# TURKISH JOURNAL of TRAUMA & EMERGENCY SURGERY

Ulusal Travma ve Acil Cerrahi Dergisi



# TURKISH JOURNAL OF TRAUMA & EMERGENCY SURGERY ULUSAL TRAVMA VE ACIL CERRAHI DERGISI

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# Evaluation of hepatic and remote organ injury in an experimental liver ischemia-reperfusion model in rats and the effects of quercetin on this damage

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#### **ABSTRACT**

**BACKGROUND:** This study aims to show the changes in the liver, lung, kidney, and heart in the liver ischemia-reperfusion model in rats and the effect of quercetin on these changes histopathologically and immunohistochemically.

METHODS: Eighteen Sprague Dawley rats were classified into three groups: Group I sham, Group 2 ischemia-reperfusion (IR), Group 3 ischemia-reperfusion + quercetin (IR+Q). For three days, distilled water was given to Group I, and quercetin was given to Group 3 via gavage. At the end of the third day, abdominal opening-closing was applied to Group I, and 4 hours of reperfusion was applied to Groups 2 and 3 after I hour of ischemia by clamping the hepatoduodenal ligament, and all rats were euthanized. Liver, lung, kidney, and heart tissue samples were stained with Hematoxylin Eosin (HE), Masson Trichrome, Periodic Acid-Schiff (PAS), and TUNEL (Terminal deoxynucleotidyl transferase (TdT) deoxyuridine triphosphate nick end labeling assay) to assess apoptosis and examined histopathologically and immunohistochemically under a light microscope.

**RESULTS:** In the liver, the damage score was significantly higher in the IR group than in the sham group, while it was significantly lower in the IR+Q group than in the IR group. While there was no significant difference between the groups in semi-quantitative scoring parameters, the Apoptotic Index was significantly higher in the IR group than in the sham group and significantly lower in the IR+Q group than in the IR group. In the lung, no significant difference in lung damage scores between the groups was observed. While the Apoptotic Index was significantly higher in the IR group than in the sham group, it was significantly lower in the IR+Q group than in the IR group. In the kidneys, tubular cell degeneration and intertubular vascular congestion were significantly higher in the IR group than in the sham group. While the Apoptotic Index was higher in the IR group than in the sham and IR+Q groups, it was higher in the IR+Q group than in the sham group. In the heart, there was no difference between the groups in terms of myocardial cell degeneration and vascular damage. The apoptotic index was significantly higher in the IR group than in the sham and IR+Q groups.

**CONCLUSION:** Our results indicate that histopathological damage occurs in the liver, lung, kidney, and heart in the experimentally created IR model, and quercetin application decreases IR-related damage and apoptosis in these organs.

**Keywords:** Ischemia-reperfusion injury; liver; quercetin; remote organ.

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#### INTRODUCTION

An organ's inability to meet oxygen and nutrient demands due to impaired blood flow causes depletion of energy stores, metabolite accumulation, and oxidative stress, resulting in ischemia within a specified time.

Reinstating blood flow aggravates cellular damage through the enhancement of reactive oxygen radicals (ROS) and the inflammatory response. This condition is called ischemia-reperfusion damage (IRD). The risk of liver ischemia-reperfusion damage is heightened in liver tissue following trauma or prolonged surgical procedures like tumor resection and transplantation.<sup>[1]</sup>

Experimental animal models, in which inflammatory factors like chemokines, cytokines, and transcription factors are released due to oxidative stress and reperfusion following ischemia, have helped elucidate the pathophysiology of IRD. <sup>[2]</sup> Mitochondrial peptides from necrotic cells during ischemia stimulate Kupffer cells, macrophages in the liver. Kupffer cells release ROS and inflammatory mediators, inducing apoptosis in endothelial cells of vascular structures. The inflammatory response intensifies with the presence of neutrophils and inflammatory mediators that infiltrate the liver parenchyma. <sup>[3]</sup>

The presence of IRD in the liver can also threaten other organs. This phenomenon occurs because the inflammatory response is carried to distant organs with the help of cytokines released as a result of oxidative stress. In some cases, this response can lead to fatal outcomes by causing multiple organ dysfunction syndrome (MODS) or systemic inflammatory response syndrome (SIRS).<sup>[4]</sup> Oxidative stress and increased ROS levels are the main pathologies targeted for the prevention and treatment of IRD. Antioxidant treatment mitigates liver problems caused by IRD.<sup>[2]</sup>

Quercetin, a flavonoid present in numerous plants such as seeds, red onions, blueberries, and apples, is a natural antioxidant. This pigment exhibits antioxidant, anti-inflammatory, and antifibrotic activities. Quercetin mitigates ischemia-reperfusion injury in multiple organs and tissues. [5] Quercetin's antioxidant properties include free radical scavenging, nitric oxide synthase reduction, and xanthine oxidase inhibition. [6] It exerts its anti-inflammatory effect by inhibiting cyclooxygenase and lipoxygenase enzymes and by reducing inflammatory mediators such as prostaglandins and leukotrienes. [7] The heme oxygenase I enzyme, crucial for antioxidant and anti-inflammatory responses, is activated by it. [2]

This study explored the histopathological alterations in the liver, lung, kidney, and heart tissues of rats caused by IRD in the liver, assessing the impact of quercetin.

#### **MATERIALS AND METHODS**

The experimental procedures were carried out at Karadeniz Technical University Medical Faculty Surgical Research Center in Trabzon, Türkiye. Eighteen female Spraque Dawley rats

weighing between 250 and 300 g were used for the study. The animals were treated in accordance with the National Institutes of Health's Guide for the Care and Use of Laboratory Animals. The Institutional Animal Ethical Committee of Karadeniz Technical University, Trabzon, Türkiye approved our study (protocol no: 2017-25). The rats were housed in type III cages, provided with tap water and standard rat chow (Bayramoğlu Yem ve Un Sanayi Tic. A.Ş., Erzurum, Türkiye), and maintained at a temperature of 22±1°C under a 12 hours light-12 hours dark cycle.

#### **Experimental Design**

In the study, rats were classified into three groups.

Group I (Sham group, n=6): The rats, which received I mL of distilled water by gavage for 3 days before the experiment, were sacrificed by exsanguination, and their organs were removed 4 hours after opening the abdomen, waiting I hour, and then closing it.

Group 2 (Ischemia-Reperfusion (IR) group, n=6): On the day of the experiment, rats reperfused for 4 hours after I hour of ischemia were sacrificed by exsanguination, and their organs were removed.

Group 3 (Ischemia-Reperfusion + Quercetin (IR+Q) group, n=6): The rats that were given quercetin (Sigma-Aldrich; Merck KGaA, Darmstadt, Germany) by gavage for 3 days before the experiment and reperfused for 4 hours after I hour of ischemia were sacrificed by exsanguination, and their organs were removed.

#### **Experimental Protocol**

The hepatic ischemia was induced through clamping of the portal vein, hepatic artery, and bile duct (hepaticoduodenal ligament) during the abdominal median laparotomy under general anesthesia. After an hour, the liver was reperfused for 4 hours before the rats were sacrificed by exsanguination. For histological analysis, the liver, lung, kidney, and heart were removed.

#### **Histological Procedures**

In the tissues prepared for examination with a light microscope, Hematoxylin-Eosin (H&E) staining was performed to observe the histological structure, and Masson's trichrome staining was performed to examine connective tissue. Periodic acid-Shiff (PAS) staining was performed to investigate glycogen accumulation in the liver, lung, kidney, and heart; microvilli and basal membranes of epithelial cells in kidney tubules; and goblet cells in the lung.

Hepatic ischemia/reperfusion damage was graded (0 for minimal, 1 for mild, 2 for moderate, and 3 for severe) based on patterns of cytoplasmic vacuolization, nuclear pyknosis, hypereosinophilia, loss of cell borders, and neutrophil infiltration. <sup>[8]</sup> A semi-quantitative score from 0-3 (ranging from none to

severe) was assigned to hepatocytes degeneration, pyknotic nuclei, sinusoidal dilatation, mononuclear cell infiltration, vascular congestion, and hemorrhage in the liver.<sup>[9]</sup>

Semi-quantitative damage scoring in the evaluation of lung tissue was performed as follows: Grade 0, normal morphology; Grade 1, mild intra-alveolar edema and inflammatory cell infiltration; Grade 2, moderate alveolar edema and inflammatory cell infiltration; Grade 3, inflammatory cell infiltration with severe alveolar edema and focal hemorrhage; Grade 4, diffuse inflammatory cell infiltration and deterioration in the alveolar structure. [10]

In the evaluation of kidney tissue, degeneration of tubular cells (tubular dilatation, shedding, and vacuolization of tubular epithelial cells) and intertubular vascular congestion were scored semi-quantitatively as Grade 0, none; Grade 1, mild; Grade 2, moderate; and Grade 3, severe.<sup>[11]</sup>

Myocardial cell degeneration scoring in the evaluation of heart tissue was performed as Grade 0 (normal), no degeneration in myocytes; Grade I (mild), few degenerated myocytes; Grade 2 (moderate), myocyte degeneration around 50%; Grade 3 (severe), myocyte degeneration over 50%.<sup>[12]</sup>

#### **Immunohistochemical Procedures**

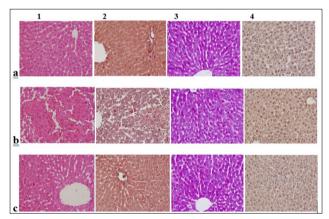
Terminal deoxynucleotidyl transferase (TdT) deoxyuridine triphosphate (dUTP) nick end labeling assay (TUNEL) staining was performed to evaluate apoptosis in organs (11 684 817 910 Roche Diagnostic, Mannheim, Germany). TUNEL (+) cells with homogeneously stained brown nuclei without areas of necrosis were defined as apoptotic. In the evaluation, apoptotic and normal cells were recorded by counting 100 cells in 5 different areas at ×400 magnification, and the Apoptotic Index (AI) was calculated as follows: AI=TUNEL (+) cell number/total cell number × 100.

#### RESULTS

## Histological and Immunohistochemical Evaluation of Liver Tissue

Pyknotic hepatocyte nuclei with eosinophilic cytoplasm, hepatocyte degeneration, sinusoidal dilatation and congestion, centrilobular necrosis, hemorrhage, apoptosis, and reduced glycogen accumulation were observed in the liver of the IR group. In the IR+Q group, sinusoidal dilatation, hepatocytes with occasional eosinophilic cytoplasm and pyknotic nuclei, and a higher glycogen accumulation were detected compared to the IR group (Fig. I).

While the damage score in the IR group was significantly higher than in the sham group (p<0.008), the damage score in the IR+Q group was significantly lower than that in the IR group (p=0.015). No statistically significant difference in semi-quantitative scoring was found between the groups (p>0.05) (Table 1).



**Figure 1.** Liver (Line a: Sham group, Line b: IR group, Line c: IR+Q group); Column 1: H&E, Column 2: Masson trichrome, Column 3: PAS, Column 4: TUNEL staining (X400)

<b>Table 1.</b> Liver scoring results and Apoptotic Index (AI) eval
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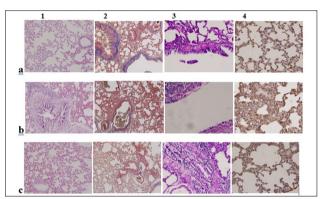
	Sham mean±SD	IR mean±SD	IR+Q mean±SD	Р
Liver Dam. Score	0.5±0.84	2.5±0.84 <sup>x</sup>	0.67±1.21 <sup>s</sup>	<0.013
Hep. Deg.	0.33±0.51	2.17±1.32	0.67±1.21	<0.055
Pic. Nuc.	0.33±0.51	2.17±1.32	0.67±1.21	<0.055
Sin. Dil.	0.0±0.0	0.83±0.75	0.33±0.81	<0.052
Mon. Cell Inf.	0.0±0.0	0.83±0.75	0.33±0.81	<0.052
Vas. Cong.	0.0±0.0	1.50±1.22	1.50±1.22	<0.052
Hemorrhage	0.0±0.0	0.33±0.81	0.33±0.81	<0.588
Apoptotic Index (%)	26.33±0.51	63.97±6.84*	22.7±11.16°	p≤0.0001

Data were given as mean  $\pm$  standard deviation. n=6 rats in each group. Liver Dam. Score: Liver Damage Score; Hep. Deg: Hepatocyte Degeneration; Pic. Nuc.: Pyknotic Nucleus; Sin. Dil.: Sinusoidal Dilation; Mon. Cell Inf: Mononuclear Cell Infiltration; Vas. Cong.: Vascular Congestion.\*: (p<0.008) Damage score in the IR group was found to be significantly higher than in the sham group. \*: (p<0.015) In the IR+Q group, the damage score was significantly decreased compared to the IR group. \*: (p≤0.0001) Apoptotic Index was found to be higher in the IR group than in the sham group. \*: (p≤0.0001) The Apoptotic Index was decreased in the IR+Q group compared to the IR group. No significant differences were found in the comparison of other parameters among the groups.

Table 2. Lung damage score and Apoptotic Index (AI) evaluation

	Sham mean±SD	IR mean±SD	IR+Q mean±SD	Р
Lung Damage	1.17±0.41	2.17±1.17	1.50±0.55	p<0.152
Apoptotic Index (%)	25.12±7.84	59.21±9.46 <sup>x</sup>	35.22±5.8 <sup>s</sup>	p≤0.0001

Data were given as mean  $\pm$  standard deviation. n=6 rats in each group.  $^{x}$ : (p $\leq$ 0.0001) The apoptotic index was found to be higher in the IR group than in the sham group.  $^{s}$ : (p $\leq$ 0.0001) The apoptotic index was decreased in the IR+Q group compared to the IR group.



**Figure 2.** Lung (Line a: Sham group, Line b: IR group, Line c: IR+Q group); Column 1: H&E, Column 2: Masson trichrome, Column 3: PAS, Column 4: TUNEL staining (X400).

In the liver, the AI% obtained through the TUNEL method was markedly increased in the IR group compared to the sham group ( $p\le0.0001$ ), but was substantially diminished in the IR+Q group relative to the IR group ( $p\le0.0001$ ) (Table I).

## Histological and Immunohistochemical Evaluation of Lung Tissue

While an increase in alveolar epithelial thickness, vascular congestion, interalveolar hemorrhage, intra-alveolar edema, neutrophil infiltration were observed in the lung in the IR group, in the IR+Q group, there was a slight decrease in the thickening of the alveolar epithelium and interalveolar hemorrhage compared to the IR group. In addition, when the lung was evaluated with PAS staining, an increase in mucin secretion and goblet cells in the bronchial wall was observed in the IR and IR+Q groups (Fig. 2).

When the groups were evaluated in terms of lung damage score, no significant difference was found between the groups (p<0.152) (Table 2).

The apoptotic index in the IR group was significantly higher than that in the sham group ( $p \le 0.0001$ ), but it was significantly lower in the IR+Q group relative to the IR group ( $p \le 0.0001$ ).

# Histological and Immunohistochemical Evaluation of Kidney Tissue

In the cortex of the kidney's IR group, detached and vacuolized tubular epithelial cells, dilated tubules, congested intertubular vessels, and increased intertubular collagen were detected, while the renal medulla showed cast structures and necrotic tubular epithelial cells within the lumen. In the IR+Q group, both cortical intertubular congestion with epithelial shedding and medullary shedding and necrosis with cast structures were observed. In Figure 3, interruptions in the brush border epithelium and basal membrane structures of the kidney were minimally observed in the sham group, infrequently in the IR+Q group, and significantly in the IR group upon PAS staining evaluation.

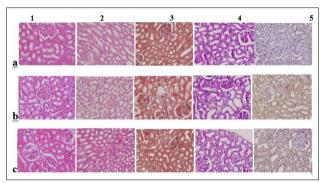
Tubular cell degeneration was significantly higher in the IR group than in the sham group (p<0.004) (Table 3). Again, intertubular vascular congestion was significantly higher in the IR group than in the sham group (p<0.015) (Table 3).

In the evaluation of the apoptotic kidney index, the apoptotic index in the IR group was significantly higher than in the sham and IR+Q groups ( $p \le 0.0001$ ,  $p \le 0.0001$ , respectively); the apoptotic index in the IR+Q group was higher than in the sham group (p < 0.001) (Table 3).

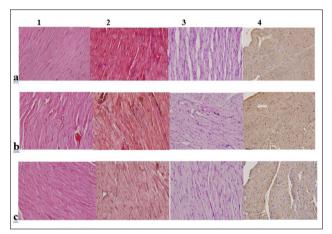
Table 3. Kidney damage score and Apoptotic Index (AI) evaluation

	<u> </u>	<u> </u>		
	Sham mean±SD	IR mean±SD	IR+Q mean±SD	Р
Tub. Cell Deg.	0.50±0.55	2.17±0.75 <sup>x</sup>	1.00±0.90	p<0.014
Vas. Cong.	0.33±0.52	1.50±0.55°	0.50±0.55	p<0.014
Apoptotic Index (%)	17.25±20.89	76.6±10.15*	45.08±12.76∞	p≤0.0001

Data were given as mean  $\pm$  standard deviation. n=6 rats in each group. Tub. Cell Deg.: Tubular Cell Degeneration; Vas. Cong.: Vascular Congestion.  $^{x}$ : (p<0.004) Tubular cell degeneration was significantly higher in the IR group than in the sham group.  $^{\circ}$ : (p<0.015) Intertubular vascular congestion was significantly higher in the IR group than in the sham group.  $^{*}$ : (p<0.0001) Apoptotic index was found to be significantly higher in the IR group than in the sham group.  $^{\circ}$ : (p<0.0001) The apoptotic index was significantly lower in the IR+Q group than in the IR group.



**Figure 3.** Kidney (Line a: Sham group, Line b: IR group, Line c: IR+Q group); Column 1: H&E, Column 2: H&E (renal medulla), Column 3: Masson trichrome, Column 4: PAS, Column 5: TUNEL staining (X400).



**Figure 4.** Heart (Line a: Sham group, Line b: IR group, Line c: IR+Q group); Column 1: H&E, Column 2: Masson trichrome, Column 3: PAS, Column 4: TUNEL staining (X400).

## Histological and Immunohistochemical Evaluation of Heart Tissue

In the heart tissue of the IR group, degeneration and loss of striation in cardiac muscle fibers, perinuclear edema between muscle fibers, and vascular hemorrhage were observed; in the IR+Q group, a decrease in edema between perinuclear and muscle fibers was observed locally. When the groups were

examined with Masson's trichrome staining, there was no difference between the groups in terms of collagen distribution. When the groups with PAS staining were evaluated, no difference was observed between the groups in the glycogen accumulation in the muscle fibers (Fig. 4).

When myocardial cell degeneration was evaluated, no significant difference was found between the groups (p<0.090). In addition, myocardial fibrosis and vascular congestion were scored semi-quantitatively. There were no patients with myocardial fibrosis. There were no significant differences between the groups in terms of vascular damage (Table 4).

The evaluation of the apoptotic index performed by the TU-NEL technique in the heart showed that the apoptotic index was significantly higher in the IR group than in the sham and IR+Q groups ( $p \le 0.0001$ ,  $p \le 0.0001$ , respectively) (Table 4).

#### **DISCUSSION**

Ischemia—reperfusion damage is the name given to the damage caused by the ischemic and inflammatory response that develops in the tissue after the blood flow is interrupted and restored. It is a common complication of the liver following prolonged liver surgery such as transplantation or tumor resection, after trauma, or in situations of shock. Using an experimental liver IR model, we evaluated IRD in our study.

The complex, multifactorial pathophysiological process gives rise to IRD. Local tissue acidosis and ischemia triggering inflammatory response mediators and leukocyte migration in the blood lead to systemic damage and dysfunction. Acidosis and local ischemia developing in the tissue that cannot meet oxygen and nutrient needs cause systemic inflammatory response syndrome, which results in distant tissue damage and dysfunction through inflammatory mediators and leukocytes that mix with the blood.<sup>[4]</sup>

In the creation of the IRD model in the liver, clamping durations have varied. In our study, we imposed ischemia for an hour followed by reperfusion for four hours. A previous study investigated the impact of quercetin on the liver under experimentally induced IRD (45 minutes ischemia, I hour reperfusion). [13] Jaeschke distinguished between the acute (first

Table 4. Myocardial cell degeneration, heart vascular congestion score results, and Apoptotic Index (AI) evaluation

	Sham mean±SD	IR mean±SD	IR+Q mean±SD	P
Myo. Cell Deg.	1.17±0.98	2.33±0.82	1.67±0.52	p<0.090
Vas. Cong.	1.33±0.82	2.17±0.75	1.83±0.41	p<0.166
Apoptotic Index (%)	29.33±6.45	61.39±16.9 <sup>x</sup>	37.09±7.41 <sup>s</sup>	p≤0.000 I

Data were given as mean  $\pm$  standard deviation. n=6 rats in each group. Myo. Cell Deg.: Myocardial Cell Degeneration; Vas. Cong.: Vascular Congestion.  $^{x}$ : (p $\leq$ 0.0001) The Apoptotic Index was found to be significantly higher in the IR group than in the sham group.  $^{s}$ : (p $\leq$ 0.0001) The Apoptotic Index was significantly lower in the IR+Q group than in the IR group.

6 hours) and late/subacute (later 6 hours) phases of liver IRD. The acute phase is the period of increased ROS production, activation of Kupffer cells, and increased proinflammatory cytokines; the subacute phase is characterized by intense inflammatory cytokine and neutrophil infiltration. [14] The acute phase after IRD was evaluated in our study.

The researchers Taghizadieh et al.<sup>[15]</sup> observed a marked reduction in the hepatic antioxidants, including glutathione peroxidase (GPX) and superoxide dismutase (SOD), during the IRD process. These changes result in oxidative stress and cell damage.<sup>[1]</sup> Numerous studies have investigated the cellular impacts of excessive ROS activity in IRD, as well as the use of antioxidants to counteract these effects. The positive effects of several antioxidant agents like melatonin,<sup>[15-16]</sup> carnosine,<sup>[16]</sup> quercetin, and desferrioxamine<sup>[13]</sup> have been shown to improve IRD in previous research.

Quercetin is a potent antioxidant and anti-inflammatory flavonoid. Previous research reveals its ability to quench oxidative stress and inflammation through various mechanisms, including inhibiting lipid peroxide radical formation, binding metal ions, scavenging radicals, affecting inducible nitric oxide synthase activity, suppressing xanthine oxidase, reducing leukocyte immobilization, and inhibiting tumor necrosis factoralpha (TNF- $\alpha$ ). [6,13]

In Baykara's research, matching our IR durations, the IR group exhibited damaged hepatocyte cell cords, numerous and scattered hepatocyte necrosis, neutrophil infiltration within parenchymal regions, and sinusoidal enlargement and congestion, similar to our findings.[16] According to Tokyol et al.'s study,[13] histopathological findings and liver damage scores following a 45-minute ischemia and 1-hour reperfusion period were consistent with our results. In Baykara's study, whose IR durations were the same as in our research, in the IR group, the integrity of hepatocyte cell cords was impaired, multiple and diffuse hepatocyte necrosis areas, neutrophil infiltration in parenchymal areas, enlargement and congestion in sinusoids were observed in the IR group, compatible with the findings of our study.[16] The difference in general damage between the groups was statistically significant, whereas the differences in individual parameters were not. The insufficient number of rats might account for this outcome.

In the IRD of one organ, damage to distant organs may occur in addition. Systemic inflammation occurs due to oxidative mediators released during IRD and subsequent leukocyte adhesion through these mediators.<sup>[3]</sup> In our study, lung, kidney, and heart tissues were used to evaluate distant organ damage.

As it is the initial capillary bed the blood encounters following hepatic circulation, the liver experiences the greatest impact from the inflammatory mediators generated during IRD.[17] Major liver surgeries can result in both acute lung damage and acute respiratory failure syndrome, which are significant complications in IRD patients.[18] The IR+Q group showed de-

creased thickening of alveolar epithelium, vascular congestion, interalveolar hemorrhage, intra-alveolar edema, neutrophil infiltration, and increase in apoptosis, as well as decreased Al, compared to the IR group, but no significant difference was noted in damage scoring between the two groups. Although Oğuz et al.'s study[19] revealed histopathological changes due to liver IRD-induced lung tissue damage, they found that sulforaphane—an antioxidant and anti-inflammatory agent like quercetin-failed to mitigate this damage. Ninety minutes of ischemia and 18 hours of reperfusion increased high-mobility group box I (HMGBI) protein levels linked to inflammation in rat lungs.[18] Eight hours of liver reperfusion following 75 minutes of ischemia resulted in increased apoptosis and stress response enzymes in type II alveolar cells, inflammatory cytokines in plasma, and greater neutrophil ratio in bronchoalveolar lavage.[17] Similarly, we think the increase in mucin secretion and goblet cells in the bronchi in our study's IR and IR+Q groups is related to airway inflammation.

An organ most frequently affected by IRD in the liver is the kidney. The reported incidence of acute kidney damage after liver operations is between 40% and 85%.<sup>[20]</sup> When the kidney tissue after IRD was examined in our study, cellular degeneration and necrosis findings were observed in both cortex and medulla regions in the IR group. Again, in damage scoring, tubular cell degeneration and vascular congestion scores were higher in the IR group. However, although quercetin partially reduced histopathological deterioration, it was not effective in improving damage scoring. Al that increased in the IR group was found to be slightly lower in the IR+Q group. Miranda et al.<sup>[21]</sup> reported increased malondialdehyde (MDA) and myeloperoxidase (MPO) levels in the kidneys after liver IRD in rats. This study showed that the event is related to oxidative stress. In a study in which apoptosis and related Fas gene expression were measured in kidney tissue after liver transplantation, it has been shown that both events began I hour after transplantation and increased up to 12 hours. [22] In our study, sufficient IRD time was applied to apoptosis formation in accordance with these data. In a study by Takhtfooladi et al.,[23] in which ischemia for 30 minutes and reperfusion for 24 hours was applied in the liver, kidney damage was evaluated and, unlike our study, diffuse necrosis and glomerular fibrosis findings were observed. This difference may be because the study included the subacute period in terms of reperfusion.

In the IR+Q group, histopathological degeneration findings noted in the IR group, including nuclear pyknosis, perinuclear and interstitial edema, vascular hemorrhage, and congestion, were partially alleviated but without statistical significance. No evidence of myocardial cell degeneration, vascular damage, or myocardial fibrosis was found. A study with 150 minutes of ischemia and 12 hours of reperfusion yielded a high damage score due to myocardial necrosis and edema. <sup>[24]</sup> The difference is attributed to varying durations. In the IR+Q group, the heart tissue exhibited a decrease in Al levels

compared to the IR group. Applying IRD to heart tissue, as in our study, resulted in apoptosis, yet quercetin diminished this effect. [25]

We did not find any significant difference between the groups, except for a slight increase in intertubular collagen in the IR group, in the connective tissue of the sections of each of the four organs we stained with Masson Trichrome. This result may be due to the fact that our experimental period was not sufficient for collagen increase. We think that more precise results can be obtained by including the 6-24 hour subacute period of IRD in the experiment.

#### **CONCLUSION**

In the light of the findings, it was shown that the experimentally created IR model in the liver causes histopathological damage to the liver and distant organs, and quercetin has positive effects on this damage. For these results to be clinically applicable, there is a need for experimental and clinical studies to be carried out at different IRD times, at different doses of quercetin, supported by further investigations.

**Ethics Committee Approval:** This study was approved by the Karadeniz Technical University Ethics Committee (Date: 19.07.2017, Decision No: 2017-25).

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept: N.S.A., E.Y., C.K., O.K.; Design: N.S.A., E.Y., T.A.; Supervision: N.S.A, C.K., T.Z., E.Y.; Resource: N.S.A., E.Y., T.Z., T.A.; Materials: N.S.A., E.Y., B.A., E.Y.; Data collection and/or processing: N.S.A., B.A., G.D.R.K., E.Y.; Analysis and/or interpretation: N.S.A., B.A., C.K., E.Y.; Literature review: N.S.A., E.Y., O.K., T.A.; Writing: N.S.A., E.Y., G.D.R.K., O.K.; Critical review: N.S.A., C.K., T.Z., O.K.

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#### DENEYSEL ÇALIŞMA - ÖZ

# Sıçanlarda deneysel karaciğer iskemi-reperfüzyon modelinde karaciğer ve uzak organ hasarının değerlendirilmesi ve bu hasara *quercetin*'in etkileri

AMAÇ: Bu çalışma, sıçanlarda karaciğer iskemi-reperfüzyon modelinde karaciğer, akciğer, böbrek ve kalpte meydana gelen değişiklikleri ve quercetin'in bu değişiklikler üzerindeki etkisini histopatolojik ve immünohistokimyasal olarak göstermeyi amaçlamaktadır.

GEREÇ VE YÖNTEM: On sekiz Sprague Dawley sıçan 3 gruba ayrıldı: Grup 1 sham, Grup 2 iskemi-reperfüzyon, Grup 3 iskemi-reperfüzyon + quercetin. 3 gün boyunca Grup 1'e distile su, Grup 3'e ise quercetin gavaj yoluyla verildi. 3. günün sonunda Grup 1'e abdominal açma-kapama, Grup 2 ve 3'e ise hepatoduodenal ligament klemplenerek 1 saatlik iskeminin ardından 4 saatlik reperfüzyon uygulandı ve tüm sıçanlar sakrifiye edildi. Karaciğer, akciğer, böbrek ve kalp doku örnekleri hematoksilen eozin (HE), Masson Trikrom, Periyodik Asit-Schiff (PAS) ve apoptozu değerlendirmek için TUNEL (Terminal deoksinükleotidil transferaz (TdT) deoksiüridin trifosfat nick end labeling assay) ile boyandı ve ışık mikroskobu altında histopatolojik ve immünohistokimyasal olarak incelendi.

BULGULAR: Karaciğerde hasar skoru; IR grubunda sham grubuna göre anlamlı derecede yüksek iken, IR+Q grubunda IR grubuna göre anlamlı derecede düşüktü. Yarı kantitatif skorlama parametrelerinde gruplar arasında anlamlı bir fark bulunmazken, apoptotik indeks İR grubunda sham grubuna göre anlamlı derecede yüksek, İR+Q grubunda ise İR grubuna göre anlamlı derecede düşüktü. Akciğerde, akciğer hasarı skorlarında gruplar arasında anlamlı bir fark gözlenmedi. Apoptotik indeks IR grubunda sham grubuna göre anlamlı derecede yüksekken, IR+Q grubunda IR grubuna göre anlamlı derecede düşüktü. Böbreklerde, tübüler hücre dejenerasyonu ve intertübüler vasküler konjesyon IR grubunda sham grubuna göre anlamlı derecede yüksekti. Apoptotik indeks IR grubunda sham ve IR+Q gruplarına göre daha yüksek iken, IR+Q grubunda sham grubuna göre daha yüksekti. Kalpte, miyokardiyal hücre dejenerasyonu ve vasküler hasar açısından gruplar arasında fark yoktu. Apoptotik indeks IR grubunda sham ve IR+Q gruplarına göre anlamlı olarak daha yüksekti.

SONUÇ: Sonuçlarımız, deneysel olarak oluşturulan IR modelinde karaciğer, akciğer, böbrek ve kalpte histopatolojik hasar oluştuğunu ve *quercetin* uygulamasının bu organlarda IR ile ilişkili hasarı ve apoptozisi azalttığını göstermektedir.

Anahtar sözcükler: İskemi-reperfüzyon hasarı; karaciğer; quercetin; uzak organ hasarı.

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# Does infliximab attenuate oxidative stress following traumatic brain injury?

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#### **ABSTRACT**

**BACKGROUND:** Traumatic brain injury is a global health problem. Infliximab is used daily to treat a variety of inflammatory systemic disorders. The goal of this study was to compare the pathological and biochemical changes induced by dexamethasone and infliximab usage in rats with blunt head trauma.

METHODS: Thirty-two adult rats were used in our study. Groups of eight animals were used, and those with skin incision without any additional trauma were called sham (Group 1); those with skin incision and head trauma were called control (Group 2); those who received I mg/kg intraperitoneal dexamethasone immediately after head trauma were called steroid (Group 3); and those who received 5 mg/kg subcutaneous infliximab immediately after trauma were called infliximab (Group 4). The animals were euthanized seven days after the operation.

**RESULTS:** Brain tissue malondialdehyde (MDA), superoxide dismutase (SOD), and glutathione peroxidase (GPx) values of the four groups were compared and a statistically significant difference was shown. However, no significant difference was observed between the infliximab and dexamethasone groups in terms of tissue MDA, SOD, and GPx concentrations. Pathological sections showed that trauma-induced cortical damage, interstitial edema, and perivascular edema were reduced in the infliximab group.

**CONCLUSION:** Infliximab demonstrates comparable neuroprotective effects to dexamethasone in oxidative stress markers, while providing superior efficacy in edema reduction.

Keywords: Infliximab; rat model; head injury; antioxidant.

#### INTRODUCTION

Traumatic brain injury is a global health problem as well as a growing socioeconomic problem. In the United States alone, more than 1.5 million people suffer from traumatic brain injury each year. [1] While traffic accidents are responsible for more than 50% of cases of acute trauma, falls are the second-most common cause. [2] In a study conducted in Southeastern Anatolia, Berber et al. observed a mean age of 7.7 years among patients with traumatic head injury and underscored the importance of causes of head trauma such as traffic accidents and falls. They additionally concluded that traumatic brain in-

jury warrants attention as a problem for public health.[3]

Infliximab, developed by Merck & Co., Inc. (Whitehouse Station, NJ, USA) and approved by the U.S. Food and Drug Administration for managing various inflammatory systemic conditions, acts as an antagonist to tumor necrosis factor-alpha (TNF- $\alpha$ ). As a chimeric monoclonal antibody, infliximab neutralizes elevated levels of TNF- $\alpha$  both within the bloodstream and at sites of inflammation. A review of the literature indicates that several types of anti-TNF- $\alpha$  therapy, including infliximab, are recommended for treating spinal cord injuries.<sup>[4]</sup>

However, infliximab's effect on head trauma has not been in-

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vestigated. Therefore, in our study, we investigated the effects of infliximab and dexamethasone on malondialdehyde (MDA), superoxide dismutase (SOD), and glutathione peroxidase (GPx) in cases of blunt head injury in a rat model and compared their effects pathologically.

#### MATERIALS AND METHODS

#### Rat Model

The study was conducted in accordance with the Declaration of Helsinki. Ethical considerations concerning our study's experimental protocol were meticulously reviewed and subsequently approved by the Local Ethics Agency (No. 795, November I, 2024). The animal subjects employed in our investigation were sourced from the Experimental Animal Breeding Laboratory affiliated with Health Sciences University, Ankara Training and Research Hospital and all experimental procedures were conducted within the Experimental Animal Research Laboratory at the same institution. The biochemical analyses associated with the study were performed by trained staff at the Medical Biochemistry Department at Ankara Bestepe Hospital.

Our experiment involved 32 male adult Wistar rats, each weighing 250–300 g, which were maintained under standardized laboratory conditions and provided unrestricted access to food and water.

#### **Anesthesia and Surgical Procedure**

Anesthesia was administered via the intramuscular injection of 45 mg/kg of ketamine hydrochloride in conjunction with 10 mg/kg of xylazine. After checking anesthetic depth by corneal reflex and tail pinch test, physiological values such as breathing, pulse, and rectal temperature of the animals were recorded preoperatively, postoperatively, and after one week (Table 1).

Prior to the surgical intervention, the frontoparietal regions of the rats' heads were shaved and disinfected using a 10% solution of polyvinylpyrrolidone-iodine. The surgical procedure involved inducing head trauma following the method outlined by Marmarou et al.<sup>[5]</sup> A midline incision spanning the coronal and lambdoid sutures was made in the scalp, after which a stainless-steel disc I cm in diameter was meticulously affixed to the central portion of the calvarium. Once the trauma device was prepared, the rat was positioned in a prone orientation to ensure that the disc was located beneath the lower end of the device. A weight was subsequently allowed to drop freely from a height of I m onto the disc (Fig. 1). None of the rats exhibited respiratory arrest or seizures shortly after trauma. Post-impaction, the calvarium was carefully analyzed for any resulting fractures, after which the scalp was sutured.

#### **Definition of Groups**

The rats were assigned to four groups with eight rats each:

**Table 1.** Distribution of physiological parameters of groups measured preoperatively, postoperatively, and after one week (values are presented as the median scores (25th and 75th percentiles))

	Sham	Control	Dexamethasone	Infliximab		
Weight						
Preoperatively	284.5 (279.5-293.25)	292.5 (276.5-295.5)	280.5 (275.5-291.5)	279 (276-290.75)	*	-
Postoperatively	289 (283.5-290.25)	283.5 (277.75-291.25)	288.5 (284.5-293.75)	280 (272-289.25)	*	
I week after	285.5 (280-289)	288 (283.5-296.5)	288 (277.5-291.25)	290.5 (283.75-297.25)	*	
Rectal tempera-ture						
Preoperatively	36.55 (36.48-36.82)	36.3 (36.25-36.6)	36.6 (36.4-36.78)	36.75 (36.68-36.9)	*	-
Postoperatively	36.65 (36.38-36.82)	36.3 (36-36.4)	36.45 (36.4-36.53)	36.7 (36.5-36.82)	*	
I week after	36.25 (36.18-36.85)	36.45 (36.35-36.85)	36.5 (36.35-36.85)	36.55 (36.4-36.7)	*	
Number of respirations						
Preoperatively	97.5 (94.5-99.75)	104.5 (93.5-112)	84.5 (77.75-89.75)	103 (94.25-106.75)	*	
Postoperatively	97 (89.25-105.5)	100 (84-110.25)	88 (77.75-93.5)	91 (88.5-92.5)	*	
I week after	91 (83.75-103)	92 (75.75-105.5)	93 (90-100.25)	82.5 (79.5-93.25)	*	
Hearth rate						
Preoperatively	354.5 (311.25-378)	359.5 (323-390.25)	347 (306.25-411)	344 (272.25-413.5)	*	
Postoperatively	352 (324.75-405)	302 (280.5-334.5)	359 (305.25-420)	393 (326.75-412.5)	*	
I week after	368 (338-390.25)	277.5 (268.5-322.75)	354 (295.75-412.5)	418 (296.5-429.75)	*	

<sup>\*</sup>No significant differences among the groups (p>0.05). †No significant differences among all groups (p>0.05)

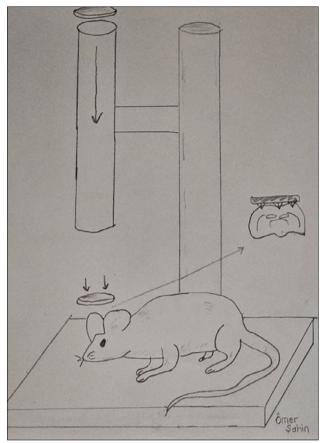


Figure 1. Schema presenting Marmarou weight drop model.

(1) a sham group that received a scalp incision without any additional trauma being inflicted; (2) a control group that received a scalp incision, underwent head trauma, but had no medical treatment administered; (3) a dexamethasone group that received 1 mg/kg intraperitoneal dexamethasone immediately following head trauma; and (4) an infliximab group that received 5 mg/kg subcutaneous infliximab immediately following trauma.<sup>[4]</sup>

The animals were euthanized seven days after the operation. The cranial bones, including the scalp, were extracted as a single unit. After dividing from the midline, one hemisphere was sent for pathological sections. The other side was used for biochemical evaluations.

#### **Evaluation of Pathologic Sections**

The samples were fixed in a 10% formaldehyde solution, after which standard processing procedures were conducted utilizing the LEICA ASP 300S apparatus. Subsequently, paraffin blocks were created, and 4-micron-thick cross-sections were obtained using the LEICA RM 2255 microtome. The sections underwent staining with hematoxylin and eosin. Following these steps, examinations were conducted with an OLYMPUS BX51 microscope. The examiner who evaluated the sections was unaware of the group information of the samples. Following the evaluation of sections for neuronal

degeneration, perivascular edema, and interstitial edema, all parameters were quantified as a percentage of the affected area. The classification system employed was as follows: 0 (no edema), I (slight) 5%, 2 (minimal) 6–20%, 3 (moderate) 21–50%, 4 (severe) 51–75%, 5 (very severe) 76–100%. [6]

#### Measurement of MDA, GPx, and SOD Activity

Tissue samples were processed via homogenization using I mL of distilled water in an Ultra Turrax tissue homogenizer. The resulting homogenates served as the basis for quantifying the activities of MDA, GPx, and SOD. All experimental procedures were conducted at a temperature of 4°C to ensure enzymatic integrity. The protein content of the brain samples was analyzed according to Lowry's method, [7] while the level of lipid peroxidation in the samples was determined by measuring concentrations of MDA using the NWLSS NWKMDA01 assay, with results expressed in micromoles per gram of protein. Meanwhile, GPx activity was assessed using a colorimetric assay kit, based on methods established by Paglia and Valentine, and concentrations of GPx were recorded as milliunits per gram of protein.[8] Last, SOD activity was evaluated using a superoxide dismutase assay kit, with results expressed in units per gram of protein.

#### **Statistical Analysis**

As each group had a sample size of eight, we reported median values alongside the interquartile range (25th and 75th percentiles), and we used non-parametric tests as suggested in previous research. [9] For overall group comparisons, we applied the Kruskal-Wallis test. If significant differences were detected, we performed pairwise subgroup comparisons using the Mann-Whitney U test. The significance level (type I error) was set at 5%, and we adjusted p-values using the Bonferroni correction to account for multiple comparisons. All analyses were conducted using IBM SPSS Statistics version 23 (IBM Corp., Armonk, NY, USA).

#### **RESULTS**

Physiological parameters of groups are given in Table I. No statistically significant difference was found between the groups (p>0.05).

