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ABOUT

The Journal of Cardio-Vascular-Thoracic Anaesthesia and Intensive Care Society (GKDAYB Journal) is an official scientific journal of Cardio-Vascular-Thoracic Anaesthesia and Intensive Care Society journal (GKDA-YBD).

AIM AND SCOPE

The purpose of the journal; to publish clinical and experimental studies including new developments related to anesthesia and intensive care of the chest, heart and vascular surgery.

The journal publishes clinical and experimental studies, case reports, editorial letters, review articles and reports of scientific meetings related to fields of Thoracic, Cardiovascular Anesthesia and Intensive Care the both in English, Review articles written upon request of the editor are not accepted.

The journal is published every three months namely in March, June, September and December. One volume is completed after publication of 4 issues (one year). GKDAYB is an open access, free and peer-reviewed journal and all published content is freely available at www.gkdaybd.org Printed copies are distributed to members of the Cardio-Vascular-Thoracic Anaesthesia and Intensive Care Society free of charge.

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Journal of The Cardiovascular Thoracic Anaesthesia and Intensive Care Society

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Research Article

Incidence of Chronic Neuropathic Pain After Open-heart Surgery: A Retrospective Cohort Analysis

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ABSTRACT

Objectives: Chronic sternal pain has been reported in 11%–56% of patients 1 year after cardiac surgery with median sternotomy. However, chronic pain after sternotomy can frequently be ignored.

Methods: Patients who received open-heart surgery between January 2020 and June 2022 were included. Data analysis was performed through file scans, hospital data processing system and patient follow-up documents, phone calls, and algology outpatient clinic records. T For the assessment of neuropathic pain, the Turkish version of the pain scale, for which validity and reliability studies were conducted, was employed.

Results: When all patients were analyzed, the incidence of chronic pain was 28.7%, and the incidence of chronic neuropathic pain was 14.7%. There was no difference in age, gender, education level, time after surgery, and smoking. Although the BMI was higher in the group with neuropathic pain when compared, there was no statistically significant difference. The presence of Diabetes Mellitus (DM) diagnosis was statistically significant in the group that created the neuropathic pain group, and no discernible difference was found in terms of other additional diseases. The rate of patients with preoperative angina was discovered to be higher in the neuropathic pain group (p: 0.030). When the type of surgery, urgency, and need for revision were compared, no significant difference was observed between the two groups. When both groups were compared in terms of l the duration of hospital stay was discovered to be longer in the neuropathic pain group (17 [15–19] days, p:0.046).

Conclusion: The incidence of chronic neuropathic pain was estimated to be 14.7%, and it was shown that the presence of DM, preoperative angina, and the long hospital stay might be factors contributing to the development of chronic neuropathic pain.

Keywords: Cardiac surgery, chronic pain, neuropathic pain, sternotomy

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Introduction

Chronic poststernotomy pain is characterized as nonanginal postoperative pain lasting longer than 3 months following median sternotomy. Allodynia, discomfort, hypoesthesia, and chronic pain are some of the possible symptoms.[1]

It has been reported that 11%–56% of patients have chronic sternal pain 1 year after cardiac surgery with median sternotomy.[2,3] Based on the Society of Thoracic Surgery database in the United States, more than 280,000 patients underwent cardiac surgery annually, and 156,800 patients have sternotomy-related chronic pain in the first year after surgery.

However, prolonged sternotomy pain is often ignorable. Chronic sternotomy pain can negatively influence the quality of life by interfering with sleep, mood, activity level, and overall satisfaction if not carefully identified, and treated.[4] There are several causes of pain following thoracotomies or sternotomies, including entrapment neuropathy, muscular damage, sternal pseudoarthrosis, and sternal wires. In addition to postoperative infection, damage to the intercostal nerves during dissection of the internal mammary artery has been identified as a potential contributing factor.[5]

The purpose of this research is to investigate the prevalence of chronic neuropathic pain and potential predispos-

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ing factors among patients who have received open-heart surgery in our hospital during the last three years.

Methods

The research was planned as a retrospective cohort study following the Helsinki Declaration. After approval by the Ethics Committee of our hospital (November 24, 2022, decision number 0528), patients who had undergone open-heart surgery at Katip Çelebi University Atatürk Education and Research Hospital between January 1, 2020, and July 1, 2022, were included in the study.

Data analysis was conducted using the hospital's data system, including patients' follow-up records, telephone calls, and file records from the algology outpatient clinic. Data from patients whose pain scores were not followed up or reported, who did not want to participate in the research, or who died were considered incomplete data, and data from these individuals were removed from the analysis.

