications[35].

Most recently, qualified publications are also required for the opening and execution of graduate education programs[36]. These criteria, introduced by law for academic appointments, promotions and rewards, have prioritized publishing with high scientific value. For this reason, it is believed that one of the most significant factors influencing the conversion of theses into publications is the academic career plan, and that doctoral graduates are more likely to publish as a result.

In some institutions, publication of at least one article from the doctoral thesis is a graduation requirement. In contrast, in some institutions, in addition to publication, the journal's impact factor in which the article is published must be above a certain level. The Organisation of PhD in Biomedicine and Health Sciences European System (ORPHEUS), as an organisation dedicated to developing quality standards and good practices in doctoral education, has published "articles produced from doctoral theses published or accepted for publication in internationally recognized peer-reviewed journals" as one of its basic quality standards [37]. It is a requirement that doctoral dissertations are published in academic institutions that are members of the organization and have received the ORPHEUS Assessment Certificate.

Our research determined that most publications produced from master's and doctoral theses were indexed in international indexes, followed by national indexes and then citation indexes. When evaluated by year, progress was observed in publishing articles derived from theses in indexed and quartile journals (Fig.s 1 and 2). Karaca et al. (2020) found that publications produced from health sciences theses were mainly published in international indexes[14]. Yilmaz et al. (2017) found that 30.7% of the publications produced from nursing theses were published in nationally indexed journals, 29.4% in internationally indexed journals, and 15.8% in citation indexes[16]. Çürük et al. (2021) found that 31.4% of internal medicine nursing master's theses were published in journals with a citation index[17].

When the journals in which articles produced from theses are published are analyzed in terms of medical sciences, a study determined that 68.9% of the articles produced from theses were published in national journals and 13.3% were published in PubMed-indexed journals[22]. In another study, it was found that 20.4% of the publications were indexed in the citation index, 21.4% in international journals, and in a separate study, 26.8% of the publications were in Scopus-indexed journals[19].

Publication of theses in indexed journals confirms the validity of the thesis and increases its quality and scientific value[20,22,30,38].

The quartiles of the journals in which the articles are published have gained importance in scoring associate professorship application requirements, amended in 2023[39]. Journal indexes and quartiles are crucial in evaluating the impact and quality of publications in the scientific literature. For this reason, the increase in the number of articles produced from theses and dissertations published in journals with high indexes and quartiles is a positive development.

## Conclusion

This study, conducted to determine the publication status of health sciences master's and doctoral theses, found that the rate of publication of theses by converting them into scientific articles was low. The publication of health sciences theses is of great importance in terms of the

benefits it provides to the graduate, the department, and the institution, as well as its contribution to the advancement of health sciences and the health professions.

The criteria for qualified publications in academic placement, promotion, and rewards will be effective for thesis advisors and thesis authors who continue their academic careers by converting their theses into publications. Graduate students who will continue their careers outside academia should be supported by advisors and institutions to publish their theses within the scope of the academic and professional benefits of publishing theses, as well as the responsibilities of authors. Factors affecting the conversion of graduate theses into publications should be investigated, and solutions should be found. Additionally, institutional arrangements to ensure the publication of theses should be strengthened and effective policies should be implemented.

### *Limitations of the Study*

The study's results include evaluations of publications produced from the graduate theses of only one institute. Therefore, they can only be generalized to postgraduate theses conducted in the fields covered by the Institute of Health Sciences.

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OLGU SUNUMU / *CASE REPORT*

# Hand Deformity in Parkinson's Disease: A Case of Striatal Hand Deformity Mimicking Rheumatoid Arthritis

*Parkinson Hastalığında El Deformitesi: Romatoid Artriti Taklit Eden Striatal El Deformite Olgusu*

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**ABSTRACT**

*Abnormal postures and deformities can be seen in the hands and feet in parkinson's disease. The most typical deformities seen in the upper extremities are flexion of the metacarpophalangeal joints, extension of the proximal interphalangeal joints, flexion of the distal interphalangeal joints, and ulnar deviation. These deformities may cause rheumatoid arthritis to be misdiagnosed and unnecessary medical treatment given to patients whose Parkinson's findings, such as tremor, bradykinesia, and rigidity, are not fully established. In our case, there was a male patient with hand deformities in his right upper extremity due to Parkinson's disease, and his differential diagnosis was made with rheumatoid arthritis. It was aimed to prevent the progression of deformities by starting physical therapy after the diagnosis was made. This case shows that there may be a diagnosis confusion due to the similar hand deformities in rheumatoid arthritis and Parkinson's disease. To draw attention to this situation, a case of Parkinson's disease with striatal hand deformity is presented.*