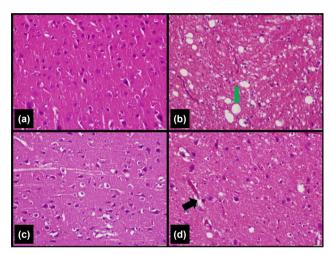
#### **Pathological Examination**

Table 2 presents a summary of the pathological findings. Regarding neuronal degeneration, significant differences were observed among all groups (p<0.05). The sham group showed no neuronal degeneration, while the control group exhibited severe neuronal damage. Both treatment groups demonstrated reduced neuronal degeneration compared to the control group, with infliximab showing slightly better results than dexamethasone, although no significant difference was found between the two treatment groups (p>0.05). Significant differences in perivascular and interstitial edema were observed among all groups (p<0.05). The sham group exhibited no edema (Fig. 2a). Notably, there was a statisti-

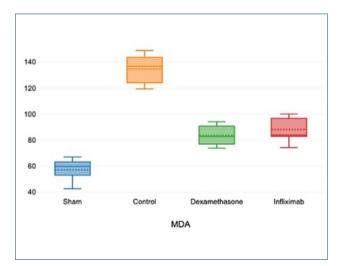
Table 2. Injury grading scores in samples (values are presented as the median scores (25th and 75th percentiles))

Score	Sham	Control	Dexamethasone	Infliximab	
Neuronal degeneration	0 (0-0)	4 (4-5)	2.5 (1.75-3.25)	2 (1-3)	† *
Perivascular edema	0 (0-0)	4 (4-5)	2 (1.75-2.25)	l (I-I.25)	† ‡
Interstitial edema	0 (0-0)	4.5 (4-5)	2 (1.75-3)	I (0-1.25)	† ‡

 $<sup>\</sup>dagger$  Significant differences among the groups (p<0.05).  $\ddagger$  Significant difference between Dexamethasone and Infliximab groups (p<0.05). \* No significant difference between Dexamethasone and Infliximab groups (p>0.05).



**Figure 2.** Hematoxylin and eosin-stained sections: **(a)** Sham group demonstrates normal brain tissue; **(b)** Trauma group shows severe perivascular and interstitial edema; **(c)** Dexamethasone group demon-strates moderate perivascular and interstitial edema; **(d)** Infliximab group shows mild perivascular and interstitial edema. (Black arrow: Perivascular edema; Green arrow: Interstitial edema).



**Figure 3.** Box and whisker plots showing malondialdehyde (MDA) levels in brain tissue. Lipid peroxidation content is expressed as micromoles per gram protein.

cally significant distinction between the trauma and infliximab groups (p<0.05). Moreover, infliximab demonstrated statistically superior results compared to the dexamethasone group (p<0.05). The control group displayed severe edema (Fig. 2b). Examination of the study group sections revealed that both infliximab and dexamethasone groups showed reduced perivascular and interstitial edema, particularly when juxtaposed with the trauma group (Fig. 2c). This observation underscores the relative effectiveness of infliximab in reducing perivascular and interstitial edema in the subjects under investigation (Fig. 2d).

#### **MDA** Levels by Group

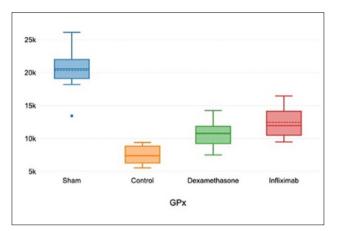
A statistically significant difference in MDA levels was detected between the control group and all the other groups (p<0.05). The presence of trauma resulted in a marked elevation in MDA levels. Meanwhile, the infliximab group displayed a statistically significant difference in MDA concentrations compared with the control group (p<0.05); however, no such significant difference was observed when compared to the dexamethasone group (p>0.05). These findings are depicted in Figure 3.

#### **GPx Levels by Group**

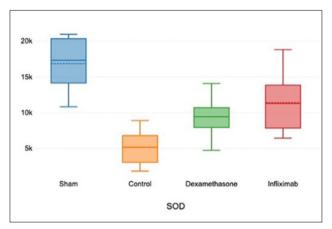
Levels of GPx in the brain were notably lower in the control group than in all other groups (p<0.05). By contrast, the groups treated with infliximab and dexamethasone demonstrated elevated GPx levels that were not statistically significant (p>0.05) (Fig. 4).

#### **SOD** Levels by Group

The control group displayed a significant reduction in SOD activity compared with the sham and drug groups (p<0.05) (Fig. 5). The infliximab group demonstrated a notable difference in SOD activity relative to the control group (p<0.05), although it did not differ significantly from the dexamethasone group (p>0.05). These results underscore the varied effects of different treatments on SOD activity in the context of trauma and inflammation.



**Figure 4.** Box and whisker plots showing glutathione peroxidase (GPx) levels in brain tissue. GPx content of the brain is expressed as milliunits per gram of protein.



**Figure 5.** Box and whisker plots showing superoxide dismutase (SOD) levels in brain tissue. SOD content of the brain is expressed as units per gram of protein.

#### **DISCUSSION**

TNF- $\alpha$ , an important proinflammatory cytokine produced by many blood cells, interacts with two distinct receptors present on various types of cells: the type I TNF- $\alpha$  receptor, commonly called "p55," and the type 2 TNF- $\alpha$  receptor, commonly called "p75."[10] Cytokines, particularly TNF- $\alpha$ , play a crucial role in the injury of endothelial cells induced by activated leukocytes. Their effect occurs not only through the activation of neutrophils but also by enhancing the expression of adhesion molecules on endothelial cells, including E-selectin, which facilitates the adhesion of activated neutrophils to those cells.[11,12] Moreover, Zheng et al. have demonstrated that TNF- $\alpha$  can directly induce damage to endothelial cells independent of the involvement of neutrophils.[13] The effects of the cytokine on oxidative stress are mediated through the activation of multiple reactive oxygen species (ROS) generation pathways. This is primarily achieved by disrupting the efficiency of the mitochondrial electron transport chain, which normally results in 2-5% electron loss during oxidative phosphorylation. However, this increases significantly in the presence of TNF- $\alpha$ , causing mitochondrial dysfunction and decreased adenosine triphosphate (ATP) production<sup>[14]</sup> TNF- $\alpha$  also activates nicotinamide adenine dinucleotide phosphate (NADPH) oxidase isoforms (NOX2, NOX4, NOX1, and dual oxidase [DUOX]) and enhances other enzymes such as xanthine oxidase, lipoxygenases, and cyclooxygenases, thereby diversifying ROS production pathways.<sup>[15]</sup> This multi-pathway activation amplifies and perpetuates oxidative stress, which explains the dramatic increase in MDA levels observed following traumatic brain injury.<sup>[16]</sup>

Numerous researchers have explored the connection between TNF- $\alpha$  and neuronal injury. Wang et al. found that the concentration of TNF- $\alpha$  was elevated in the tissues of injured spinal cords,[17] while Yakovlev and Faden reported that spinal cord injuries in rats resulted in a significant rise in TNF- $\alpha$  messenger RNA at the injury site only 30 minutes post-trauma, with a direct correlation between the level of TNF- $\alpha$  and the intensity of the injury.<sup>[18]</sup> Furthermore, Taoka et al. observed that TNF- $\alpha$  levels in injured spinal cord tissue increased markedly following compressive trauma and peaked 4 hours after the initial injury.<sup>[19]</sup> The effects of TNF- $\alpha$  on antioxidant enzyme systems are paradoxical and significantly reduce cellular antioxidant capacity. TNF- $\alpha$  suppresses the expression of cytoplasmic Cu/Zn-SOD at the transcriptional level through nuclear factor kappa B (NF-κB)-independent pathways, thereby weakening the cell's defense against superoxide radicals, particularly in neurons. [20] Conversely, TNF- $\alpha$ increases mitochondrial Mn-SOD expression via NF-κB activation as a compensatory response; however, this is usually insufficient to counteract increased mitochondrial ROS production.<sup>[21]</sup> Furthermore, TNF- $\alpha$  reduces glutathione peroxidase (GPx) activity and disrupts glutathione homeostasis by suppressing glutathione synthesis and reducing glutathione reductase activity.[22] The loss of GPx7 expression promotes TNF-α-induced NF-κB activation, creating a positive feedback loop that sustains inflammatory responses and amplifies oxidative stress. This results in a net decrease in antioxidant capacity and increased susceptibility to oxidative damage.[23]

Infliximab, an innovative inhibitor of TNF- $\alpha$ , is widely used for a variety of therapeutic and research purposes. Its clinical applications include rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, Crohn's disease, ulcerative colitis, and psoriasis, all of which infliximab is officially sanctioned for. <sup>[24]</sup> Research conducted by Olmarker et al. has demonstrated that the targeted inhibition of TNF- $\alpha$  via the intraperitoneal administration of infliximab effectively mitigated both initial focal pain and subsequent widespread responses to pain triggered by experimental disc herniation in a rat model. <sup>[25]</sup> Furthermore, Demir et al. revealed that infliximab diminishes the production of interleukins IL-1, IL-6, IL-8, and TNF- $\alpha$  in a uveitis model. <sup>[26]</sup> In the present study, infliximab caused a statistically significant increase in the levels of GPx and SOD enzymes that protect against lipid peroxidation. The neuro-

protective effects of infliximab extend beyond the neutralization of TNF- $\alpha$  alone, operating through multiple complementary mechanisms. As a chimeric monoclonal antibody, it binds with high affinity to both soluble and membrane-bound TNF- $\alpha$ , thereby preventing interaction with TNF receptors and blocking downstream signaling cascades.[27] Its fragment crystallizable (Fc) domain activates both antibody-dependent cellular cytotoxicity and complement-dependent cytotoxicity, thereby eliminating inflammatory cells and activated macrophages. [28,29] By neutralizing TNF- $\alpha$ , infliximab blocks pathways that produce reactive oxygen species, including NADPH oxidase activation and mitochondrial dysfunction, while facilitating the restoration of antioxidant enzymes.[30] Furthermore, infliximab promotes a shift in the phenotype of microglia cells from MI (pro-inflammatory) to M2 (anti-inflammatory) and preserves the integrity of the blood-brain barrier by reducing endothelial ROS production and protecting tight junction proteins. This contributes to superior neuroprotective outcomes compared to dexamethasone treatment.[31,32]

In our study, analysis of pathological sections revealed that trauma induced extensive perivascular and interstitial edema. Treatment with infliximab significantly reduced these traumarelated pathological changes. Notably, the infliximab-treated group showed statistically better outcomes compared to the dexamethasone-treated group. Following traumatic brain injury, TNF- $\alpha$  levels surge within hours, sustaining a proinflammatory state that exacerbates vascular hyperpermeability. [33,34] The role of TNF- $\alpha$  in disrupting vascular integrity is critical to edema formation. As Kunimura et al. demonstrated, TNF- $\alpha$  impairs endothelial cell junctions via the guanine nucleotide exchange factor-HI (GEF-HI)/ Ras homolog family member A (RhoA)/ Ras-related C3 botulinum toxin substrate (Rac) signaling pathway, reducing membrane localization of tight junction proteins such as Claudin-5 and Occludin.[35] Infliximab's superior efficacy over dexamethasone in mitigating edema likely stems from its specific targeting of TNF- $\alpha$ . As shown by Zhou et al., infliximab binds with high affinity to both soluble and membrane-bound TNF- $\alpha$ , directly counteracting the primary driver of vascular permeability.[36] While dexamethasone exerts broad anti-inflammatory effects, infliximab's targeted mechanism may provide more precise control over edema development.

The use of synthetic glucocorticoids such as dexamethasone for the treatment of severe traumatic brain injury has been implemented in clinical and experimental settings to reduce inflammation and edema. The target of our report was to compare the biochemical and pathological effects of infliximab, a TNF- $\alpha$  inhibitor, and dexamethasone on head trauma. The literature indicates that TNF- $\alpha$  inhibitors have been used in treating spinal cord injuries and contributed positively to recovery in such cases. However, the effect of TNF- $\alpha$  inhibitors in a head trauma model has not previously been examined. Chengke and Kurt have mentioned the protective effects of infliximab in an experimentally induced spinal cord injury model, [4,38] while Börcek et al. have reported that adali-

mumab, another TNF- $\alpha$  inhibitor, caused a statistically significant decrease in MDA levels similar to infliximab. [39] Although infliximab has been studied with different tissues other than the brain in previous publications, the data obtained in our study is seen as compatible with previous studies. We found that trauma initiated a statistically significant increase in MDA levels, while infliximab and dexamethasone triggered a statistically significant decrease in those same levels. By the same token, infliximab produced a statistically significant increase in the levels of GPx and SOD enzymes that protect against lipid peroxidation. These findings were also supported by the pathological assessment of the brain tissues. Trauma caused significant neuronal degeneration, perivascular edema, and interstitial edema; and infliximab treatment decreased it.

It is important to recognize several limitations in this research. First, the small sample size may affect the generalizability of the findings. Future studies should include larger cohorts and both male and female animals to account for potential sex differences in traumatic brain injury response. Second, the study tested only a single dose of infliximab, leaving questions about optimal dosing. Further research should explore dose-dependent effects and compare infliximab with other TNF- $\alpha$  inhibitors. Third, while the study measured oxidative stress markers and pathological changes, deeper mechanistic investigations would strengthen the findings. These should include more extensive biochemical analyses, immunostaining, and electron microscopy, such as cytokine profiling, apoptosis markers, and blood-brain barrier integrity assessments. Fourth, the seven-day observation period may not fully capture long-term recovery or delayed neurodegeneration; extended studies with behavioral tests are needed. Finally, while rat models are useful, differences in human traumatic brain injury pathophysiology necessitate caution when translating findings to humans. Future work should include non-human primates or human cell models to improve clinical relevance. Addressing these limitations will help refine infliximab's potential as a therapeutic option for traumatic brain injury.

#### **CONCLUSION**

In sum, infliximab exhibits antioxidant effects comparable to those of dexamethasone, but is superior in terms of edema control. This suggests that targeted blockade of TNF- $\alpha$  may be a more effective approach to the treatment of post-traumatic cerebral edema. Long-term results and additional studies are needed, however, before the observed neuroprotective activity of infliximab can be used, especially following head trauma in humans.

**Ethics Committee Approval:** This study was approved by the Health Sciences University, Ankara Training and Research Hospital Ethics Committee (Date: 01.11.2024, Decision No: 795).

**Peer-review:** Externally peer-reviewed.

Authorship Contributions: Concept: Ö.Ş.; Design: Ö.Ş.;

Supervision: Ö.Ş.; Resource: Ö.Ş.; Materials: F.K.K.; Data collection and/or processing: F.K.K.; Analysis and/or interpretation: F.K.K.; Literature review: F.K.K.; Writing: Ö.Ş.; Critical review: Ö.Ş.

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#### DENEYSEL ÇALIŞMA - ÖZ

#### İnfliximab travmatik beyin hasarı sonrası oksidatif stresi azaltır mı?

AMAÇ: Travmatik beyin hasarı küresel bir sağlık sorunudur. İnfliximab çeşitli enflamatuvar sistemik durumların tedavisinde günlük olarak kullanılmaktadır. Çalışmamızın amacı künt kafa travmalı sıçanlarda deksametazon ve infliximab kullanımı sonucunda ortaya çıkan patolojik ve biyokimyasal değişiklikleri karşılaştırmaktır.

GEREÇ VE YÖNTEM: Bu çalışmada 32 yetişkin erkek Wistar sıçan kullanılmıştır. Sekiz hayvandan oluşan gruplar kullanıldı ve ek travma olmaksızın deri kesisi yapılanlar sham (grup 1); kafa deri kesisi ve kafa travması olanlar kontrol (grup 2); kafa deri kesisi ve kafa travmasından hemen sonra 1 mg/kg intraperitoneal deksametazon alanlar steroid (grup 3); kafa deri kesisi ve travmadan hemen sonra 5 mg/kg subkutan infliximab alanlar infliximab (grup 4) olarak adlandırılmıştır. Hayvanlar operasyondan 7 gün sonra ötanazi ile öldürüldü.

BULGULAR: Tüm grupların doku malondialdehit, süperoksit dismutaz ve glutatyon peroksidaz verileri göz önüne alındığında, bütünde istatistiki olarak pozitif bir fark vardı (p<0.05). Öte yandan, infliximab ve deksametazon grupları arasında doku malondialdehit, süperoksit dismutaz ve glutatyon peroksidaz konsantrasyonları açısından istatistiksel olarak anlamlı bir fark tespit edilmedi. Patolojik kesitler travmaya bağlı kortikal hasarın, intertisyel ödemin ve perivasküler ödemin infliximab grubunda daha az olduğunu göstermiştir.

SONUÇ: Infliximab, oksidatif stres belirteçlerinde deksametazon ile karşılaştırılabilir nöroprotektif etkiler gösterirken, ödemin azaltılmasında üstün etkinlik sağlar.

Anahtar sözcükler: Antioksidan; infliximab; kafa travması; sıçan modeli.

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# Performance of ChatGPT-40 in thoracic trauma: A comparative evaluation with guidelines

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#### **ABSTRACT**

**BACKGROUND:** This study aims to evaluate the performance of ChatGPT-40 in thoracic trauma management by comparing its responses to established clinical guidelines.

METHODS: Five major thoracic surgery guidelines were reviewed, including the Advanced Trauma Life Support (ATLS) Guidelines 2018, Eastern Association for the Surgery of Trauma (EAST) Guidelines 2020, Evaluation and management of traumatic pneumothorax: A Western Trauma Association critical decisions algorithm 2022, European Trauma Course (ETC) Guidelines 2016, and the National Institute for Health and Care Excellence (NICE) Guidelines for Trauma 2020. Fifty open-ended questions were developed based on these guidelines and submitted to ChatGPT-4o. Five thoracic surgery specialists evaluated the artificial intelligence (AI) responses using a 5-point Likert scale.

**RESULTS:** ChatGPT-40 achieved an average score of 4.76±0.57 on the 50-question evaluation. ChatGPT-40 excelled in questions derived from well-defined guidelines, demonstrating its ability to synthesize and apply guideline-based medical knowledge. Its performance aligns with previous studies in urological trauma and emergency medicine, which reported similar reliability. However, its reliance on pre-existing data limits its effectiveness in addressing highly nuanced or novel clinical scenarios. These findings underscore its potential as a complementary tool in guideline-driven medical contexts while emphasizing the need for clinical oversight in complex cases.

**CONCLUSION:** ChatGPT-40 performed strongly in thoracic trauma management questions, demonstrating minimal errors and high reliability. These results suggest it could serve as a valuable support tool for clinical decision-making, particularly in scenarios guided by established protocols. Further exploration into broader medical domains is warranted.

**Keywords:** Thoracic trauma; clinical decision support systems; artificial intelligence in medicine; guideline adherence; natural language processing.

#### INTRODUCTION

Thoracic trauma is a significant cause of morbidity and mortality worldwide, accounting for up to 25% of trauma-related deaths. [1,2] Prompt and accurate diagnosis, coupled with timely intervention, is critical for improving outcomes. Over the past two decades, various clinical guidelines have been developed to standardize the management of thoracic trauma. [3-7]

Artificial intelligence (AI) and natural language processing (NLP) tools have emerged as innovative aids in medical decision-making. Al models such as OpenAl's ChatGPT have shown promise in synthesizing and contextualizing large volumes of medical literature.<sup>[8,9]</sup> Previous studies have evaluated ChatGPT's performance in various medical specialties, including its role in urological trauma<sup>[10]</sup> and clinical oncology,<sup>[11]</sup> demonstrating its potential to support clinicians in decision-

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making. However, its performance in the domain of thoracic trauma remains underexplored.

Thoracic injuries encompass a wide spectrum, ranging from simple rib fractures to life-threatening conditions like tension pneumothorax and flail chest. The complexity of thoracic trauma management is compounded by its dependence on rapidly evolving evidence-based practices.<sup>[12]</sup> Guideline adherence has been shown to improve outcomes, but variations in practice persist due to factors such as lack of awareness, clinical inertia, and resource limitations.<sup>[13]</sup> This underscores the need for tools that can facilitate access to guideline-based information and enhance clinical decision-making.

Recent evaluations of AI models suggest their utility in addressing these gaps by providing clinicians with concise, evidence-based answers to complex clinical questions. [14,15] For instance, ChatGPT has been reported to perform well in translating and summarizing clinical guidelines into actionable recommendations. [16] Additionally, its ability to engage in interactive dialogue has the potential to simulate case-based discussions, which are crucial in trauma scenarios where rapid decisions are required. [17]

In this study, we sought to evaluate the performance of ChatG-PT-40 in addressing thoracic trauma-related clinical questions derived from five widely recognized guidelines, including the Advanced Trauma Life Support (ATLS) Guidelines, the Eastern Association for the Surgery of Trauma (EAST), the European Trauma Course (ETC) Guidelines, the National Institute for Health and Care Excellence (NICE) Guidelines, and the Western Trauma Association Critical Decisions Algorithm.<sup>[3-7]</sup> By comparing its responses to expert opinions, this study aims to assess the model's capability to provide accurate, guideline-concordant answers and to explore its potential role in augmenting clinical practice in thoracic trauma management.

#### MATERIALS AND METHODS

#### **Study Design**

A descriptive cross-sectional study was designed to compare ChatGPT-4o's responses with guideline-based recommendations. The study involved generating clinical questions from established guidelines, obtaining answers from ChatGPT-4o, and evaluating these answers using a standardized scoring system reviewed by thoracic surgery experts.

#### **Data Source and Question Development**

Five well-recognized thoracic trauma management guidelines were selected as the basis for question development:

- Advanced Trauma Life Support (ATLS) Guidelines, 2018.<sup>[3]</sup>
- Eastern Association for the Surgery of Trauma (EAST) Practice Management Guidelines, 2020.<sup>[4]</sup>
- Evaluation and Management of Traumatic Pneumothorax:
   A Western Trauma Association Critical Decisions Algorithm,

2022.[5]

- European Trauma Course (ETC) Guidelines, 2016.[6]
- National Institute for Health and Care Excellence (NICE) Guidelines for Trauma, 2020.<sup>[7]</sup>

Fifty open-ended clinical questions addressing critical aspects of thoracic trauma management (e.g., pneumothorax, hemothorax, flail chest, rib fractures) were developed by two thoracic surgery specialists who are also authors of this study. Both had completed formal specialty training in thoracic surgery and had active clinical experience in the management of thoracic trauma. Their direct involvement in the design and objectives of the study ensured that each question was clinically relevant and explicitly linked to one or more of the selected guidelines, thereby maintaining both accuracy and comprehensiveness.

To illustrate the structure and clinical relevance of the questions and corresponding ChatGPT-40 responses, a representative question-answer pair is presented below.

#### **Example Question:**

Where is the appropriate surgical site for tube thoracostomy?

#### **ChatGPT-40 Response:**

#### **Surgical Site:**

**Location:** The fifth intercostal space, anterior to the midaxillary line (often referred to as the "safe triangle").

**Landmarks:** The tube should be inserted above the rib to avoid the neurovascular bundle that runs along the bottom of each rib. The site is chosen to allow drainage of air or fluid from the pleural space.

#### **ChatGPT-4o Query Process**

Each of the 50 questions was entered into ChatGPT-40 using a standardized format. The model was instructed to provide concise, evidence-based answers relevant to the question. No additional prompts or contextual clarifications were provided to simulate real-world clinical use.

All queries were conducted in December 2024 using the ChatGPT web interface with the default GPT-40 model available at that time (GPT-40, May 2024 release). Each clinical question was submitted only once to simulate real-world conditions, particularly in time-sensitive clinical settings where multiple iterations are not feasible. No adjustments were made to model parameters such as temperature or randomness, as these settings are not user-configurable through the ChatGPT-40 web platform.

#### **Evaluation of Responses**

The responses were evaluated by five thoracic surgery spe-

	Doctor I	Doctor 2	Doctor 3	Doctor 4	Doctor 5	Mean	Standard Deviation
How many years have you been working as a thoracic surgery specialist?	I-10 Years	I-10 Years	I-10 Years	More than 20 years	I-10 Years		
I. Which pathologies should be identified and treated during the Primary Survey in thoracic trauma?	5	5	5	5	5	5	0.00
2. Which pathologies should be identified and treated during the Secondary Survey in thoracic trauma?	5	5	5	5	3	4.6	0.89
3. How should tension pneumothorax be diagnosed, and what is the treatment?	5	5	5	5	5	5	0.00
4. What clinical findings are observed in tension pneumothorax?	5	5	5	5	4	4.8	0.45
5. How are the respiratory mechanics disrupted in open pneumothorax?	5	5	5	5	4	4.8	0.45
6. What is the first intervention for open pneumothorax outside the hospital?	5	5	5	5	4	4.8	0.45
7. How do you clinically differentiate between tension pneumothorax and massive hemothorax?	5	5	5	5	5	5	0.00
8. How is the diagnosis of pericardial tamponade made following thoracic trauma?	5	5	5	5	5	5	0.00
9. How can tension pneumothorax and pericardial tamponade be differentiated through physical examination?	5	5	5	5	4	4.8	0.45
10. How should a patient be managed if they develop circulatory arrest and no pulse is palpable after thoracic trauma?	5	5	4	5	5	4.8	0.45
II. What should be done before air transport of a patient with pneumothorax?	5	5	4	5	5	4.8	0.45
12. What are the indications for thoracotomy in a patient with hemothorax following thoracic trauma?	5	5	4	5	5	4.8	0.45
13. How is blunt cardiac injury diagnosed, and what is the follow-up and treatment?	5	5	5	5	4	4.8	0.45
14. What are the chest X-ray findings in blunt aortic injury?	5	5	5	5	4	4.8	0.45
15. On which side is traumatic diaphragmatic rupture most common? How is it diagnosed, and what are the treatment principles?	5	5	5	5	5	5	0.00
16. What is the mechanism of blunt esophageal rupture, and how is it diagnosed? What are the treatment principles?	5	5	5	5	4	4.8	0.45
17. What is the significance of subcutaneous emphysema following thoracic trauma?	5	5	5	5	5	5	0.00

18. What complications can develop after rib fractures?	5	5	5	5	5	5	0.00
19. How do lower rib fractures (10th-12th) differ from other rib fractures??	5	5	5	5	5	5	0.00
20. How should a patient be managed if they have no palpable pulse but show signs of life after a penetrating thoracic injury?	5	5	5	5	5	5	0.00
21. How should a patient be managed if they have no palpable pulse and no signs of life after a penetrating thoracic injury?	5	5	5	5	4	4.8	0.45
22. Should emergency department thoracotomy be performed in a patient with extra-thoracic penetrating trauma who has no palpable pulse but shows signs of life?	5	5	3	5	5	4.6	0.89
23. Should emergency department thoracotomy be performed in a patient with extra-thoracic penetrating trauma who has no palpable pulse and no signs of life?	5	5	5	5	3	4.6	0.89
24. How should a patient be managed if they have no palpable pulse but show signs of life after blunt thoracic trauma?	5	5	5	5	4	4.8	0.45
25. How should a patient be managed if they have no palpable pulse and no signs of life after blunt thoracic trauma?	5	5	5	5	4	4.8	0.45
26. In pneumothorax diagnosis, should inspiratory or expiratory X-rays be preferred?	5	5	5	5	4	4.8	0.45
27. In a hemodynamically stable patient with traumatic pneumothorax, what criteria on X-ray and computed tomography (CT) should indicate the need for tube thora-costomy?	5	5	5	4	4	4.6	0.55
28. How is the differentiation made between small and large pneumothorax?	5	5	I	5	4	4	1.73
29. If a patient with pneumothorax has shortness of breath, should an intervention (needle aspiration, chest tube) be performed regardless of pneumothorax size?	5	5	5	5	4	4.8	0.45
30. How should a small pneumothorax without shortness of breath be managed?	5	5	5	5	5	5	0.00
31. Is needle aspiration associated with a shorter hospital stay compared to chest tubes in pneumothorax management?	5	4	5	5	2	4.2	1.30
32. What should be done if needle aspiration fails in pneumothorax management?	5	5	5	5	5	5	0.00
33. Is there a role for large bore (>20 F) chest tubes in pneumothorax management?	5	5	5	5	2	4.4	1.34
34. Should chest tubes in pneumothorax management be routinely connected to a suction system?	5	5	5	5	4	4.8	0.45

35. Under what circumstances can a patient with a history of pneumothorax engage in scuba diving?	5	5	5	5	4	4.8	0.45
36. In pneumothorax management, which is more successful: surgical or chemical pleurodesis? Which patients are more suitable for each option?	5	5	5	5	4	4.8	0.45
37. What is the most suitable agent for chemical pleurodesis?	5	5	5	5	4	4.8	0.45
38. How is pneumothorax managed during pregnancy?	5	5	5	5	4	4.8	0.45
39. Is prophylactic antibiotic use necessary during chest tube placement for traumatic pneumothorax?	5	5	5	5	2	4.4	1.34
40. How would performing chemical pleurodesis on a patient with cystic fibrosis and pneumothorax impact a potential lung transplant?	5	5	4	5	4	4.6	0.55
41. Which imaging modality has a higher diagnostic value for pneumothorax: ultrasound or X-ray?	5	4	5	5	3	4.4	0.89
42. What are the indications for intubation in flail chest?	5	5	4	5	4	4.6	0.55
43. What radiological findings are observed in pulmonary contusion on a chest X-ray?	5	5	4	5	4	4.6	0.55
44. What is the significance of a first rib fracture?	5	5	5	5	4	4.8	0.45
45. Where is the appropriate surgical site for tube thoracostomy?	5	5	5	5	4	4.8	0.45
46. In the emergency department, if pneumothorax is not detected on extended Focused Assessment with Sonography for Trauma (eFAST) in thoracic trauma, can it be excluded?	5	5	5	5	5	5	0.00
47. Only which patients should undergo chest decompression (needle, finger, chest tube) in the pre-hospital setting?	5	5	5	5	4	4.8	0.45
48. Which imaging studies should be ordered first for a severely unstable patient with respiratory distress following chest trauma?	5	5	5	5	4	4.8	0.45
49. Is it appropriate to choose a CT scan as the first imaging modality for thoracic trauma in patients under 16 years old?	5	4	5	5	4	4.6	0.55
50. What is the first choice of analgesic following major trauma?	5	5	5	5	4	4.8	0.45

cialists who participated voluntarily, following an open call distributed via a professional communication network among thoracic surgeons. All reviewers were certified specialists with clinical experience in thoracic trauma management.

Their years of experience in thoracic surgery—ranging from I to over 20 years—are detailed in Table I. A 5-point Likert scale was used for scoring, where:

- 1: Strongly Disagree Incorrect or irrelevant response.
- 2: Disagree Partially correct but missing key details.
- 3: Neutral Adequate but lacking depth.
- 4: Agree Comprehensive and correct.
- 5: Strongly Agree Comprehensive, correct, and clinically insightful.

Reviewers assessed the accuracy, relevance, and adherence of the answers to guideline recommendations. Discrepancies in scoring were resolved through consensus.

#### **Statistical Analysis**

The mean and standard deviation of scores were calculated to determine ChatGPT-4o's overall performance. Statistical significance was defined as p<0.05. Data were analyzed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). The free-marginal multirater kappa test was used to calculate inter-rater reliability, with the tool available at "http://justusrandolph.net/kappa/" utilized for the analysis.<sup>[18]</sup>

#### **Ethical Considerations**

This study did not involve human or animal subjects and thus did not require formal ethical approval. All data used were derived from publicly available clinical guidelines. Reviewer participation was voluntary, and no personal or identifiable information was collected. According to the Declaration of Helsinki, ethical committee approval was not required for this study.

#### **RESULTS**

The mean score across all 50 questions was 4.76±0.57, indicating a high level of accuracy and adherence to guideline-based recommendations (Table 1). Median scores for all questions were consistently 5.0, reflecting a high level of agreement among reviewers regarding the model's performance. The evaluation produced a free-marginal kappa value of 0.58, with a 95% confidence interval of [0.51, 0.65], reflecting an intermediate to good level of agreement among the raters.

ChatGPT-40 performed best on questions requiring clear, guideline-based answers. For instance, it provided highly accurate and consistent responses on topics such as the diagnosis of tension pneumothorax, which are determined by standard protocols. While its performance on questions requiring more nuanced clinical judgment was also generally strong, slightly more variability was observed. Overall, there was robust agreement among the evaluating doctors, as reflected by consistently high scores.

Questions on emergency management steps, such as needle decompression for tension pneumothorax, received perfect scores ( $5.0\pm0.0$ ), emphasizing the tool's utility in high-stakes clinical scenarios.

In contrast, questions requiring the identification of clinical findings or differential diagnosis displayed slightly varied scores, with a mean of 4.6±0.89. This variability suggests that while ChatGPT-40 provides accurate answers, its depth in clinical reasoning could be further refined.

#### **DISCUSSION**

The findings of this study demonstrate that ChatGPT-40 performs exceptionally well in answering clinical questions related to thoracic trauma, with a mean score of 4.76±0.57 on a 5-point Likert scale, indicating high accuracy and adherence to established guidelines.

Previous studies have explored the role of Al in trauma-related domains with promising results. For example, ChatGPT has demonstrated robust performance in synthesizing urological trauma guidelines, [10] and Al models have been applied in emergency medicine for prioritizing acute interventions. [19] These findings support the applicability of large language models in structured, protocol-driven trauma care. However, this study is one of the first to systematically evaluate the application of ChatGPT-40 in thoracic trauma management, addressing a critical gap in the literature.

The model's ability to provide accurate and guideline-concordant responses reflects its advanced natural language processing capabilities. Questions involving straightforward diagnostic and management protocols, such as tension pneumothorax or chest tube placement, received perfect scores (5.0±0.0), showcasing ChatGPT-4o's strength in synthesizing well-established evidence. These findings are consistent with other specialties, where AI tools excel in processing explicit and structured data. [20]

Additionally, ChatGPT-4o's interactive nature enables dynamic querying, allowing clinicians to refine or expand upon initial responses. This adaptability could be particularly valuable in resource-limited settings or for less experienced practitioners who might benefit from supplemental guidance.<sup>[21]</sup> The high performance observed in this study highlights ChatGPT-4o's utility as a decision-support tool in thoracic trauma management. By synthesizing complex guidelines into actionable insights, it can enhance clinical efficiency, particularly in high-pressure environments such as trauma centers.<sup>[22]</sup>

Moreover, ChatGPT-4o's application extends beyond individual clinicians. It could potentially be integrated into electronic health record (EHR) systems to provide real-time recommendations during patient care. [23] However, Al should not replace clinical expertise but instead act as an adjunct, supporting decision-making while allowing clinicians to exercise their judgment.

#### **CONCLUSION**

This study underscores the potential of ChatGPT-40 as a reliable, guideline-concordant tool for thoracic trauma manage-

ment. Its high performance, particularly in questions derived from explicit guidelines, demonstrates its promise in augmenting clinical decision-making. However, careful consideration of its limitations and integration with clinical expertise is essential to maximize its impact on patient care.

**Ethics Committee Approval:** This study did not involve human or animal subjects and thus did not require formal ethical approval.

Peer-review: Externally peer-reviewed.

**Authorship Contributions:** Concept: İ.D., M.Y.; Design: İ.D., M.Y.; Supervision: İ.D., M.Y.; Resource: İ.D., M.Y.; Materials: İ.D., M.Y.; Data collection and/or processing: İ.D., M.Y.; Analysis and/or interpretation: İ.D., M.Y.; Literature review: İ.D., M.Y.; Writing: İ.D., M.Y.; Critical review: İ.D., M.Y.

Conflict of Interest: None declared.

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#### ORİJİNAL ÇALIŞMA - ÖZ

# Torasik travmada ChatGPT-40 performansı: Kılavuzlara dayalı karşılaştırmalı değerlendirme

AMAÇ: Bu çalışma, Chat GPT-40'nun torakal travma yönetimindeki performansını, yanıtlarını belirli klinik kılavuzlarla karşılaştırarak değerlendirmeyi amaçlamaktadır.

GEREÇ VE YÖNTEM: Beş ana torakal cerrahi kılavuz incelendi; bunlar arasında 2018 yılına ait Advanced Trauma Life Support (ATLS) Kılavuzları, 2020 yılına ait Eastern Association for the Surgery of Trauma (EAST) Kılavuzları, 2022 yılına ait Evaluation and Management of Traumatic Pneumothorax: A Western Trauma Association Critical Decisions Algorithm, 2016 yılına ait European Trauma Course (ETC) Kılavuzları ve 2020 yılına ait NICE Trauma Kılavuzları yer almaktadır. Bu kılavuzlara dayalı olarak 50 açık uçlu soru geliştirilmiş ve Chat GPT-40'ya sunulmuştur. Beş torakal cerrahi uzmanı, yapay zekânın yanıtlarını 5 dereceli Likert ölçeği ile değerlendirmiştir.

BULGULAR: Chat GPT-40, 50 soruluk değerlendirmede ortalama 4.76±0.57 puan almıştır. Chat GPT-40, iyi tanımlanmış kılavuzlardan türetilen sorularda başarılı olmuş ve kılavuzlara dayalı tibbi bilgiyi sentezleme ve uygulama yeteneğini göstermiştir. Performansı, ürolojik travma ve acil tıp alanındaki önceki çalışmalarla uyumludur ve benzer güvenilirlik bildirilmiştir. Ancak, mevcut verilere dayalı çalışması, oldukça ayrıntılı veya yeni klinik senaryoları ele almadaki etkinliğini sınırlamaktadır. Bu bulgular, kılavuz odaklı tıbbi bağlamlarda, özellikle karmaşık vakalarda klinik denetim gerekliliğine vurgu yaparak, onun tamamlayıcı bir araç olarak potansiyelini vurgulamaktadır.

SONUÇ: Chat GPT-40, torakal travma yönetimi sorularında güçlü bir performans sergilemiş, hataları minimumda tutmuş ve yüksek güvenilirlik göstermiştir. Bu sonuçlar, özellikle belirlenmiş protokollerle yönlendirilen senaryolarda, klinik karar verme sürecinde değerli bir destek aracı olabileceğini göstermektedir. Daha geniş tıbbi alanlarda daha fazla araştırma yapılması gereklidir.

Anahtar sözcükler: Doğal dil işleme; klinik karar destek sistemleri; kılavuzlara uyum; tıpta yapay zeka; torakal travma.

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# The problem-solving role of the 'wait and repeat CT' approach in the diagnosis and treatment of acute abdomen

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#### **ABSTRACT**

**BACKGROUND:** This study aims to assess the diagnostic value and problem-solving utility of follow-up abdominopelvic computed tomography (CT) scans performed within 10 days of the initial presentation for acute non-traumatic abdominal symptoms in the emergency department.

METHODS: A retrospective analysis was conducted on patients who presented with acute abdominal symptoms to the emergency department between January 1, 2013 and May 30, 2023, and underwent abdominopelvic CT scans in the acute setting. Among this cohort, 149 patients had repeat abdominopelvic CT scans during the same admission and were classified into five groups based on findings: Group A (no change in diagnosis), Group B (confirmation of suspected initial diagnosis), Group C (disease progression), Group D (disease regression), and Group E (new diagnosis).

**RESULTS:** The mean age of the cohort was 51.5±18 years (range: 19-92). The average interval between initial and repeat CT scans was 40.9±59.05 hours (range: 0.5-238). The number of patients in each group was as follows: Group A (n=21), Group B (n=60), Group C (n=32), Group D (n=25), and Group E (n=11). Partial bowel obstruction was the most common finding (27%, 41/149), with 72% (18/25) of Group D showing regression on follow-up CT. The "wait and follow-up" approach significantly guided management decisions for partial bowel obstruction (p<0.01).

**CONCLUSION:** This study emphasizes the importance of the "wait and repeat CT" strategy in enhancing diagnostic accuracy and guiding clinical management for patients with acute non-traumatic abdominal complaints. Follow-up CT scans were particularly effective in identifying conditions such as partial bowel obstruction.

Keywords: Abdominal pain; acute abdomen; computed tomography; emergency medicine; intestinal obstruction.

#### INTRODUCTION

In emergency radiology (ER) practice, abdominopelvic CT scans play an indispensable role in the assessment of patients with acute non-traumatic abdominal symptoms. Abdominal pain, one of the most frequent reasons for emergency department visits, is a key indication for CT imaging.<sup>[1]</sup> Ab-

dominopelvic CT has become a cornerstone of routine emergency practice due to its ability to provide rapid and detailed cross-sectional imaging, enabling clinicians to swiftly identify life-threatening conditions and guide treatment decisions. [2-5] However, within this patient population, there remains a lack of well-established classification systems and limited research on the clinical utility of repeat abdominopelvic CT scans. Few

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studies in the literature have evaluated the diagnostic contribution of repeat imaging.  $^{[6,7]}$ 

This study aims to address this gap by focusing on patients for whom the "wait and repeat" strategy is employed. Our objective is to identify and characterize the patient subgroup that benefit most from follow-up CT scans, particularly in cases where the initial scan fails to provide a definitive diagnosis. By analyzing the diagnostic value of repeat abdominopelvic CT scans performed within one week of the initial presentation, this study seeks to determine which patient subgroups benefit most from this approach and to define the specific scenarios in which repeat imaging serves as a crucial diagnostic tool.

#### **MATERIALS AND METHODS**

Study Design and Time Period: The study protocol was approved by the Institutional Review Board of Hacettepe University Hospital (Approval No: GO 23-566). The study was conducted in accordance with the principles of the Declaration of Helsinki. Patients who presented to the emergency department (ED) at Hacettepe University Hospital between January 1, 2013 and May 30, 2023, with acute abdominal pain and underwent abdominal CT scans were included in this retrospective study.