Pain assessment: The Turkish version of the S-LANSS (Self-Leeds Assessment of Neuropathic Symptoms and Signs) pain scale was used to evaluate neuropathic pain. The S-LANSS pain scale consists of 7 items. There is a dual rating type (yes, no). Patients can score between 0 and 24 on the test. While the test supports neuropathic pain in patients with scores of 12 and higher, it supports nociceptive pain in patients with scores below 12.

Grouping and data collection: patient demographics, comorbidities, BMI, type of surgery, history of prior Covid- 19 infection, presence of preoperative neuropathic pain diagnosis, history of covid vaccine, length of hospital stay, hospital and ICU stay were acquired from patient records. Patients were interviewed by telephone or in the algology outpatient clinic utilizing the S-LANSS scale. Those with an S-LANSS score >of 12 points were defined as the neuropathic pain group. Comparing the prevalence and risk variables with the patient population of those without neuropathic pain.

Patients younger than 18 years, who passed away after surgery, who were unable to be reached by telephone, who had been previously diagnosed with neuropathic pain, or who were taking a drug from the group of drugs used to treat neuropathic pain were removed from the study.

Statistical analyzes were conducted using IBM SPSS Statistics for Windows (version 22.0; IBM Corp., Armonk, NY, USA). Descriptive statistics were represented by mean and standard deviation or median-(IQR) for continuous variables and numbers and percentages for categorical variables. Before all analyses, skewness and kurtosis values, the Shapiro-Wilk test, and histogram plots were employed to check whether the data conformed to the normal distribution. T-test for independent variables or dependent variables T-test for variables with normal distribution to examine the differences in means between groups; the Mann–Whitney U test was employed for the variables that did not conform to the normal distribution. The chi-square test or Fischer exact test was utilized to evaluate differences in categorical variables between groups. $p<.05$ was regarded as statistically significant in all analyses.

Results

Data from a total of 129 patients were added to the study. When all patients were analyzed, the incidence of chronic pain was 28.7% and the incidence of chronic neuropathic pain was 14.7%. Table 1 provides details on the demographics, comorbidities, prior surgeries, and hospitalizations of all patients.

Compared with the patient group with neuropathic pain, no difference was observed in the patient group without neuropathic pain in terms of age, sex, education level, time following surgery, and smoking. BMI was higher in the group with neuropathic pain when it was compared, but no statistically significant difference was discovered. When the patients with neuropathic pain were analyzed for their comorbidities, it was observed that the presence of DM was statistically significant compared to the group without neuropathic pain ($p=0.048$); no significant difference was identified for the other comorbidities. The prevalence of patients with preoperative angina was greater in the group with neuropathic pain ($p=0.030$). When comparing the type of surgery, urgency, and need for revision, no discernible difference was observed between the two groups. When comparing the two groups in terms of length of stay in the ICU and hospital, it was discovered that the length of hospital stay was longer in the neuropathic pain group (17 [15–19] days, $p=0.046$) (Table 2).

Discussion

In the current study, evaluating data from 129 patients, we observed that the incidence of chronic pain was 28.7% and the incidence of chronic neuropathic pain was 14.7%. A diagnosis of DM, preoperative angina, and a longer hospital stay were all associated with a higher rate of development of chronic neuropathic pain in those patients.

Pain after chronic sternotomy may result in a variable clinical condition influencing one or more sites. Chronic pain related to cardiac surgery most frequently occurs in the anterior chest wall in patients, although chronic pain may also occur in the upper and lower extremities, neck, and back. This describes the potential challenges in accurately diagnosing chronic pain after median sternotomy. The literature reports a wide range of median incidences of

Table 1. Demographic, comorbidity and surgical data of all patients

Demographic data	n=129	%
Age (years)	60±10	
Gender		
Female	29	22.5
Male	100	77.5
Educational status		
Illiterate	11	8.5
Primary education	80	62
High school	23	17.8
University	15	11.6
Post-surgery time		
3–6 months	1	0.8
6 months–1 year	39	30.2
>1 year	89	69
Body mass index	27±3	
Smoking	28	21.7
Preoperative angina	39	30.2
Emergency surgery	11	8.5
Type of surgery		
CABG	80	62
Valve replacment	15	11.6
CABG+Valve	34	26.4
Saphenous graft	86	66.7
Internal mammarian artery graft (IMA)	54	41.9
Revision surgery (resternotomy)	19	14.7
Chronic pain	37	28.7
Chronic Neuropathic pain	19	14.7
Analgesic usage	11	8.5
Pain location		
Sternum	28	21.7
Saphenous	14	10.9
Intercostal	5	3.9
Comorbidity		
Hypertension (HT)	79	61.2
Diabetes Mellitus (DM)	54	41.9
Coronary Artery Disease	97	75
COPD	22	17
Thyroid dysfunction	12	9.3
Malignancy	5	3.9
Chronic renal failure	5	3.9
Chronic liver disease	5	3.9
Covid-19 infection	43	33.9
ICU stay (days)	3 (3–4)	
Hospital stay (days)	14 (12–17)	

n, %, n ±SD , median (25^{th}-75^{th} percentile). CABG: Coronary artery bypass graft; COPD: Chronic obstructive pulmonary disease; ICU: Intensive care unit.