**Key words:** *striatal hand deformity; Parkinson's hand deformity; hand deformity*

**ÖZET**

*Parkinson hastalığında el ve ayaklarda anormal postur ve deformiteler görülebilir. Üst extremitelerde görülen en tipik deformite metakarpofalangiel eklemlerde fleksiyon, proksimal interfalangiel eklemlerde extansiyon, distal interfalangiel eklemlerde fleksiyon ve ulnar deviasyondur. Bu deformiteler; tremor, bradikinezi, rijidite gibi parkinson bulgularının tam yerleşmediği hastalarda yanlışlıkla romatoid artrit tanısı konmasına ve gereksiz medikal tedavi verilmesine sebep olabilir. Olgumuzda Parkinson hastalığına bağlı sağ üst extremitesinde el deformiteleri olan hasta mevcut olup romatoid artrit ile ayırıcı tanısı yapılmıştır. Hastaya tanı konulduktan sonra fizik tedavi başlanarak deformitelerin progresyonunun engellenmesi amaçlanmıştır. Bu olgu; romatoid artrit ve parkinson hastalığında benzer el deformitelerinin olması sebebiyle bir tanı karışıklığı yaşanabileceğini göstermektedir. Bu duruma dikkat çekmek amacıyla striatal el deformitesine sahip parkinsonlu bir vaka sunulmuştur.*

**Anahtar kelimeler:** *striatal el deformitesi, Parkinson el deformitesi, el deformitesi*

## Introduction

Parkinson's Disease(PD) is a progressive disease characterised by dopamine depletion resulting in motor and non-motor symptoms. Motor signs include bradykinesia, rigidity, tremor and postural instability. Dopamine-enhancing drugs such as levodopa are used in the treatment[1–3].

Abnormal postures and deformities of the hands and feet can occur in Parkinson's disease. The most characteristic deformities in the upper extremities include flexion of the metacarpophalangeal (MCP) joints, extension of the proximal interphalangeal (PIP) joints, flexion of the distal interphalangeal (DIP) joints and ulnar deviation[4,5]. These deformities can resemble those seen in rheumatoid arthritis (RA), potentially leading to misdiagnosis and unnecessary treatments, especially in cases where classic Parkinsonian features such as tremor, bradykinesia and rigidity are not yet fully established.

This case highlights the diagnostic confusion that may arise due to similar hand deformities in RA and PD. To emphasize this clinical overlap, we present a case of PD with striatal hand deformity.

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***Figure 1.*** *Swelling and deformities in the hand when the patient comes.*


***Figure 2.*** *Right hand radiograph of the patient.*

## Case

A 69-year-old male was referred to our Physical Medicine and Rehabilitation (PM&R) rheumatology outpatient clinic with a preliminary diagnosis of RA, due to complaints of swelling and pain in the right hand. In the patient's medical history, it was noted that he had undergone surgery for stomach cancer one year prior and coronary bypass surgery six months prior, but had not sought medical attention afterward.

The patient denied prior joint swelling or morning stiffness. On examination, swelling and restricted movement in the right wrist, along with swelling, pain and deformity in the MCP, PIP and DIP joints of the right hand were observed (Fig. 1). Bunnell-Littler and MCP squeeze tests were performed on examination. Rigidity and cogwheel phenomenon were present in both the right upper and lower limbs. A resting tremor was noted on the tongue and lips, along with marked bradykinesia. The patient exhibited a flexed posture and a slowed gait. He was able to maintain balance while standing, but had impaired balance when attempting to sit upright in bed for prolonged periods.

Laboratory tests revealed normal acute-phase reactants except for anemia. Rheumatoid factor (RF), anti-CCP, ANA, ENA, thyroid antibodies, infectious and hepatitis markers were all within normal limits (Table 1). Magnetic resonance imaging of the hand and wrist showed mild joint effusion and tendon sheath fluid consistent with mild tendinitis. There was no evidence of hyperalgesia, allodynia or vasomotor changes suggestive of shoulder-hand syndrome. Trophic changes observed in the right hand and both toenails were referred to dermatology, but no additional pathology was found. X-rays showed deformities without erosions (Fig. 2). Doppler ultrasound ruled out deep vein thrombosis or thrombophlebitis. Except for the hand swelling and mild pain, the patient's general condition was stable.