Population and Sample Size: A total of 16,474 patients were admitted to the emergency department with abdominal complaints. Among these patients, 228 underwent repeat abdominal CT examinations during the same admission. After excluding 79 patients for the following reasons: being under 18 years of age (n=12), images with artifacts (n=49), known chronic organic gastrointestinal disease (n=11), or complications of known malignancy (n=7), a total of 149 patients with appropriate CT images were included in the final analysis.

Study Setting: CT scans were performed using a 2-slice scanner (until 2016) and a 64-multislice CT scanner (after 2016). The standard protocol for non-traumatic abdominal pain included administering 50 cc of oral contrast (iopamidol-300) diluted in 600 mL of water, consumed one hour prior to the CT scan, and 80 cc of intravenous contrast (iopamidol-370), injected 90 seconds before CT scanning. For CT scans performed with a renal protocol, no intravenous contrast was administered. Images were acquired at 3-mm intervals, spanning from the middle of the heart to the ischial tuberosities, with routine coronal reconstructions performed. The distribution of initial CT examinations according to contrast agent utilization was as follows: 92 scans (61.7%) without intravenous (IV) contrast, 32 scans (21.4%) with only IV contrast, 17 scans (11.4%) with both IV and oral contrast, and 8 scans (5.3%) with only oral contrast. For follow-up CT examinations, the breakdown was: 75 scans (50.3%) with only IV contrast, 31 scans (20.8%) without oral or IV contrast, 26 scans (17.4%) with both IV and oral contrast, and 17 scans (11.4%) with only oral contrast.

Intervention and Outcome Measures: Medical records, including CT reports, physician notes, nursing notes, and specialty consultations, were comprehensively reviewed. Vital signs, laboratory test results, and all imaging studies conducted in the ED were also included in the analysis.

Patients were categorized based on the similarity or difference between initial and repeat CT findings into the following groups:

- Group A: No change in preliminary diagnosis on repeat CT.
- Group B: Confirmation of the initially suspected diagnosis.
- Group C: Disease progression after initial diagnosis.
- Group D: Regression of findings after initial diagnosis.
- Group E: Identification of a completely different diagnosis.

#### **Data Analysis**

Continuous variables were summarized as mean ± standard deviations or median (range), depending on distributional characteristics. Normality was tested using the Kolmogorov-Smirnov test. Categorical variables were evaluated with the chi-square test or Fisher's exact test, as appropriate. Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA). A two-tailed p<0.05 was considered statistically significant.

#### **RESULTS**

This study included 149 patients who met the inclusion criteria: age over 18 years, absence of chronic conditions or known malignancies, and exclusion of cases with image artifacts. The mean age of the cohort was 51.5±18 years, with a median of 53 years (range: 19-92 years). Of the patients, 91 (61.07%) were male and 58 (38.93%) were female. The average interval between the initial and repeat CT scans was 40.9±59.05 hours (range: 0.5-238 hours) (Table 1).

The diagnostic outcomes from the repeat CT scans were classified into five groups based on changes relative to the initial scans (Fig. 1, Fig. 2):

- Group A (No change in the preliminary diagnosis): 21 patients (14%) showed no change in CT findings between the initial and follow-up scans, maintaining the original diagnosis.
- Group B (Confirmation of suspected diagnosis on follow-up CT): 60 patients (40%) had their initial suspected diagnoses confirmed on repeat CT.
- Group C (Disease progression after initial diagnosis): 32 patients (22%) showed progression of findings compared with the initial scan.
- Group D (Disease regression of initial findings on followup CT): 25 patients (17%) demonstrated regression of initial findings on repeat CTs.

Table 1. Demographic characteristics of patients and contrast agent use in computed tomography (CT) scans

Parameter	Mean±SD or Number
Mean age in years (range)	51.5±18 (19-92)
Number of males/total (%)	91/149 (61.7%)
Mean interval between CT scans (range)	40.9±59.05 (0.5-238)
Initial CT scan (number, percentage)	
Non-contrast	92 (61.7%)
IV contrast	32 (21.4%)
Oral contrast	8 (5.3%)
IV + oral contrast	17 (11.4%)
Repeat CT scan (number, percentage)	
Non-contrast	31 (20.9%)
IV contrast	75 (50.3%)
Oral contrast	17 (11.4%)
IV + oral contrast	6 (17.4%)

• Group E (Completely different diagnosis): I I patients (7%) were found to have a completely different diagnosis on repeat CT, not suspected during the initial examination.

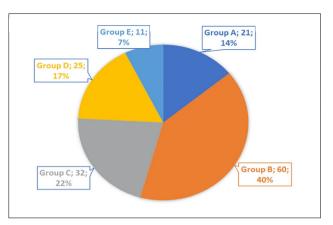
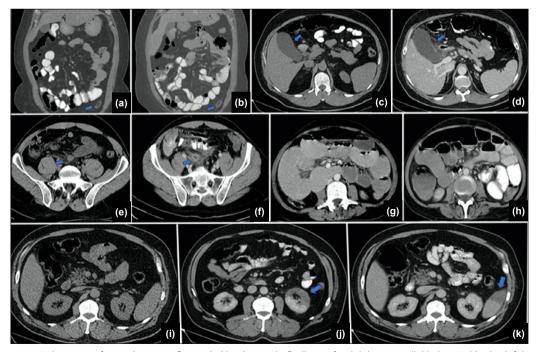


Figure 1. The number and percentage of patients in each group.

In Group A (n=21), the most common diagnoses were urolithiasis (seven patients), epiploic appendagitis (six patients), and partial bowel obstruction (six patients). In Group B (n=60), frequent diagnoses included enterocolitis, partial bowel obstruction, acute appendicitis, acute cholecystitis, pelvic inflammatory disease, acute pyelonephritis, and serositis. In Group C (n=32) predominant diagnoses were partial bowel obstruction, acute appendicitis, urolithiasis, renal infarction, enterocolitis, and acute pyelonephritis. In Group D (25 patients), the most prevalent condition was partial bowel obstruction, followed by enterocolitis, serositis, and urolithiasis. Group E (11 patients) revealed diverse new diagnoses on



**Figure 2.** Representative cases for each group. Group A: No change in findings of epiploic appendicitis located in the left lower quadrant on repeat computed tomography (CT) scan (a, b, arrows). Group B: Initially suspicious findings of acute cholecystitis on the first CT scan were confirmed on follow-up CT (c, d, arrows). Group C: Findings of acute appendicitis showed progress (e, f, arrows). Group D: Findings of partial bowel obstruction improved (g, h). Group E: Initial CT was negative (i), while the follow-up CT revealed renal infarction (j, arrow) and splenic infarction (k, arrow).

Table 2.	Distribution and frequency of findings across groups, presented as the number of patients in each category. Group sizes are
	shown in brackets.

Group A (n=21)	Group B (n=60)	Group C (n=32)	Group D (n=25)	Group E (n=11)
Urolithiasis (7)	Enterocolitis (14)	Partial bowel obstruction (8)	Partial bowel obstruction (18)	Renal infarction (5)
Epiploic appendagitis (6)	Partial bowel obstruction (7)	Acute appendicitis (3)	Enterocolitis (4)	Partial bowel obstruction (2)
Partial bowel obstruction (6)	Acute appendicitis (7)	Urolithiasis (3)	Serositis (2)	Acute pancreatitis (I)
Omental infarction (I)	Pelvic inflammatory disease (5)	Renal infarction (2)	Urolithiasis (I)	Cholelithiasis (I)
Acute diverticulitis (I)	Acute cholecystitis (5)	Enterocolitis (2)		Urolithiasis (I)
	Acute pyelonephritis (3)	Acute pyelonephritis (2)		Cystitis (I)
	Serositis (2)	Others (12)		
	Others (17)			

repeat CT, including renal infarction, partial bowel obstruction, acute pancreatitis, cholelithiasis, urolithiasis, and cystitis (Table 2).

In Group A, all six patients diagnosed with epiploic appendagitis initially underwent non-contrast CT imaging. However, due to persistent symptoms, follow-up contrastenhanced CT scans were subsequently performed. Similarly, among the seven patients with urolithiasis in Group A, six underwent non-contrast CT as their initial imaging modality. Of these, two required contrast-enhanced repeat CT due to anuria, while the remaining patients underwent repeat imaging because of ongoing pain. In Group B (60 patients with confirmed suspected diagnoses on repeat CT), the initial imaging was non-contrast in 48 cases. Of these, 42 underwent repeat CT with IV contrast. In Group E, non-contrast CT was used as the initial imaging modality in 9 of the 11 patients, with contrast-enhanced CT performed during repeat evaluations. In one patient, the initial contrast-enhanced CT scan failed to clearly identify a stone at the ureterovesical junction, which was retrospectively noted to have been difficult to detect. However, the stone was successfully visualized on the follow-up non-contrast CT scan.

The average time interval between the initial and repeat CT scans was 40.9±59.05 hours (range: 0.5-238 hours). When analyzing the intervals for each group individually, the mean durations were: Group A, 49.3±59.05 hours (range: 1-181 hours); Group B, 30.8±54.5 hours (range: 0.5-229 hours); Group C, 62±71.2 hours (range: 1.5-238 hours); Group D, 28.1±43.7 hours (range: 1.5-205 hours); and Group E, 47.6±66.6 hours (range: 1.5-210 hours). The highest average time interval between CTs was observed in Group C. Although no statistically significant differences were identified between the mean time intervals across the groups, the considerable variability in the duration between examinations suggests that direct comparisons may not be appropriate.

A particularly notable finding was the high prevalence of partial bowel obstruction, which was observed in 41 of 149 patients (27%), making it the most frequent condition across all groups. In Group D, 18 of the 25 patients (72%) with partial bowel obstruction experienced regression of findings on repeat CT scans, indicating that many of these patients benefit from the "wait and repeat" approach. Among the 18 patients with partial intestinal obstruction in Group D, obstruction in two cases was attributed to ventral and inguinal hernias and resolved following surgery. The remaining patients were managed conservatively without surgery, using nasogastric tube decompression, during which the obstruction resolved. Oral contrast was administered in the initial CT scan of eight patients, whereas it was used in repeat CT imaging in only five of these patients. In the progression group, the most frequently observed condition was partial intestinal obstruction, affecting eight patients. However, partial bowel obstruction was significantly more prevalent in the regression group compared to other groups (p<0.01), and follow-up CT imaging appeared particularly valuable for both monitoring these patients and informing treatment decisions. Importantly, no patients experienced significant adverse events from either the initial or repeat CT scans, although the potential longterm radiation risks from CT exposure were not directly addressed in this study.

## **DISCUSSION**

Acute non-traumatic abdominal pain is a frequent presenting complaint in emergency departments and often necessitates abdominopelvic CT scans for accurate diagnosis. Multi-detector CT scanners provide high diagnostic accuracy and play a key role in guiding critical patient management decisions.<sup>[8-11]</sup> In particular, the "wait and repeat CT" strategy has gained attention for its potential to yield additional diagnostic information without requiring immediate surgical intervention.

Our findings demonstrate that the "wait and repeat CT" approach plays a significant role in refining diagnoses and guiding clinical management. By categorizing patients based on changes between initial and follow-up CT findings, we identified several diagnostic outcomes: confirmation of initial suspicions, detection of disease progression, regression of findings, and identification of new diagnoses. This study specifically aimed to evaluate the diagnostic contribution and problemsolving role of repeat CT imaging performed within 10 days for acute non-traumatic abdominal conditions. Through this analysis, we sought to establish the value of follow-up CT in confirming or modifying initial diagnoses, as well as detecting disease changes or previously unrecognized conditions.

Our data also highlight the potential utility of performing contrast-enhanced CT scans following non-contrast imaging in selected clinical scenarios. Among patients with a confirmed suspected diagnosis, the transition from non-contrast to contrast-enhanced CT in 42 of 48 cases improved diagnostic assessment and management, underscoring its importance in refining diagnostic accuracy. Furthermore, in Group E, contrast-enhanced imaging during repeat evaluations was beneficial in many cases. However, findings from one patient suggest that non-contrast imaging may sometimes be more effective, particularly in specific contexts such as identifying stones at the ureterovesical junction. The importance of IV contrast in confirming diagnoses has been demonstrated, particularly in patients whose suspected diagnosis was validated. Performing with IV contrast in these patients, when clinically indicated, may improve diagnostic accuracy while reducing the rate of unnecessary CT scans.

Our findings contribute to the ongoing discussion regarding the diagnostic utility of repeat imaging in acute abdominal cases. Lee et al.[7] reported that repeat abdominopelvic CT scans within one month revealed new or worsening findings in 30% of patients presenting to the emergency department with acute abdominal pain, emphasizing the importance of repeat imaging in clinical decision-making. In our study, which used a shorter interval of 10 days compared to their one-month interval, 14% of patients exhibited no change on repeat CT, in contrast to the 43% reported in their study. We observed progression in 22% of patients (Group C) among 149 cases, compared to their study, which reported a progression rate of 15% in 53 patients. Similarly, 17% of our patients showed regression (Group D), compared with 26% in their study. Finally, 7% of our patients were diagnosed with a different condition on repeat CT (Group E), compared to 15% in the same group in their study. These differences may reflect the potential influence of varying time intervals on the outcomes of repeat imaging.

In contrast, Nojkov et al.<sup>[12]</sup> concluded that repeat abdominal CT scans after an initially negative CT in non-traumatic abdominal pain cases had a low diagnostic yield (6.5%). Our findings suggest a different perspective: 14% of patients retained their original diagnosis, 40% had their initial suspected

diagnosis confirmed, 22% demonstrated disease progression, 17% showed regression, and 7% received an entirely new diagnosis. These findings emphasize the higher diagnostic yield of repeat CT in our patient population compared to the results reported by Nojkov et al.<sup>[12]</sup> In their study, the most frequently observed findings were obstructive nephrolithiasis, gastrointestinal mural thickening or masses, and diverticulitis. In contrast, the most common findings in our study were partial bowel obstruction, enterocolitis, urolithiasis, and acute cholecystitis.

The diagnostic utility of follow-up CT scans was particularly notable in cases of partial bowel obstruction, which was the most frequently encountered condition in our study, affecting 27% of patients. Regression of findings on follow-up imaging was observed in 72% of these patients (Group D), supporting the "wait and repeat" approach as a valuable strategy, particularly for managing partial bowel obstruction. Among the patients with partial obstruction who showed regression, no clear underlying cause was identified in most cases, except for two (ventral and inguinal hernias). These cases were managed with nasogastric tube decompression, which led to symptom resolution and was attributed to adhesions. Oral contrast was administered during follow-up CT in only five of these patients. Although no statistically significant benefit (p<0.05) of oral contrast in resolving partial obstruction was observed, the unequal data distribution and small sample size suggest that its impact should be further investigated in larger studies.

This study has several limitations. The retrospective design may introduce selection bias, and the single-center setting in a tertiary-care teaching hospital may limit the generalizability of the findings to smaller community hospitals. Furthermore, the relatively small sample size reduces the robustness of the study, emphasizing the need for future prospective studies to confirm these findings. The small sample size limits the ability to assess the utility of repeat CT imaging for diagnosing rare but potentially fatal conditions that might be overlooked. Large-scale studies using standardized equipment and imaging protocols are needed to validate these findings. The repetition of CT imaging despite unchanged diagnosis highlights a limitation in the use of follow-up imaging. In Group A, all six patients with epiploic appendagitis underwent repeat contrast-enhanced CT scans solely due to persistent symptoms, yet the findings did not alter the initial diagnosis. Similarly, among the six patients with urolithiasis who initially underwent non-contrast CT, repeat imaging with contrast was performed in two cases due to anuria and in the remaining cases for ongoing pain, but the diagnostic outcomes remained unchanged. These observations suggest potential overutilization of repeat imaging in situations where it may not significantly influence clinical decision-making, underscoring the need for more judicious use of follow-up CT scans to balance patient care with resource efficiency. When comparing the mean time intervals between examinations across groups, no statistically significant differences were observed.

However, the considerable variability in these intervals may have introduced selection bias in group formation, representing a potential limitation of the study. Furthermore, imaging performed up to 10 days later may reflect entirely different disease processes, making it impractical to apply a single time frame to the management of conditions with widely varying urgency. Additionally, the heterogeneous use of oral and intravenous contrast agents, the limited imaging phases acquired, and the use of both 2-slice and 64-slice CT scanners may have reduced image quality and consistency, posing another limitation of this study.

## **CONCLUSION**

Our study highlights the significant diagnostic contribution of repeat abdominopelvic CT scans performed within 10 days in patients with acute non-traumatic abdominal pain. The "wait and repeat" strategy is invaluable for confirming or revising diagnoses, detecting disease progression or regression, and identifying new conditions. Despite ongoing concerns about radiation exposure and economic costs, the clinical benefits, particularly in dynamic conditions such as partial bowel obstruction, support the continued use of this approach. Future research should focus on optimizing imaging protocols to balance diagnostic accuracy with patient safety and cost-effectiveness.

**Ethics Committee Approval:** This study was approved by the Hacettepe University Hospital Ethics Committee (Date: 11.07.2023, Decision No: GO 23-566).

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**Authorship Contributions:** Concept: E.A., A.G.E.; Design: E.A.; Supervision: E.A., M.R.O., A.G.E.; Data collection and/or processing: E.A., A.G.E.; Analysis and/or interpretation: E.A., A.G.E., M.R.O., İ.İ.; Literature review: E.A., A.G.E.; Writing: E.A.; Critical review: M.R.O., İ.İ., B.E.

Conflict of Interest: None declared.

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## ORİJİNAL ÇALIŞMA - ÖZ

## Akut batın tanı ve tedavisinde 'bekle ve BT'yi' yönteminin sorun çözmedeki rolü

AMAÇ: Bu çalışma, acil servise akut travmatik olmayan karın ağrısı şikayetiyle başvuran hastalarda, ilk başvurudan sonraki 10 gün içinde gerçekleştirilen takip abdomenopelvik bilgisayarlı tomografi (BT) taramalarının tanısal değerini ve sorun çözme potansiyelini değerlendirmeyi amaçlamaktadır. GEREÇ VE YÖNTEM: I Ocak 2013 ile 30 Mayıs 2023 tarihleri arasında akut karın şikayetleri ile acil servise başvuran ve akut dönemde abdomenopelvik BT çekilen hastalar retrospektif olarak analiz edildi. Bu kohort içerisinde, aynı yatış süresi içinde tekrar abdomenopelvik BT çekilen 149 hasta belirlendi ve bulgulara göre beş gruba ayrıldı: Grup A (ilk tanıda değişiklik yok), Grup B (başlangıçta şüphelenilen tanının doğrulanması), Grup C (hastalığın progresyonu), Grup D (hastalığın regresyonu) ve Grup E (tekrarlayan BT'de yeni tanı).

BULGULAR: Kohortun ortalama yaşı 51.5±18 yıl (19–92) idi. İlk ve tekrarlayan BT çekimleri arasındaki ortalama süre 40.9±59.05 saat (0.5–238) olarak belirlendi. Gruplara göre hasta sayısı şu şekildeydi: Grup A (n=21), Grup B (n=60), Grup C (n=32), Grup D (n=25) ve Grup E (n=11). En sık karşılaşılan bulgu parsiyel barsak obstrüksiyonu idi (%27, 41/149); Grup D'nin %72'sinde (18/25) takip BT'de regresyon izlendi. "Bekle ve BT'yi tekrarla" yaklaşımı, parsiyel barsak obstrüksiyonunda klinik yönetim kararlarını anlamlı şekilde yönlendirdi (p<0.01).

SONUÇ: Bu çalışma, travmatik olmayan akut karın şikayeti olan hastalarda tanısal doğruluğun artırılması ve klinik yönetimin yönlendirilmesinde "bekle ve BT'yi tekrarla" stratejisinin önemini vurgulamaktadır. Takip BT'leri özellikle parsiyel barsak obstrüksiyonu gibi durumların belirlenmesinde etkili bulunmuştur.

Anahtar sözcükler: Acil tıp; akut batın; barsak tıkanıklığı; bilgisayarlı tomografi; karın ağrısı.

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## Hyperbaric oxygen therapy in patients with thoracic injuries: Is it safe?

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- © Gözde Büşra Sarıyerli Dursun,¹ © Gamze Aydın,² © Taylan Zaman,¹ © Şahin Kaymak³

## **ABSTRACT**

**BACKGROUND:** This retrospective cohort study aimed to evaluate the safety of hyperbaric oxygen therapy (HBOT) in patients with blunt thoracic trauma, with particular focus on crush injuries sustained during the 2023 Kahramanmaraş earthquakes.

**METHODS:** Twenty-five patients with documented thoracic trauma who underwent HBOT at a tertiary care center were included. HBOT was delivered at 2.4 atmospheres absolute (ATA) for two hours per session in a multiplace chamber. Data on demographics, clinical findings, treatment outcomes, and adverse events were analyzed.

**RESULTS:** The median age was 23 years (range: 10-57), and 64% were female. The median number of HBOT sessions was 11 (range: 2-37). Three patients (12%) died during follow-up due to severe crush injuries, unrelated to HBOT. Five patients (20%) developed respiratory or cardiac symptoms during treatment, including dyspnea (n=2), chest pain (n=1), dyspnea with chest pain (n=1), and arrhythmia with convulsions (n=1). Pneumomediastinum was incidentally detected in one intubated patient post-session and was managed conservatively, allowing HBOT to continue without further complications. One patient experienced a generalized seizure attributed to central nervous system oxygen toxicity; HBOT was discontinued, neurological evaluation was performed, and no permanent sequelae occurred.

**CONCLUSION:** Although HBOT is generally considered safe, it may cause cardiopulmonary complications in patients with thoracic trauma, especially those with poor clinical reserve or requiring mechanical ventilation. Most complications observed in this cohort were minor and manageable. HBOT can be safely administered in carefully selected thoracic trauma patients when individualized risk assessment and multidisciplinary monitoring are ensured. Future prospective studies with larger cohorts are needed to further clarify safety profiles and risk stratification strategies.

Keywords: Hyperbaric oxygen therapy; thoracic trauma; blunt chest injury; pulmonary complications.

## INTRODUCTION

Thoracic trauma refers to injury of the chest wall, pleural space, or intrathoracic organs caused by blunt or penetrating mechanisms and accounts for a significant proportion of trauma-related deaths.<sup>[1]</sup> Most thoracic traumas present as blunt injuries, commonly resulting from traffic accidents, falls from

height, assaults, or crush injuries.<sup>[1]</sup> Between 45% and 65% of patients admitted to the emergency department with multiple trauma have an associated thoracic injury.<sup>[2]</sup>

Hyperbaric oxygen treatment (HBOT) is a therapeutic method in which 100% oxygen is administered, either intermittently or continuously, at pressures higher than I atmosphere

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absolute (ATA) within a closed chamber.[3] It enhances oxygen diffusion into hypoxic tissue regions and is used for various clinical indications, such as early administration in crush injuries, which has been shown to reduce hypoxia-related tissue damage, necrosis, and the risk of infection. [4,5] Although HBOT is generally considered a safe treatment modality, it carries certain risks of complications. Patients at increased risk for developing pulmonary barotrauma (PBT) during HBOT include those with air-trapping lesions in the lungs, a history of spontaneous pneumothorax, underlying pulmonary disease, mechanical ventilation, or a history of thoracic trauma. [6] Existing lung injuries resulting from thoracic trauma, such as pulmonary contusion, laceration, hematoma, pseudocyst, hemothorax, and tracheobronchial injury, are particularly sensitive to pressure changes during HBOT and may increase the risk of pulmonary complications due to the vulnerability of damaged pulmonary structures. [6-8]

Although the incidence of PBT during HBOT has been reported to be very low in the literature, at approximately 4.5 cases per one million treatments, [8] complications may still occur in high-risk patient groups. [7,9-11] Published case reports on these complications have mostly involved patients treated for carbon monoxide poisoning or chronic wounds, whereas systematic data specific to the thoracic trauma population remain limited. There is currently no consensus in the literature regarding the degree of pulmonary complication risk or their optimal management strategies.

The small sample sizes, reliance on retrospective designs, and variability in patient characteristics across current studies limit the ability to draw definitive conclusions about the safety of HBOT in patients with thoracic trauma. Therefore, conducting studies to fill this gap is essential to guide the safer and more effective use of HBOT in this patient group. The aim of this study is to evaluate the safety profile of HBOT in patients with thoracic trauma and to support clinical decision-making.

## **MATERIALS AND METHODS**

## **Ethical Approval**

The research was carried out in alignment with the ethical guidelines of the Declaration of Helsinki and was approved by the Gulhane Ethics Board of the University of Health Sciences (05/25: 2025-50).

## **Design and Participants**

This retrospective cohort study evaluated patients with accompanying thoracic trauma related to the 2023 Kahramanmaraş earthquake who underwent HBOT at the Department of Underwater and Hyperbaric Medicine, Gülhane Training and Research Hospital.

The study population consisted of both male and female patients, with no age restrictions applied. Patients with missing or incomplete data were excluded from the study. Data col-

lected included age, sex, demographic characteristics, clinical indications for HBOT, and follow-up information regarding morbidity and mortality. In addition, the number of HBOT sessions administered and any complications that occurred during the treatment process were recorded.

HBOT was administered to all patients at 2.4 ATA for a duration of two hours per session in a multi-place chamber (Hipertech ZYRON 12, 2008, Istanbul, Türkiye).

## **Statistical Analysis**

Statistical analyses were performed using Jamovi software (version 2.4.7; The Jamovi Project, Sydney, Australia). The normality of distribution for continuous variables was assessed using the Shapiro-Wilk test. Descriptive statistics were presented as mean  $\pm$  standard deviation, median (minimum–maximum), or number and percentage [n (%)], as appropriate.

## **RESULTS**

A total of 25 patients were included in the study. The median age was 23 years (range: 10-57). Of these, 16 patients (64%) were female and nine patients (36%) were male. All patients included in the study had sustained thoracic trauma during the earthquake and underwent HBOT due to indications such as crush injury and/or compartment syndrome. The median number of HBOT sessions administered was 11 (range: 2-37). At the end of the treatment process, nine patients (36%) were discharged with complete recovery, while three patients (12%) died during follow-up after the HBOT schedule ended; these deaths were not attributed to HBOT. The remaining 13 patients (52%) could not complete the full course of HBOT as initially scheduled due to poor tolerance, voluntary discontinuation, or transfer to another facility.

Of the 25 patients, two (8%) had asthma, while the remaining 23 patients (92%) had no known chronic pulmonary disease. All patients (100%) had sustained blunt thoracic trauma. The radiological findings observed in these patients are presented in Figure 1.

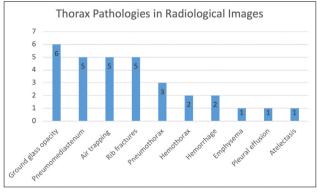


Figure 1. Thoracic pathologies identified on radiological imaging.

Pre-HBOT: Chest tube insertion was required in two patients (8%) prior to HBOT due to pneumothorax secondary to blunt thoracic trauma.

During HBOT: Adverse events were observed in a small number of patients during HBOT sessions. Dyspnea occurred in two patients (8%), chest pain in one patient (4%), both chest pain and dyspnea in one patient (4%), and one patient (4%) developed arrhythmia and convulsions. The remaining 20 patients (80%) completed the treatment without any complaints.

Post-HBOT: Pulmonary barotrauma in the form of pneumo-mediastinum occurred in only one patient (4%). The patient did not report any symptoms such as chest pain or dyspnea during or after HBOT sessions. Pneumomediastinum was incidentally detected on a routine thoracic computed tomography (CT) scan performed by the primary clinical team for follow-up evaluation. No additional intervention was required, and conservative management was deemed appropriate by the thoracic surgery team. Following multidisciplinary consultation, HBOT was resumed the next day under close clinical monitoring. No additional complications were observed during subsequent HBOT sessions in this patient.

## **DISCUSSION**

In this retrospective study, the safety of HBOT was evaluated in 25 patients with blunt thoracic trauma. While some patients (n=5, 20%) experienced transient symptoms such as dyspnea, chest pain, arrhythmia, and convulsions during treatment, only one case (4%) of pneumomediastinum was recorded after HBOT. These findings indicate that strict and close monitoring is critical in patients with thoracic trauma during and after HBOT. Physicians, attending staff, and primary caregivers should remain vigilant for signs of pulmonary complications both during and after HBOT sessions.

The potential complications of HBOT arise from the physiological effects of pressure changes and high oxygen concentrations.[12] Barotrauma can develop during the pressurization and decompression phases of treatment due to significant pressure-volume fluctuations. PBT results from pulmonary overexpansion in response to a reduction in ambient pressure.[13] PBT of ascent can present in four clinical forms: local pulmonary injury, pneumomediastinum, pneumothorax, and arterial gas embolism (AGE).[14] Pulmonary pathologies that may increase the risk of barotrauma during decompression include reduced pulmonary compliance, a history of spontaneous pneumothorax, acute lower respiratory tract infection, atelectasis, bullous emphysema, pulmonary cysts, blunt chest trauma, subpleural blebs, pulmonary fibrosis, and chronic obstructive pulmonary disease with air trapping.[13] Clinicians should carefully evaluate patients for the risk of PBT prior to initiating HBOT in those with thoracic trauma. To our knowledge, there is only one case report in the literature describing the development of PBT in patients with existing thoracic trauma.[15] In our study, pneumomediastinum was

observed in only one patient. Pneumomediastinum is defined as the presence of air within the mediastinal cavity and may occur spontaneously or as a result of iatrogenic factors such as trauma, mechanical ventilation, or endoscopic procedures. [16,17] Intubation and positive-pressure ventilation—especially when high pressures are applied—can lead to alveolar rupture and subsequent leakage of air into the mediastinum.[18] During HBOT, pressure fluctuations, particularly during the decompression phase, may exacerbate pre-existing air leaks or reveal subclinical pulmonary injuries.[19] The possibility of an occult or subclinical pneumothorax should always be considered, and clinicians must remain vigilant for potential complications such as tension pneumothorax.[19] Nevertheless, the literature suggests that HBOT may still be safely administered in carefully selected, asymptomatic, and hemodynamically stable cases of pneumomediastinum under close clinical observation.[20] In our case, the patient was intubated and receiving mechanical ventilation due to critical illness. The patient did not report any complaints at any stage of HBOT. However, pneumomediastinum was incidentally detected on a thoracic CT scan performed for routine monitoring by the primary clinical team. Therefore, it is difficult to definitively attribute the pneumomediastinum to either intubation or HBOT. In this clinically stable patient, HBOT was continued under close monitoring without any complications. This underscores the importance of multidisciplinary evaluation and individualized clinical decision-making in patients undergoing HBOT, particularly those with thoracic trauma or prior airway interventions.

Patients who developed dyspnea, chest pain, convulsions, or arrhythmia during HBOT were evaluated on a case-by-case basis. In our study, dyspnea was observed in two patients. In one of these, the pre-HBOT posteroanterior chest radiograph was interpreted as normal. However, dyspnea persisted throughout the entire fourth session of HBOT. A post-session thoracic CT scan revealed pericardial effusion, bilateral pleural effusions with adjacent passive atelectasis, and complete collapse of the right middle and lower lobes. This patient had undergone two surgical procedures under general anesthesia with endotracheal intubation prior to HBOT and was concurrently receiving dialysis treatment for renal failure. In the literature, atelectasis is described as one of the most frequently observed respiratory complications, particularly after upper abdominal and thoracic surgeries.<sup>[21]</sup> This clinical picture may be explained by atelectasis secondary to repeated surgical interventions and fluid accumulation in the pleural and pericardial spaces due to postoperative fluid overload and inadequate renal function. It is also possible that HBOT contributed to the aggravation of this condition, as the increased pressure within the hyperbaric environment may elevate the respiratory workload in patients with limited cardiopulmonary reserve, thereby exacerbating clinical dyspnea.[22]

In our study, another patient who developed dyspnea was evaluated in the intensive care unit with a posteroanterior chest radiograph and arterial blood gas analysis after the session. The patient had a history of multiple blood transfusions and was diagnosed with transfusion-related acute lung injury (TRALI) based on clinical assessment. Due to progressive clinical deterioration and an increasing need for respiratory and systemic support, the patient was unable to continue HBOT sessions.

Pulmonary injuries commonly associated with blunt chest trauma include pneumothorax, hemothorax, pulmonary contusion, and tracheobronchial disruption.<sup>[23]</sup> Among these, untreated pneumothorax is considered an absolute contraindication for HBOT.[12] However, pneumothorax may not constitute a contraindication to HBOT if it is properly treated. In our study, two patients with thoracic trauma had chest tubes. One of these patients experienced chest pain during the compression phase of HBOT, while the other reported both chest pain and dyspnea during the compression phase. In the first patient, chest pain began during the compression phase of the HBOT session. Evaluation by the thoracic surgery team confirmed that the chest tube was correctly positioned and that oscillation within the tube appeared normal. However, due to recurrence of similar pain during the descent phase in subsequent sessions, it was considered that the increasing ambient pressure during HBOT may have led to a reduction in intrathoracic gas volumes in accordance with Boyle's law. Consequently, the resulting increase in negative intrapleural pressure may have caused the chest tube to come into contact with the pleura, potentially triggering the pain. Based on this clinical assessment, the patient's primary care team decided to discontinue HBOT. The other patient with a chest tube reported experiencing chest pain and dyspnea during the compression phase of all four HBOT sessions. As these symptoms persisted in subsequent sessions, they were, similar to the previous case, attributed to the presence of the chest tube. Once the patient's pneumothorax had resolved, the chest tube was removed. However, following chest tube removal, the thoracic surgery team considered further HBOT sessions to pose a high risk for barotrauma. Consequently, the patient did not continue HBOT.

In our study, another patient developed an arrhythmic episode during HBOT. Blunt thoracic trauma can affect not only pulmonary structures but also cardiovascular components, potentially influencing clinical outcomes and the safety of adjunctive therapies such as HBOT. Although often less evident, cardiac injury remains a relevant concern in such cases. [24] It may result from direct chest impact—particularly during end-diastole—compression of the heart between the sternum and vertebrae, sudden deceleration, or increased intracardiac pressure due to elevated venous return. Other contributing mechanisms include blast injuries, rib or sternal fractures, and concussive forces capable of inducing arrhythmias or even myocardial rupture. [25] In our case, the patient's thorax was compressed under debris; however, no radiological signs of cardiac injury or skeletal fracture were identified.

HBOT itself has been associated with certain cardiovascular effects. It may lead to left ventricular (LV) dysfunction or bradycardia by increasing afterload and filling pressures.

<sup>[26]</sup> Therefore, optimizing cardiac function prior to HBOT is recommended, particularly in high-risk patients. <sup>[27]</sup> Furthermore, HBOT may influence cardiac conduction, likely through enhanced parasympathetic activity. <sup>[28]</sup> Although rare, arrhythmias such as extrasystoles and premature ventricular contractions have been reported without major clinical consequences. <sup>[28,29]</sup> Retrospective evaluation of this patient revealed a history of arrhythmia prior to hospitalization. It is plausible that HBOT either triggered or unmasked an underlying arrhythmogenic tendency. This case highlights the importance of comprehensive cardiovascular assessment and continuous electrocardiographic monitoring in patients with a history of blunt thoracic trauma undergoing HBOT.

One patient experienced a generalized tonic-clonic seizure during an HBOT session. Central nervous system (CNS) oxygen toxicity is a known but rare complication of HBOT.<sup>[30]</sup> This condition is thought to result from the accumulation of oxygen-derived free radicals in neural tissue, leading to neuronal hyperexcitability, which in some cases can trigger generalized tonic-clonic seizures.<sup>[31]</sup>

To mitigate this risk, air breaks were incorporated into the treatment protocol, alternating periods of oxygen breathing with short intervals of breathing ambient air. This approach aims to reduce the risk of CNS oxygen toxicity and associated convulsions. However, despite these precautions, such adverse events may still occasionally occur.

In our case, HBOT was discontinued following the seizure, and the patient was evaluated by neurology specialists. The patient had no prior history of epilepsy or seizure susceptibility, and no metabolic or structural abnormalities were identified. In the absence of alternative etiologies, the seizure was considered possibly related to central nervous system oxygen toxicity induced by HBOT. It should be noted, however, that this complication is not specific to thoracic trauma and may potentially occur in any patient receiving HBOT. This case underscores the importance of individualized risk assessment and strict adherence to treatment protocols to minimize the likelihood of such adverse events.

Furthermore, in our study, three patients died during the follow-up period after completion of the planned HBOT sessions. All three patients had sustained severe crush injuries and exhibited poor clinical status at baseline. Importantly, none of these patients experienced any HBOT-related adverse effects or clinical deterioration during the treatment sessions. Therefore, the observed mortalities were not temporally or causally linked to HBOT but were instead attributed to the underlying severity of trauma and systemic complications.

This study has several limitations. Its retrospective nature limits causal inference, and the small sample size reduces generalizability. Additionally, not all patients underwent standardized imaging or pulmonary function testing before and after HBOT, which may have led to underrecognition of subclinical complications. The presence of multiple comorbidi-

ties also made it difficult to isolate the effects of HBOT from other clinical factors.

## **CONCLUSION**

In this study, various respiratory and cardiac symptoms occurred during HBOT in patients (n=5, 20%) with blunt thoracic trauma, and one patient (4%) developed pneumomediastinum. These findings emphasize the importance of thorough clinical evaluation and close monitoring in thoracic trauma patients during and after HBOT. Therefore, HBOT should be administered only in carefully selected post-trauma cases, guided by a multidisciplinary approach and individualized risk assessment, with patients being closely monitored throughout the treatment process.

**Ethics Committee Approval:** This study was approved by the Gulhane University of Health Sciences Ethics Committee (Date: 08.05.2025, Decision No: 2025/50).

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## ORİJİNAL ÇALIŞMA - ÖZ

## Toraks yaralanması olan hastalarda hiperbarik oksijen tedavisi: Güvenli mi?

AMAÇ: Bu retrospektif kohort çalışmada, 2023 Kahramanmaraş depremleri sonrasında künt toraks travması geçiren hastalarda hiperbarik oksijen tedavisinin (HBOT) güvenliğini değerlendirmek amaçlanmıştır.

GEREÇ VE YÖNTEM: Çalışmaya, toraks travması tanısı alarak Gülhane Eğitim ve Araştırma Hastanesi Hiperbarik Tıp Kliniği'nde HBOT uygulanan 25 hasta alındı. HBOT, çok kişilik bir odada 2.4 ATA basınçta, günde bir kez, iki saat süreyle uygulandı. Hastaların demografik verileri, klinik endikasyonları, seans sayıları ve tedavi sırasında gelişen komplikasyonlar retrospektif olarak analiz edildi.

BULGULAR: Hastaların medyan yaşı 23 (dağılım: 10–57) olup, %64'ü kadındı. Medyan HBOT seans sayısı 11 (2–37) idi. Üç hasta (%12), HBOT tamamlandıktan sonraki takip sürecinde, altta yatan ağır crush yaralanmalarına bağlı olarak hayatını kaybetmiştir; bu ölümler HBOT ile ilişkili bulunmamıştır. Tedavi sırasında beş hastada (%20) solunum ve kardiyak semptomlar gözlenmiştir: Dispne (n=2), göğüs ağrısı (n=1), hem dispne hem ağrı (n=1), aritmi ve konvülsiyon (n=1). Bir entübe hastada seans sonrası rutin çekilen toraks BT'de tesadüfen pnömomediastinum saptanmış, hasta stabil seyretmiş ve tedaviye komplikasyonsuz şekilde devam edilmiştir. Ayrıca bir hastada seans sırasında jeneralize tonik-klonik nöbet gelişmiş, santral sinir sistemi oksijen toksisitesine bağlı olabileceği düşünülerek HBOT sonlandırılmış ve hasta nörolojik açıdan değerlendirilmiştir.

SONUÇ: HBOT, toraks travması olan hastalarda potansiyel faydalar sağlayabilecek destekleyici bir tedavi seçeneğidir. Ancak özellikle solunum rezervi kısıtlı, entübe edilen ya da ciddi eşlik eden yaralanmaları bulunan hastalarda komplikasyon riski artabilir. Bu nedenle, tedavi kararı hasta bazında dikkatle değerlendirilmelidir. HBOT'nin bu özel hasta grubunda uygulanabilirliğini artırmak için multidisipliner yaklaşım, bireyselleştirilmiş risk analizi ve yakın klinik izlem gereklidir.

Anahtar sözcükler: Hiperbarik oksijen tedavisi; toraks travmaları; künt toraks yaralanmaları; pulmoner komplikasyonlar.

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## Emergency department nurses' knowledge and practices related to extravasation injuries of non-cytotoxic medications

## **ABSTRACT**

**BACKGROUND:** Extravasation of non-cytotoxic medications can lead to serious complications such as pain, tissue necrosis, limb loss, and even death. This descriptive cross-sectional study aims to assess the knowledge levels of emergency department (ED) nurses regarding extravasation incidents involving non-cytotoxic medications and to highlight the importance of effective management and prevention.

**METHODS:** The study was conducted in the EDs of three hospitals in Istanbul, Türkiye, between November 19, 2020 and December 31, 2020. A total of 100 ED nurses participated in the study. Inclusion criteria required nurses to be working full-time in the EDs during the study period and to provide written and verbal consent. The study utilized a survey to assess sociodemographic characteristics, knowledge of non-cytotoxic medications (e.g., epinephrine), symptoms of extravasation, prevention strategies, and intervention practices.

**RESULTS:** The mean age of the nurses was 29.43 years, with 57% female and 73% holding a bachelor's degree. Among participants, 52% had 0-3 years of ED experience. Ninety-one percent reported not receiving education on extravasation after graduation, and 82% indicated no extravasation protocol was in place at their workplace. Knowledge about non-cytotoxic medications causing extravasation significantly increased with ED experience (p=0.035). Nurses in units with an extravasation protocol had significantly higher knowledge levels (p=0.007). Female nurses demonstrated better knowledge of extravasation symptoms than male nurses (p=0.012). Nurses with a bachelor's or higher degree had significantly better knowledge than others (p=0.015). The knowledge rate for the extravasation care protocol was 64%, with the most recognized protocol item being "immediately stop the infusion" (97%) and the least recognized being "aspirate the medication not to exceed 3-5 mL" (33%). Strong correlations were found between non-pharmacological factors and knowledge of non-cytotoxic medications (r=0.601; p<0.001), as well as between knowledge of extravasation care protocols and non-pharmacological factors (p<0.001).

**CONCLUSION:** The study highlights the need for targeted education and the establishment of institutional protocols for managing and preventing extravasation in EDs. Nurses' knowledge significantly impacts their adherence to prevention and care protocols. To ensure patient safety, it is important to provide ongoing education and implement evidence-based intervention protocols for the management of extravasation in ED settings.

Keywords: Emergency department; extravasation; complication management.

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## INTRODUCTION

The primary goals of care provided by Emergency Department (ED) nurses in healthcare systems around the world are to protect health, ensure patient safety, and improve health. Medication errors are a key indicator of patient safety.[1-3] The ED's multitasking environment, overcrowding, and need for quick decisions can contribute to medication errors. Medication administration errors can threaten patient safety, leading to incorrect treatments, various complications, injuries, limb loss, and even death.<sup>[4,5]</sup> There can be many complications in the administration of medications. Examples of these complications include bleeding, hematoma, thromboembolism, infection, and extravasation of the medication.[6,7] Extravasation is an iatrogenic complication that occurs when medications or solutions administered to the patient via intravenous (IV) infusion leaks into the surrounding tissues such as subcutaneous tissue, adipose tissue, connective tissue, and muscle tissue, rather than staying within the vein. Extravasation not only prolongs the patient's hospital stay but also has an impact on their daily life; it may cause critical and irreversible local injuries. If left untreated, medications that cause extravasation and are used in the ED can cause tissue necrosis, dysfunction, and permanent disfigurement.[8-11] Extravasation injuries and non-standardized nursing care caused by non-cytotoxic medications administered by ED nurses may negatively affect the patient's health and quality of life.[12-15]

The aim of this descriptive study is to draw attention to the fact that extravasation can cause serious complications such as pain, limb loss, tissue necrosis, and death and to determine the knowledge levels of ED nurses about extravasation. Although the causes, symptoms, and nursing process of extravasation have been addressed in various independent articles in the literature, the knowledge levels of nurses about extravasation have not been examined in detail and systematically. This study aims to fill this gap in the literature.

## **MATERIALS AND METHODS**

## **Design and Setting**

This descriptive cross-sectional study was conducted in the Emergency Departments of three hospitals located in Istanbul, Türkiye, under the jurisdiction of the Ministry of Health, between November 19, 2020 and December 31, 2020. The sample included 100 ED nurses (n=100) who met the inclusion criteria and were actively working in the EDs during the study period. The minimum required sample size was calculated using the G\*Power software with a 95% power ( $\alpha$ =0.05), resulting in 76 participants. To ensure sufficient statistical power and account for potential non-responses or data loss, the final sample consisted of 100 participants, exceeding the minimum required sample size.

## **Inclusion Criteria**

The study included ED nurses who were working full-time in

the Emergency Departments of the selected hospitals during the study period and who agreed to participate by providing both verbal and written consent.

## **Exclusion Criteria**

Nurses who were excluded from the study included those who refused participation or did not provide the necessary verbal and written consent, part-time workers, nurses on leave, those with physical or psychological conditions that hindered participation, and those who were assigned to different units during the study period. Nurses who left their positions during the study period were also excluded.

## **Data Collection Process and Data Collection Tools**

The data collection tool was developed by adapting questions from existing literature and previous studies on extravasation injuries and related practices. [3,8,15] To ensure the validity and relevance of the survey, the opinions of five nurse academicians with expertise in the field were sought. Their feedback was incorporated into the final version of the survey, leading to revisions in wording and structure. The expert validation process confirmed that the tool was both valid and reliable for assessing the knowledge and practices of ED nurses regarding non-cytotoxic medication extravasation.

A pilot study was conducted with a small sample of ED nurses to test the reliability and clarity of the survey. The feedback from the pilot study confirmed that the questions were clear and understandable, and the survey was revised accordingly.

The final survey included questions regarding the sociodemographic characteristics of ED nurses, such as age, education, and work experience. It also assessed their knowledge about non-cytotoxic medications, such as epinephrine, used in the ED that may cause extravasation. The survey further explored their understanding of extravasation symptoms, prevention strategies, and the interventions they would implement when dealing with extravasation injuries. Additionally, nurses were asked to respond to protocol-based statements concerning the current practices they would follow in managing extravasation.

## **Ethical Considerations**

The study was conducted in accordance with the ethical principles outlined in the Helsinki Declaration, ensuring the privacy and confidentiality of all participants. The survey was administered only after obtaining written consent from each participant. Personal and medical information was kept confidential, with all data stored securely. The study received ethical approval from the Istanbul University-Cerrahpaşa, Social and Human Sciences Research Ethics Committee (January 7, 2020, decision no: 2019/165) and the necessary institutional permissions from the Ministry of Health.

## **Data Analysis**

The collected data were analyzed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics (e.g., frequencies, percentages, means, medians, and standard deviations) were calculated to summarize the sociodemographic characteristics and responses of the participants. To examine differences between groups, the Independent Samples t-test was used for continuous variables, and One-Way Analysis of Variance (ANOVA) was used to compare means across different groups. When significant differences were found in the ANOVA, multiple comparisons were conducted using the Tukey test. The relationship between two continuous variables was assessed using the Pearson correlation test. A significance level of p<0.05 was applied for all statistical tests, and results were evaluated within a 95% confidence interval.

## **RESULTS**

The mean age of the participating ED nurses was 29.43 (standard deviation [SD]=5.90). It was determined that 57% (n=57) of them were female, and 73% (n=73) had received a bachelor's degree. When looking at their ED experience, ED nurses with 0-3 years of experience comprised 52% (n=52) of the study. Ninety-one percent (n=91) of the ED nurses stated that they had not received any education on extravasation after graduation, and 82% (n=82) indicated that there was no extravasation protocol implemented in their work-place (Table 1).

With the increase in the ED experience of ED nurses, it was determined that their knowledge about the extravasation potential of non-cytotoxic medications increased (p=0.035). Depending on whether there was an extravasation protocol implemented in the unit where ED nurses worked, it was found that ED nurses had significantly higher knowledge levels regarding non-cytotoxic medications causing extravasation (p=0.007) (Table 2). When the extravasation symptom knowledge levels of ED nurses were examined according to gender, it was determined that women had a statistically significantly higher level of knowledge about extravasation symptoms compared to men (p=0.012). It was found that the extravasation symptom knowledge levels of ED nurses varied significantly according to their educational level (p=0.015); the group with the highest knowledge level about extravasation symptoms was composed of ED nurses with a bachelor's degree and postgraduate education (Table 2). When looking at the knowledge level of ED nurses about the extravasation prevention protocol according to their sociodemographic and professional characteristics, it was observed that the knowledge levels of ED nurses regarding the extravasation prevention protocol varied significantly according to their educational level (p=0.033); the group with the highest knowledge level about the extravasation prevention protocol was composed of ED nurses with a bachelor's degree and postgraduate education (Table 2).

When the knowledge levels of ED nurses regarding the ex-

travasation care protocol were examined, the rate of being knowledgeable was determined as 64% (n=64); it was found that the protocol item about which ED nurses were most knowledgeable was "immediately stop the infusion," with a rate of 97% (n=97), and the least knowledgeable protocol item was "aspirate no more than 3-5 mL of the medication," with a rate of 33% (n=33) (Table 3).

The Pearson correlation coefficients (r) demonstrate significant relationships between nurses' knowledge levels and their extravasation management practices. The strongest correlation was observed between non-pharmacological fac-

**Table 1.** Sociodemographic and professional characteristics of emergency department nurses

Variables	N*
Number of nurses	100
Age, years#	29.4±5.9
Age group	
<30 years	66
≥30 years	34
Sex: Female	57
Education	
High School	10
Associate's Degree	13
Bachelor's Degree	73
Graduate Degree	4
Hospital	
Α	33
В	33
С	34
Duration of professional experience	
<3 years	38
4-6 years	27
7-10 years	8
≥II years	27
Emergency department experience	
0-3 years	52
4-6 years	17
7-10 years	15
≥II years	16
Received extravasation training after graduation	ı
Yes	9
No	91
Implementation of extravasation protocol in the	e work unit
Yes	18
No	82

**Table 2.** Nurses' knowledge levels on factors causing extravasation and prevention protocols according to their sociodemographic and professional characteristics

	Knowledge of Non-Cytotoxic Medications		Knowledge of Extravasation Symptoms		Knowledge of Extravasation Prevention Protocol	
Variables	X±SD	P Value	X±SD	P Value	X±SD	P Value
Sex	0.722		0.012		0.820	
Female	7.8±4.7		3.4±0.7		9.5±3.1	
Male	7.5±4.6		3.1±0.8		9.3±3.3	
Education		0.380		0.015		0.033
High School	7.9±4.9		2.9±0.6		7.2±3.3	
Associate's Degree	6.0±4.1		2.9±1.1		8.7±3.8	
Bachelor's & Graduate Degree	7.9±4.7		3.4±0.7		9.8±2.9	
Emergency Department Experience		0.035	0.459		0.662	
0-3 years	7.5±4.5		3.3±0.7		10.4±2.3	
4-6 years	6.4±4.9		3.0±0.7		8.4±3.5	
7-10 years	6.8±4.5		3.3±0.9		9.3±3.9	
≥II years	10.6±3.9		3.3±0.7		9.2±3.5	
Received extravasation training after graduation		0.007	0.561	0.447		
Yes	10.3±4.7		3.2±0.8		8.9±3.3	
No	7.1±4.5		3.3±0.7		9.5±3.2	

X: Mean; SD: Standard deviation. \*P value was evaluated with the Mann-Whitney U test, with p<0.05.

tors, that is, elevation, cold/heat application, etc., and non-cytotoxic medications knowledge, with a correlation coefficient of r=0.601 (p<0.001), indicating a strong relationship between these two variables. Additionally, a moderate positive correlation was found between knowledge of non-pharmacological factors and extravasation symptoms (p<0.001) (Table 4).

There was also a significant correlation between extravasation care protocols and non-pharmacological factors (p<0.001), as well as with non-cytotoxic medications (p<0.001), indicating that as nurses' knowledge of these factors increased, their adherence to extravasation care protocols also improved (Table 4).

Other notable correlations include the relationship between extravasation prevention protocols and extravasation symptoms (p<0.001) and the relationship between extravasation prevention protocols and non-pharmacological factors (p<0.001). These findings suggest that nurses' knowledge across various aspects of extravasation management is consistently related to their practical implementation of both prevention and care protocols. All correlations reported were statistically significant, with p-values less than 0.05, indicating meaningful associations between knowledge and practice in extravasation management (Table 4).

Table 3. Management of extravasation and nursing care **Statements** Practice Rate (%) Extravasation Care Protocol 97 Immediately stop the infusion 56 Inform the physician Aspirate the medication (not exceeding 3-5 mL) 33 Remove the peripheral venous catheter 68 Elevate the affected area 78 77 Apply hot and cold compresses Administer the antidote, if necessary and available, as per physician's order 55 Complete the recording and reporting 48 process related to extravasation

## **DISCUSSION**

The primary aim of this study was to examine the knowledge levels and nursing practices of ED nurses regarding extravasation caused by non-cytotoxic medications. The results obtained showed that the general knowledge levels of ED nurs-

Table 4. Correlation between nurses' knowledge and extravasation management practices
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	Non-Pharmacological Factors	Non-Cytotoxic Medications	Extravasation Symptoms	Extravasation Prevention Protocols
Non-Cytotoxic Medications	0.601*			
Extravasation Symptoms	0.591*	0.420*		
Extravasation Prevention Protocols	0.521*	0.328**	0.412*	
Extravasation Care Protocols	0.599*	0.577*	0.270**	0.498*
*p<0.001; **p<0.01; Pearson correlation t	est.			

es about extravasation were at a moderate level. The findings of this study are parallel to similar studies in the literature. [16-18] For example, in a study conducted to determine the knowledge levels of nurses working in a university hospital intensive care unit about extravasation, it was reported that the average general knowledge of nurses about extravasation was 80.41%.<sup>[19]</sup>

This study also examined the relationship between the knowledge level of ED nurses about medications that cause extravasation and their postgraduate extravasation training and professional experience. It was found that nurses with more ED experience and those who received postgraduate extravasation training had significantly higher knowledge levels about medications that cause extravasation. This finding is supported by previous studies. Yıldız and Avcı (2020)[19] reported that half of the nurses (53.8%) had knowledge about non-cytotoxic medications that can cause extravasation. Atay et al.[18] (2023) reported that 74.5% of nurses stated that they did not receive any postgraduate training on extravasation management during in-service training programs, and 89.7% of nurses reported that they had knowledge about medications that cause extravasation. According to Kahraman et al.[20] (2020), 89.9% of nurses reported that they did not receive any training on extravasation, and 55.7% did not consider extravasation as a medical error. There are studies reporting that in-service training programs provided a statistically significant improvement in nurses' knowledge and practices in minimizing extravasation. [20-22] This situation shows that nurses' knowledge level about medications that cause extravasation can be increased with increased ED experience and postgraduate extravasation training. In addition, the findings of the study conducted by Sisan et al.[23] (2018) were inconsistent; it was reported that only a small proportion of ED nurses (19.6%) had knowledge about non-cytotoxic medications that cause extravasation. It can be suggested that informing ED nurses about medications that can cause extravasation will reduce the risk of encountering this complication.

The research results provide an important starting point for understanding the educational level of ED nurses and their knowledge levels about extravasation symptoms. In particular, as the educational level of nurses increases, their knowledge levels about extravasation symptoms increase, providing a deeper understanding beyond previous general studies on

this subject.

One of the important findings of this study was the educational level of ED nurses and their knowledge level about extravasation prevention protocols. As the educational level of ED nurses increases, their knowledge level about extravasation prevention protocols also increases. This finding is consistent with prior research. Pluschnig et al.<sup>[24]</sup> (2015) stated that implementing a protocol or standardized treatment for extravasation improves the management of the extravasation process. It can therefore be argued that providing ED nurses with training on the management of extravasation caused by non-cytotoxic medications would be beneficial.

In this study, the management of extravasation by ED nurses and what they do in nursing care were also questioned (Table 3). The findings obtained from this study were found to be parallel to similar studies in the literature.  $^{[21,25,26]}$  Atay et al.  $^{[18]}$ (2023) reported that the nursing care applied by nurses after extravasation was stopping the IV infusion (98.6%), elevation (89.7%), applying cold (76.6%), and aspirating the medications (40.7%). Elsayed et al.[25] (2024) reported that the management of intravenous chemotherapy extravasation of oncology nurses was positively affected by training. According to the study by Maasand et al.[26] (2019), nurses reported that the majority (91.0 %) of patients with radiographic contrast material injuries only elevated the injured area. The differences in extravasation management and nursing care may be attributed to the lack of standardized extravasation management and nursing care protocols in hospitals.

## Limitations

The limitations of the study are, firstly, that the results have limited applicability to the general ED nursing population due to factors such as sample size and demographic characteristics. In addition, there are methodological limitations in the data collection method and research design. In this study, the use of a questionnaire as a data collection method may not fully reflect the participants' actual thoughts and behaviors due to social desirability bias, which may limit the accuracy of the results. In future studies, using larger and more varied groups of ED nurses can help address these issues, and including new medications that might cause extravasation can make the findings more applicable to a wider audience.

## **CONCLUSION**

The study's findings recommend regular training on extravasation management and high-risk medications for ED nurses starting to work in the ED. Lack of knowledge among nurses may lead to failure to perform effective interventions, especially in critical situations that may affect patient safety. In light of the findings, it is suggested that in-service training programs be developed or updated regularly to align with internationally accepted practices for extravasation management. It is recommended that in-service training programs in EDs provide training on extravasation based on the Targeted Medication Safety Best Practices for Hospitals, prepared by the Institute for Safe Medication Practices (ISMP), and the Infusion Therapy Standards of Practice. [27,28] Moreover, extravasation management and related nursing care should be conducted in accordance with a standardized, up-to-date, and evidence-based protocol (e.g., checklists). Finally, it is recommended that a general standard for extravasation management be developed and supported by additional studies conducted across different healthcare institutions and on a broader scale.

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## ORİJİNAL ÇALIŞMA - ÖZ

## Acil servis hemşirelerinin sitotoksik olmayan ilaçların ekstravazasyon yaralanmalarıyla ilgili bilgi ve uygulamaları

AMAÇ: Non-sitotoksik ilaçların ekstravazasyonu, ağrı, doku nekrozu, uzuv kaybı ve hatta ölüme kadar ciddi komplikasyonlara yol açabilir. Bu tanımlayıcı kesitsel çalışma, acil servis (AS) hemşirelerinin non-sitotoksik ilaçlarla meydana gelen ekstravazasyon vakalarına ilişkin bilgi düzeylerini değerlendirmeyi ve etkili yönetim ve önlemenin önemini vurgulamayı amaçlamaktadır.

GEREÇ VE YÖNTEM: Çalışma, 19 Kasım 2020 ile 31 Aralık 2020 tarihleri arasında İstanbul, Türkiye'deki üç hastanenin AS'lerinde gerçekleştirilmiştir. Çalışmaya toplamda 100 AS hemşiresi katılmıştır. Dahil edilme kriterleri, hemşirelerin çalışma dönemi boyunca AS'lerde tam zamanlı çalışıyor olmalarını ve yazılı ve sözlü onay vermelerini gerektirmiştir. Çalışmada, hemşirelerin sosyodemografik özelliklerini, non-sitotoksik ilaçlar (örneğin epinefrin), ekstravazasyon belirtileri, önleme stratejileri ve müdahale uygulamalarına yönelik bilgilerini değerlendiren bir anket kullanılmıştır.

BULGULAR: Hemşirelerin yaş ortalaması 29,43 yıl olup, katılımcıların %57'si kadın ve %73'ü lisans diplomasına sahiptir. Katılımcıların %52'si AS deneyimi olarak 0-3 yıl arasında bir süreye sahiptir. Katılımcıların %91'i, mezuniyet sonrası ekstravazasyonla ilgili eğitim almadıklarını belirtmiş ve %82'si işyerlerinde ekstravazasyon protokolü bulunmadığını ifade etmiştir. AS deneyimi arttıkça, non-sitotoksik ilaçların ekstravazasyona yol açmasıyla ilgili bilgi seviyelerinin anlamlı bir şekilde arttığı gözlemlenmiştir (p=0.035). Ekstravazasyon protokolü bulunan birimde çalışan hemşirelerin bilgi seviyeleri, protokolsüz birimde çalışanlara göre anlamlı şekilde daha yüksektir (p=0.007). Kadın hemşireler, erkek hemşirelere göre ekstravazasyon belirtileri hakkında daha yüksek bilgiye sahipti (p=0.012). Lisans veya daha yüksek eğitim düzeyine sahip hemşirelerin, diğer gruplara göre daha yüksek bilgiye sahip olduğu bulunmuştur (p=0.015). Ekstravazasyon bakım protokolüne dair bilgi oranı %64 olup, en bilinen protokol maddesi "enfüzyonu hemen durdurma" (%97) ve en az bilinen maddesi "ilacı 3–5 ml'yi geçmeyecek şekilde aspirasyon yapma" (%33) olmuştur. Non-farmakolojik faktörler ile non-sitotoksik ilaç bilgisi arasında güçlü bir ilişki bulunmuş (r = 0.601; p<0.001) ve ekstravazasyon bakım protokolleri ile non-farmakolojik faktörler arasında anlamlı ilişkiler gözlemlenmiştir (p<0.001).

SONUÇ: Çalışma, AS'lerde ekstravazasyon yönetimi ve önlenmesi için hedeflenmiş eğitimlerin ve kurumsal protokollerin oluşturulması gerekliliğini vurgulamaktadır. Hemşirelerin bilgisi, önleme ve bakım protokollerine uyumlarını önemli ölçüde etkilemektedir. Hasta güvenliğini sağlamak için, AS ortamlarında ekstravazasyon yönetimi için sürekli eğitim sağlanması ve kanıta dayalı müdahale protokollerinin uygulanması önemlidir.

Anahtar sözcükler: Acil servis, ekstravazasyon, komplikasyon yönetimi

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# Is endoscopic retrograde cholangiopancreatography a reliable procedure in advanced age? A single tertiary center experience

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## **ABSTRACT**

**BACKGROUND:** This study aimed to determine the reliability and efficacy of endoscopic retrograde cholangiopancreatography (ERCP) in elderly patients compared with younger patients.

METHODS: In this retrospective study, ERCP procedures performed in our endoscopy unit between December 2020 and October 2024 were reviewed. Elderly patients aged ≥80 years (AA group) and younger patients aged <65 years (control group) were included. Their demographics, comorbidities, American Society of Anesthesiologists (ASA) scores, ERCP indications, procedural success, and complications were compared.

**RESULTS:** There were significant differences in ASA scores, comorbidities, and the use of anticoagulant or antiplatelet drugs between the groups (p<0.05, p<0.01, and p<0.05, respectively). Juxtapapillary diverticula were more common in the AA group than in the control group (21% vs. 5.1%, p<0.01). Regarding indications, choledocholithiasis and obstructive jaundice were the most common in both groups (p=0.456 and p=0.064, respectively). The rate of cannulation success was not significantly different between the groups (p=0.956). Sphincterotomy and stone extraction with balloon or basket were the most frequent interventions in both groups (p=0.22 and p=0.563, respectively). Postprocedural pancreatitis was significantly more common in the control group than in the AA group (p=0.041). No significant differences were found in other complications, including bleeding, perforation, infection, basket impaction, and cardiopulmonary events between the groups (p=0.436, p=0.354, p=0.958, p=0.254, and p=0.289, respectively).

**CONCLUSION:** Therapeutic ERCP procedures can be performed safely and efficiently in elderly patients, as their outcomes are comparable to those observed in younger patients.

**Keywords:** Advanced age; safety; endoscopic retrograde cholangiopancreatography; complications; indications.

## INTRODUCTION

According to data from the Turkish Statistical Institute, the population aged 65 years and older, which is considered the

elderly population, was 7,550,727 in 2019, and increased by 20.7% over the last five years to 9,112,298 in 2024. The proportion of the elderly population in the total population rose from 9.1% in 2019 to 10.6% in 2024. Life expectancy is in-

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creasing worldwide due to improvements in public health and advances in medical care. In parallel with this rise, the terminology of aging has also evolved. In the past, advanced-age (AA) patients were defined as those aged ≥65 years. Today, however, individuals aged 65-74 are considered "early elderly," while those aged ≥80 years are referred to as "advanced age." [2,3] As the geriatric population grows, hepatobiliary diseases, such as bile duct stones and tumors, and postoperative complications following various pancreatic surgeries [4,5] are becoming more prevalent in AA individuals. [6,7] For instance, biliary surgery in patients over 82 years of age carries a mortality rate of 9.7% and a complication rate of 62%. [6]

Endoscopic retrograde cholangiopancreatography is primarily a therapeutic technique that provides a safer alternative to surgery for AA patients and, in some circumstances, allows for direct treatment of many pancreaticobiliary diseases. <sup>[6]</sup> Consequently, endoscopic procedures, particularly ERCP, are increasingly being performed in AA patients as the size of this population grows, and as equipment, operator experience, and interventional modalities develop to address the challenges in this patient group.<sup>[8]</sup>

In the literature, ERCP has a reported complication rate of 4%-11%, [9,10] while the mortality rate has been reported as 0.3%-0.5%, [9,11] However, in AA patients, complications and mortality rates may be higher and less predictable due to several factors. To provide precise information to elderly patients and to balance risks and benefits in geriatrics, it is crucial to better understand the success and safety of ERCP in this population.

Therefore, we aimed to evaluate the reliability and performance of ERCP in AA patients compared with younger control patients (<65 years), focusing on cannulation success, indications, procedure details, and complication rates between the groups.

## MATERIALS AND METHODS

Following approval from the Kanuni Sultan Süleyman Health Application and Research Center Ethics Committee (protocol no: KAEK 2023.05.71), patients aged ≥80 years or <65 years who underwent ERCP in our general surgery endoscopy unit between December 2020 and October 2024 were reviewed using patient files, outpatient clinic records, and the hospital's electronic archives. Patients with incomplete data, those under 18 years of age, patients aged 65-79 years, pregnant individuals, patients with major psychiatric disorders, those with recurrent ERCPs, cases with prior gastrectomy, and patients with active pancreatitis were excluded from the study.

While evaluating the reliability and effectiveness of ERCP in AA patients, we divided the patients into two groups: the AA group, aged ≥80 years (n=105), and the control group aged <65 years (n=350). Demographics (age, sex), comorbid

diseases, ASA scores, indications for ERCP, details of interventions, and complications, if any, were compared between the two groups.

All ERCPs were performed by five experienced endoscopists at our single center, each conducting at least 250 cases per year. After the intervention, patients were monitored for one day for any adverse events. Written informed consent was obtained from all patients, and the research was conducted in accordance with the principles of the Declaration of Helsinki.

## **ERCP Procedure**

Patients were placed in the prone or left lateral decubitus position according to the standardized technique. Procedures were performed under deep sedation using propofol (I-I.5 mg/kg), ketamine (I-4.5 mg/kg intravenously [IV]), and midazolam (10-20 mg IV). Vital signs, including oxygen saturation, arterial pressure, and heart rate, were measured and monitored with a digital pulse oximeter. Standard sideviewing duodenoscopes (Fujinon ED-450XT5) were used for all procedures. Endoscopic sphincterotomy was performed when necessary using either a standard sphincterotome or a precut sphincterotome. For the precut technique, either suprapapillary fistulotomy or precut papillatomy was applied. For bile duct stone removal, standard techniques such as dormia basket, extraction balloon, or both were employed. For bile duct drainage or other indications, plastic (10F, 8.5F, 10 cm, double-pigtail) and metallic self-expandable metal stents (SEMS) biliary stents were used as appropriate.

The British Society of Gastroenterology (BSG) and European Society of Gastrointestinal Endoscopy (ESGE) guideline recommendations for the management of patients on antiplatelet therapy or anticoagulants were applied to the study population. [12] Low-thrombosis-risk conditions were defined as ischemic heart disease without coronary stents, cerebrovascular accidents, and peripheral vascular disease, whereas high-thrombosis-risk conditions were defined as the presence of coronary artery stents. ERCP with sphincterotomy is classified as a high-risk procedure for bleeding in the guidelines.

I. Low-thrombosis-risk patients: P2Y12 inhibitors (clopidogrel, ticagrelor, prasugrel) were discontinued seven days before the procedure and restarted I-2 days after ERCP if there was no bleeding. In patients on dual antiplatelet therapy, acetylsalicylic acid was continued. Warfarin was discontinued five days before the procedure, International Normalized Ratio (INR) was checked prior to ERCP and confirmed to be <1.5, and warfarin was restarted on the evening of the procedure. INR was rechecked one week later to ensure adequate anticoagulation. For patients on direct oral anticoagulants (DOACs: dabigatran, rivaroxaban, apixaban, edoxaban), the last dose was taken three days before the procedure, and therapy was resumed 2-3 days after ERCP.

2. High-trombosis-risk patients: Acetylsalicylic acid was continued, and the risk/benefit of discontinuing P2Y12 receptor antagonists was evaluated in consultation with an interventional cardiologist. For patients on warfarin, treatment was stopped five days before ERCP, and low-molecular-weight heparin (LMWH; enoxaparin sodium 4000 IU/day) was initiated two days after stopping warfarin. LMWH was omitted on the day of ERCP. Warfarin was restarted on the evening of ERCP at the usual daily dose, and LMWH was continued until the INR target was achieved. As acetylsalicylic acid is considered safe with respect to bleeding risk, it was continued without interruption. These recommendations were applied to all patients included in the study.

Bleeding related to intervention was classified as follows: mild bleeding was defined as a hemoglobin drop of <3 g/dL without the need for transfusion; moderate bleeding required transfusion (≤4 units) but not an interventional procedure; and severe bleeding required transfusion of >5 units of erythrocyte suspension or an interventional procedure (surgical or angiographic) to control the bleeding.<sup>[13]</sup>

Basket impaction was defined as the entrapment of a stone by a dormia or lithotripsy basket that could not be retrieved from the common bile duct.

Cholangitis was diagnosed when the body temperature exceeded 38°C within 24-48 hours after ERCP, and no other focus was identified, suggesting a biliary source.<sup>[13]</sup>

Cardiopulmonary complications included hypoxemia (oxygen saturation <90%), myocardial infarction, congestive heart failure, cerebrovascular accident, cardiac or respiratory arrest, arrhythmia, and hypotension (systolic blood pressure <90 mmHg).<sup>[13]</sup>

Mortality, whether directly related to the procedure or not, was considered intervention-related when death occurred within 48 hours due to complications or incomplete endoscopic treatment (e.g., failure to relieve bile duct obstruction).<sup>[13]</sup>

Postprocedural pancreatitis (PPP)\*\* was defined as the onset or worsening of abdominal pain after ERCP, serum amylase levels  $\geq 3$  times the upper limit of normal, or hospitalization prolonged by at least three days.<sup>[7]</sup>

Perforations occurring during ERCP were classified into four types according to the Stapfer classification: Type I, duodenal wall perforation; Type 2, perforation around the ampulla; Type 3, choledochus wall perforation; and Type 4, retroperitoneal free air. Emergency surgery was required for Type I perforations, while conservative management was appropriate for the other types of perforations depending on the patient's clinical condition.<sup>[7]</sup>

## **Statistical Analysis**

All analyses were performed using the Statistical Package for the Social Sciences, Version 24.0. (Armonk, New York, United States). Continuous variables were expressed as mean ± SD, and categorical variables were presented as percentages and frequencies. The student's t-test and the Chi-square test were used for comparisons between groups for continuous and categorical variables, respectively. A p value <0.05 was considered statistically significant.

## **RESULTS**

Between December 2020 and October 2024, a total of 2,865 therapeutic ERCP procedures were performed in our general surgery endoscopy-ERCP unit. Of these, 117 patients aged ≥80 years with a naïve papilla who underwent 165 ERCP procedures were identified, accounting for 4% of all cases (117/2,865). Twelve patients (two with previous gastrectomy and 10 with incomplete data) were excluded from the study. Thus, 105 patients aged ≥80 years (mean age: 85.8 years, range: 80-92 years) who underwent 135 ERCP procedures were included in group AA. After applying the selection criteria, the control group consisted of 350 consecutive patients with a naïve papilla, with a mean age of 44.3 years (range: 22-64 years) (Fig. 1).

Of the 105 patients in group AA, 65 (62%) were female and 40 (38%) were male (F/M=1.6). In the control group, 200 (57%) patients were female and 150 (43%) were male. The difference was not statistically significant (p=0.857). Compared with the control group, the group AA had higher ASA scores, higher rates of anticoagulant or antiplatelet usage, and more comorbidities, all of which were statistically significant (p<0.05, p<0.05, and p<0.01, respectively). The mean hospital stay was  $4.1\pm1.8$  days in group AA and  $4.3\pm1.2$  days

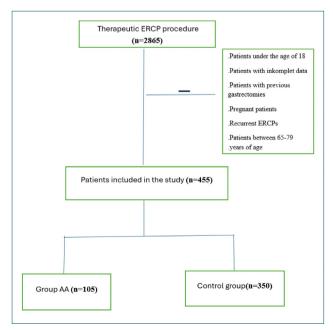


Figure 1. Study design.

	AA Group	Control Group	p value
	n=105 (%)	n=350 (%)	
ASA score			
1	_	95 (27)	
II	55 (52)	222 (64)	<0.05
III	44 (42)	33 (7)	
IV	6 (6)	7 (2)	
٧			
Mean age, years (range)	85.8 (80-92)	44.3 (22-64)	
Drugs	61 (58)	57 (16)	<0.05
Anticoagulant	41(39)	41 (11)	
Antiaggregant	8 (8)	10 (3)	
Both	12 (11)	6 (2)	
Comorbidity	92 (88)	135 (39)	<0.01
DM	13 (12)	25 (7)	
HT	8 (7.6)	21 (6)	
COPD	11(10)	17 (4.8)	
Dementia	6 (6)	3 (0.9)	
CAD	15 (14)	15 (4)	
CHF	11 (10)	3 (0.9)	
Cancer	5 (4.7)	2 (0.6)	
At least two	23 (22)	49 (14)	
Hospital stay (days)	4.l±1.8	4.3±1.2	0.254
Sex			
Male	40	150	0.857
Female	65	200	

Data are given as mean ± standard deviation (SD) or n (%). ASA: American Society of Anaesthesiologists; DM: Diabetes Mellitus; COPD: Chronic Obstructive Pulmonary Disease; CAD: Coronary Artery Disease; CHF: Congestive Heart Failure; BMI: Body Mass Index; AA: Advanced age.

	AA Group n=105 (%)	Control Group n=350 (%)	p value
		555 (/3)	
Choledocholithiasis	55 (52)	190 (54)	0.456
Obstructive jaundice	32 (30)	56 (16)	0.064
Cholangitis	6 (5.7)	26 (7.4)	0.258
Dilated bile duct	11 (10)	36 (10)	0.479
Acute pancreatitis	0	12 (3.4)	
Papillary adenoma	2 (1.9)	5 (1.4)	0.368
Biliary/pancreatic leak	0	20 (19)	
Primary sclerosing cholangitis	0	5 (1.4)	

In terms of indications, the most common ERCP indication in both groups was choledocholithiasis (52% in group AA and 54% in the control group) (p=0.456). Although obstructive jaundice was more common in group AA (30%) than in the control group (16%), the difference was not statistically significant. Acute pancreatitis, pancreatic or biliary leak, and primary sclerosing cholangitis were not indications in group AA compared with the control group (Table 2).

Diverticulum in the second part of the duodenum and juxtapapillary diverticulum were more common in group AA, occurring in 22 (21%) patients, compared with 18 (5.1%) in the control group, which was a statistically significant difference (p<0.01).

Common bile duct cannulation was successful in 98 (94%) patients in group AA and 336 (96%) patients in the control group, with no statistically significant difference (p=0.956). In group AA, the indications for failed cannulation were obstructive jaundice in four cases, dilated bile duct in two cases, and cholangitis due to choledocholithiasis in the remaining two patients. In three cases of failed cannulation, the papilla

was located inside a large diverticulum and could not be detected. In two of these failed cannulation cases, a rendezvous technique was used for cannulation, while in the remaining six patients, external drainage with percutaneous transhepatic cholangiography was performed to drain the bile duct (Table 3).

Sphincterotomy and stone extraction with balloon or basket were the most frequently performed interventions in both groups (p=0.22 and p=0.563, respectively), and although more common in group AA, the differences were not statistically significant. For bile duct stenting, plastic stents were used in 33.3% of patients in group AA and 31.4% in the control group (p=0.548). The indications for plastic stent use in group AA were impacted stones, cholangitis, and pancreatic malignancy, while in the control group, the most common indications were residual stone or sludge, cholangitis, and postoperative bile fistula. Self-expandable metal stents (SEMS) were used in both groups: 2 (1.9%) in group AA and 5 (1.42%) n the control group (p=0.445). In group AA, SEMS was preferred as a permanent stent in two patients with inoperable pancreatic

Table 3. Endoscopic retrograde cholangiopancreatography (ERCP) intervention details and complications

	AA Group n=105 (%)	Control Group n=350 (%)	p value
Sphincterotomy	88 (84)	248 (71)	0.22
Stone extraction with balloon or basket	71 (67)	193 (55)	0.563
Bile duct stenting	37 (35.2)	110 (31.4)	
Biliary plastic	35 (33.3)	105 (30)	0.548
Biliary SEMS	2 (1.9)	5 (1.42)	0.445
Ampullectomy	I (0.95)	3 (0.85)	0.468
Mechanic lithotripsy	7 (6.6)	16 (4.57)	0.356
Success rate	98 (94.1)	337 (96.4)	0.956
Complications	12 (11.4)	44 (12.5)	0.432
Pancreatitis	4 (3.8)	21 (6)	0.041
Bleeding	4 (3.8)	9 (2.6)	0.436
Mild	3 (2.8)	7 (2)	0.417
Moderate	I (I)	I (0.3)	0.423
Severe	-	I (0.3)	
Perforation	I (0.95)	2 (0.6)	0.354
Basket impaction	2 (1.9)	6 (1.7)	0.254
Infection (cholangitis, cholecystitis)	3 (2.9)	10 (2.85)	0.958
Cardiopulmonary events	2 (1.9)	3 (0.9)	0.289
Juxtapapillary diverticula	22 (21)	18 (5.1)	<0.01
ERCP-related death			0.654
During procedure	I (I)	I (0.3)	0.551
After the procedure	l (l)	I (0.3)	0.728

Data are given as mean ± SD or n (%). AA: Advanced age; SEMS: Self-expendable metallic stent; ERCP: Endoscopic retrograde cholangiopancreatography.

cancer, while in the control group, it was used in one case to control moderate bleeding after precut sphincterotomy, in two cases due to suspected Stapfer type II and III perforations after sphincterotomy, and in the remaining three cases for drainage of a locally advanced pancreatic head tumor before neoadjuvant therapy (Table 3).

A mass in the papilla was identified in two (1.9%) cases in group AA and five (1.4%) cases in the control group (p=0.368). Ampullectomy was performed in one (0.95%) case in group AA and three (0.85%) cases in the control group (p=0.468). The histopathological diagnosis was adenoma with high-grade dysplasia and clear margins, which was accepted as a cure in geriatric patients. In the control group, one patient had papillary adenoma with benign hyperplasia and clear margins, whereas the remaining two patients had invasive adenocarcinoma and underwent pancreaticoduodenectomy, as decided by the multidisciplinary oncology council (Table 3).

Mechanic lithotripsy was performed in seven (6.6%) cases in group AA and 16 (4.57%) cases in the control group (p=0.356).

The most common complication in the control group was PPP, detected in 21 (6%) cases, whereas it was detected in four (3.8%) cases in group AA. The rate of PPP was higher in the control group than in group AA (6% vs. 3.8%, respectively), and the difference was statistically significant (p=0.041). The ages of group AA patients with PPP ranged from 82 to 88 years. Of these, three were female and one was male. The indications were choledocholithiasis in three cases and obstructive jaundice in one case. In the control group, 74% of PPP patients were female and 26% were male. The indications for ERCP were choledocholithiasis in 17 (80%) patients, cholangitis in two (10%), papillary adenoma in one (5%), and bile leakage after liver hydatid surgery in one (5%). In group AA, one of the four PPP patients had a juxtapapillary diverticulum; however, diverticulum was not present in any of the control group PPP cases.

Bleeding complications occurred in four (3.8%) cases in group AA and nine (2.6%) cases in the control group (p=0.436). In group AA, three cases had minor and one case moderate bleeding, whereas in the control group, seven cases had minor, one case moderate, and one case major bleeding. A major bleeding case occurred in a patient receiving anticoagulant therapy, with the indication being obstructive jaundice. Our treatment modality was the application of a fully covered self-expendable metallic stent, through which the bleeding was gradually controlled. The stent was withdrawn after three weeks (Table 3).

Perforations were detected in one (0.95%) case in group AA and two (0.6%) cases in the control group (p=0.354).

Basket impaction was another complication observed in both groups: two (1.9%) cases in group AA and six (1.7%) cases in the control group (p=0.254). In group AA, one patient un-

derwent open surgery with an upper midline incision, cholecystectomy, choledochotomy, stone extraction, basket wire removal, and choledochal T-tube drainage. The t-tube was removed in the third postoperative week following a patent T-tube cholangiography. In another patient in group AA, the basket was successfully removed after endoscopic withdrawal attempts, and a plastic biliary stent was placed. In the control group, two patients underwent surgery due to basket impaction. Both underwent upper midline incision, cholecystectomy, choledochotomy, stone and basket wire extraction, and choledochal T-tube placement, after which they were discharged uneventfully. In the remaining four patients, recurrent endoscopic withdrawal attempts were successful, and plastic stents application were subsequently placed.

Infectious complications (cholecystitis, cholangitis) were observed in three (2.9%) cases in group AA and 10 (2.9%) cases in the control group (p=0.958).

Cardiopulmonary side effects (hypoxia, aspiration, cardiac arrhythmia, or angina pectoris) occurred in two (1.9%) patients in group AA and three (0.9%) patients in the control group (p=0.289), with no statistically significant difference.

Endoscopic retrograde cholangiopacreatography-related death was observed in two patients (2%) in group AA and two patients (2%) in the control group. In both groups, one patient died during the procedure and another died during the hospitalization follow-up period.

## **DISCUSSION**

With the increase in average life expectancy, the frequency of endoscopic examinations in elderly patients has also risen. Differences in disease prevalence, concomitant systemic diseases, and the risk of complications that may occur highlight the need for more careful evaluation of endoscopic procedures in the elderly. <sup>[14]</sup> In the present study, we evaluated the outcomes of ERCP procedures performed in our clinic on AA patients and compared them with younger patients.