The patient was referred to the neurology department, where a diagnosis of Parkinson's disease was made. Treatment with pramipexole and selegiline (dopaminergic agents) was initiated. The hand swelling and deformities were interpreted as striatal hand deformity due to Parkinson's disease. A rehabilitation program was started. During inpatient follow-up, the swelling and deformities regressed with rehabilitation, but reappeared after the exercises were discontinued. The patient was discharged with a home exercise program, and follow-up with neurology and PM&R clinics was recommended.

***Table 1.*** *Lab values*

| | | | | | |
|---|---|---|---|---|---|
| WBC | 5.46 | Normal | CCP | <10 | Negative |
| HMG | 11.5 | Normal | ALT | 19 | Normal |
| PLT | 284000 | Normal | AST | 26 | Normal |
| CRP | <2 | Normal | KREATİNİN | 0.7 | Normal |
| ESR | 15 | Normal | ANTİ-HBS | 493.3 | Positive |
| TİT | Negative | Normal | ANTİ-HBC IGM | 0.071 | Negative |
| RF | <20 | Normal | ANTİ-HBC IGG | 1.73 | Negative |
| ANA | Negative | Negative | ANTİ-HAV IGG | 0.009 | Positive |
| ENA | Negative | Negative | ANTİ-HCV | 0.031 | Negative |

## Discussion and Conclusion

Hand and foot deformities in Parkinson's disease were first described in 1864 and later elaborated upon by various researchers[6]. When flexion and ulnar deviation of the MCP joints are observed, differential diagnoses should include RA, systemic lupus erythematosus (SLE), Osteoarthritis, Jaccoud's arthritis, Dupuytren's contracture, Trigger finger, De Quervain's tenosynovitis, dystonia, Parkinson's disease, and advanced age[4,5,7].

The term striatal hand deformity is used based on the hypothesis that lesions in the neostriatum (putamen and caudate nucleus) contribute to these deformities[5]. However, the exact pathogenesis remains unclear. Potential contributing factors include dystonia, little finger spasm and rigidity. These deformities may progress to fixed contractures over time, underscoring the importance of early recognition and intervention to preserve quality of life.

In rheumatoid arthritis, deformities typically present symmetrically, involving both hands and are accompanied by radiological evidence of joint involvement. In contrast, striatal hand deformities are usually unilateral at onset, appearing on the side where Parkinson's disease (PD) first manifests and where motor symptoms are more pronounced, despite normal radiographic findings[8].

Striatal hand deformities in Parkinson's disease can mimic RA and lead to misdiagnosis and inappropriate treatment. Accurate diagnosis requires careful clinical evaluation. The absence of arthritis, lack of erosions on radiographs and normal laboratory values can help rule out inflammatory arthritis. Recognizing these Parkinson-related deformities is crucial to avoid unnecessary therapies and maintain functional independence.

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# Erratum: Comparison of the Effects of Femoral Nerve Block and Adductor Canal Block on Postoperative Analgesia in Patients to Undergo Unilateral Knee Arthroplasty

In the article published in **(Kafkas J Med Sci 2025;15(1):64-70 (DOI: 10.5505/06787))** titled **"Comparison of the Effects of Femoral Nerve Block and Adductor Canal Block on Postoperative Analgesia in Patients to Undergo Unilateral Knee Arthroplasty"**, the address and contact information for the first author, Soner Kina appeared incorrectly as **"Department of Cardiology, Kafkas University School of Medicine, Kars"**. The corrected address and information are as follows. We apologize to our readers.

# Comparison of the Effects of Femoral Nerve Block and Adductor Canal Block on Postoperative Analgesia in Patients to Undergo Unilateral Knee Arthroplasty

*Tek Taraflı Diz Artroplastisi Geçirecek Hastalarda Femoral Sinir Bloğu ile Adduktor Kanal Bloğunun Postoperatif Analjezi Üzerine Etkilerinin Karşılaştırılması*

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