In two large meta-analyses, the incidence of PPP was reported to be 4.8%-11.9%, while mortality among patients who developed PPP was reported as 0.1%-0.7%.[15] A meta-analysis of 15 prospective and 52 retrospective cohort studies examining the risk factors of PPP found that young age, female sex, sphincter of Oddi dysfunction, a history of pancreatitis, absence of bile duct dilation (bile duct diameter < 1 cm), normal bilirubin levels, and difficult cannulation were the main risk factors.[16] Conversely, Sökmen et al.,[17] in a retrospective study, reported that periampullary diverticulum was more common in elderly and female patients and was associated with an increased risk of PPP. They suggested that difficult cannulation due to periampullary diverticulum might be the leading cause of PPP. However, Jayaraj et al.,[18] in their meta-analysis, concluded that ERCP was both successful and feasible, with comparable complication rates in patients with and without periampullary diverticulum. Finkelmeier et al.,[19]

in a retrospective study including 758 patients, reported that PPP occurred less frequently in patients aged ≥80 years compared to younger patients (0.9% vs. 5.3%; p<0.05). Similarly, in another retrospective study of 624 cases, both the frequency and severity of PPP were lower in patients aged ≥80 years compared to the younger control group (1.3% vs. 2.9%, p=0.262). [20] In studies investigating the feasibility of ERCP in elderly patients, Rodriguez-Gonzalez et al.[21] and Ergin et al.[22] reported no cases of PPP among patients aged ≥90 years. In line with the literature, in the present study, the rate of PPP was lower in elderly patients compared to the control group (3.8% vs. 6%). The difference was statistically significant (p=0.041). The ages of group AA patients suffering from PPP ranged from 82 to 88 years. No mortality related to PPP was detected, and the majority of patients with PPP were female in both groups. In group AA, one of the four patients with PPP had a juxtapapillary diverticulum, whereas none of the PPP patients in the control group had a diverticulum. Although cannulation time was longer, the complication rate was not different from those without diverticulum. We suggest that, as a result of aging, decreased secretory capacity, fibrosis, and atrophy of the pancreatic tissue might reduce the response to trauma, as seen in ERCP.

Post-interventional bleeding might be a fatal complication after ERCP. In the literature, although some authors[20,22] have reported no significant difference in post-ERCP bleeding in patients over 80 years old compared to younger ones, despite higher antiaggregant and anticoagulant use in the 80-year-old group, Elmi et al.[23] and Chong et al.[24] reported that nonagenarians had twice the risk of bleeding compared with younger patients. They pointed out that the increased prevalence of coagulopathy, the use of medications that could increase bleeding risk, and the need for larger sphincterotomies to extract large stones require more therapeutic maneuvers. In our series, there was no severe bleeding in either groups, but three minor and one moderate bleeding events occurred in group AA. Although a higher rate of bleeding is expected in elderly patients due to the frequent use of nonsteroidal anti-inflammatory drug (NSAIDs) and antithrombotic drugs, there was no statistically significant difference between the two groups (3.8% vs. 2.6%, p=0.417). In our daily practice, for patients using two antiaggregant drugs, one is discontinued if the patient is at high cardiac risk. Low-molecular-weight heparin was initiated in patients using warfarin or new-generation anticoagulants as bridging therapy before the procedure.

Considering ERCP-related perforations, it is an uncommon but very serious complication, with an incidence of 0.2% to 1.6%. [25,26] In the literature, factors such as prolonged intervention duration, precut sphincterotomy, advanced age, and sphincter of Oddi dysfunction have been found to increase the risk of ERCP-related perforations. [27,28] In our study, there was no statistically significant difference between the AA and control groups in terms of post-ERCP perforations (0.95 vs. 0.6, p=0.354). In group AA, one patient had a Stapfer type 2

perforation, which was detected during the procedure. The defect was closed with endoclip application, and after 10 days of follow-up, the patient was discharged. In the control group, two patients had Stapfer type 2 and type 3 perforations detected during the procedure, and SEMS placement was the treatment modality. Both patients had uneventful follow-up periods and were discharged on days 10 and 12, respectively.

Obstructive cholangitis is a clinical entity that requires urgent drainage to prevent cholangiosepsis. Bodger et al., [29] in their study analyzing 20,246 ERCPs nationwide in England, reported that the mortality risk of cholangitis is not related to patient age but mainly depends on the timing of drainage. Cholangitis was the indication in six (5.7%) cases in group AA and 26 (7.4%) cases in the control group, and the difference was not statistically significant (p=0.258). In the presence of cholangitis, the application of early (<24 hours) ERCP in our patients prevented an increased risk of complications in the elderly of the study group.

Lemmel's syndrome was first described by Dr. Gerhard Lemmel in 1934 and is a rare cause of biliary obstruction. [30] Its pathophysiology is nonspecific, but reported mechanisms include three leading causes: chronic fibrosis of the papilla, periampullary diverticulitis, and chronic inflammation of the ampulla. In addition, the location of the duodenal diverticulum may cause malfunction of the sphincter of Oddi, leading to functional obstruction. Alternatively, obstructive jaundice may result from external compression of the common bile duct or ampulla of Vater. [31] In group AA, we detected two cases of Lemmel's syndrome causing obstructive jaundice without choledocholithiasis or malignancy but with a large juxtapapillary diverticulum causing obstruction in the pancreatic part of the bile duct. Our treatment modality was sphincterotomy and biliary stenting.

In our study, comorbidities and ASA physical status scores were significantly higher in group AA (p<0.01, p<0.05), but differences in post-ERCP complication rates were not statistically significant (p=0.432). In a retrospective study, the authors, finding the same results, explained that the ASA physical status score was not a quantitative index but a qualitative one, which is not sufficient to measure the health status of the AA population. Instead, a comprehensive elderly assessment (CEA) was suggested for use in geriatric patients.<sup>[32]</sup>

Studies evaluating the safety and effectiveness of ERCP in AA patients are very limited. Fritz et al., [33] in their retrospective study with 502 cases, reported that in patients ≥80 years of age, the success rate was 88%, compared with 86% in patients <80 years of age, while the complication rate was 6.8% versus 5.1%, with no statistically significant difference detected. In another study conducted by Katsinelos et al., [34] patients over 90 years of age and patients between 70-90 years were compared, and the early complication rate was 6.3% in patients ≥90 years and 8.4% in patients between 70-90 years. The mortality rate due to ERCP was 1.6% in patients ≥90

years of age and 0.6% in patients between 70-90 years of age. In our study, in line with the literature, there was no statistically significant difference between the two groups in terms of success rate and postprocedural complications (complication and success rates were 11.4% and 94.1% in group AA vs. 12.5% and 96.4% in the control group). ERCP-related mortality was 1.9% and 0.57% in groups AA and control, respectively, in line with previous reports. [35,36]

Tyagi et al.,[37] in their prospective study, reported that the incidence of periampullary diverticulum was 7.5% and showed that the size of the diverticulum and the location of the papilla had no effect on cannulation success or post-ERCP complications. Jayaraj et al.,[18] in their meta-analysis, reported that ERCP was successful and feasible with comparable complication rates in patients with and without periampullary diverticulum. In our study, periampullary diverticulum was more commonly seen in group AA at 22 (21%) compared with the control group at 18 (5.1%), which was statistically significant (p<0.01). Cannulation time was longer, but the complication rate was not different from those without diverticulum. We think that as the experience and number of cases performed by the endoscopist increase, failure of selective cannulation and complications due to periampullary diverticulum will proportionally decrease.

Many studies have shown that lower complication rates and higher success rates in terms of selective biliary cannulation are achieved in high-volume centers and by highly experienced endoscopists. This study was conducted in a high-volume center with at least 1,000 cases per year. Therefore, our results may not be generalizable to centers with lower ERCP volume or less operator experience.

The retrospective design and being a single-center study were the main limitations of this study. Additionally, the study period was extended and had a relatively small sample size. Further multicenter prospective studies with larger case series are needed to confirm and support these results.

## **CONCLUSION**

Endoscopic retrograde cholangiopancreatography is increasingly being used in the diagnosis and treatment of elderly patients, since the incidence of bile duct and pancreatic cancer increases with age and surgical intervention in these patients carries high mortality and morbidity. We think that ERCP is a reliable, applicable, and feasible method in AA patients, but clinicians should be alert to potential adverse events.

**Ethics Committee Approval:** This study was approved by the Kanuni Sultan Süleyman Health Application and Research Center Ethics Committee (Date: 01.05.2023, Decision No: KAEK 2023.05.71).

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## ORİJİNAL ÇALIŞMA - ÖZ

## Endoskopik retrograd kolanjiyopankreatografi ileri yaşlarda güvenilir bir işlem midir? Üçüncü basamak tek merkez deneyimi

AMAÇ: Bu çalışmanın amacı ileri yaşlı hastalarda endoskopik retrograd kolanjiyopankreatografinin (ERCP) güvenilirliğini, daha genç kontrol grubuyla karsılastırarak belirlemektir.

GEREÇ VE YÖNTEM: Bu retrospektif çalışmada, Aralık 2020 ile Ekim 2024 tarihleri arasında endoskopi ünitemizde gerçekleştirilen ERCP prosedürleri incelenerek, ileri yaş hastalar (≥80 yaş) (Grup AA) ve daha genç hastalar (<65 yaş) (Kontrol grubu) dahil edilerek demografik özellikler, eşlik eden hastalıklar, Amerikan Anestezistler Derneği (ASA) skorları, ERCP endikasyonları, işlem başarısı ve komplikasyonlar açısından birbirleriyle karsılastırıldı.

BULGULAR: İki grup arasında ASA skorları, komorbiditeler ve antikoagülan ve antiplatelet ilaç kullanımı açısından anlamlı fark vardı (p<0.05, p<0.01 ve p<0.05). Juxtapapiller divertikül grup AA'da kontrol grubuna göre daha yaygındı (%21'e karşı 5,1, p<0.01). Endikasyonlar açısından her iki grupta da en sık koledokolitiyazis ve obstrüktif sarılık görüldü (p=0.456, p=0.064). Kanülasyon başarısı açısından iki grup arasında anlamlı fark yoktu (p=0.956). Her iki grupta da en çok yapılan girişimler sfinkterotomi ve balon ve basket ile taş ekstraksiyonu idi (sırasıyla p=0.22 ve p=0.563). İşlem sonrası pankreatit oranı genç grupta istatistiksel anlamlı olarak daha yüksekti (p=0.041). Kanama, perforasyon, enfeksiyon, basket sıkışması ve kardiyopulmoner komplikasyon oranları açısından iki grup arasında anlamlı fark saptanmadı (p=0.436; p=0.354; p=0.958; p=0.254; p=0.289). SONUÇ: Terapötik ERCP işlemleri ileri yaş hastalarda da uygun endikasyonlarla, genç yaş grubu ile karşılaştırılabilir komplikasyon ve sonuçlarla güvenli ve etkin bir şekilde uygulanabilir.

Anahtar sözcükler: Endoskopik retrograd kolanjiyopankreatografi; endikasyonlar; güvenlik; ileri yaş; komplikasyonlar.

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# Management of abdominal gunshot injuries: Surgical intervention or conservative follow-up? A single-center experience

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## **ABSTRACT**

**BACKGROUND:** This study aims to retrospectively evaluate treatment approaches and clinical outcomes in patients with penetrating abdominal trauma caused by gunshot injuries—one of the most complex and controversial areas in trauma surgery.

METHODS: A total of 101 patients diagnosed and treated for penetrating abdominal trauma due to gunshot injuries between 2015 and 2025 were included in the study. Demographic data (age and sex); vital signs at admission to the emergency department (blood pressure, pulse, respiratory rate, body temperature); level of consciousness (Glasgow Coma Scale); hemodynamic status (stability/instability, need for fluid or inotropic support); intra-abdominal (liver, spleen, small intestine, colon, etc.) and extra-abdominal (thorax, extremities, head, etc.) organ injuries; laboratory findings (hemoglobin, leukocyte count, creatinine, pH level); treatment modality (surgical intervention or conservative management); surgical techniques used; blood and blood product transfusions; and hospital length of stay were retrospectively analyzed. Patients were divided into two groups: those who underwent surgical treatment and those managed conservatively. Factors influencing treatment decisions and variables affecting mortality were evaluated statistically.

**RESULTS:** Of the patients, 83.2% were male, with a mean age of 28.3±10.5 years. Surgical treatment was performed in 81.2% of cases, while 18.8% received conservative management. No mortality occurred in the conservatively managed group, whereas the surgically treated group had a mortality rate of 15.9%. Mortality among female patients (29.4%) was significantly higher than among males (9.5%) (p=0.026). Hemodynamic instability, intra-abdominal organ injury, presence of free air in the abdomen, and the need for blood product transfusion were associated with both the decision for surgical intervention and higher mortality. Additionally, damage control surgery and multiple organ injuries were linked to increased mortality.

**CONCLUSION:** Management of abdominal trauma caused by gunshot injuries requires a multidisciplinary approach to ensure appropriate patient selection and treatment planning. In hemodynamically stable patients, selective non-operative management (SNOM) is a safe and effective option, whereas surgical intervention—particularly in cases requiring damage control surgery—is associated with higher mortality. The increased mortality rate among female patients underscores the need for closer monitoring of this subgroup and further investigation into potential additional risk factors. These findings align with current literature and provide practical guidance for clinical decision-making.

**Keywords:** Gunshot injury; selective non-operative management (SNOM); surgical intervention; mortality; hemodynamic instability; damage control surgery; abdominal trauma.

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## INTRODUCTION

Penetrating abdominal trauma is one of the most complex and debated challenges in trauma surgery. In regions where gunshot and stab wounds are prevalent, such injuries continue to be a major cause of morbidity and mortality.<sup>[1]</sup> Even in the absence of death, gunshot injuries can lead to permanent disability, reduced quality of life, loss of employment, and high treatment costs.<sup>[2]</sup>

Despite advances in surgical techniques, imaging modalities, and intensive care, the management of abdominal trauma caused by gunshot injuries continues to vary depending on patient- and injury-specific characteristics.<sup>[3]</sup>

Traditionally, surgical exploration has been the mainstay of treatment for such injuries. [4] Damage control surgery remains the first-line approach for surgical exploration, [5,6] and physiological criteria can provide an objective basis for decision-making in this context. [7] However, diagnostic laparotomy for abdominal gunshot injuries has been reported to result in negative laparotomy rates as high as 53%. [8,9] Gunshot wounds to the abdomen represent the most challenging subgroup for decision-making among penetrating abdominal trauma cases. Although selective non-operative management (SNOM) remains difficult in these patients, it has been shown to be successful in carefully selected cases. [10,11,12]

In recent years, the outcomes of SNOM in hemodynamically stable patients have gained increasing acceptance and clinical application. This approach offers several advantages, including the prevention of unnecessary laparotomies, shorter hospital stays, and lower complication rates. The literature emphasizes that with proper patient selection, SNOM is a safe and effective strategy; however, meticulous monitoring is essential. [1]

In this study, we retrospectively evaluated the clinical characteristics, treatment modalities, and outcomes of 101 patients treated for abdominal trauma caused by gunshot injuries. Our aim was to assess these findings in the context of existing literature, focusing on how treatment approaches in abdominal gunshot trauma vary depending on factors such as hemodynamic status, organ injury, presence of free intraperitoneal air, and the mechanism of injury.

## MATERIALS AND METHODS

This study involved a retrospective evaluation of 101 patients who presented to our hospital and were treated for abdominal trauma caused by gunshot injuries between 2015 and 2025. Ethical approval was obtained from the institutional review board of the hospital (Ethics Committee Approval No: 2025/01-37). The research was conducted in accordance with the principles of the Declaration of Helsinki.

## **Inclusion and Exclusion Criteria**

Patients aged 15-64 years with a diagnosis of abdominal trauma caused by gunshot injuries and complete medical records were included in the study. Exclusion criteria were incomplete medical records, stab wounds, non-penetrating (blunt) abdominal trauma.

## **Data Collection**

Patient data were retrieved from medical files and the hospital information management system. Collected variables included demographic characteristics (age, sex), clinical findings at admission, treatment modality (surgical or conservative), type of surgery (definitive or damage control), hemodynamic status, level of consciousness, presence of abdominal penetration, intraperitoneal free air, intra-abdominal and extra-abdominal organ injuries, laboratory parameters, need for blood product transfusion, and lengths of stay in the intensive care unit and inpatient wards.

## **Treatment Groups**

Patients were classified into two groups based on treatment modality: surgical and conservative. For the surgically treated group, detailed data were recorded on the type of surgery, hemodynamic and neurologic status, intra-abdominal and extra-abdominal injuries, laboratory findings, and clinical outcomes. For the conservatively managed group, clinical and laboratory data, as well as treatment outcomes, were analyzed.

## **Statistical Analysis**

Statistical analysis was performed using IBM SPSS Statistics, version 28 (IBM Corp., Armonk, NY, USA). Categorical variables were expressed as frequencies and percentages, and continuous variables as mean ± standard deviation or median (minimum-maximum), depending on distribution. Differences between categorical variables were analyzed using the chisquare test, and differences between continuous variables were assessed using the independent samples t-test or the Mann-Whitney U test, as appropriate. A p-value <0.05 was considered statistically significant.

## **RESULTS**

The study population consisted of 101 patients, including 17 females ( $25.41\pm12.88$  years, range: 15-64 years) and 84 males ( $28.88\pm9.93$  years, range: 16-56 years), with a mean age of  $28.30\pm10.49$  years (range: 15-64 years).

The mortality rate was higher among patients who underwent surgical treatment (15.9%) compared to those managed conservatively, in whom no mortality was observed. This finding suggests that surgically treated patients presented with more severe and higher-risk clinical profiles. Regarding sex, the mortality rate among female patients (29.4%) was significantly higher than that among males (9.5%) (p=0.026),

0 (0%)

13 (33.3%)

possibly reflecting more severe presentations or additional risk factors in female patients. By type of surgery, no mortality occurred among patients who underwent definitive surgery, whereas the mortality rate was 33.3% in those who underwent damage control surgery (Table 1).

Hemodynamically stable patients were less likely to undergo surgery and had lower mortality rates. Similarly, patients with

Definitive

Damage control

Type of surgery

preserved consciousness had lower mortality (Table 2), indicating that the patient's overall condition at presentation directly influenced treatment decisions and outcomes.

Patients who underwent surgery had significantly longer intensive care unit (ICU) and ward stays, reflecting their more severe clinical status and greater demand for hospital resources. In terms of laboratory parameters, pH and he-

43

39

<0.001

Table I. Clinical and demographic characteristics and outcomes **V**ariable Total Category **No Mortality Mortality** p-value Treatment approach Surgical 69 (84.1%) 13 (15.9%) 82 0.063 Conservative 19 (100%) 0 (0%) 19 Sex Male 76 (90.5%) 8 (9.5%) 84 0.026 Female 12 (70.6%) 5 (29.4%) 17

43 (100%)

26 (66.7%)

Treatment Approach	Hemodynamically Stable (n, %)	Hemodynamically Unstable (n, %)	Conscious (n, %)	Unconscious (n, %)	Total	p-value
Surgical	31 (37.8%)	51 (62.2%)	54 (65.9%)	28 (34.1%)	82	<0.001 (stability)
Conservative	19 (100%)	0 (0%)	19 (100%)	0 (0%)	19	
Total	50	51	73	28	101	0.003 (consciousne

Parameter	Surgical (n=82)	Conservative (n=19)	p-value
ICU stay duration (days)	6 [1-300]	I [0-4]	<0.001
Ward stay duration (days)	4 [0-12]	2 [1-5]	0.007
pH	7.31 [6.80-7.52]	7.40 [7.35-7.42]	<0.001
INR	1.26 [0.91-3.93]	1.07 [0.97-1.86]	<0.001
WBC	12.78 [1.86-27.90]	14 [9.77-6]	0.332
Hemoglobin (Hb)	12.90 [4.80-17.58]	15 [13-18.6]	<0.001
ALT	40.50 [8-974]	27 [9-108]	0.023
AST	48 [12-714]	27 [17-127]	0.001
Creatinine	0.85 [0.32-4.22]	0.80 [0.66-1.09]	0.266
Abdominal penetration (yes/no)	81/1	11/8	<0.001
Presence of free air in abdomen (yes/no)	79/3	11/8	<0.001
Blood product transfusion (yes/no)	49/33	0/19	<0.001

pH: Blood acidity level; INR: International Normalized Ratio; WBC: White blood cell count; Hb: Hemoglobin; ALT: Alanine aminotransferase; AST: Aspartate

aminotransferase.

Variable	Category	Surgical (n=82)	Conservative (n=19)	Total (n=101)	p-value
Injury region	Right upper	35 (42.7%)	7 (36.8%)	42 (41.6%)	0.098
	Left upper	12 (14.6%)	I (5.3%)	13 (12.9%)	
	Right lower	11 (13.4%)	7 (36.8%)	18 (17.8%)	
	Left lower	24 (29.3%)	4 (21.1%)	28 (27.7%)	
Firearm type	Rifled	70 (85.4%)	8 (42.1%)	78	<0.001
	Smoothbore	12 (14.6%)	11 (57.9%)	23	
Blood product transfusion	Yes	49 (59.8%)	0 (0%)	49	<0.001
	No	33 (40.2%)	19 (100%)	52	
Time to surgery	Immediate	64 (63.4%)	-	-	-
	12-48 hours later	18	<del>-</del>	_	-

moglobin (Hb) levels were significantly lower in the surgical group, suggesting impaired tissue perfusion and more extensive blood loss. Conversely, international normalized ratio (INR), alanine aminotransferase (ALT), and aspartate aminotransferase (AST) levels were higher in the surgical group, indicating more pronounced coagulopathy and liver injury. The presence of intra-abdominal injury and free air was markedly more common in the surgical group, supporting the preference for surgical intervention in cases of visceral organ injury. Blood product transfusion was significantly more frequent in the surgical group, whereas no transfusions were required in the conservatively managed patients (Table 3).

The most commonly affected anatomical region was the right upper quadrant (41.6%). There was no significant association between the site of injury and the treatment approach, suggesting that treatment decisions were more strongly influenced by the patient's overall condition and organ injury rather than the location of trauma. Analysis by firearm type revealed that the majority of surgically treated patients were injured by rifled firearms (85.4%), whereas injuries from smoothbore firearms were more often managed conservatively. This finding supports the notion that rifled firearms tend to cause deeper and more severe injuries, thereby increasing the likelihood of surgical intervention. Blood product transfusion was significantly more common in the surgical group, further indicating a higher incidence of hemorrhage and shock in these patients. Among the surgically treated group, 63.4% underwent immediate surgery, while the remaining patients were operated on within 12-48 hours (Table 4).

## **DISCUSSION**

According to the literature, mortality rates in abdominal trauma caused by gunshot injuries range between 10-20%, with factors such as multiple organ injury, hemodynamic instability, and advanced age being associated with higher mortality.<sup>[13]</sup> In our study, the overall mortality rate was 12.9%,

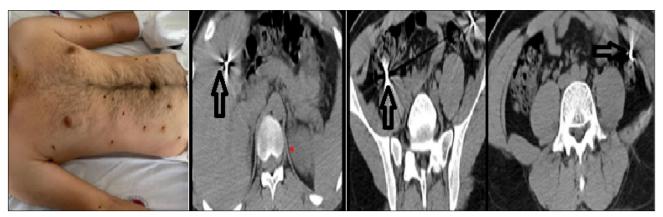
and the factors associated with mortality were analyzed in detail (Tables I and 2).

Gunshot injuries are more frequently observed in males and tend to occur more often in young adults.<sup>[14,15]</sup> Similarly, in our study, 84 of the 101 patients were male, with a mean age of 28 years.

Surgical treatment was performed in the majority of patients (81.2%), while conservative management was applied in 18.8%. Notably, no mortality occurred in the conservatively managed group, whereas the mortality rate among surgically treated patients was 15.9%. These findings align with previous studies reporting mortality rates of 10-20% in surgically treated gunshot-related abdominal trauma cases. [4] For instance, Demetriades reported a 13.5% mortality rate in surgically treated patients with abdominal gunshot injuries. [11]

The significantly higher mortality rate in female patients compared to males (29.4% vs. 9.5%, p=0.026) raises the question of whether sex plays a prognostic role in abdominal gunshot trauma. Although data on sex-related differences in mortality are limited, some studies have suggested that mortality may indeed be higher among female patients. [1] In our study, the higher mortality in women was not associated with surgical type, hemodynamic or neurological status, intra-abdominal involvement, presence of free air, injury location, firearm type, or blood transfusion (Table 3). This suggests the potential presence of non-standard risk factors in female patients. Further multicenter studies with larger cohorts are needed to better evaluate the effect of sex on mortality (Table 1).

In many studies, the small intestine has been reported as the most frequently injured organ in abdominal gunshot trauma. Adesanya and Feliciano reported small bowel injuries in 52.4% and 60% of their patients, respectively. [16,17] However, other studies have found colon injuries to be more common. [15] In our study, colon injuries were more frequent than small bowel injuries, although the latter were also common. Among the patients who underwent surgery, 45 had colon injuries



**Figure 1.** A 17-year-old male patient admitted with a firearm injury involving multiple injury sites in the abdominal region. Foreign body densities are visible in the liver parenchyma, sigmoid colon, and cecal lumen (black arrows). The patient was managed non-operatively and discharged after treatment.

and 39 had small bowel injuries. Given the broad spectrum of organ involvement, gunshot wounds to the abdomen are often associated with multiple injuries. The thoracic region is the most commonly affected extra-abdominal site.<sup>[18]</sup> In our series, 15 patients had lung injuries and six had diaphragm injuries (Table 3).

Mortality was significantly higher in patients who underwent damage control surgery compared to those who underwent definitive procedures (p<0.001). This likely reflects the fact that damage control surgery is typically performed in critically ill, hemodynamically unstable patients with multiple injuries. Rotondo emphasized that while damage control surgery can be life-saving in patients with severe physiological derangements and multiple injuries, it is also associated with high mortality rates.<sup>[19]</sup>

When dividing the abdomen into four quadrants—right upper, right lower, left upper, and left lower—the literature commonly identifies the right upper quadrant as the most frequently injured area. [20] Our findings were consistent with this pattern. However, no significant correlation was found between injury location and mortality (p=0.154) (Table 4).

Other variables influencing treatment decisions and prognosis included intra-abdominal organ injury, presence of free intraperitoneal air, and the need for blood product transfusion. Intra-abdominal injury was present in 98.8% of surgically treated patients compared to 57.9% in the conservative group. Similarly, free air was observed in 96.3% of the surgical group. Mortality was significantly higher among patients who received blood transfusions (p<0.001). Consistent with previous reports, these findings indicate that injury severity and associated organ damage are key prognostic factors. Leppäniemi reported that multiple organ injuries and massive hemorrhage are major determinants of mortality.<sup>[21]</sup>

A notable case in our series involved a patient with a left lower quadrant entry wound and an exit wound near the umbilicus who developed signs of acute abdomen and underwent surgery. Despite the absence of a clear intra-abdominal trajectory, the patient was found to have a sigmoid colon perforation. This case highlights the unpredictable clinical presentations of gunshot injuries and the importance of clinical judgment in determining the appropriate treatment modality (Fig. 1).

In our study, all patients managed conservatively were hemodynamically stable, and none experienced mortality. These findings support the view that SNOM is a safe and effective approach in appropriately selected patients. The 2010 Guidelines for Selective Nonoperative Management of Penetrating Abdominal Trauma also state that SNOM is a safe strategy in hemodynamically stable patients and helps reduce unnecessary laparotomies. [1] Leppäniemi further reported that the success rate of SNOM exceeds 90% in stable patients. Moreover, hospital and ICU stays were significantly shorter in the conservatively treated group, underscoring the benefits of SNOM in terms of patient comfort and resource utilization.

This study has several limitations. Its retrospective and single-center design and limited sample size restrict the generalizability of the findings. Additionally, the relatively small number of female patients necessitates caution when interpreting sex-related results.

## **CONCLUSION**

This study demonstrates that treatment approaches and clinical outcomes in patients with abdominal trauma caused by gunshot injuries are influenced by multiple factors. Our findings indicate that SNOM is a safe and effective treatment option in hemodynamically stable patients.

The management of abdominal gunshot trauma requires a multidisciplinary approach to ensure appropriate patient selection and treatment planning. Hemodynamically stable patients should be primarily considered for SNOM, whereas those requiring surgical intervention should be closely moni-

tored in an intensive care setting.

**Ethics Committee Approval:** This study was approved by the Van Yüzüncü Yıl University Ethics Committee (Date: 04.02.2025, Decision No: 2025/01-37).

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Authorship Contributions: Concept: S.B., F.A., M.E.; Design: S.B., F.A., A.A., E.O.; Supervision: S.B., M.E., F.A., B.B., O.B.; Resource: S.B., M.Ç.K., F.A., E.O.; Materials: S.B., F.A., İ.Ç., A.A.; Data collection and/or processing: S.B., E.O., F.A., M.E.; Analysis and/or interpretation: S.B., M.Ç.K., F.A., İ.Ç.; Literature review: S.B., F.A., O.B., B.B.; Writing: S.B., İ.Y., F.A., B.B.; Critical review: S.B., F.A., M.E., M.Ç.K.

Conflict of Interest: None declared.

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## ORİJİNAL ÇALIŞMA - ÖZ

## Abdominal ateşli silah yaralanmalarının yönetimi: Cerrahi müdahale mi yoksa konservatif takip mi? Tek merkez deneyimi

AMAÇ: Bu çalışma, travma cerrahisi alanında en karmaşık ve tartışmalı konulardan biri olan, abdominal bölgeyi penetran olarak etkileyen ateşli silah yaralanmalarında uygulanan tedavi yöntemleri ve klinik sonuçları geriye dönük olarak değerlendirmeyi amaçlamaktadır.

GEREÇ VE YÖNTEM: 2015-2025 yılları arasında ateşli silah yaralanması nedeniyle penetran abdominal travma tanısı konulan ve tedavi edilen toplam 101 hasta çalışmaya dahil edildi. Hastaların yaş, cinsiyet, acil servise başvuru anındaki vital bulguları (kan basıncı, nabız, solunum sayısı, vücut sıcaklığı), bilinç durumu (Glasgow Koma Skalası), hemodinamik durumu (stabil/instabil, sıvı ve/veya inotrop desteği ihtiyacı), intra-abdominal (karaciğer, dalak, ince bağırsak, kolon vb.) ve ekstra-abdominal (toraks, ekstremite, kafa vb.) organ yaralanmaları, laboratuvar bulguları (hemoglobin, lökosit sayısı, kreatinin, pH seviyesi), uygulanan tedavi yöntemleri (cerrahi müdahale veya konservatif takip), cerrahi teknikler, kan ve kan ürünü transfüzyonları ile hastanede kalış süreleri geriye dönük olarak analiz edilmiştir. Hastalar cerrahi tedavi uygulanan grup ve konservatif yönetilen grup olmak üzere ikiye ayrılmış, tedavi kararlarını etkileyen faktörler ve mortaliteye etki eden değişkenler istatistiksel olarak değerlendirilmiştir.

BULGULAR: Hastaların %83.2'si erkek olup, ortalama yaş 28.3±10.5 yıl olarak bulunmuştur. Hastaların %81.2'sine cerrahi tedavi uygulanırken, %18.8'ine konservatif tedavi verilmiştir. Konservatif tedavi uygulanan grupta mortalite gözlenmezken, cerrahi tedavi görenlerde mortalite oranı %15.9 olarak kaydedilmiştir. Kadın hastalarda mortalite oranı (%29.4) erkeklere (%9.5) göre anlamlı derecede yüksek bulunmuştur (p=0.026). Hemodinamik instabilite, intra-abdominal organ yaralanması, karın içinde serbest hava varlığı ve kan ürünü transfüzyonu ihtiyacı hem cerrahi tedavi kararını hem de mortaliteyi artıran faktörler arasında yer almıştır. Ayrıca, hasar kontrol cerrahisi ve çoklu organ yaralanmaları da mortalite ile ilişkilendirilmiştir.

SONUÇ: Ateşli silah yaralanmasına bağlı abdominal travmanın yönetimi, uygun hasta seçimi ve tedavi stratejisi için multidisipliner bir yaklaşım gerektirmektedir. Hemodinamik olarak stabil hastalarda seçici non-operatif yönetim (SNOY) güvenli ve etkili bir seçenektir. Cerrahi müdahale, özellikle hasar kontrol cerrahisi gerektiren vakalarda mortalite ile ilişkilidir. Kadın hastalarda gözlenen yüksek mortalite oranı, bu hasta grubunun daha yakından izlenmesi ve ek risk faktörlerinin araştırılması gerekliliğini ortaya koymaktadır. Elde edilen bulgular mevcut literatürle uyumludur ve klinik uygulamalara rehberlik etmektedir.

Anahtar sözcükler: Abdominal travma; ateşli silah yaralanması; cerrahi müdahale; hemodinamik instabilite; hasar kontrol cerrahisi; mortalite; SNOY.

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## Pediatric burns in low-income countries: An example from Somalia

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## **ABSTRACT**

**BACKGROUND:** Epidemiological data are needed to develop pediatric burn prevention strategies and guide interventions in lowand middle-income countries.

METHODS: In this observational retrospective study, the characteristics of 140 consecutive pediatric patients who were hospitalized and treated for burns at the Burns Unit of a hospital in Mogadishu, Somalia, between November 2022 and April 2024 were analyzed.

**RESULTS:** The patients included 50% males and 50% females, with a mean age of 4.96±4.07 years. The most common burn etiologies were hot water (75.7%), open flame (15.7%), and hot oil (8.6%). Burns involving two or more anatomical regions were observed in 44.2% of the cases. The mean total body surface area (TBSA) affected was 16.2±10.42% (min: 4%, max: 90%). Superficial second-degree burns were present in 50.7% of the patients, and deep second-degree burns in 28.6%. No statistically significant relationship was found between gender and burn degree, burn percentage, or burn etiology (p>0.05). Analysis by age group revealed a statistically significant but weak association (24%) between the 0-4 years age group and burn degree. This was attributed to a higher proportion of more severe burns in children aged 0-4 years compared to those aged 5 years and older. The most common complication was anemia (37.1%), and no mortality was observed. The average hospital stay was 24.1±27.8 days (range: 2-179 days).

**CONCLUSION:** This study presents the first epidemiological data on in-patient pediatric burn cases in Somalia, a country classified as low-income. The risk of mortality can be eliminated if effective burn management is provided in pediatric burn cases, even in low-resource countries. These findings support the expectation of survival in major pediatric burns. Nurses and all healthcare professionals share responsibility for the protection and promotion of health. Therefore, training on burn injury prevention strategies should be targeted and implemented in areas where the incidence is high.

Keywords: Burn; burn care; pediatric burn.

## INTRODUCTION

Burns are a significant health problem in low- and middle-income countries, where 95% of burn-related deaths occur. In addition to high mortality rates, burns cause body deformities, lifelong disability, and social stigmatization and rejection among survivors. In the Guidelines for Burn Prevention and Care published in 2008, the World Health Organization (WHO) reported the burn-related mortality rate in Africa as

6.1 per 100,000 population per year.<sup>[1]</sup> Epidemiological data highlight the burden of childhood burns in low- and middle-income countries. One study from 2000 reported that 16,000 children aged 5 years and younger died from burns.<sup>[2]</sup> In another single-center study focusing on pediatric burn mortality, the rate was reported to be 7.1%.<sup>[3]</sup> Globally, 111,292 burn-related deaths were recorded in 2019, with the majority occurring in the 1-4 years age group.<sup>[4]</sup>

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Table 1. Demographic characteristics and burn-related factors of the patients (n=140)		
Variable	Mean±SD (Min-Max)	n (%)
Age (years)	4.96±4.07 (I-I7)	
Age Distribution		
0-4 years		88 (62.9)
5-9 years		32 (22.9)
10-14 years		13 (9.3)
≥15 years		7 (5.0)
Gender		
Female		70 (50.0)
Male		70 (50.0)
Family Type		
Nuclear		5 (3.6)
Extended		135 (96.4)
Family Income Level		
Low		23 (16.4)
Medium		115 (82.1)
High		2 (1.5)
Average Number of Children per Family	6.68±2.3 (2-15)	
Place of Burn Incident		
Home		139 (99.3)
School		I (0.7)
Cause of Burn		
Hot water		106 (75.7)
Open flame		22 (15.7)
Hot oil		12 (8.6)
Point of Initial Medical Contact		
Home		20 (14.3)
Emergency Department		108 (77.1)
Outside Center		12 (8.6)
Burn Severity		
≤5% (minor)		2 (1.4)
5%-10% (moderate)		28 (20.0)
>10% (major)		110 (78.6)
Patients Undergoing Surgery		
Yes		79 (56.4)
No		61 (43.6)
Anatomic Burn Locations		
Head		7 (5.0)
Trunk (front)		16 (11.4)
Upper extremity		22 (15.7)
Lower extremity		23 (16.4)
Perineum		I (0.7)
Trunk (front) + upper extremity		17 (12.1)
Head + upper extremity		2 (1.4)
Lower extremity + perineum		26 (18.6)
Back + upper extremity		3 (2.1)
Head + trunk (front)		4 (2.9)
Trunk (front + back)		3 (2.1)

Head + upper + lower extremities		4 (2.9)
Trunk (front) + upper + lower extremities		2 (1.4)
Whole body		I (0.7)
Burn Percentage	16.2%±10.42% (4-90)	
Burn Degree		
First Degree		4 (2.9)
Second Degree (Superficial)		71 (50.7)
Second Degree (Deep)		40 (28.6)
Third Degree		25 (17.8)
Bacterial Culture Results		
No growt		119 (85.0)
E. col		4 (2.8)
Proteus spp.		7 (5.0)
Klebsiella spp.		3 (2.1)
Other		2 (1.4)
Local Wound Infection		
Yes		25 (17.9)
No		115 (82.1)
Sepsis		
Yes		34 (24.3)
No		106 (75.7)
Burn-related complications		
None		54 (38.6)
Anemia		52 (37.1)
Sepsis + Anemia		34 (24.3)
Length of Hospital Stay (days)	24.1±27.8 (2-179)	

The prevalence of poverty and unsafe living conditions in rural areas of low-income countries significantly affects the epidemiological profile and risk factors associated with childhood burns. Risk factors such as low socioeconomic status, extended family structures, lack of supervision, the presence of flammable materials, and low maternal education levels are significant contributors to burn injuries.<sup>[5,6]</sup> The literature has primarily focused on three types of burns: scalds from hot liquids, burns from contact with hot surfaces, and burns from open flames.<sup>[7]</sup> A study investigating the causes of burns in patients under 18 years of age reported that scald burns, commonly resulting from falling into or spilling hot liquids, occurred more frequently than other types of burns. [7] Despite the availability of studies on childhood burns in high-income countries, epidemiological data for low- and middle-income countries remain insufficient, underscoring the need for comprehensive data to support the development of prevention strategies.[8]

Research findings can provide an evidence-based foundation for the prevention and management of pediatric burns. However, the scarcity of data in low- and middle-income countries hinders the creation of effective action plans. The demographic and prognostic features of pediatric burn patients in East

Africa are not well defined, largely due to the rural nature of life in the region. [9] In the absence of a national surveillance system, epidemiological data are often derived from hospital-based studies. Therefore, the development of effective prevention strategies for pediatric burns is contingent upon the availability of robust epidemiological data. [3]

The aim of this study was to investigate the epidemiology of pediatric burns in Somalia, which is classified as a low-income country, and to determine the characteristics of burn injuries at the time of hospital admission.

## **MATERIALS AND METHODS**

This observational retrospective study included 140 consecutive patients diagnosed with pediatric burn injuries who were admitted for treatment to the Burns Unit of the Turkish Training and Research Hospital in Mogadishu, Somalia, between November 2022 and April 2024. Ethical approval for the study was obtained from the Local Ethics Committee prior to commencement (Approval number: 962; Date: 30.03.2024). Inclusion criteria were defined as consecutive patients aged ≤18 years, diagnosed with burn injuries, and admitted to the Burns Unit. Exclusion criteria included burn

injuries occurring outside the study period and patients seen in the Emergency Department who either died or were not treated at the specified hospital. Data collected and analyzed included demographic information, family structure, number of children, family economic status, place of admission, cause of burns at the time of admission, location of burns, burn degree as diagnosed by debridement after admission, and any subsequent complications.

#### **Statistical Analysis**

Data obtained in the study were analyzed statistically using SPSS for Windows, Version 25.0 (IBM Corporation, Armonk, NY, USA). The conformity of the data to a normal distribution was assessed using the Shapiro-Wilk W-test. Continuous variables were expressed as mean ± standard deviation, and categorical variables as number and percentage. The Chisquare test was used to analyze categorical data. A significance level 0.05 was applied for all analyses.

#### RESULTS

A total of 140 pediatric patients hospitalized and treated for burn injuries were evaluated. The cohort included 70 males (50%) and 70 females (50%), with a mean age of 4.96±4.07 years. A significant majority of the families (96.4%) were classified as extended families, with an average of 6.68±2.3 children per family. Only 1.5% of families identified themselves as high-income. Burn injuries occurred at home in 99.3% of the cases, with 41.0% specifically taking place in the kitchen. The most common burn etiologies were hot water (75.7%), open flames (15.7%), and hot oil (8.6%).

Burns were most frequently located on the lower extremities and perineum (18.6%), followed by the lower extremities alone (16.4%) and upper extremities (15.7%). Burns involving multiple anatomical regions were observed in 44.2% of cases. The mean total body surface area (TBSA) affected was 16.2±10.42% (range: 4%-90%). The most common severity

was second-degree superficial burns (50.7%), followed by second-degree deep burns (28.6%) and third-degree burns (17.8%).

Microbiological cultures showed no bacterial growth in 85% of patients. Sepsis was diagnosed in 24.3% of cases, all of whom also had anemia, while 17.9% had local wound infections. No burn-related complications developed in 38.6% of the patients, with anemia being the most frequently observed complication (37.1%). The mean length of hospital stay was 24.1±27.8 days (range: 2-179 days). The demographic data and burn-related factors are presented in Table 1.

No statistically significant relationship was found between gender and burn degree, burn percentage, or cause of burn (p>0.05). In the analyses conducted by age group, a statistically significant but weak association (24%) was identified between the 0-4 years age group and burn degree. This was attributed to a higher frequency of more advanced burn degrees in the 0-4 years group compared to children aged  $\geq$ 5 years. Second-degree superficial and second-degree deep burns were more frequently observed in the 0-4 years group, with the leading causes being hot water (Fig. 1), open flames (Fig. 2), and hot oil (Fig. 3), respectively (Table 2.

#### DISCUSSION

According to the World Bank income classifications, countries are categorized based on Gross National Income per capita, an indicator related to a country's level of development. As of the World Bank's 2022 update, Somalia was classified as a low-income country. The WHO's 2022 Africa Health Statistics Atlas reported that no health-related epidemiological data were available for the region. Given this situation, available epidemiological data are limited to local and single-center studies. A systematic review published in 2016, which provided an overview of global burn epidemiology, noted that reporting conclusive results in low-income

	0-4 Years	>5 Years	р
	n (%)	n (%)	
Cause of Burn			
Hot water	70 (66.0)	36 (34.0)	p<0.05
Open flame	12 (54.5)	10 (45.5)	
Hot oil	6 (50.0)	6 (50.0)	
Burn Degree			
First Degree	2 (50.0)	2 (50.0)	
Second Degree (Superficial)	49 (69.0)	22 (31.0)	
Second Degree (Deep)	26 (65.0)	14 (35.0)	
Third Degree	II ( <del>44</del> .0)	14 (56.0)	

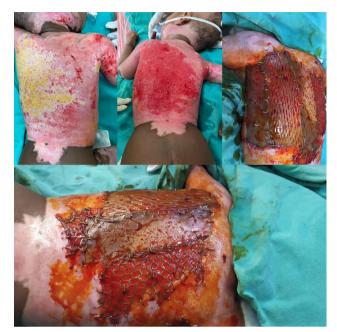


Figure 1. Burns caused by hot water.



Figure 2. Burn injuries resulting from open flames.

countries was difficult due to the lack of data and publications. The review emphasized the urgent need for epidemiological studies on burns, especially in low-income settings.<sup>[11]</sup>

The current study represents the first investigation into epidemiological data on pediatric burn cases requiring hospitalization in Somalia, which is categorized as a low-income country. Previous research in similar settings reported that the mean age of pediatric burn patients was 4.0±3.6 years, with over half being male, and that hot water was the leading cause of burn injuries (68.5%).<sup>[7]</sup> A study conducted in South Africa found a mean age of 25 months, 58% of the sample were male, and the most frequently encountered type of burn injury in this pediatric group was scalding, at a rate of 84%.<sup>[12]</sup> Our findings were consistent with these studies.

The results of the current study were found to be in line with the literature from other low-income countries. Addi-



Figure 3. Burn injuries caused by hot oil.

tionally, the family structure of pediatric burn patients was typically extended, with most families having a medium to low economic status and an average of six or more children. Considering that most burn cases occurred at home, particularly in the kitchen, crowded family environments, economic challenges, and especially floor-level stoves used for cooking (Fig. 4) can be considered key predisposing factors for scald burns in children.

These risk factors are clearly preventable. Great care must



Figure 4. Floor-level cooking stoves.

be taken when using hot water or preparing food. Given the high treatment and care costs associated with burn injuries, the World Health Organization has reported that preventative measures are cost-effective. Nurses and all healthcare professionals are responsible for promoting and preserving health. Therefore, targeted family education on burn injury prevention strategies should be developed and implemented in regions with high incidence.

The anatomic localizations of pediatric burns in the current study were most frequently observed in the lower extremities and perineal region. In a previous study conducted in Africa examining the general characteristics of burns, the most common anatomic sites were in the upper part of the body. These were often the result of curiosity-driven behaviors, such as touching, pulling, or grasping objects, especially among toddlers who had just begun to walk.<sup>[13]</sup> Differences in the anatomic localization of burns between countries and regions are likely due to factors such as social living conditions, the education level of the family, and whether children have access to flames or hot liquids.

According to the American Burn Association guidelines, burn severity is classified based on the total body surface area affected (%). Pediatric burns involving ≥10% TBSA are considered major, 5-10% as moderate, and <5% as minor.[3] In the current study, half of the cases involved burns covering more than 10% TBSA and were classified as superficial and deep second-degree burns, most commonly affecting children aged 0-4 years. It was also observed that many of the patients lived in rural areas and often presented late to the hospital, which may be a contributing factor to increased burn severity. Patients are often admitted to the Burns Unit after first being evaluated in the Emergency Department. Preventing the causes of severe burns, such as preparing food and hot liquids in areas inaccessible to children, and placing hot substances above floor level, is essential when planning parental education on burn prevention and first-aid interventions.

Decreases in hemoglobin levels due to intraoperative or repeated surgical debridement shortly after burn injury can lead to anemia as a result of both the burns themselves and their treatment.[14] While acute blood loss is one of the primary causes of anemia, other contributing factors include reduced hemoglobin concentration during the resolution of the acute phase and the demands of surgical wound healing.[14] In the pediatric group included in this study, burn-related anemia can be explained by the high TBSA involvement, which is consistent with the literature, and by the fact that more than half of the patients underwent surgical intervention. Following major burns, there is an increase in catecholamines, acutephase reactants, and inflammatory cytokines. These create a catalytic effect on whole-body catabolism, inefficient glucose utilization, and a dysregulated host immune response. [15] Burns patients are at significant risk of infection and sepsis due to these physiological changes. Burn depth, TBSA%, and the use of invasive or urinary catheters have been reported

as risk factors for the development of infection-related complications. The literature emphasizes a strong correlation between infections and cases involving >20% TBSA. Infection and sepsis are the leading causes of morbidity and mortality in both pediatric and adult burns patients. Despite advances in burn care, sepsis-related mortality rates remain high.<sup>[8,16]</sup>

The current study was conducted in the Burns Unit of a training and research hospital where multidisciplinary care is provided. Although septic conditions were observed in the pediatric cases during follow-up, a systematic treatment and care approach was implemented. This included regular debridement at intervals, dressing follow-up, and the use of antimicrobials, which helped keep sepsis under control and prevented mortality in all patients. The most important factor contributing to recovery without mortality in pediatric burn cases has been associated with the systematic approach to infection control, particularly the presence of specialist healthcare professionals in hospitals with dedicated pediatric burn units. In the literature, the most significant predictor of mortality in pediatric burn cases has been linked to limited access to intensive care services.[17] Pediatric burn care ranges from simple to complex and advanced management.[18] In low-income countries, the lack of anesthesiologists, nurses, and surgeons specialized in pediatric burns, as well as the lack of access to pediatric-specific products, has been associated with the inability to provide comprehensive, multidisciplinary care.[19,20,21]

In the Burns Unit where this research was conducted, pediatric burn care is provided across the full spectrum, from basic to complex cases. With this comprehensive approach, no sepsis-related mortality was observed in the pediatric patients included in this study, and the results are consistent with findings reported in the literature.<sup>[18,19,20,21]</sup>

Some research in the literature has reported prolonged hospital stays in burn patients. The length of hospital stay has been associated with survival after burn injury and the implementation of key aspects of burn care, including wound closure, infection control, and reduction of the hypermetabolic response.<sup>[22]</sup>

An important finding of this study was that the risk of mortality can be significantly reduced if effective burn management is provided for pediatric burn cases in low-income countries. Effective burn injury management involves systematic care in a Burns Unit, where comprehensive treatment is provided. This includes intermittent debridement and dressing changes, infection control through antibiotics, anemia management, nutritional support, and access to intensive care. This finding supports the expectation of survival for pediatric patients with major burns. Moreover, burns are largely preventable through family education, home safety precautions, and appropriate first-aid interventions. The risk of morbidity and mortality can be further reduced through timely access to healthcare services during the acute phase and management by a professional healthcare team. [23,24]

#### **CONCLUSION**

This study is the first to examine the epidemiological characteristics of pediatric burn cases in Somalia. The findings show that the majority of cases occurred in the 0-4 years age group, scald burns were the most common cause, and the lower extremities and perineal region were the most frequently affected body areas. The results also indicate that proper burn management can significantly reduce mortality risks for pediatric patients in low-income countries. It is recommended that families be educated on burn prevention strategies and that access to healthcare services be improved.

**Ethics Committee Approval:** This study was approved by the Somalia–Türkiye Recep Tayyip Erdoğan Training and Research Hospital Ethics Committee (Date: 30.03.2024, Decision No: 962).

Peer-review: Externally peer-reviewed.

**Authorship Contributions:** Concept: S.A.; Design: S.A., Y.A.; Supervision: S.A., Y.A.; Resource: S.A.; Data collection and/or processing: Y.A.; Analysis and/or interpretation: S.A.; Literature review: S.A.; Writing: S.A.; Critical review: S.A., Y.A.

Conflict of Interest: None declared.

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#### ORİJİNAL ÇALIŞMA - ÖZ

#### Düşük gelirli ülkelerde pediatrik yanıklar: Somali'den bir örnek

AMAÇ: Düşük-orta gelirli ülkelerde pediatrik yanık önleme stratejileri geliştirmek ve harekete geçmek için epidemiyolojik verilere ihtiyaç vardır. GEREÇ VE YÖNTEM: Bu gözlemsel retrospektif çalışmada, Kasım 2022 ile Nisan 2024 arasında Somali, Mogadişu'daki bir hastanenin Yanık Ünitesi'nde pediatrik yanık tanısıyla hastaneye yatırılan ve tedavi edilen 140 ardışık hastanın özellikleri analiz edildi.

BULGULAR: En sık görülen yanık etyolojileri sıcak su (%75.7), alev (%15.7) ve sıcak yağ (%8.6) olarak değerlendirildi. Yanıkların %44.2'sinin iki veya daha fazla anatomik lokasyonda meydana geldiği analiz edildi. Hastaların %50'si erkekti ve ortalama yaş 4.96±4.07 idi. Tüm pediatrik hastalardaki ortalama yanık yüzdesi %16.2±10.42 (min %4-maks %90) iken; yanık dereceleri sıklıkla %50.7'sinde ikinci derece yüzeysel ve %28.6'sında ikinci derece derindi. Cinsiyet ile yanık derecesi, yanık yüzdesi ve yanık oluşum nedenleri arasında istatistiksel olarak anlamlı bir ilişki bulunmamıştır (p>0.05). Ancak 0-4 yaş grubu 5 ve üzeri yaş grubu ile karşılaştırıldığında 0-4 yaş grubu ile yanık dereceleri arasında istatistiksel olarak düşük %24 anlamlı ilişki bulunmaktadır. Bu durum 0-4 yaş grubundaki çocukların yanık derecelerinin 5 ve üzeri yaş grubundakilere göre daha ileri düzeyde olabileceği ile ilişkilidir. En sık görülen komplikasyon (%37.1) anemiydi ve mortalite görülmedi. Ortalama hastanede kalış süresi 24.1±27.8 (2-179) idi.

SONUÇ: Araştırmamız, düşük gelirli ülke kategorisinde yer alan Somali bölgesindeki pediatrik yanık vakalarına ilişkin ilk epidemiyolojik veridir. Düşük gelirli ülkelerde pediatrik yanık vakalarında etkili yanık yönetimi sağlanırsa ölüm riski ortadan kaldırılabilir. Bu sonuç, majör pediatrik yanıklarda hayatta kalma beklentisini desteklemektedir. Hemşireler ve tüm sağlık profesyonelleri sağlığın korunması ve geliştirilmesinden sorumludur. Bu nedenle, yanık yaralanması önleme stratejileri konusunda eğitim, insidansın yüksek olduğu bölgelere hedeflenmeli ve uygulanmalıdır.

Anahtar sözcükler: Pediatrik yanık; yanık; yanık tedavisi.

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# Prognostic value of lactate-enhanced quick sequential organ failure assessment (qSOFA) versus standard qSOFA in predicting mortality among sepsis patients in the emergency department: A retrospective cohort study

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#### **ABSTRACT**

**BACKGROUND:** The quick Sequential Organ Failure Assessment (qSOFA) score is widely used for bedside risk stratification in sepsis patients. However, its limited sensitivity may hinder early identification. The lactate-enhanced qSOFA (LqSOFA), which incorporates serum lactate levels into the qSOFA score, may improve prognostic accuracy. This study aimed to evaluate the diagnostic performance of LqSOFA in predicting early (24-hour) and late (30-day) mortality, as well as intensive care unit (ICU) admission, among patients with sepsis.

METHODS: This retrospective descriptive study included patients aged ≥18 years who were diagnosed with sepsis based on Sepsis-3 criteria and admitted to the emergency department (ED) of a tertiary-care teaching hospital between July I, 2024 and December 3I, 2024. Patients were identified through ICD-I0 (International Classification of Diseases, 10th Revision) codes, and diagnoses were clinically confirmed. qSOFA and LqSOFA scores were calculated using initial vital signs and venous lactate levels. The primary outcomes were 24-hour and 30-day mortality; ICU admission was assessed as a secondary outcome. Statistical analyses were conducted using SPSS v27 and Jamovi v2.5.7. The diagnostic performance of the scores was evaluated using receiver operating characteristic (ROC) curve analysis. Area under the curve (AUC), sensitivity, specificity, and predictive values were calculated, and AUC comparisons were performed using the DeLong test (p<0.05 considered significant).

**RESULTS:** A total of 236 patients were included (median age: 75 years; 53% male). The 24-hour and 30-day mortality rates were 20.3% and 36.4%, respectively. LqSOFA demonstrated significantly higher diagnostic accuracy than qSOFA for predicting 24-hour mortality (AUC: 0.709 vs. 0.673; p<0.05). Although LqSOFA also showed a higher AUC for 30-day mortality, the difference was not statistically significant. Nevertheless, LqSOFA exhibited superior specificity and positive predictive value. For ICU admission, LqSOFA demonstrated greater sensitivity than qSOFA (79% vs. 57%).

**CONCLUSION:** LqSOFA outperforms qSOFA in predicting mortality and ICU admission among sepsis patients in the emergency department. Given its simplicity, objectivity, and ease of implementation, LqSOFA may serve as a practical tool to support clinical decision-making in emergency settings.

Keywords: Sepsis; emergency service; hospital; lactic acid; qSOFA score; intensive care units; mortality.

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#### INTRODUCTION

Sepsis is a systemic condition characterized by life-threatening organ dysfunction resulting from a dysregulated host response to infection. It is recognized as one of the leading causes of mortality encountered in emergency departments. [1] In cases where early diagnosis is not established, the risk of progressive multiorgan failure and death increases significantly. Therefore, the need for rapid and accurate diagnostic tools, risk stratification methods, and timely initiation of appropriate treatment in the early phase of the disease remains critical and continues to grow. [2]

The quick Sequential Organ Failure Assessment (qSOFA) score, defined by the "Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)," is a simple bed-side scoring system based on three parameters: systolic blood pressure, respiratory rate, and mental status. qSOFA has been widely adopted due to its noninvasive nature and reliance on easily measurable clinical variables.<sup>[3]</sup> However, several studies have demonstrated that qSOFA may be insufficient for the early identification of sepsis due to its low sensitivity, and that its performance in predicting mortality is limited.<sup>[4,5]</sup>

In recent years, numerous studies have demonstrated that serum lactate levels are an independent predictor of poor prognosis. Lactate is considered an early indicator of cellular hypoperfusion and, in this context, provides valuable guidance for clinical decision-making. Moreover, elevated lactate levels have been found to be strongly associated with mortality, even in patients who are normotensive and not tachypneic.<sup>[6,7]</sup>

In light of this evidence, the Lactate-enhanced qSOFA (LqSOFA) score was developed by incorporating serum lactate levels into the conventional qSOFA scoring system. The literature suggests that LqSOFA outperforms qSOFA in predicting both in-hospital and 28-day mortality. In a study conducted by Liu et al., [8] the LqSOFA score was compared with other rapid scoring systems such as qSOFA, Systemic Inflammatory Response Syndrome (SIRS), Modified Early Warning Score (MEWS), and Mortality in Emergency Department Sepsis score (MEDS); LqSOFA demonstrated the highest overall accuracy. Similarly, in a multicenter prospective cohort study conducted in Southeast Asia, Wright et al. [9] reported that the LqSOFA score significantly outperformed qSOFA in predicting 28-day mortality.

LqSOFA has garnered attention as a practical and predictive tool, particularly in emergency department settings within low- and middle-income countries, where access to laboratory and imaging resources may be limited. However, the validity, clinical performance, and predictive value of the LqSOFA score in the Turkish patient population have not yet been adequately investigated. This gap underscores the need for further studies evaluating the applicability of LqSOFA across different geographical regions and patient cohorts.

This study aims to retrospectively evaluate the performance of the LqSOFA score at the time of emergency department

admission in predicting 24-hour and 30-day mortality among adult patients diagnosed with sepsis. The findings are expected to support the use of LqSOFA as a simple, rapid, and effective risk stratification tool in resource-limited clinical settings. Furthermore, by examining the association between LqSOFA scores and key clinical outcomes such as hospital admission, intensive care unit (ICU) requirement, and patient prognosis, the study is anticipated to make a meaningful contribution to the literature regarding the practical utility of the LqSOFA score.

#### MATERIALS AND METHODS

#### Study Design and Ethical Approval

This study was designed as a single-center, retrospective, descriptive, and analytical observational investigation. Ethical approval was obtained from the Clinical Research Ethics Committee of Etlik City Hospital (Approval No: AEŞH-BADEK1-2025-0177). The study was conducted in accordance with the principles of the Declaration of Helsinki. Due to its retrospective nature, the requirement for informed consent was waived.

#### **Participants**

This study included adult patients aged 18 years and older who presented to the Emergency Medicine Department of Etlik City Hospital and were diagnosed with sepsis between July 1, 2024 and December 31, 2024. Eligible cases were retrospectively identified through the hospital's electronic medical record system.

#### **Inclusion Criteria**

- Presentation to the emergency department with suspected infection and a subsequent diagnosis of sepsis
- An increase in the baseline SOFA score by ≥2 points
- Documented respiratory rate, systolic blood pressure (SBP), Glasgow Coma Scale (GCS) score, and serum lactate levels at the time of admission

#### **Exclusion Criteria**

- Presentation due to non-sepsis-related causes such as trauma or convulsions
- · Patients admitted to the hospital in cardiac arrest
- Inability to reliably assess mental status due to factors such as psychotropic drug use, alcohol intoxication, altered consciousness, or pre-existing neurological disorders
- Immunosuppression (e.g., history of chemotherapy, hematologic malignancy, Human Immunodeficiency Virus [HIV] infection, or long-term immunosuppressive therapy)
- Other critical non-infectious conditions that could elicit a severe systemic response and potentially influence qSOFA scores and lactate levels such as myocardial infarction, pulmo-

nary embolism, aortic dissection, or gastrointestinal bleeding

- · Missing clinical or laboratory data
- · Age under 18 years
- Pregnancy.

These criteria were established to ensure methodological homogeneity and to enable an isolated evaluation of the impact of lactate levels and qSOFA scores on sepsis prognosis.

#### Definition of Sepsis, qSOFA, and LqSOFA Scores

According to the Sepsis-3 guidelines, sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection. Organ dysfunction is identified by an increase of  $\geq 2$  points in the SOFA score. The qSOFA score ranges from 0 to 3, assigning I point each for a systolic blood pressure  $\leq 100$  mmHg, respiratory rate  $\geq 22$  breaths/min, and altered mental status. A score  $\geq 2$  indicates a high risk of poor outcomes in patients with suspected sepsis.<sup>[3,10]</sup>

The qSOFA score was calculated based on triage notes recorded at emergency department admission. Patients were excluded from the study if this information was unavailable or incomplete. The LqSOFA score is a modified version of qSOFA, which incorporates serum lactate as an additional fourth parameter. One point was added if the initial serum lactate level was ≥2 mmol/L. Lactate levels were measured using venous blood gas samples.

#### **Data Collection Process**

The following variables were collected for each patient: age, sex, vital signs [respiratory rate, GCS, SBP, diastolic blood pressure (DBP), and body temperature], laboratory parameters, and clinical outcomes in the emergency department. Laboratory variables included serum levels of lactate, pH, base excess, procalcitonin, C-reactive protein (CRP), and albumin, along with complete blood count components such as white blood cell (WBC) count, hemoglobin (HGB), platelet (PLT) count, and immature granulocyte count (IGC).

All laboratory values were obtained from blood samples collected within the first hour of emergency department admission to assess the early course of pathophysiological changes. Previous studies have demonstrated a significant correlation between venous and arterial lactate levels, indicating that venous lactate is also sufficient for predicting mortality. [11,12] Accordingly, venous lactate values were used in this study.

The diagnosis of sepsis was initially identified through the hospital's information management system using the International Classification of Diseases, 10th Revision (ICD-10) codes A41.1, A41.2, A41.4, A41.5, A41.8, and A41.9. These cases were then retrospectively reviewed in detail, including their clinical and laboratory data. The diagnosis of sepsis was further confirmed based on clinical findings documented in hospital records and emergency department admission notes.

This two-step verification process was employed to reduce false-positive identifications due to coding errors and to enhance the diagnostic reliability of the study population.

The calculation of qSOFA and LqSOFA scores in this study was performed by an independent researcher who was blinded to patient mortality outcomes. This approach minimized assessor bias and ensured the objectivity of the scoring process.

The qSOFA and LqSOFA scores were calculated for each patient. Patient groups were compared using descriptive, clinical, and laboratory data. The primary outcome was mortality within 24 hours and within 30 days. Secondary outcome measures included emergency department disposition (discharge, ward admission, or intensive care unit admission).

All data were recorded in accordance with the study's exclusion criteria, and no data imputation was performed. For patients with a suspected diagnosis of sepsis, consultation with the Infectious Diseases Department was obtained to confirm the diagnosis. Patients whose diagnosis could not be definitively confirmed were excluded from the study.

#### **Statistical Analysis**

All statistical analyses were performed using SPSS version 27.0 (IBM Corp., Armonk, NY, USA) and Jamovi version 2.5.7. Descriptive statistics for categorical variables were presented as frequencies and percentages, while continuous variables were summarized using median and interquartile range (IQR, 25th–75th percentile). The distribution of continuous variables was assessed using histograms and the Kolmogorov–Smirnov test.

The chi-square test was used to compare categorical variables. For continuous variables with normal distribution, comparisons were made using the Student's t-test or Welch's t-test, depending on the equality of variances. For non-normally distributed variables, the Mann–Whitney U test was applied. Homogeneity of variances was assessed using Levene's test.

To assess the diagnostic performance of qSOFA and LqSOFA scores in predicting mortality, Receiver Operating Characteristic (ROC) curve analysis was performed. The cut-off values, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (+LR), and negative likelihood ratio (-LR) were calculated. The DeLong test was used to compare the AUCs of different scoring systems. A p-value <0.05 was considered statistically significant for all analyses.

#### **RESULTS**

A total of 493 patients were initially identified based on ICD-10 codes through the hospital information management sys-

Table I.	Distribution of patients' demographic character-
	istics, vital signs, laboratory values, and clinical
	features

Sex	
Male	125 (53.0%)
Female	111 (47.0%)
Age	75 (64-84)
Vital Parameters	
Systolic Blood Pressure (mmHg)	95 (80-117)
Diastolic Blood Pressure (mmHg)	59 (50-70)
Heart Rate (beats/min)	100 (86-118)
Oxygen Saturation (%)	94 (91-96)
Respiratory Rate (breaths/min)	21 (20-23)
Body Temperature (°C)	36.8 (36.5-37.8)
Laboratory Parameters	
WBC (×10 <sup>9</sup> /L)	13.9 (8.5-19.8)
Hemoglobin (g/dL)	11.1 (9.1-12.7)
Platelet (×10 <sup>9</sup> /L)	219 (133-328)
IGC (×10³/μL)	0.16 (0.08-0.48)
рН	7.38 (7.30-7.40)
Base excess	7.4 (-2.5 to 12.6)
Lactate (mmol/L)	1.77 (2.38-3.84)
Lactate ≥2 mmol/L	150 (63.6%)
Procalcitonin (ng/mL)	3.1 (0.5-21.3)
CRP (mg/L)	178 (98-271)
Albumin (g/dL)	30.4 (25.8-33.3)
Altered Mental Status	133 (56.4%)
Vasopressor Requirement	139 (58.9%)
qSOFA	
0	35 (14.8%)
I	91 (38.6%)
2	74 (31.4%)
3	36 (15.3%)
LqSOFA	
0	20 (8.5%)
I	55 (23.3%)
2	70 (29.7%)
3	62 (26.3%)
4	29 (12.3%)
Emergency Department Outcome	
Discharge	13 (5.5%)
Ward Admission	34 (14.4%)
ICU Admission	189 (80.1%)
ICU Transfer After Ward Admission	9 (3.8%)
24-hour Mortality	48 (20.3%)
30-day Mortality	86 (36.4%)

WBC: White Blood Cell Count; IGC: Immature Granulocyte Count; CRP: C-Reactive Protein; ICU: Intensive Care Unit. Values are expressed as n (%) or median (IQR), as appropriate.

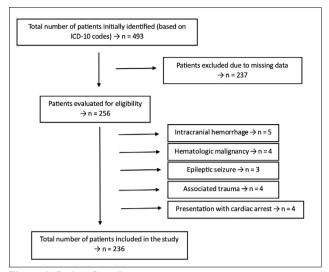


Figure 1. Patient flow diagram.

tem. Of these, 237 patients were excluded due to missing data. Among the remaining 256 patients, five were excluded due to intracranial hemorrhage, four due to hematologic malignancy, three due to epileptic seizures, four due to concomitant trauma, and four due to presentation with cardiac arrest. Consequently, a total of 236 patients were included in the final analysis (Fig. 1).

The median age of the 236 patients included in the study was 75 years, with a balanced gender distribution (53% male). Evaluation of vital signs at admission revealed a median systolic blood pressure of 95 mmHg and diastolic blood pressure of 59 mmHg, with borderline tachycardia (median heart rate: 100 bpm). The most prominent laboratory abnormality was that 63.6% of patients had a serum lactate level ≥2 mmol/L. Altered mental status was observed in 56.4% of patients at admission, and vasopressor requirement was documented in 58.9%. Approximately 50% of patients presented with a qSO-FA score ≥2, while 68.3% had an LqSOFA score ≥2. Clinical outcomes showed a 24-hour mortality rate of 20.3% and a 30-day mortality rate of 36.4% (Table 1).

Table 2 demonstrates statistically significant differences in several clinical and laboratory variables associated with both 24-hour and 30-day mortality. Regarding 24-hour mortality, patients who died had significantly lower pH levels and higher lactate levels (both p<0.001). Hemoglobin levels were also significantly higher in the group with fatal outcomes (p=0.025). Additionally, altered mental status (AMS) was significantly more prevalent among patients who died within 24 hours (p<0.001).

Among these variables, AMS, pH, and lactate levels were also significantly associated with 30-day mortality (p<0.001, p=0.012, and p<0.001, respectively). Furthermore, a significantly lower serum albumin level and a higher need for vasopressor support were observed in patients who died within 30 days (both p<0.001).

**Table 2.** Association of patients' demographic characteristics, vital signs, laboratory values, and clinical features with 24-hour and 30-day mortality

	24-hour	mortality		30-day n	30-day mortality	
	Yes (n=48)	No (n=188)	p value	Yes (n=86)	No (n=150)	p value
Sex						
Male	22 (45.8%)	103 (54.8%)	0.2671	44 (51.2%)	81 (54.0%)	0.6741
Female	26 (54.2%)	85 (45.2%)		42 (48.8%)	69 (46.0%)	
Age	74 (66-82)	75 (64-84)	0.8752	74 (64-84)	75 (65-83)	0.9272
Vital Parameters						
SBP (mmHg)	89 (71-114)	98 (80-118)	$0.132^{2}$	90 (75-110)	100 (83-119)	0.1322
DBP (mmHg)	56 (47-66)	60 (50-70)	0.2623	55 (47-68)	60 (50-70)	0.1383
HR (beats/min)	108 (89-120)	99 (85-116)	0.200 <sup>3</sup>	107 (88-121)	98 (85-112)	0.1633
Oxygen (%)	93 (89-95)	94 (92-96)	$0.132^{2}$	94 (90-96)	94 (91-96)	0.7212
RR (breaths/min)	20 (20-23)	21 (20-23)	0.6242	21 (20-24)	20 (19-23)	0.1542
BT (°C)	36.6 (36.5-37.3)	36.8 (36.5-37.8)	0.5022	36.6 (36.5-37.1)	36.8 (36.5-37.9)	0.1022
Laboratory Parame-ters						
WBC (×10 <sup>9</sup> /L)	13.2 (7.3-23.0)	14.2 (8.7-19.7)	0.8702	11.7 (7.2-19.8)	14.9 (9.1-19.8)	0.1422
Hemoglobin (g/dL)	11.3 (9.8-13.0)	10.9 (9.0-12.7)	0.0253	10.9 (8.4-12.4)	11.2 (9.3-12.8)	0.3733
Platelet (×10 <sup>9</sup> /L)	179 (114-332)	233 (138-327)	0.5373	184 (105-337)	237 (154-323)	0.6714
IGC (×10³/μL)	0.16 (0.06-0.57)	0.16 (0.09-0.47)	0.8242	0.14 (0.05-0.57)	0.18 (0.09-0.45)	0.3212
pН	7.30 (7.20-7.39)	7.40 (7.30-7.41)	<0.0012	7.32 (7.24-7.40)	7.40 (7.30-7.41)	0.0122
Base excess	2.1 (-9.8 to 14.1)	7.5 (-0.3 to 12.3)	0.0594	7.4 (-4.9 to 13.4)	7.4 (-0.7 to 12.2)	0.288⁴
Lactate (mmol/L)	4.56 (2.45-7.33)	2.23 (1.73-3.08)	<0.0012	2.95 (2.04-5.23)	2.23 (1.68-3.13)	<0.0012
Procalcitonin (ng/mL)	4.3 (0.9-34.2)	2.8 (0.5-19.0)	0.2462	2.9 (0.9-21.6)	3.5 (0.4-21.0)	0.5672
CRP (mg/L)	163 (83-265)	179 (101-285)	0.6813	181 (97-261)	177 (99-291)	0.9773
Albumin (g/dL)	30.1 (23.8-32.8)	30.4 (26.3-33.6)	0.1643	28.1 (24.3-31.9)	31.2 (27.3-34.6)	<0.0013
AMS	39 (81.3%)	94 (50.0%)	<0.001	64 (74.4%)	69 (46.0%)	<0.001
Vasopressor Re-quirement	34 (70.8%)	105 (55.9%)	0.0601	65 (75.6%)	74 (49.3%)	<0.001
Emergency Depart-ment Outcome						
Discharge	0	13 (6.9%)		0	13 (8.7%)	
Ward Admission	I (2.1%)	33 (17.6%)		5 (5.8%)	29 (19.3%)	
ICU Admission	47 (97.9%)	143 (76.1%)		81 (94.2%)	108 (72.0%)	
ICU Transfer After Ward Admission	1 (2.1%)	8 (4.3%)		5 (2.7%)	8 (4.3%)	

SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; HR: Heart Rate; RR: Respiratory Rate; BT: Body Temperature; WBC: White Blood Cell Count, IGC: Immature Granulocyte Count; CRP: C-Reactive Protein; AMS: Altered Mental Status; ICU: Intensive Care Unit. 'Chi-square test; 'Student's t-test; 'Mann-Whitney U test; 'Welch's t-test. Values are expressed as n (%) or median (IQR), as appropriate.

As shown in Figure 2, both LqSOFA and qSOFA scores demonstrated diagnostic value in predicting 24-hour and 30-day mortality. For 24-hour mortality, the LqSOFA score with a cut-off value of ≥3 yielded an area under the curve (AUC) of 0.709 (95% confidence interval [CI]: 0.629–0.789), which was higher than that of the qSOFA score (AUC: 0.673). The sensitivity and specificity of LqSOFA were 62% and 68%, respectively, with a positive predictive value of 33% and a negative predictive value of 88%. These findings indicate that while LqSOFA has higher specificity and comparable NPV compared

to qSOFA in predicting early mortality, it has relatively lower sensitivity (Table 3).

For 30-day mortality prediction, the LqSOFA score with a cutoff value of ≥3 yielded an AUC of 0.676 (95% CI: 0.607– 0.746), while the qSOFA score with a cutoff of ≥2 demonstrated an AUC of 0.669. Although the AUC values were relatively similar for both scores, the LqSOFA score exhibited higher specificity and positive predictive value compared to qSOFA (Table 3).

**Table 3.** Cut-off values of Lactate-enhanced quick Sequential Organ Failure Assessment (LqSOFA) and quick Sequential Organ Failure Assessment (qSOFA) scores for predicting 24-hour and 30-day mortality in patients with sepsis

	Cut-off	AUC (95% CI)	SEN (95% CI)	SPE (95% CI)	PPV (95% CI)	NPV (95% CI)	+LR (95% CI)	-LR (95% CI)	p value
24-hour mortality									
LqSOFA	3	0.709	62 (47-76)	68 (60-74)	33 (27-40)	88 (83-91)	1.93	0.56	<0.001
		(0.629-0.789)					(1.43-2.61)	(0.38-0.82)	
qSOFA	2	0.673 (0.587-0.759)	69 (54-81)	59 (52-66)	30 (25-36)	88 (83-92)	1.68	0.53	<0.001
							(1.30-2.17)	(0.34-0.82)	
30-day mortality									
LqSOFA	3	0.676	55 (44-65)	71 (63-78)	52 (44-59)	73 (68-78)	1.86	0.64	<0.001
			(0.607-0.746)				(1.36-2.55)	(0.50-0.82)	
qSOFA	2	0.669	65 (54-75)	64 (56-72)	51 (44-57)	76 (70-81)	1.81	0.55	<0.001
		(0.598-0.740)					(1.39-2.36)	(0.40-0.75)	

AUC: Area under the curve; SEN: Sensitivity; SPE: Specificity; PPV: Positive predictive value; NPV: Negative predictive value; +LR: Positive likelihood ratio; -LR: Negative likelihood ratio.

**Table 4.** Cut-off values of Lactate-enhanced quick Sequential Organ Failure Assessment (LqSOFA) and quick Sequential Organ Failure Assessment (qSOFA) scores for predicting Intensive Care Unit (ICU) admission in patients with sepsis

	Cut-off	AUC (95% CI)	SEN (95% CI)	SPE (95% CI)	PPV (95% CI)	NPV (95% CI)	+LR (95% CI)	-LR (95% CI)	p value
LqSOFA	2	0.824	79 (72-84)	74 (60-86)	93 (88-95)	47 (39-55)	3.09	0.28	<0.001
		(0.758-0.891					(1.89-5.06)	(0.20-0.39)	
qSOFA	2	0.820	57 (49-64)	94 (82-99)	97 (92-99)	35 (31-39)	8.87	0.46	<0.001
		(0.756-0.885)					(2.95-26.7)	(0.38-0.55)	

AUC: Area under the curve; SEN: Sensitivity; SPE: Specificity; PPV: Positive predictive value; NPV: Negative predictive value; +LR: Positive likelihood ratio; -LR: Negative likelihood ratio.

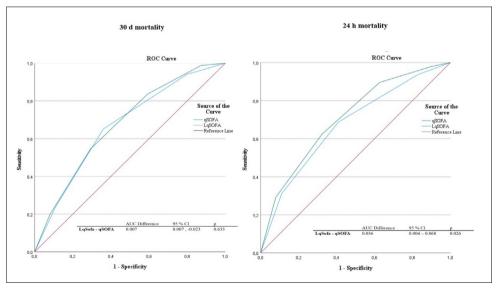
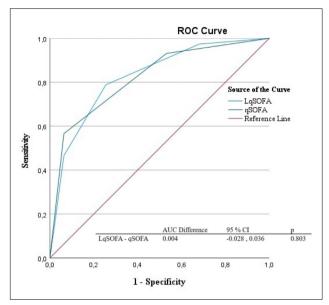


Figure 2. ROC Curves of qSOFA and LqSOFA Scores in Predicting 24-Hour and 30-Day Mortality.



**Figure 3.** ROC Curves of LqSOFA and qSOFA Scores for Predicting ICU Admission.

Figure 2 demonstrates that the LqSOFA score exhibits higher diagnostic accuracy than qSOFA in predicting both 24-hour and 30-day mortality. For 24-hour mortality, the LqSOFA curve lies above that of qSOFA, with an AUC difference of 0.006 (95% CI: 0.004–0.026), which was statistically significant according to the DeLong test (p<0.05). This suggests that LqSOFA may offer superior performance in predicting early mortality. For 30-day mortality, although the LqSOFA score again demonstrated a higher AUC compared to qSOFA, the difference was 0.007 and did not reach statistical significance (95% CI: -0.023 to 0.633, DeLong test, p>0.05).

Both LqSOFA and qSOFA scores demonstrated diagnostic value in predicting ICU admission (Fig. 3). As shown in Table 4, the diagnostic performance of the two scores was comparable: the AUC for the LqSOFA score (cut-off ≥2) was 0.824 (95% Cl: 0.758-0.891), which was similar to that of the qSOFA score (AUC: 0.820, 95% Cl: 0.756-0.885). Both scores showed strong discriminative ability (p<0.001). The sensitivity and specificity of LqSOFA were 79% (95% Cl: 72-84) and 74% (95% Cl: 60-86), respectively. While qSOFA exhibited higher specificity (94%), it had considerably lower sensitivity (57%). These findings suggest that LqSOFA, with its higher sensitivity and balanced specificity, allows for more effective identification of high-risk patients, whereas qSOFA—despite its high specificity—may fail to detect a subset of critically ill patients due to its lower sensitivity.

In Figure 3, the diagnostic accuracy of qSOFA and LqSOFA scores for predicting ICU admission was compared using ROC curves. Although the LqSOFA curve lies slightly above that of qSOFA, the AUC difference between the two scoring systems was 0.004 (95% CI: -0.028 to 0.036), which was not statistically significant (DeLong test, p=0.803).

#### **DISCUSSION**

This study aimed to evaluate the predictive performance of the LqSOFA score, which incorporates serum lactate levels into the conventional qSOFA score, for both early and late mortality among adult patients diagnosed with sepsis in the emergency department. Our findings indicate that the LqSOFA score demonstrated higher diagnostic accuracy than the qSOFA score in predicting both 24-hour and 30-day mortality. Additionally, LqSOFA exhibited greater sensitivity than qSOFA in predicting ICU admission.

Sepsis represents a heterogeneous clinical spectrum characterized by systemic inflammatory response, hypoperfusion, organ dysfunction, and increased risk of death. Therefore, there is a critical need for tools that can enable both early diagnosis and risk stratification.<sup>[1,4]</sup> In this context, the qSOFA score is widely used due to its simplicity and bedside applicability. However, multiple studies have reported that it may be insufficient for early recognition of sepsis and prediction of mortality.<sup>[13-15]</sup>

Lactate is recognized as an early biochemical marker of tissue hypoperfusion in patients with sepsis or critical illness and has been identified in the literature as an independent predictor of mortality. [6,16,17] Moreover, elevated lactate levels may indicate poor prognosis even in patients who appear clinically stable, including those who are normotensive, nontachypneic, or afebrile. [18] In this context, the LqSOFA score has emerged as a tool that may better reflect early pathophysiological deterioration in sepsis.

In our study, the AUC of the LqSOFA score for predicting 24-hour mortality was found to be 0.709, which was significantly higher than that of the qSOFA score. This finding supports the results of the study by Liu et al., [8] in which LqSOFA was compared with other scoring systems. Liu and colleagues demonstrated that LqSOFA yielded a higher AUC than SIRS, MEWS, and MEDS in predicting in-hospital mortality and identified it as the scoring system with the highest overall accuracy. Similarly, in a prospective cohort study conducted in Southeast Asia, Wright et al. [9] found that LqSOFA significantly outperformed qSOFA in predicting 28-day mortality (AUROC: 0.78 vs. 0.68). In parallel, Bou Chebl et al. [6] showed that lactate is an independent predictor of mortality in patients diagnosed with sepsis in the emergency department.

Hemoglobin levels are a critical biomarker in sepsis, as they reflect oxygen-carrying capacity and tissue perfusion. Accordingly, low hemoglobin levels in septic patients have been associated with increased mortality. However, in our study, hemoglobin levels were found to be significantly higher in the 24-hour mortality group. In a study by Sheng et al., a nonlinear association between hemoglobin levels and in-hospital mortality was observed in sepsis patients, with both low and high hemoglobin values linked to poor outcomes. Elevated hemoglobin levels may increase blood viscosity and impair microcirculation. Therefore, maintaining hemoglobin levels

within an optimal range may be important in the management of sepsis.

In our study, patients who died within both 24 hours and 30 days exhibited significantly lower pH levels, higher lactate concentrations, and a greater frequency of AMS. These findings support the strong association between hypoperfusion, metabolic dysfunction—core components of sepsis pathophysiology—and mortality.[21] Additionally, hypoalbuminemia was significantly associated with 30-day mortality, suggesting that low albumin levels may serve as an additional independent biomarker for late-phase sepsis prognosis. In line with this, a study by Seo et al.[22] identified a nomogram incorporating hypoalbuminemia, tachypnea, and low base excess as a reliable predictor of 28-day mortality among septic patients in the emergency department. Similarly, the significant association between vasopressor requirement and 30-day mortality in our cohort reinforces the prognostic value of hemodynamic instability. In septic patients, vasopressor use is commonly linked to septic shock, which is a major contributor to increased mortality.[23]

In predicting ICU admission, the LqSOFA score demonstrated higher sensitivity compared to qSOFA (79% vs. 57%), albeit with lower specificity. This suggests that LqSOFA may be a safer triage tool in emergency department settings, as it is less likely to miss high-risk patients. Conversely, the higher specificity of qSOFA (94%) may offer an advantage in reducing false-positive identifications. Therefore, it is important to consider not only the diagnostic accuracy of scoring systems but also the intended clinical purpose when applying them in decision-making processes.

The literature has emphasized the applicability of the LqSO-FA score particularly in low- and middle-income countries, where emergency departments often operate with limited resources. In such settings, the use of simple, time-efficient, and objectively measurable scoring systems is of critical importance.<sup>[24,25]</sup>

In our study, only venous lactate measurements were used, which supports the feasibility and sustainability of this scoring system in emergency departments where arterial sampling may be challenging in practice. Several studies have reported a strong correlation between venous and arterial lactate levels. [12,26]

#### **CONCLUSION**

In conclusion, our study demonstrated that the LqSOFA score provides superior performance compared to qSOFA in predicting both mortality and the need for ICU admission. Given its simplicity, rapid applicability, and utility in guiding clinical decision-making, we believe that the LqSOFA score should be more widely adopted in emergency department settings. Future multicenter, prospective studies with larger sample sizes are warranted to further evaluate and validate the diagnostic accuracy of this scoring system.

**Ethics Committee Approval:** This study was approved by the Etlik City Hospital Clinical Research Ethics Committee (Date: 07.05.2025, Decision No: AEŞH-BADEK I-2025-0177).

Peer-review: Externally peer-reviewed.

**Authorship Contributions:** Concept: V.S.; Design: V.S. A.B.E.; Supervision: A.B.E.; Resource: V.S.; Materials: V.S. A.B.E.; Data collection and/or processing: V.S. A.B.E.; Analysis and/or interpretation: V.S.; Literature review: V.S.; Writing: V.S.; Critical review: V.S. A.B.E.

Conflict of Interest: None declared.

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#### ORİJİNAL ÇALIŞMA - ÖZ

# Acil serviste sepsis hastalarında mortaliteyi tahmin etme konusunda laktatla geliştirilmiş qSOFA'nın standart qSOFA'ya karşı prognostik değeri: Retrospektif bir kohort çalışması

AMAÇ: Quick Sequential Organ Failure Assessment (qSOFA) skoru, sepsis hastalarında yatak başı risk sınıflandırması için yaygın olarak kullanılmaktadır. Ancak sınırlı duyarlılığı, erken tanı konmasını zorlaştırabilir. Serum laktat düzeylerinin qSOFA skoruna entegre edilmesiyle oluşturulan Lactate-enhanced qSOFA (LqSOFA) skoru, prognostik doğruluğu artırabilir. Bu çalışmanın amacı, LqSOFA skorunun erken (24 saat) ve geç (30 gün) mortalite ile yoğun bakım ünitesi (YBÜ) yatışını öngörmedeki tanısal performansını değerlendirmektir.

GEREÇ VE YÖNTEM: Bu retrospektif tanımlayıcı çalışma, 1 Temmuz 2024 – 31 Aralık 2024 tarihleri arasında üçüncü basamak bir eğitim ve araştırma hastanesinin acil servisine başvuran ve Sepsis-3 kriterlerine göre sepsis tanısı alan ≥18 yaş hastaları kapsamaktadır. Hastalar ICD-10 kodları ile belirlenmiş, tanılar klinik olarak doğrulanmıştır. qSOFA ve LqSOFA skorları, başvuru anındaki vital bulgular ve venöz laktat düzeylerine göre hesaplanmıştır. Birincil sonuçlar 24 saat ve 30 günlük mortalite; ikincil sonuç ise YBÜ yatışıdır. İstatistiksel analizler SPSS v27 ve Jamovi v2.5.7 ile yapılmıştır. Tanısal performans değerlendirmesi için ROC eğrisi analizi uygulanmış; AUC, duyarlılık, özgüllük ve kestirim değerleri hesaplanmıştır. AUC karşılaştırmaları DeLong testi ile yapılmış; p<0.05 anlamlı kabul edilmiştir.

BULGULAR: Toplam 236 hasta dahil edilmiştir (medyan yaş: 75 yıl; %53 erkek). Yirmi dört saatlik ve 30 günlük mortalite oranları sırasıyla %20.3 ve %36.4 olarak bulunmuştur. LqSOFA, 24 saatlik mortaliteyi öngörmede qSOFA'ya göre anlamlı derecede daha yüksek tanısal doğruluk göstermiştir (AUC: 0.709 ve 0.673; p<0.05). LqSOFA'nın 30 günlük mortalite için AUC değeri daha yüksek olmasına rağmen, fark istatistiksel olarak anlamlı değildir. Bununla birlikte, LqSOFA daha yüksek özgüllük ve pozitif kestirim değeri sergilemiştir. YBÜ yatışını öngörmede, LqSOFA skoru qSOFA'ya göre daha yüksek duyarlılığa sahiptir (%79 ve %57).

SONUÇ: LqSOFA skoru, mortalite ve YBÜ yatışını öngörmede qSOFA skoruna göre daha iyi tanısal performans sunmaktadır. Basitliği, nesnelliği ve hızlı uygulanabilirliği sayesinde, LqSOFA acil servislerde klinik karar verme sürecini destekleyen pratik bir araç olarak kullanılabilir.

Anahtar sözcükler: Hastane acil servisi; laktik asit; sepsis; mortalite; qSOFA skoru, yoğun bakım üniteleri.

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### Predictive value of disability scoring systems for return-towork outcomes in hand and forearm injuries

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#### **ABSTRACT**

**BACKGROUND:** Predicting return-to-work (RTW) outcomes following upper extremity trauma is crucial for optimizing patient care, guiding rehabilitation, and reducing the socioeconomic burden. Although several disability scoring systems have been proposed to assess injury severity, their ability to estimate RTW status and duration remains underexplored. This study aimed to evaluate the predictive value of the Modified Hand Injury Severity Score (MHISS), Upper Extremity Disability Rate (UEDR), and Total Body Disability Rate (TBDR) for RTW outcomes in patients with hand, wrist, and forearm injuries.

METHODS: A retrospective cross-sectional study was conducted on 69 patients who presented to the Forensic Medicine Department of Ondokuz Mayıs University between 2020 and 2024. Eligible participants were adults with documented hand, wrist, or forearm injuries and complete treatment records, including MHISS scoring. Demographic data, injury characteristics, and disability rates (UEDR, TBDR) were collected. Statistical analyses included Spearman correlation, receiver operating characteristic (ROC) analysis, and logistic regression to assess associations between scoring systems and RTW status and duration.

**RESULTS:** The median MHISS score was 20.0, with corresponding UEDR and TBDR values of 3.0% and 2.0%, respectively. Occupational injuries, observed in 37.7% of cases, were associated with significantly higher disability scores (p<0.05). ROC analysis demonstrated strong predictive ability for MHISS (area under the curve [AUC]: 0.886), UEDR (AUC: 0.903), and TBDR (AUC: 0.897) in identifying RTW status. While MHISS effectively predicted RTW status, it did not correlate with RTW duration (p=0.082). In contrast, UEDR and TBDR showed weak but statistically significant correlations with RTW duration (r=0.295 and r=0.296, respectively). Multivariate logistic regression did not identify any independent predictors of RTW.

**CONCLUSION:** Disability scoring systems such as MHISS, UEDR, and TBDR are useful tools for predicting whether patients will return to work following hand and forearm injuries. However, their ability to estimate the duration of work absence is limited. Future research should integrate psychosocial, occupational, and rehabilitation-related variables to develop more comprehensive models for RTW prognosis.

**Keywords:** Hand injuries; return to work; disability evaluation; occupational injuries.

#### **INTRODUCTION**

Hand injuries are frequently encountered in regions where small- and medium-sized industrial enterprises and agriculture-based activities are prevalent. Owing to the functional significance of the hand, such injuries are associated with high morbidity and prolonged loss of workforce.<sup>[1]</sup> A substantial

proportion of workers' compensation claims and applications to traffic compensation systems are related to acute orthopedic trauma. To mitigate the individual, social, and economic impacts of such trauma, it is crucial to identify prognostic factors associated with a low likelihoods of return to work at an early stage.<sup>[2]</sup>

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While some studies have identified injury severity as the most significant factor influencing the ability to return to work, [3, 4] others suggest that sociodemographic factors such as occupation, age, gender, and educational level also play a critical role. [5,6] Notably, Urso Baiarda et al., [4] building upon the Hand Injury Severity Score (HISS) developed by Campbell and Kay to assess the extent and potential outcomes of hand injuries, introduced the Modified Hand Injury Severity Score. They proposed that MHISS severity, independent of other factors, significantly affects the duration of return to work. [7]

Determining the patient's recovery period, the time required to return to work, and the presence of any permanent disability is crucial after an injury. In Türkiye, disability rates for patients are assessed according to the Regulation on Disability Assessment for Adults. [8] In a previous study, Çapkın et al. [9] found that the MHISS was statistically significantly correlated with the upper extremity disability rate, total body disability rate, and return-to-work duration, as determined by this regulation. MHISS has also been used in numerous studies to predict long-term functionality in the affected region, return-to-work timelines, the likelihood of prolonged work absence, and triage decisions. [10-13]

The aim of this study was to examine whether scoring systems used to assess disability can serve as predictive factors for return to work and the time required to return to work.

#### MATERIALS AND METHODS

#### **Study Design**

This retrospective cross-sectional study included 69 patients who presented to the Forensic Medicine Department of Ondokuz Mayıs University Health Practice and Research Center between January 1, 2020 and January 1, 2024, for disability assessment following hand, wrist, and forearm injuries. Ethical approval was obtained from the Ethics Committee of Ondokuz Mayıs University (2025000001-1), and the study was conducted in accordance with the Declaration of Helsinki.

#### **Patient Selection**

Patients aged 18 years or older with documented hand, wrist, or forearm injuries during emergency department visits, evaluated by plastic surgery or orthopedic specialists with expertise in hand surgery, with fully calculated MHISS scores, and with complete treatment, surgical, and physical therapy rehabilitation records were included in the study.

Patients with incomplete treatment, surgical, or rehabilitation records; those under 18 years of age; or those with additional trauma outside the upper extremity were excluded from the study.

#### **Data Collection**

Recorded data included patients' age, gender, injury etiology, the device causing the injury, occupational category, injury direction, and whether the dominant hand was affected. MHISS, UEDR, and TBDR scores were calculated and documented by a forensic medicine specialist.

#### **Scoring Systems**

The Modified Hand Injury Severity Score, derived from the Hand Injury Severity Score, is used to evaluate hand, wrist, and forearm injuries. MHISS assesses injury severity across four components: skin, skeleton, motor function, and nerves. Each component is scored based on absolute scores, the functional importance of the affected region, and additional factors such as wound contamination, compound fractures, crush injuries, or amputations. The total score is obtained by summing the component scores and classifying them into MHISS severity levels. In Türkiye, patients' disability rates are determined according to the Regulation on Disability Assessment for Adults, which primarily evaluates disability based on the active range of motion (ROM) of the injured hand, the amputation level, and the location of motor and sensory loss.<sup>[8]</sup>

#### Statistical Analysis

Data analysis was performed using IBM SPSS version 21.0 (SPSS Inc., Chicago, IL, USA). Categorical variables were summarized as frequencies, counts (n), and percentages (%). Non-normally distributed continuous variables were presented as medians (min-max). Spearman correlation analysis was applied to non-normally distributed data. Receiver operating characteristic analysis was conducted to evaluate the predictive ability of the scoring systems for return-to-work status, and cutoff values were determined using the Youden index. Results were expressed with 95% confidence intervals. Multivariate logistic regression analysis was performed to determine independent predictors of return-to-work status. A p-value of <0.05 was considered statistically significant for all analyses.

#### RESULTS

The median age of the patients was 40 years (range: 16-65), with the majority being male (71%). The median MHISS score was 40.0 (range: 2.0-1740.0), the upper extremity disability rate was 5.0% (range: 0.0-95.0), and the total body disability rate was 3.0% (range: 0.0-57.0). Dominant hand injuries were reported in 59.4% of cases. Regarding injury etiology,traffic accidents were the most common cause (55.1%), followed by occupational accidents (37.7%). Patients with occupational injuries had significantly higher MHISS, UEDR, and TBDR scores compared with those whose injuries had other causes (p<0.05). By injury type, sharp-force injuries were associated with significantly higher MHISS, UEDR, and TBDR scores compared with blunt or crush injuries (p<0.001) (Table 1).

Patients who successfully returned to work had a median age of 41 years (range: 18-65), while those who did not had a median age of 36 years (range: 18-65). Statistically significant

			Median (m	in-max)		
Age (years)			40.0 (16.0	)-65.0)		
RTW time (days)	90.0 (7.0-900.0)					
	n	%	MHISS	UEDR	TBDR	
Gender						
Male	49	71.0	40.0 (2.0-1740.0)	5.0 (0.0-95.0)	3.0 (0.0-57.0)	
Female	20	29.0	37.0 (4.0-631.0)	5.0 (0.0-40.0)	3.0 (0.0-24.0)	
$P^{\dagger}$			0.921	0.716	0.746	
Etiology of injuries						
Traffic accident	38	55.1	20.0 (2.0-1331.0) <sup>a</sup>	1.0 (0.0-95.0) <sup>a</sup>	1.0 (0.0-57.0)	
Work accident	26	37.7	96.0 (10.0-1740.0) <sup>b</sup>	11.0 (0.0-77.0) <sup>b</sup>	6.5 (0.0-46.0) <sup>t</sup>	
Assault	5	7.2	20.0 (4.0-90.0) <sup>a,c</sup>	0.0 (0.0-5.0) <sup>a,c</sup>	0.0 (0.0-3.0) <sup>a,c</sup>	
P <sup>‡</sup>			<0.001	<0.001	<0.001	
Type of injury						
Crush injury	52	75. <del>4</del>	20.0 (2.0-1740.0)	4.0 (0.0-95.0)	2.5 (0.0-57.0)	
Sharp-force injury	17	24.6	102.0 (10.0-1008.0)	9.0 (0.0-45.0)	5.0 (0.0-28.0)	
$P^\dagger$			0.002	0.016	0.013	
Occupational category						
Blue-collar worker	57	82.6	56.0 (2.0-1740.0)	8.0 (0.0-95.0)	5.0 (0.0-57.0)	
White-collar worker	12	17.4	20.0 (6.0-262.0)	0.0 (0.0-22.0)	0.0 (0.0-13.0)	
$P^\dagger$			0.181	0.011	0.010	
Side of injury						
Right	41	59.4	42.0 (3.0-1740.0)	8.0 (0.0-95.0)	5.0 (0.0-57.0)	
Left	25	36.2	28.0 (2.0-631.0)	5.0 (0.0-45.0)	3.0 (0.0-25.0)	
Both	3	4.3	40.0 (22.0-80.0)	18.0 (9.0-28.0)	10.0 (5.0-17.0)	
P <sup>‡</sup>			0.701	0.166	0.186	
Dominant hand affected						
Yes	41	59.4	42.0 (3.0-1331.0)	8.0 (0.0-95.0)	5.0 (0.0-57.0)	
No	28	40.6	31.0 (2.0-1740.0)	5.0 (0.0-77.0)	3.0 (0.0-46.0)	
p <sup>†</sup>			0.580	0.622	0.613	

†Mann-Whitney U test; ‡Kruskal-Wallis test. \*\*:No significant differences between groups with the same letter (Dunn's test). RTW: Return to work.

differences were observed in MHISS scores (20.0 vs. 196.0; p<0.001), UEDR (3.0% vs. 24.5%; p<0.001), and TBDR (2.0% vs. 24.5%; p<0.001). A significantly higher proportion of patients with occupational accidents (38.5%) did not return to work compared with those injured by other causes (Table 2).

Correlation analysis revealed a weak positive correlation between return-to-work duration and both UEDR (r=0.295, p=0.029) and TBDR (r=0.296, p=0.028). MHISS was not significantly correlated with return-to-work duration (p=0.082) (Table 3).

In univariate logistic regression analysis, MHISS (odds ratio [OR]: 1.0; 95% confidence interval [CI]: 1.00-1.01; p=0.010),

UEDR (OR: 1.12; 95% CI: 1.05-1.19; p<0.001), and TBDR (OR: 0.40; 95% CI: 0.22-0.81; p<0.001) were identified as significant predictors of return to work. However, multivariate logistic regression analysis did not identify any statistically significant predictors (p>0.05) (Table 4).

The ROC analysis demonstrated high predictive accuracy for MHISS (AUC: 0.886; 95% CI: 0.801-0.971; p<0.001), UEDR (AUC: 0.903; 95% CI: 0.825-0.982; p<0.001), and TBDR (AUC: 0.897; 95% CI: 0.814-0.979; p<0.001). The optimal cut-off values for predicting return to work were MHISS  $\leq$ 82.0, UEDR  $\leq$ 10.0, and TBDR  $\leq$ 6.0 (Fig. I, Table 5).

Table 2. Comparative analysis of return-to-work (RTW) and non-return-to-work (nRTW) groups

	, ,	, , , , ,	
	RTW, median (min-max)	nRTW, median (min-max)	$\mathbf{p}^{\dagger}$
Age	41.0 (18.0-65.0)	36.0 (18.0-65.0)	0.638
MHISS	20.0 (2.0-1008.0)	196.0 (22.0-1740.0)	<0.001
UEDR	3.0 (0.0-43.0)	24.5 (5.0-95.0)	<0.001
TBDR	2.0 (0.0-26.0)	15.0 (3.0-57.0)	<0.001
	RTW, n (%)	n <b>RTW</b> , n (%)	P <sup>‡</sup>
Gender			
Male	39 (79.6%)	10 (20.4%)	0.969
Female	16 (80.0%)	4 (20.0%)	
Etiology of injury			
Traffic accident	34ª (89.5%)	4 <sup>b</sup> (10.5%)	0.012
Work accident	16ª (61.5%)	10 <sup>b</sup> (38.5%)	
Assault	5ª (100.0%)	O <sup>a</sup> (0.0%)	
Type of injury			
Crush injury	42 (80.8%)	10 (19.2%)	0.734
Sharp-force injury	13 (76.5%)	4 (23.5%)	
Occupational category			
Blue-collar worker	43 (75.4%)	14 (24.6%)	0.107
White-collar worker	12 (100.0%)	0 (0.0%)	
Dominant hand affected			
Yes	32 (78.0%)	9 (22.0%)	0.912
No	23 (82.1%)	5 (17.9%)	

†Mann-Whitney U test; †Chi-square test of independence, RTW: Return to work; MHISS: Modified Hand Injury Severity Score; UEDR: Upper Extremity Disability Rate; TBDR: Total Body Disability Rate. \*\*:No significant differences between groups with the same letter (Bonferroni correction).

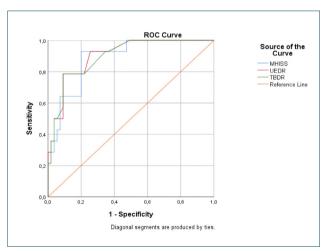
 Table 3.
 Correlation between scoring systems and return-to-work duration

	RTW tim	RTW time (days)		
	r	<b>p</b> *		
MHISS	0.236	0.082		
UEDR	0.295	0.029		
TBDR	0.296	0.028		

<sup>\*</sup>Spearman correlation. MHISS: Modified Hand Injury Severity Score; UEDR: Upper Extremity Disability Rate; TBDR: Total Body Disability Rate.

#### **DISCUSSION**

Injuries or trauma affecting the upper extremities are significant conditions that prolong the return-to-work process and contribute to economic losses.<sup>[14]</sup> The MHISS, developed by Urso-Baiarda et al.,<sup>[4]</sup> is a scoring system for upper extremity injuries that predicts both the likelihood of returning to work



**Figure 1.** ROC Analysis Results for MHISS, UEDR, and TBDR in Predicting Return-to-Work.

and the duration required for return. Their study demonstrated that as the MHISS score and classification increased, the probability of returning to work decreased, and this finding could not be explained by factors such as dominant ex-

**Table 4.** Univariate and multivariate logistic regression analysis of predictors of return to work

	Multivariate		Univariate	
	OR (95% CI)	р	OR (95% CI)	P
Age	0.92 (0.840-1.00)	0.054	0.99 (0.95-1.03)	0.613
Female gender	1.67 (0.24-11.80)	0.606	0.98 (0.27-3.57)	0.969
Sharp-force injury	2.57 (0.23-28.72)	0.445	0.77 (0.21-2.89)	0.702
MHISS	1.00 (0.99-1.00)	0.203	1.00 (1.00-1.01)	0.010
UEDR	2.18 (0.36-13.09)	0.396	1.12 (1.05-1.19)	<0.001
TBDR	0.40 (0.02-7.81)	0.544	1.20 (1.09-1.34)	<0.001
Dominant hand affected	0.99 (0.15-6.53)	0.993	1.29 (0.38-4.37)	0.678
Constant	0.04 (0-0)	0.182		

Cox & Snell R2=0.377; Nagelkerke R2=0.593; Model accuracy=0.870. MHISS: Modified Hand Injury Severity Score; UEDR: Upper Extremity Disability Rate; TBDR: Total Body Disability Rate.

**Table 5.** Receiver Operating Characteristic (ROC) analysis of the Modified Hand Injury Severity Score (MHISS), Upper Extremity Disability Rate (UEDR), and Total Body Disability Rate (TBDR) for predicting return to work

	MHISS	UEDR	TBDR
Cut-off	≤82.0	≤10.0	≤6.0
AUC (95% CI)	0.886 (0.801-0.971)	0.903 (0.825-0.982)	0.897 (0.814-0.979)
Sensitivity	78.6% (49.2-95.3)	78.6% (49.2-95.3)	78.6% (49.2-95.3)
Specificity	80.0% (67.3-89.6)	78.2% (65.0-88.2)	78.2% (65.0-88.2)
PPV	50.0% (35.5-64.5)	47.8% (34.1-61.9)	47.8% (34.1-61.9)
NPV	93.6% (84.2-97.6)	93.5% (83.9-97.5)	93.5% (83.9-97.5)
Accuracy	79.7% (68.3-88.4)	78.3% (66.7-87.3)	78.3% (66.7-87.3)
p value	<0.001	<0.001	<0.001

tremity involvement, household income, or compensation claims. However, other studies in the literature have emphasized the influence of physical, psychosocial, demographic, and employment-related factors on return-to-work duration. [15-17] The present study examined patients who sustained hand or forearm injuries within the past five years and presented to our clinic for disability evaluation.

We observed that individuals who experienced occupational accidents had a lower likelihood of returning to work compared to those injured from other etiologies. Previous studies have also shown that occupational accidents are associated with longer recovery periods before return to work than hand injuries resulting from other factors. This has been attributed to the fact that occupational accidents predominantly occur among workers who use hand tools, requiring advanced manual skills to resume their jobs.<sup>[18-21]</sup> Our findings are consistent with those reported in the literature.

We found no statistically significant differences between pa-

tients who returned to work and those who did not in terms of age, gender, type of injury, job category (white-collar vs. blue-collar), or dominant hand involvement. Although these findings contradict studies suggesting that age and gender are significant factors influencing the time to return to work,<sup>[22]</sup> they are consistent with the results of a systematic review by Shi et al.,<sup>[23]</sup> which examined prognostic factors for return to work following work-related traumatic hand injuries.

Independent predictors of return to work were evaluated using logistic regression analysis, and the scoring systems examined were found to be significant in univariate analyses. Subsequently, we assessed these scoring systems as predictors of return to work using ROC analysis. MHISS, UEDR, and TBDR were all significant predictors of return to work, with the following thresholds and AUC values: MHISS ≤82.0 (AUC: 0.886), UEDR ≤10.0 (AUC: 0.903), and TBDR ≤6.0 (AUC: 0.897). These findings support Urso-Baiarda's<sup>[4]</sup> assertion that MHISS is a strong standalone marker for return to work. However, no significant correlation was found between

MHISS and the duration of return to work. While UEDR and TBDR showed significant correlations with return-to-work duration, these correlations were weak (r=0.295 for UEDR, r=0.296 for TBDR). By contrast, the study by Çapkın et al.<sup>[9]</sup> reported a very strong positive correlation between MHISS, UEDR, TBDR, and return-to-work duration. Our findings suggest that although scoring systems are effective in predicting return-to-work status, they are not sufficient on their own to predict the duration of return to work among patients who eventually resume employment.

The negative legal processes often encountered by patients presenting to the forensic medicine department, particularly in disputes with their employers, may influence both their return-to-work duration and their ability to return to work. Consequently, the data from patients seen in the forensic medicine clinic may inherently differ from those of patients presenting to other clinics, who typically experience more favorable legal processes and receive adequate social and medical support.

#### **CONCLUSION**

In conclusion, scoring systems such as MHISS, UEDR, and TBDR can be used as predictive tools for evaluating return-to-work status. However, relying solely on these systems is insufficient for assessing the duration of return to work. To better understand the return-to-work timeline for patients with hand and forearm injuries, future studies should explore the impact of psychosocial and environmental factors (e.g., anxiety levels, economic and social support) as well as the optimization of rehabilitation processes. Such research could help develop more comprehensive and effective evaluation methods that extend beyond the current limitations of existing scoring systems.

A key limitation of this study is the inability to confirm whether patients who did not return to work failed to do so solely for medical reasons. Factors such as employer dynamics, adherence to an effective physical rehabilitation, medical follow-up, and sociodemographic influences were not clearly delineated. In addition, it was not possible to determine whether individuals who returned to work resumed their previous roles under the same job descriptions or were reassigned to modified duties. This lack of information may affect the interpretation of functional recovery. Moreover, the relatively small sample size and the fact that all patients included in the study were seeking disability-related reports (raising the possibility of simulation) further constrain the findings.

**Ethics Committee Approval:** This study was approved by the Ondokuz Mayıs University Ethics Committee (Date: 16.01.2025, Decision No: 2025000001-1).

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**Authorship Contributions:** Concept: N.C.A., M.S.A, B.A., A.T.; Design: N.C.A., M.S.A, B.A., A.T.; Supervision: N.C.A.,

M.S.A, B.A., A.T.; Resource: N.C.A., B.A., A.T.; Materials: N.C.A., B.A., A.T.; Data collection and/or processing: N.C.A., M.S.A, B.A., A.T.; Analysis and/or interpretation: M.S.A, A.T.; Literature review: N.C.A., M.S.A, B.A.; Writing: N.C.A., M.S.A, B.A., A.T.; Critical review: AT.

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#### ORİJİNAL ÇALIŞMA - ÖZ

# El ve ön kol yaralanmalarında işe dönüşle ilişkili sonuçların öngörülmesinde engellilik puanlama sistemlerinin rolü

AMAÇ: Üst ekstremite travmalarını takiben işe dönüş sonuçlarını öngörebilmek, hasta bakımının optimize edilmesi, rehabilitasyon sürecinin yönlendirilmesi ve sosyoekonomik yükün azaltılması açısından kritik öneme sahiptir. Travma şiddetini değerlendirmek amacıyla çeşitli engellilik puanlama sistemleri önerilmiş olsa da bu sistemlerin işe dönüş durumu ve süresini tahmin etme konusundaki yeterliliği sınırlı düzeyde araştırılmıştır. Bu çalışma, el, el bileği ve ön kol yaralanmaları bulunan hastalarda Modifiye El Yaralanması Şiddet Skoru (MHISS), Üst Ekstremite Özürlülük Oranı (UEDR) ve Toplam Vücut Özürlülük Oranı'nın (TBDR) işe dönüş sonuçlarını öngörme değerini değerlendirmeyi amaçlamaktadır.

GEREÇ VE YÖNTEM: Bu retrospektif kesitsel çalışma, 2020–2024 yılları arasında Ondokuz Mayıs Üniversitesi Adli Tıp Anabilim Dalı'na başvuran 69 hasta üzerinde gerçekleştirilmiştir. Çalışmaya, el, el bileği veya ön kol yaralanması olan, tam tedavi kayıtlarına ve MHISS skorlamasına sahip erişkin bireyler dahil edilmiştir. Demografik veriler, yaralanma özellikleri ve özürlülük oranları (UEDR, TBDR) toplanmıştır. İstatistiksel analizlerde Spearman korelasyonu, ROC analizi ve lojistik regresyon kullanılmıştır.

BULGULAR: Ortanca MHISS skoru 20, UEDR %3, TBDR ise %2 olarak hesaplanmıştır. Olguların %37.7'sinde gözlenen iş kazaları, anlamlı düzeyde daha yüksek engellilik skorlarıyla ilişkili bulunmuştur (p<0.05). ROC analizi, MHISS (AUC: 0.886), UEDR (AUC: 0.903) ve TBDR'nin (AUC: 0.897) işe dönüş durumunu öngörmede yüksek doğrulukla çalıştığını göstermiştir. MHISS, işe dönüş durumunu başarılı şekilde tahmin etmesine karşın, işe dönüş süresiyle anlamlı bir korelasyon göstermemiştir (p=0.082). Buna karşılık, UEDR ve TBDR ile işe dönüş süresi arasında zayıf ancak anlamlı korelasyonlar bulunmuştur (sırasıyla, r=0.295 ve r=0.296). Çok değişkenli lojistik regresyon analizinde bağımsız bir prediktör saptanmamıştır.

SONUÇ: MHISS, UEDR ve TBDR gibi engellilik puanlama sistemleri, el ve ön kol yaralanmaları sonrasında hastaların işe dönüp dönemeyeceğini öngörmede faydalı araçlardır. Ancak, işe dönüş süresini tahmin etme kapasiteleri sınırlıdır. Gelecekte yapılacak çalışmalarda, psikososyal, mesleki ve rehabilitasyonla ilişkili değişkenlerin de dahil edilmesiyle daha kapsamlı öngörü modelleri geliştirilebilir.

Anahtar sözcükler: El yaralanmaları; engellilik değerlendirmesi; işe dönüş; mesleki yaralanmalar.

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# Management of Thoracolumbar Injury Classification and Severity Score (TLICS) 4 thoracolumbar fractures after natural disasters: Comparative outcomes of conservative and surgical treatments following the 2023 Türkiye earthquake

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#### **ABSTRACT**

**BACKGROUND:** This study examines the outcomes of conservative versus surgical treatment for Thoracolumbar Injury Classification and Severity Score (TLICS) 4 thoracolumbar fractures in patients injured during the 2023 Türkiye earthquake. It aims to assess clinical and radiographic outcomes while considering the impact of crush syndrome-related complications on treatment decisions.

METHODS: Twenty-three patients with TLICS 4 spinal injuries were evaluated and divided into surgical (n=12) and conservative (n=11) groups. Clinical parameters, including age, gender, preoperative spinal measurements, and one-year postoperative outcomes, were assessed. The Roland-Morris score was used to evaluate clinical outcomes. Additionally, complications such as cardiac, renal, and respiratory issues, infections, and length of hospital stay were analyzed.

**RESULTS:** The surgical group had significantly higher Roland-Morris scores (RM: 79.3±12.7 vs. 15.0±8.5, p<0.001). Preoperative acute kidney injury was more common in the conservative group (36.4% vs. 8.3%, p<0.05), whereas preoperative pulmonary complications were more frequent in the surgical group (83.3% vs. 36.4%, p<0.05). No significant differences were found in gender, age, or other complications. Radiological outcomes, including Cobb angle, sagittal index, and anterior central vertebral body height (ACVBH) restoration, showed no significant differences between groups. Length of hospital stay was similar between groups.

**CONCLUSION:** Our study demonstrates that both conservative and surgical treatments are effective for managing TLICS 4 thoracolumbar fractures in disaster settings. Treatment decisions should be guided by patient-specific factors and available resources.

Keywords: Spine; fracture; Thoracolumbar Injury Classification and Severity Score (TLICS); earthquake; posterior instrumentation.

#### **INTRODUCTION**

The devastating earthquake that struck Türkiye on February 6, 2023 resulted in over 50,000 deaths and caused injuries

to more than 107,000 individuals.<sup>[1]</sup> This catastrophe led to severe traumatic injuries, including crush syndrome, which required urgent and complex medical care. Crush syndrome is a

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systemic condition that occurs due to prolonged compression of muscle tissue, leading to ischemia-reperfusion injury, rhabdomyolysis, and life-threatening complications such as acute kidney injury (AKI), electrolyte imbalances, metabolic acidosis, and multi-organ failure. [2,3] The management of patients with crush syndrome is further complicated by associated comorbidities, including renal failure, respiratory distress, and cardiovascular complications, all of which can significantly influence the treatment approach for concurrent traumatic injuries. [4,5]

Spinal injuries, though less common than extremity injuries among earthquake victims, carry a high risk of long-term disability and functional loss.<sup>[6]</sup> Among these, thoracolumbar fractures are the most frequently observed due to the biomechanical vulnerability of the thoracolumbar junction, where the rigid thoracic spine transitions into the more flexible lumbar spine.<sup>[7,8]</sup> The Thoracolumbar Injury Classification and Severity Score (TLICS) system is widely used to guide the management of vertebral fractures by assessing injury morphology, integrity of the posterior ligamentous complex, and neurological involvement.[9] While conservative treatment is generally recommended for stable fractures with a TLICS score of ≤3 and surgical intervention is preferred for scores of ≥5, the optimal approach for TLICS 4 fractures remains debated. Some studies suggest that conservative management may be sufficient, while others advocate surgical stabilization to achieve better clinical and radiographic outcomes.[10,11]

The presence of crush-related comorbidities further complicates the decision-making process for managing TLICS 4 fractures. Renal failure resulting from crush syndrome may limit the feasibility of prolonged immobilization, while respiratory complications can increase perioperative risks. Therefore, treatment decisions must be made through a multidisciplinary approach, considering both the immediate and long-term implications for the patient.

This study aims to analyze the outcomes of conservative versus surgical management of TLICS 4 thoracolumbar fractures in patients affected by the 2023 Türkiye earthquake. By evaluating clinical and radiographic parameters, we aim to provide evidence on the efficacy and risks associated with both treatment approaches, particularly in patients with crush-related complications.

#### **MATERIALS AND METHODS**

This retrospective study evaluated patients referred to our institution with injuries sustained during the Kahramanmaraş earthquake on February 6, 2023. It was conducted in accordance with the ethical principles of the Declaration of Helsinki and approved by the Ethics Committee of Ankara Etlik City Hospital, Türkiye (Approval Number: Ek1-2024-1221). A total of 11,346 earthquake victims presented to the hospital, and 790 neurosurgical and orthopedic procedures were performed. The study included patients with earthquake-related spinal injuries categorized as TLICS 4 or higher who

were eligible for either conservative or surgical treatment based on their TLICS score.

We specifically included patients with a TLICS score of 4 who were treated either surgically or conservatively. Patients were excluded if they were in the pediatric age group, had a prior history of spinal surgery, did not sustain earthquake-related injuries, or lacked concomitant extremity injuries. Those with spinal injury levels exceeding TLICS 4 were also excluded, as they underwent posterior instrumentation and fusion surgery, which was outside the scope of this research. Among the earthquake victims, 43 patients with spinal injuries were identified, all with a TLICS score of 4 or higher. Of these, 20 had spinal injury levels exceeding TLICS 4 and were excluded from the study due to the type of surgery performed.

A total of 23 patients with TLICS 4 were included in the study and divided into two groups: the surgical group (12 patients) and the conservative group (11 patients). Clinical parameters evaluated included age, gender, preoperative Cobb angle, anterior vertebral body compression percentage, and sagittal index. Postoperative outcomes were assessed at the one-year follow-up, focusing on changes in Cobb angle, sagittal index, and anterior compression angles.

To assess clinical outcomes, the Roland-Morris score was used. This highly sensitive tool evaluates acute, subacute, and chronic back pain and is particularly effective for detecting and assessing mild to moderate lumbar and back conditions. The Roland-Morris score was used to assess clinical outcomes at the one-year postoperative follow-up.

The study also examined pre-treatment complications, including cardiac, renal, and respiratory issues. The presence of infections, both at the surgical site and elsewhere, was documented. Additional factors such as hospital stay duration and time spent under debris were also analyzed. The objective was to determine whether major surgery contributed to additional complications in patients with earthquake-related spinal injuries.

#### **Statistical Analysis**

Statistical analyses were conducted using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY, USA). Normality of the dataset was assessed using the Kolmogorov-Smirnov and Shapiro-Wilk tests, with significance values evaluated alongside skewness and kurtosis metrics. Based on these assessments, the variables were determined to follow a normal distribution.

For group comparisons, the Independent Samples t-test was applied to normally distributed continuous variables, while the Mann-Whitney U test was used for non-normally distributed variables. The Chi-square test was employed to assess differences between categorical variables. A 95% confidence

level was used for all analyses, and a p-value of less than 0.05 was considered statistically significant.

#### **RESULTS**

A total of 23 patients were included in the study, divided into two groups: the surgical group (n=12) and the conservative group (n=11). The mean age was  $50.4\pm11.5$  years in the surgical group and  $58.0\pm14.5$  years in the conservative group. The age difference between groups was not statistically significant (p>0.05). Regarding gender distribution, the conservative group had a higher proportion of female patients (81.8%) compared to the surgical group (66.7%). Across both groups, 73.9% of patients were female and 26.1% were male, with no statistically significant difference in gender distribution (p>0.05).

Acute kidney injury was significantly more common in the conservative group (36.4%) than in the surgical group (8.3%) (p<0.05). Conversely, pulmonary complications were significantly more prevalent in the surgical group (83.3%) compared to the conservative group (36.4%) (p<0.05).

The time under debris, used as a measure of exposure, was longer in the conservative group ( $14.6\pm37.9$  hours) compared to the surgical group ( $7.4\pm20.4$  hours). However, this difference was not statistically significant (p>0.05).

Cardiac complications occurred at similar rates in both groups: 8.3% in the surgical group and 9.1% in the conservative group, with no statistically significant difference (p>0.05) (Table 1).

Wound infection rates were similar between groups, with 33.3% of patients in the surgical group and 36.4% in the conservative group affected. The difference between the two groups was not statistically significant (p>0.05). The rate of additional infections was higher in the conservative group (62.9%) than in the surgical group (41.7%), but this difference was also not statistically significant (p>0.05).

A significant difference was observed in the Roland-Morris (RM) score between the two groups, with the surgical group scoring significantly higher (79.3 $\pm$ 12.7) than the conservative group (15.0 $\pm$ 8.5) (p<0.001).

Regarding sagittal alignment, no statistically significant differences were found in either initial or follow-up sagittal index measurements. The initial sagittal index was  $10.2\pm5.4$  in the surgical group and  $6.6\pm16.2$  in the conservative group (p>0.05). The follow-up sagittal index was  $8.6\pm6.4$  in the surgical group and  $6.6\pm10.2$  in the conservative group (p>0.05).

Similarly, no significant differences were observed in Cobb angle measurements between the two groups. The initial Cobb angle was  $18.9^{\circ}\pm10.5$  in the surgical group and  $17.1^{\circ}\pm7.0$  in the conservative group (p>0.05). Follow-up Cobb angles were similar between the two groups, with values of  $17.6^{\circ}\pm7.5$  in the surgical group and  $18.0^{\circ}\pm6.2$  in the conservative group (p>0.05).

The percentage of anterior vertebral body height (ACVBH) restoration was similar in both groups at both the initial assessment and follow-up. The initial ACVBH restoration was  $69.8\%\pm14.5$  in the surgical group and  $69.3\%\pm15.1$  in the conservative group (p>0.05), while the follow-up values were  $75.1\%\pm15.6$  in the surgical group and  $74.8\%\pm16.4$  in the conservative group (p>0.05).

The length of hospital stay was notably longer in the conservative group  $(58.0\pm101.4 \text{ days})$  compared to the surgical group  $(26.9\pm18.6 \text{ days})$ , but the difference was not statistically significant (p>0.05) (Table 2).

Additional surgical procedures were performed in 50.0% of patients in the surgical group (n=6) and 45.5% in the conservative group (n=5). The remaining patients in both groups did not require further operations (50.0% in the surgical group vs. 54.5% in the conservative group). There was no statistically significant difference in the need for additional surgical interventions (p>0.05).

 Table 1.
 Comparison of demographic, clinical parameters, and gender distribution between surgical and conservative groups

	Surgical (n=12)	Conservative (n=11)	p Value
Age	50.4±11.5	58.0±14.5	>0.05
Gender			
Female	8 (66.7%)	9 (81.8%)	
Male	4 (33.3%)	2 (18.2%)	-
Acute Kidney Injury (%)	8.3%	39.4%	<0.05
Pulmonary Complications (%)	83.3%	36.4%	<0.05
Time Under Debris (hours)	7.4±20.4	14.6±37.9	>0.05
Cardiac Complications (%)	8.3%	9.1%	>0.05

Table 2. Comparison of clinical, radiological, and outcome parameters between surgical and conservative groups

	Surgical (n=12)	Conservative (n=11)	p Value
Wound Infection (%)	33.3%	36.4%	>0.05
Additional Infection (%)	41.7%	62.9%	>0.05
RM Score	79.3±12.7	15.0±8.5	<0.001
Initial Sagittal Index (%)	10.2±5.4	6.6±16.2	>0.05
Follow-up Sagittal Index (%)	8.6±6.4	6.6±10.2	>0.05
Initial Cobb Angle (°)	18.9±10.5	17.1±7.0	>0.05
Follow-up Cobb Angle (°)	17.6±7.5	18.0±6.2	>0.05
Initial ACVBH (%)	69.8%±14.5	69.3%±15.1	>0.05
Follow-up ACVBH (%)	75.1±15.6	74.8%±16.4	>0.05
Hospital Stay (days)	26.9±18.6	58.0±101.4	>0.05

<sup>\*</sup>RM Score: Roland-Morris Score. \*Initial ACVBH: Anterior Central Vertebral Body Height.

#### **DISCUSSION**

This study compared surgical and conservative treatments in patients with TLICS 4 thoracolumbar fractures following the 2023 Türkiye earthquake. The results showed that surgical treatment was associated with significantly better functional outcomes at one year, as measured by the Roland-Morris score. These findings align with previous research showing that surgical stabilization improves pain management and facilitates earlier mobilization in TLICS 4 fracture patients. [12] Similarly, Mohamadi et al. reported that posterior instrumentation leads to better pain control and faster return to daily activities, particularly in cases with intermediate injury severity. [13]

In mass disasters, conservative treatment is often the initial approach due to limited resources, logistical constraints, and delays in surgical care. [14] However, several studies have shown that delayed surgical stabilization, when feasible, still provides substantial biomechanical and clinical benefits. [15] Our findings support the use of early surgical intervention when patient and environmental conditions permit, particularly in cases where fracture morphology predisposes to progressive deformity or instability.

Despite the superiority in functional outcomes, radiographic parameters such as Cobb angle, sagittal index, and anterior vertebral height restoration did not differ significantly between the two groups. These findings suggest that conservative management, when carefully selected and closely monitored, can effectively preserve spinal alignment, as supported by Hitchon et al.<sup>[16]</sup> and Wood et al.<sup>[17]</sup> Our results indicate that with appropriate patient selection and close follow-up, nonoperative treatment can be a viable option in resource-limited settings or during disaster situations.

An important observation in this cohort was the higher prevalence of pulmonary complications, particularly in the surgical group. However, these conditions were primarily pre-existing and did not worsen postoperatively. This supports the premise that surgical treatment can be safely performed in patients with pulmonary comorbidities when adequate perioperative care is provided. Previous concerns about elevated risks in this patient population have been addressed in recent literature, which emphasizes the importance of respiratory optimization rather than the avoidance of surgery. [18,19]

Finally, our findings are consistent with recommendations from international spine trauma working groups, which advocate individualized treatment strategies for TLICS 4 fractures, taking into account clinical status, logistical constraints, and comorbidities.<sup>[20,21]</sup>

The limitations of this study include its retrospective design and relatively small sample size, which may affect generalizability. Furthermore, long-term outcomes beyond 12 months were not assessed, and we acknowledge that late complications or deformity progression may alter the final results. Future prospective, multicenter studies with larger cohorts and extended follow-up are needed to confirm these findings and refine treatment protocols in disaster settings.

#### **CONCLUSION**

This study demonstrates that both surgical and conservative treatments are viable options for managing TLICS 4 thoracolumbar fractures in the aftermath of natural disasters. Surgical management offers superior functional outcomes and pain relief when patient condition and available resources allow. However, conservative treatment remains a valid alternative,

particularly in settings with limited surgical capacity or elevated patient risk.

Treatment decisions should be guided by fracture characteristics, systemic health status, and the healthcare system's capacity during and after disasters. Individualized approaches that balance clinical needs with logistical realities are essential for optimizing patient outcomes in these challenging environments.

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**Availability of Data and Materials:** The data used and/ or analyzed during the current study are available from the corresponding author on reasonable request.

**Ethics Committee Approval:** This study was approved by the Ankara Etlik City Hospital Ethics Committee (Date: 25.12.2024, Decision No: Ek1-2024-1221).

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**Authorship Contributions:** Concept: H.G.; Design: H.G., A.E.; Supervision: H.D.; Resource: B.A., M.E.E.; Materials: A.E., H.G.; Data collection and/or processing: A.D., N.B.O.; Analysis and/or interpretation: E.A.; Literature review: A.E.; Writing: H.G., A.E.; Critical review: H.D.

Conflict of Interest: None declared.

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#### ORİJİNAL ÇALIŞMA - ÖZ

# 2023 Türkiye depremi sonrasında TLICS 4 torakolomber kırıkların yönetimi: Konservatif ve cerrahi tedavilerin karşılaştırmalı sonuçları

AMAÇ: Deprem gibi kitlesel afetler, yalnızca primer yaralanmalarla sınırlı kalmayıp, crush sendromu ve diğer sistemik komplikasyonlar gibi ikincil sağlık sorunlarını da beraberinde getirerek tedavi sürecini karmaşıklaştırmaktadır. Bu çalışma, 2023 Türkiye depremi sonrası yaralanan TLICS 4 torakolomber kırıklı hastalarda konservatif ve cerrahi tedavi sonuçlarını değerlendirmeyi amaçlamaktadır. Ayrıca, crush sendromu ile ilişkili komplikasyonların tedavi kararları üzerindeki etkisi incelenmiştir.

GEREÇ VE YÖNTEM: Çalışmada 23 TLICS 4 spinal yaralanmalı hasta, cerrahi (n=12) ve konservatif (n=11) tedavi gruplarına ayrıldı. Yaş, cinsiyet, ameliyat öncesi spinal ölçümler ve I yıllık postoperatif klinik sonuçlar Roland Morris skoru ile değerlendirildi. Kardiyak, renal ve solunum komplikasyonları, enfeksiyonlar ve hastanede kalış süreleri de analiz edildi.

BULGULAR: Cerrahi grup, Roland Morris skorlarında anlamlı daha iyi sonuçlar gösterdi (79.3±12.7 ve 15.0±8.5, p<0.001). Akut böbrek hasarı konservatif grupta daha yaygındı (%36.4 ve %8.3, p<0.05), pulmoner komplikasyonlar ise cerrahi grupta daha sık gözlendi (%83.3 ve %36.4, p<0.05). Yaş, cinsiyet ve diğer komplikasyonlarda anlamlı fark yoktu. Radyolojik sonuçlar (Cobb açısı, sagittal indeks, vertebral yüksekliğin restorasyonu) gruplar arasında farklılık göstermedi. Hastanede kalış süreleri benzerdi.

SONUÇ. Çalışmamız, doğal afet ortamlarında TLICS 4 torakolomber kırıkların konservatif ve cerrahi tedavi ile etkili şekilde yönetilebileceğini göstermektedir. Tedavi kararları, hasta özellikleri ve mevcut kaynaklar dikkate alınarak bireyselleştirilmelidir.

Anahtar sözcükler: Deprem; kırık; omurga; posterior enstrümantasyon; TLICS.

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### Comparison of hematoma block and dexmedetomidine for reduction of distal radius fractures in the emergency department: a prospective randomized controlled study

- © Emin Fatih Vişneci,¹ © Demet Acar,¹ © Ebubekir Eravşar,² © Betül Kozanhan,³ © Osman Lütfi Demirci,¹
- Mehmet Gül<sup>1</sup>

#### **ABSTRACT**

**BACKGROUND:** This study aimed to compare the effects of hematoma block (HB) and dexmedetomidine administration on pain control, reduction quality, and physician satisfaction during the reduction of distal radius fractures (DRFs) in the emergency department (ED).

METHODS: A total of 60 patients presenting to the ED with DRFs were enrolled. Patients were randomly assigned to two groups: one received HB, while the other underwent conscious sedation with dexmedetomidine. Pain levels were assessed using the Visual Analog Scale (VAS) at three time points: before the procedure, 10 minutes after administration of the intervention, and post-reduction. Physician satisfaction during reduction was measured using the 5-point Likert Satisfaction Scale (LSS). Post-reduction quality was evaluated on control radiographs using the Sarmiento criteria.

**RESULTS:** Among the patients included in the study, 28 were female, 19 were male, and 13 were children (<12 years). The mean age was 32.97 $\pm$ 20.48 years in the dexmedetomidine group (DG) and 35.25 $\pm$ 18.92 years in the hematoma block group (HBG), with no statistically significant difference between the groups (t=-0.448, p=0.65). There was no significant difference in physician satisfaction during reduction between the two groups according to LSS results ( $\chi^2$ =2.296, p=0.512). Pre-procedure VAS scores were comparable between the two groups (t=-0.148, p=0.883). However, VAS scores 10 minutes after the intervention were significantly lower in the DG compared to the HBG (p=0.009, t=-2.773). Post-reduction quality based on the Sarmiento criteria showed no significant difference between the groups ( $\chi^2$ =0.64, p=0.89). No adverse effects related to either method were observed in any of the patients.

**CONCLUSION:** Dexmedetomidine provides faster and more effective pain management than HB for DRF reduction in the ED. Given its minimal systemic side effects, dexmedetomidine may represent a viable alternative for procedural sedation and analgesia (PSA) in fracture reductions requiring sedation in the ED.

Keywords: Distal radius fracture; dexmedetomidine; hematoma block; emergency department.

#### INTRODUCTION

Distal radius fractures (DRFs) are among the most common upper extremity fractures presenting to the emergency department (ED), accounting for approximately one-sixth of all

fractures treated there. DRFs typically result from high-energy trauma in young and otherwise healthy individuals, whereas in elderly and osteoporotic patients, they are usually caused by low-energy trauma.<sup>[1,2]</sup>

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Table I.	Sarmianta	Padiological	Score	(Madified	Lidetröm	Critoria)
iable i.	Sarmiento	Kadiologicai	Score	(IMOGITIEG	Liastrom	Criteria

Outcome	Loss of Palmar Tilt	Radial Shortening	Loss of Radial Deviation
Excellent	<0°	<3 mm	<4°
Good	I-10°	3-6 mm	5-9°
Fair	II-14°	7-11 mm	10-14°
Poor	>15°	I2 mm	>15°

The primary goal in the management of DRFs is proper joint reconstruction and alignment of fracture fragments. Consequently, closed reduction followed by casting plays a crucial role in treatment.<sup>[3-6]</sup> The success of reduction depends heavily on patient cooperation, which is directly influenced by the level of pain experienced during the procedure. Pain not only causes discomfort and stress but also compromises the quality of the reduction. Reduction quality in DRFs is commonly evaluated using the Sarmiento criteria (Table 1).<sup>[7]</sup>

Effective sedation and analgesia are essential for ensuring patient compliance. Procedural sedation and analgesia (PSA) is defined as the administration of sedatives or dissociative agents, with or without analgesics, to induce a state that allows patients to tolerate painful procedures while maintaining cardiorespiratory function. PSA is widely used in the ED to minimize patient discomfort during the manual reduction of displaced DRFs outside the operating room.<sup>[8,9]</sup> Benzodiazepines, either alone or in combination with opioid analgesics, are commonly used for PSA in the ED.<sup>[10]</sup> Other sedatives, including etomidate and propofol, are also incorporated into PSA protocols.<sup>[11]</sup> However, conventional PSA agents are associated with significant systemic side effects such as apnea, hypotension, and respiratory depression, which may prolong post-procedure observation in the ED.<sup>[12]</sup>

Hematoma block (HB) involves the direct injection of lidocaine into the fracture hematoma. Due to concerns about PSA-related complications, HB is often preferred for analgesia before DRF reduction. The most immediate adverse effect of HB is an allergic reaction to the local anesthetic, while delayed complications may include compartment syndrome and local infection. Despite its advantages, HB is an invasive technique, and the inherently painful and stressful nature of DRFs, particularly in pediatric patients, often shifts physician preference toward PSA. Furthermore, unlike PSA, HB does not induce muscle relaxation, which can make reduction more challenging. [12,14]

Dexmedetomidine is a selective  $\alpha_2$ -adrenergic agonist with analgesic, sedative, and anxiolytic properties. Its analgesic effects make it useful for procedural and minor surgical interventions. The primary side effects of dexmedetomidine include bradycardia, hypotension, and hypertension. [15,16] Although not yet routinely used in the ED, dexmedetomidine is increasingly employed for sedation in intensive care patients,

non-invasive mechanical ventilation, endoscopic procedures, endoscopic retrograde cholangiopancreatography (ERCP), and various minor surgical interventions.[17-19]

This study aimed to compare dexmedetomidine with hematoma block in terms of reduction success, patient compliance, and physician satisfaction during DRF reduction in the ED.

#### **MATERIALS AND METHODS**

#### **Study Design and Participants**

This prospective randomized controlled study was conducted between June 2024 and December 2024 in a tertiary-level ED. A total of 60 patients presenting with DRFs were randomly assigned to two groups. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki. Ethical approval was obtained from the Clinical Research Ethics Committee of Selçuk University (Approval Date: 04.04.2024, Document No: KAD-FR-42, Decision No: 2024/33).

#### I. Hematoma Block Group (HBG):

Thirty patients diagnosed with DRF based on direct radiographs were randomly assigned to this group. The HB was performed by an emergency physician. Patients were not continuously monitored but had intravenous access maintained in case of potential allergic reactions to the local anesthetic. After disinfecting the dorsal wrist with povidone-iodine, 10 mL of 1% lidocaine solution was prepared for injection. Before administration of the anesthetic into the fracture site from the dorsal aspect of the wrist, an attempt was made to aspirate the hematoma into the syringe. Lidocaine was then injected into the fracture site (Fig. I and 2). Pain was assessed using the Visual Analog Scale (VAS) at three time points: preprocedure (Pre-Method VAS), 10 minutes post-procedure (Post-Method-10 minute VAS), and post-reduction (Post-Reduction VAS). Reduction was performed, and physician satisfaction was evaluated using the Likert Satisfaction Scale (LSS). Reduction quality was assessed on post-reduction radiographs according to the Sarmiento Criteria.

#### 2. Dexmedetomidine Group (DG):

Thirty patients were randomly assigned to receive dexmedetomidine for PSA. Patients were continuously monitored



Figure 1. Fracture site from the dorsal aspect of the wrist.

throughout the procedure, and intravenous access was maintained. Dexmedetomidine (Precedex) was administered at a dose of 0.5-1 µg/kg via intravenous infusion over 10 minutes. In the literature, the Post-Method-10 minute VAS score is typically measured 10 minutes after the infusion of dexmedetomidine, based on studies evaluating its analgesic activity using the VAS.<sup>[20,21]</sup> The same pain assessment protocol was applied in the HBG. Reduction was performed by the orthopedic team, and physician satisfaction was documented. Reduction quality was evaluated using the Sarmiento criteria.

In both groups, the post-reduction VAS score was obtained 10 minutes after the reduction procedure, at the same time point for all patients.

#### **Evaluation Criteria:**

- I. Demographic characteristics
- 2. Pain levels (VAS: 0=no pain, 10=worst pain)
- Pre-Method VAS
- Post-Method VAS (10 minutes)
- Post-Reduction VAS



Figure 2. Injection of lidocaine into the fracture site.

- 3. Reduction quality (Sarmiento classification) (Table 1)
- 4. Physician satisfaction (Likert Satisfaction Scale) (Table 2).

#### **Statistical Analysis**

Categorical variables were expressed as frequencies and percentages, while continuous variables were summarized as means and standard deviations. Differences between groups were analyzed using the t-test, chi-square test, and Mann-Whitney U test, with statistical significance set at p<0.05. The normality of continuous variables was assessed using the Shapiro-Wilk test. Depending on whether statistical assumptions were met, within-subjects tests were used to compare continuous variables between the two groups. All analyses were performed using IBM SPSS Statistics, Version 20.0, with a significance threshold of 0.05.

#### **RESULTS**

A total of 60 patients were included in the study: 28 (46.6%) females, 19 (31.6%) males, and 13 (21.6%) pediatric patients (<12 years). Although the proportion of female patients was higher overall, there was no significant difference in gender distribution between the two groups when pediatric patients were excluded ( $\chi^2$ =0.102, p=0.942). Similarly, no significant

Table 2.	Comparison of hemorrhage, edema, vasocongestion,	inflammation, and Johnsen scores between rat groups

Very Satisfied	Satisfied	Neutral	Dissatisfied	Very Dissatis-fied
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How would you evaluate the patient's compliance with reduction?

How would you evaluate your own comfort during reduction?

Table 3. Comparison between groups by age, gender, Sarmiento criteria, Visual Analog Scale (VAS), and Likert Satisfaction Scale

	Total Patients	Hematoma Block Group (n=20)	Dexmedetomidine Group (n=20)	P Value *	χ² <b>Val</b> ue **	t Value ***
Age (years)		39.95±3.003	41.25±2.92	0.758		0.310
Gender						
Male/Female	16/24	9/11	7/13	0.342	0.902	
Sarmiento						
Criteria				0.868	0.722	
Excellent	17	9	8			
Good	12	6	6			
Moderate	6	2	4			
Poor	5	3	2			
VAS						
Pre-Method VAS		8.65±0.23	8.60±0.24	0.883		-0.148
Post-Method VAS (10 min)		3.5±0.30	2.40±0.25	0.009		-2.773
Post-Reduction VAS		1.7±0.17	1.95±0.19	0.356		0.938
LSS						
(Physician Satisfaction)				0.512	2.296	
Very Satisfied		10	12			
Satisfied		11	10			
Neutral		7	8			
Dissatisfied		2	0			
Very Dissatis-fied		0	0			

difference was found between the groups regarding pediatric patient distribution ( $\chi^2$ =0.10, p=0.75).

The mean age was 32.97±20.48 years in the dexmedetomidine group and 35.25±18.92 years in the hematoma block group, with no significant difference between the groups (t=-0.448, p=0.65).

Each patient underwent three VAS evaluations. Comparisons revealed that in the Pre-Method VAS there was no significant difference between the groups (t=-0.148, p=0.883). In the Post-Method VAS (10 minutes), pain scores were significantly lower in the DG compared with the HBG (t=-2.773, p=0.009). In the Post-Reduction VAS, no significant difference was observed between the groups (t=0.935, p=0.356), although the DG demonstrated a more pronounced reduction in pain 10 minutes after intervention.

Table 3 presents a comparative analysis of age, gender, Sarmiento criteria, VAS scores, and Likert Satisfaction Scale scores between the groups.

Within-subject tests indicated significant changes in VAS scores over time (F=646.585, p<0.001), with these changes being statistically significant in both groups. According to pairwise comparisons:

- In the Dexmedetomidine Group, Pre-Method VAS was 8.6, Post-Method VAS was 2.4, and Post-Reduction VAS was 1.95.
- In the Hematoma Block Group, Pre-Method VAS was 8.65, Post-Method VAS was 3.5, and Post-Reduction VAS was 1.7.

The reduction in pain was more pronounced in the DG (Fig. 3).

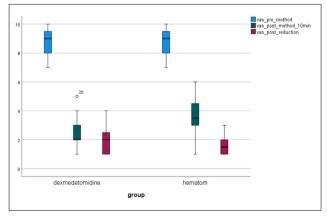


Figure 3. Box plots of Visual Analog Scale (VAS) scores.



**Figure 4.** Pre-reduction radiograph of a 52-year-old female patient with a Type V distal radius fracture (DRF).



**Figure 5.** Post-reduction radiograph of a 52-year-old female patient with a Type V distal radius fracture (DRF).



**Figure 6.** Post-surgical radiograph of a 52-year-old female patient with a Type V distal radius fracture (DRF).

Physician satisfaction was assessed using the Likert Satisfaction Scale:

- HBG: 10 orthopedic surgeons rated the reduction as "very satisfied," 11 as "satisfied," 7 as "neutral," and 2 as "dissatisfied"
- DG: 12 orthopedic surgeons rated the reduction as "very satisfied," 10 as "satisfied," and 8 as "neutral."

There was no statistically significant difference in physician satisfaction between the two groups ( $\chi^2=2.296$ , p=0.512).

Reduction quality was evaluated using the Sarmiento criteria.

- HBG: 13 cases were classified as "excellent," 10 as "good," 4 as "fair," and 3 as "poor."
- DG: 12 cases were classified as "excellent," 10 as "good," 6 as "fair," and 2 as "poor."

No significant difference was observed between the two groups regarding reduction quality ( $\chi^2$ =0.64, p=0.89).

No adverse effects related to either method were observed in any patient. Of the 60 patients included in the study, 12 required surgical intervention, with a mean age of 33.75±21.56 years.

#### DISCUSSION

The lifetime risk of distal radius fractures is 18% in women and 2% in men, primarily due to the higher prevalence of osteoporosis in females. [6] In our study, 46.6% of patients were female, consistent with findings in the literature. Previous studies comparing PSA (typically with benzodiazepines and opioids) with HB in terms of reduction quality (according to the Sarmiento criteria) have shown that PSA results in better reduction quality than HB. [22,23] However, in our study, no significant difference was observed between the DG and the HBG in terms of reduction quality. This discrepancy may be attributed to the consistency of the orthopedic team performing all reductions in our study.

The decision to treat DRFs non-surgically depends on factors such as patient age, comorbidities, and osteoporosis. [24] Among the 12 patients who required surgery, the mean age was higher than that of the overall study population, which aligns with previous reports (Figures 4, 5, and 6 depict prereduction, post-reduction, and post-surgical radiographs of a 52-year-old female patient with a Type V DRF).

A previous study comparing HB and PSA with benzodiaze-pine-opioid combinations found that HB had a superior safety profile. [25]

In our study, all patients had intravenous (IV) access secured prior to the procedure, and patients in the DG were continuously monitored throughout the intervention and reduction process. Additionally, bedside post-reduction radiographs were obtained for DG patients. No early complications re-

lated to either method were observed. Previous studies have suggested that a major advantage of HB over PSA is a shorter ED observation time and hospital stay. [26] However, in our study, the time elapsed after intervention (before reduction), the duration of reduction and casting, radiographic evaluations, and post-procedural monitoring provided sufficient observation time for both the DG and HBG groups. Thus, no significant difference was observed in ED observation time or length of hospital stay between the two groups.

There was also no statistically significant difference between the groups in the distribution of responses on the LSS, which was used to assess procedural ease and physician satisfaction during reduction. Similar findings have been reported in studies comparing PSA with agents other than dexmedetomidine against HB.<sup>[27]</sup> Pain sensitivity is typically higher in pediatric patients than in adults, making PSA the preferred option for fracture reduction in children. The use of dexmedetomidine in pediatric PSA has increased significantly in recent years.<sup>[14]</sup> Thus, dexmedetomidine may represent a promising alternative for pediatric procedural sedation in the ED, particularly for minor surgical procedures and fracture reductions.

One study comparing HB and PSA (with benzodiazepines and opioids) for pain control in DRFs found HB to be more effective. [28] However, another study reported no significant difference between the two methods. [13]

In our study, baseline VAS scores were similar between the two groups (t=-0.148, p=0.883).

However, 10 minutes post-intervention, VAS scores were significantly lower in the DG compared to the HBG (t=-2.773, p=0.009). Recent studies support our findings, showing that HB provides moderate analgesia at the wrist level but is ineffective for pain experienced in the fingers.<sup>[29]</sup> Another study reported that HB was ineffective for post-operative pain control in pediatric supracondylar humerus fractures and recommended the use of non-opioid PSA agents instead.<sup>[30]</sup> Furthermore, multiple studies have demonstrated that dexmedetomidine provides faster and more effective analgesia than traditional PSA agents such as benzodiazepines and opioids.<sup>[31,32]</sup>

To date, no study has directly compared the analgesic effects of dexmedetomidine and HB. Our study is the first to assess their analgesic efficacy in DRF reduction, demonstrating that dexmedetomidine provides stronger and faster pain relief than HB. This finding is of particular importance for guiding future research.

#### **CONCLUSION**

Procedural sedation and analgesia play a crucial role in fracture reduction and minor surgical procedures in the ED. Our findings indicate that dexmedetomidine is superior to HB for pain control, suggesting its potential future integration into standard PSA protocols for DRF reduction and other ortho-

pedic procedures.

**Ethics Committee Approval:** This study was approved by the Selçuk University Ethics Committee Ethics Committee (Date: 04.04.2024, Decision No: 2024/33).

Peer-review: Externally peer-reviewed.

**Authorship Contributions:** Concept: E.F.V., D.A., E.E.; Design: E.F.V., B.K., M.G.; Supervision: E.F.V., D.A.; Resource: E.F.V., O.L.D., D.A.; Materials: E.F.V., B.K.; Data collection and/or processing: E.F.V., M.G., D.A.; Analysis and/or interpretation: E.F.V., D.A., E.E.; Literature review: E.F.V., O.L.D.; Writing: E.F.V., D.A., B.K.; Critical review: E.F.V., M.G.

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#### ORİJİNAL ÇALIŞMA - ÖZ

# Acil serviste distal radius kırıklarının redüksiyonunda hematom bloğu ile deksmedetomidin kullanımının karşılaştırılması: Prospektif randomize kontrollü bir çalışma

AMAÇ: Distal radius kırıklarının (DRKs) redüksiyonu öncesinde yapılan hematom bloğu (HB) ile deksmedetomidin uygulamasının ağrı kontrolüne, redüksiyon kalitesine ve doktor memnuniyetine olan etkilerini karşılaştırmayı amaçladık.

GEREÇ VE YÖNTEM: Çalışmamıza acil servise (AS) başvuran DRK'lı 60 hasta dahil edildi. Hastalar rastgele iki gruba ayrıldı. İlk gruba HB, ikinci gruba ise deksmedetomidin ile bilinçli sedasyon uygulandı. Her iki grupta ağrı düzeyleri; Görsel Analog Skala (VAS) ile, yöntem öncesi, yöntemden 10 dakika sonra ve redüksiyon sonrası olmak üzere her bir hasta için 3 kez değerlendirildi. Redüksiyonu yapan doktorların redüksiyon sırasındaki konfor ve memnuniyetleri 5'li Likert Memnuniyet Ölçeği (LMÖ) kullanılarak ölçüldü. Redüksiyon sonrası kontrol direk grafi ile Sarmiento kriterlerine göre redüksiyon kalitesi değerlendirildi.

BULGULAR: DRK ile AS'ye başvuran hastaların 28'i kadın, 19'u erkek, 13'ü çocuk (<12 yıl) idi. Hastaların yaş ortalaması; deksmedetomidin grubunda (DG) 32.97 $\pm$ 20.48, hematom bloğu grubunda (HBG) 35.25 $\pm$ 18.92 idi. İki grup arasında yaş ortalaması açısından anlamlı fark yoktu (t=-0.448, p=0.65). Redüksiyon sırasındaki hasta uyumuna ilişkin doktor memnuniyetinin değerlendirildiği LMÖ sonuçlarında iki grup arasında anlamlı fark bulunmadı ( $\chi^2$ =2.296, p=0.512). Yöntem öncesi VAS değerleri açısından da iki grup arasında anlamlı fark yoktu (t=-0.148, p=0.883). Yöntem sonrası 10. dakikadaki VAS değerleri ise DG'de, HBG'ye göre anlamlı derecede düşüktü (t=-2.773, p=0.009). Bununla birlikte, Sarmiento kriterlerine göre değerlendirilen redüksiyon kalitesinde iki grup arasında anlamlı fark yoktu ( $\chi^2$ =0.64, p=0.89). Her iki gruptaki hastaların hiçbirinde uygulanan yönteme bağlı yan etki görülmedi.

SONUÇ: Deksmedetomidin AS'de DRK redüksiyonu öncesinde hızlı ve etkili ağrı yönetimi ve hasta memnuniyeti açısından HB'ye üstün, etkili bir yöntemdir. Sistemik yan etkilerinin az olması nedeniyle de, prosedürel sedasyon ve analjezi (PSA) gerektiren kırık redüksiyonlarında AS'de rutin olarak kullanılabilecek alternatif bir PSA yöntemi olabilir.

Anahtar sözcükler: Acil servis; distal radius kırığı; deksmedetomidin; hematom bloğu.

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# Clinical and radiological outcomes of bioactive glass in the treatment of benign bone tumors: a retrospective study of 64 cases

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#### **ABSTRACT**

**BACKGROUND:** Benign and benign-aggressive bone tumors, though non-metastatic, may require surgical intervention due to pain, fracture risk, or functional impairment. In many cases, bone grafting may be required in benign or benign-aggressive bone tumors. Although autografts remain the gold standard, they present disadvantages, especially in pediatric patients. Synthetic alternatives such as bioactive glass (BG) have emerged as viable options. This study aims to evaluate the clinical and radiological outcomes of BG in the treatment of benign bone tumors.

METHODS: This retrospective single-center study evaluated 64 patients (71 procedures) treated with curettage and BG grafting for benign bone tumors between 2004 and 2023. Functional outcomes were assessed using the Musculoskeletal Tumor Society (MSTS) score, and radiological healing was evaluated using the Neer classification.

**RESULTS:** The mean follow-up was 25.0±12.6 months. Significant improvement was observed in MSTS scores (from 17.6±4.8 to 28.1±2.0; p<0.05). Neer classification indicated high union rates. Complications included tumor recurrence in four patients (five procedures), fractures in nine patients, and superficial infections in four patients. No deep infections or any other material-related adverse effects were reported.

**CONCLUSION:** Bioactive glass is a safe and effective bone substitute for managing benign bone defects, especially in pediatric populations where autograft options are limited. Its osteoconductive durability, infection resistance, and compatibility with bone remodeling make it a strong alternative to traditional grafting techniques.

**Keywords:** Bioactive glass; benign bone tumors; pediatric bone tumors.

#### **INTRODUCTION**

Benign and benign-aggressive bone tumors are non-invasive, non-metastatic lesions that can affect individuals at any age. While some cases may resolve spontaneously with conservative treatment, some cases require surgical intervention.

Treatment options for these tumors include corticosteroid injections, curettage with or without bone grafting and fixation, percutaneous sclerotherapy, and wide excision with or without reconstruction.

Curettage is among the most selected surgical options with low complication rates. However, post-curettage bone defects

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Table 1. Demographics of patients			
	N	%	
Gender			
Male	45	70.3	
Female	19	29.7	
Side			
Left	32	45.1	
Right	39	54.9	
	Mean±SD (M	1in-Max)	
Age (years)	19.1±13.3 (3	3.4-65.2)	
Follow-up (months)	25.0±12.6 (	(12-72)	

often require filling. Even though autografts are the gold standard option due to their osteoinductive and osteoconductive features, they pose several drawbacks: prolonged operative time, donor-site morbidity, the need for a second surgical site, and limited harvest volume—particularly problematic in pediatric patients and large defects. [1] As a result, the orthopedic community has explored alternative bone substitutes, including allografts, xenografts, and synthetic materials.

Most non-autogenous bone substitutes have no osteoinductive effect and may result in non-union or delayed union. Bioactive glass (BG), however, is a synthetic graft that possesses osteoinductive, osteoconductive, and antimicrobial properties, making it a promising solution for bone defects across age groups.<sup>[2-4]</sup>

The purpose of this study is to evaluate the clinical and radiological outcomes, as well as potential complications, associated with the use of BG in bone defects following curettage of benign and benign-aggressive bone tumors.

#### **MATERIALS AND METHODS**

This retrospective single-center study included patient records between 2004 and 2023. Institutional Review Board (IRB) approval was obtained (IRB file date and number: 06/25//2025 - E-10840098-202.3.02-3962). This study was conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from all patients or their legal guardians.

A total of 77 patients underwent curettage and BG grafting for benign bone tumors. Ten patients were lost to follow-up, and three patients were excluded due to intraoperative suspicion of malignancy confirmed by frozen section. Only patients who received BG as the sole grafting material were included. The final cohort comprised 64 patients who underwent 71 surgical procedures. Descriptive statistics are presented in Table 1.

All surgeries were performed by the same two orthopedic surgeons (AS and LE). The surgical approach typically involved creating a cortical window to access the lesion. Curettage was performed using a high-speed burr, followed by chemical cauterization with 5% phenol. After thorough irrigation, the cavity was filled with BG granules. The cortical window was replaced, and fixation was performed using plates or intramedullary nails when cortical support was insufficient. Case examples for the tibia, femur, and humerus are shown in Figures 1, 2, and 3.

All patients underwent preoperative magnetic resonance imaging (MRI) and biopsy. Follow-up assessments occurred at 6 weeks, 3 months, I year, and up to 3 years postoperatively. Functional outcomes were evaluated using the Musculoskeletal Tumor Society (MSTS) score (range 0–30), and radiological healing was assessed with the Neer cyst classification. Standard biplanar radiographs were obtained at each visit.

The MSTS scoring system evaluates patients functionally and ranges from 0 to 30 points, with 0 indicating total functional loss and 30 indicating no functional impairment.<sup>[5]</sup> The Neer radiographic classification system evaluates bone healing in four categories: healing, healing with defect, persistent cyst, and recurrent cyst (Table 2).<sup>[6-8]</sup>

#### **Statistical Analysis**

All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., NY, USA). Descriptive statistics were used to summarize patient demographics, lesion characteristics, and clinical outcomes. Continuous variables were presented as means with standard deviations and ranges. To evaluate the change in functional outcomes, a paired-sample t-test was used to compare preoperative and postoperative Musculoskeletal Tumor Society scores. A p-value of less than 0.05 was considered statistically significant.

Table 2. Neer	cyst classification	
Category	Description	Details
Α	Healed	Cyst filled with new bone with small radiolucent area (<1 cm)
В	Healed with Defect	Radiolucent area (<50% diameter) with sufficient cortical thickness
С	Persistent Cyst	Radiolucent area (>50% diameter) with thin cortical rim
D	Recurrent Cyst	Cyst reappears in the obliterated area or increased residual radiolucent area

	N	%
Location		
Humerus	18	25.35
Radius-Ulna	4	5.63
Hand	3	4.22
Femur	21	29.57
Tibia	6	8.45
Foot-Ankle	8	11.26
Other	- 11	15.49
Type of Lesion		
Unicameral Bone Cyst	22	30.98
Aneurysmal Bone Cyst	13	18.3
Chondroblastoma	5	7.04
Enchondroma	6	8.45
Non-Ossifying Fibroma (NOF)	8	11.26
Fibrous Dysplasia	7	9.85
Langerhans Cell Histiocytosis	4	5.63
Intraosseous Lipoma	3	4.22
Desmoplastic Fibroma	1	1.41
Osteoblastoma	1	1.41
Spindle Cell Tumor	1	1.41

#### **RESULTS**

The study included 64 patients (45 males, 19 females). The mean age was 19.1±13.3 years (range: 3.4-65.2). The mean follow-up period was 25.0±12.6 months (range: 12-72 months). A total of 71 surgeries were conducted at the final follow up; one patient had three surgeries for recurrence of unicameral bone cysts; three patients had two surgeries for recurrence of bone cysts; and two patients had two surgeries for different types of tumors and different locations.

The femur and humerus were the most commonly affected bones. The most frequent lesion types were unicameral bone cysts and aneurysmal bone cysts, followed by non-ossifying fibromas (Table 3).

Functional outcomes were evaluated with MSTS and showed significant improvement at the final follow-up. Preoperative and postoperative MSTS scores were 17.6±4.8 vs. 28.11±2.0, respectively (p<0.05) (Table 4). Radiographic evaluation using the Neer classification indicated high union rates, with most cases classified as healed or healed with defect (Table 4).

The main undesirable complication was recurrence of the tumor, which required reoperation. Five operations in four patients were performed for recurrence. All four patients had fair results, and no recurrence was seen after reoperation during the follow-up period. The most common complication

**Table 4.** Outcomes and complications of curettage and bioactive glass (BG) treatment

Outcomes	Mean±SD	P¹
MSTS		
Preoperative	17.6±4.8	<0.05
Postoperative	28.11±2.0	
	N	%
Neer Cyst Classification		
1	38	53.5
2	20	28.17
3	9	12.67
4	4	5.63
	Mean±SD	Min-Max
Osseointegration seen on	4.3±0.8	3-6
X-ray (months)		
Complications	Present	Absent
Recurrence	5	66
Postoperative Fracture	9	62
Surgical Site Infection	4	67

was fracture, which occurred in nine patients (Table 4). Surgical site infection was seen in four patients and treated with oral antibiotics. No deep infections or graft-related adverse effects were reported.

#### **DISCUSSION**

This study demonstrates that BG is an effective alternative to autografts and other allograft options in the management of benign bone tumors. Its osteoconductive, osteoinductive, and antimicrobial properties contribute to favorable clinical and radiological outcomes, especially in cases of benign and benign-aggressive bone tumors.

For over ten decades, many surgeons have searched for an appropriate bone substitute material. [9] The main aim has been to find an alternative material to autogenous bone that mimics the same features of osteoinduction and osteoconduction, since the harvesting of autogenous bone has many disadvantages. Hench et al. [10] introduced BG in 1967, proposing that glass containing calcium and phosphorus could be biocompatible in bone defects.

Bioactive glass has a slow resorption rate.<sup>[11]</sup> Autogenous bone grafts, in contrast, diminish more rapidly than BG, and their osteoconductive features may disappear in the short term. Lindfors et al.<sup>[12]</sup> compared BG and autograft and demonstrated a significant difference at 12 and 24 months in terms

of cavity volume. The granules of BG disappear gradually by surface reaction and osteoclastic activity, generally within I-4 years depending on the cavity size.<sup>[12]</sup> There is also evidence of the osteoinductive capacity of BG when used alone.<sup>[2,12-15]</sup> In conclusion, the long-term osteoconductive effect of BG may influence and improve its osteoinductive capacity during that period.

In our study, BG showed no resorption during the median 25-month follow-up period in any patient. This suggests that BG granules consistently support bone defects from the time of surgery through at least the second year.

In addition to its bone-healing properties, BG offers resistance to infection, which is particularly beneficial in contaminated bone defects or compromised surgical fields. The antimicrobial feature of BG is a unique property among bone grafting materials and can also be used in contaminated bone defects. [2.4,16-18] Studies have demonstrated that BG is a well-tolerated graft option with a lower risk of infections, and no material-related adverse effects have been observed during or after clinical use. [12,19,20]

Deep infection requiring surgical intervention or debridement was seen in none of the patients in our study cohort. Even though benign bone tumors are considered sterile lesions, the absence of postoperative deep infection in this study may be attributed to the antimicrobial feature of BG.

Another advantage of BG is that it can be used with good results even in children, without disturbing the remodeling capacity of the bone. [19] Most benign bone cysts and tumors are treated in childhood. Younger children may not be suitable for autograft options due to the limited harvesting capacity of autografts.

In our study, participants were mostly below the age of 18, with the minimum age being 3.4 years. Results demonstrate that even in children, BG has high union rates with no or minimal complications. Therefore, BG should be considered an alternative to autograft, especially at early ages.

The advantage of dissolution over long periods may become a disadvantage in some cases. BG is not suitable for clinical application if the applied region must be operated on within a short period after the primary operation, especially if drilling is needed.

Bioactive glass resembles other types of glass in terms of mechanical strength. It is fragile, rigid, and mechanically weak. Due to BG's mechanically weak structure, in cases with insufficient cortical support, osteosynthesis may be required at the end of the procedure.

Most of our cases underwent only curettage and grafting with BG. A limited number of cases had insufficient cortical support, which required osteosynthesis. Only four patients experienced tumor recurrence, which did not require any implantation before or after the recurrence. It should be noted

that if there is a high risk of recurrence and/or a need for implantation after the primary surgery may arise, BG should be considered a second choice.

Our study has several limitations. The retrospective design of the study introduces selection bias and limits control over the cohort. Even though all patients had benign bone lesions, the types of lesions and their locations varied and may have affected the results with different recurrence rates and complications. Another main limitation of our study is the heterogeneity of age, which potentially influenced the union rate and union period. Lastly, the median two-year follow-up period may not demonstrate long-term complications, especially recurrence of the lesion.

#### CONCLUSION

In conclusion, BG has many advantages over autograft and other non-autogenous graft options. Our study demonstrated fair results with high union rates and MSTS scores post-operatively, along with low recurrence rates. Especially in the younger population, BG is a safe and reliable bone grafting option that should be considered in benign bone defects.

**Ethics Committee Approval:** This study was approved by the Istanbul Medipol University Ethics Committee (Date: 25.06.2025, Decision No: E-10840098-202.3.02-3962).

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#### ORİJİNAL ÇALIŞMA - ÖZ

# İyi huylu kemik tümörlerinin tedavisinde biyoaktif camın klinik ve radyolojik sonuçları: 64 vakanın retrospektif çalışması

AMAÇ: İyi huylu ve agresif iyi huylu kemik tümörleri, metastatik olmasalar da ağrı, kırık riski veya fonksiyonel bozukluk nedeniyle cerrahi müdahale gerektirebilir. Bu olgularda cerrahi tedavi sırasında kemik grefti kullanılabilir. Otogreftler altın standart olarak kabul edilse de, özellikle pediatrik hastalarda dezavantajlı olabilir. Biyoaktif cam (BG), bu gibi durumlarda uygulanabilir bir alternatif olarak öne çıkmaktadır. Bu çalışmada, iyi huylu kemik tümörlerinin tedavisinde BG'nin klinik ve radyolojik sonuçları değerlendirildi.

GEREÇ VE YÖNTEM: Bu retrospektif, tek merkezli çalışmada 2004-2023 yılları arasında iyi huylu kemik tümörleri için küretaj ve BG grefti ile tedavi edilen 64 hasta (71 cerrahi işlem) incelendi. Fonksiyonel sonuçlar Musculoskeletal Tumor Society Score (MSTS) ile, radyolojik iyileşme ise Neer sınıflandırması ile değerlendirildi.

BULGULAR: Ortalama takip süresi 25.0±12.6 aydı. MSTS skorlarında anlamlı iyileşme saptandı (17.6±4.8'den 28.1±2.0'a; p<0.05). Neer sınıf-landırmasına göre yüksek kaynama oranları elde edildi. Komplikasyonlar arasında 4 hastada (5 cerrahi işlemde) tümör nüksü, 9 hastada kırık ve 4 hastada yüzeyel enfeksiyon gözlendi. Derin enfeksiyon veya materyale bağlı başka olumsuz bir sonuç bildirilmedi.

SONUÇ: BG, özellikle otogreft seçeneklerinin sınırlı olduğu pediatrik popülasyonda, iyi huylu kemik defektlerinin tedavisinde güvenli ve etkili bir greft alternatifidir. Osteokondüktif özellikleri, enfeksiyon direnci ve kemik remodelingi ile uyumluluğu sayesinde geleneksel greftleme tekniklerine güçlü bir seçenek oluşturmaktadır.

Anahtar sözcükler: Biyoaktif cam; çocuk kemik tümörleri; iyi huylu kemik tümörü.

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