chronic pain following sternotomy, from 11% to 56% 1 year after surgery. Moreover, the number of patients reporting the development of chronic pain reduces over time. Several factors, including differences in the definition and diagnosis of pain after chronic sternotomy, variations in surgical methods and techniques, additional medical and psychological issues that may impact the ability to manage pain, physical and emotional stress, and individual patient-specific factors may contribute to this increased incidence, which is considered variable in the literature. The prevalence of chronic pain following cardiac surgery may be influenced by heterogeneity in study designs.[6]

The emergence of persistent sternotomy-related discomfort may be influenced by age. A higher incidence of chronic postoperative pain, as well as higher pain intensity, has been observed in patients older than 70 years compared with younger patients.[7] In a recent multicenter retrospective analysis, although no difference was seen in the incidence of chronic pain 3 months and 1 year after surgery, a considerably greater incidence of chronic pain 3 years after surgery was observed in patients older than 75 years.[1] However, in our research, no significant difference was discovered between the mean age of the two groups. Nevertheless, because the period following open-heart surgery was 2 years or less, the findings addressing the incidence of developing discomfort after chronic sternotomy in the long-term are unknown in the research group of patients.

Gender may also contribute to the development of chronic pain. After sternotomy, women are more likely to suffer from chronic sternal discomfort in the first year. According to reports, this difference was not there a year following surgery.[8] In the WREST -E study, which particularly analyzed the incidence of chronic pain after sternotomy in women, an incidence of 47% was reported 1 year after surgery; these findings were greater than in previous studies involving both men and women.[9] In our research, no considerable difference in the development of neuropathic pain was found when comparing the gender. Similar to other risk factors for the development of chronic pain, the evidence for gender as a predictor is not satisfactory, as other studies have not demonstrated a consistent relationship between patient gender and chronic pain. The lower percentage of female patients who received cardiac surgery and were included in these studies may describe the variable impact of gender on pain.[10]

In our study, patients' comorbidities were compared between those with and without chronic neuropathic pain. DM was observed to be more prevalent in the group with chronic neuropathic pain. However, no significant difference was observed between the groups in terms of other comorbidities. According to the research, people with hypothyroidism are more likely to experience chronic discomfort following sternotom. Hypothyroidism is thought to contribute to neuropathic pain, although the precise underlying mechanism is still unclear. It has been proposed that demyelination, ami-

Table 2. Comparison of patients with and without chronic neuropathic pain

Comparison between groups	Neuropathic pain n=19	No-Neuropathic pain n=110	p
Age	56±13	60±10	0.141
Gender			
Female/Male	7/12	22/88	0.135
Educational status			
Illiterate	4	7	0.150
Primary education	10	70	
High school	4	19	
University	1	14	
Post-surgery time			
3–6 months	15	74	0.573
6 months–1 year	4	35	
>1 year	0	one	
Body mass index	28±3	27±2	0.070
Smoking	6	22	0.364
Emergency surgery	2	9	0.257
Preoperative angina	10	29	**0.030***
Pain location			
Sternum	14		
Saphenous	7		
Intercostal	3		
Type of surgery			
CABG	12	68	0.288
Valve replacment	3	12	0.345
CABG+Valve	4	30	0.279
Saphenous graft	12	74	0.794
Internal mammarian artery graft (IMA)	12	42	0.592
Revision Surgery (resternotomy)			
Yes/no	1	18	0.304
Comorbidity			
Hypertension (HT)	12	67	1
Diabetes Mellitus (DM)	12	42	**0.048***
Coronary Artery Disease	14	83	0.869
COPD	2	20	0.526
Thyroid dysfunction	2	10	0.690
malignancy	2	4	1
Chronic renal failure	1	4	1
Chronic liver disease	2	3	0.157
Covid-19 infection	8	35	0.443
ICU stay (days)	4 (3–4)	3 (3–4)	0.496†
Length of stay in hospital (days)	17 (15–19)	14 (12–16)	**0.046†**

n, n ±SD , median (25^{th}-75^{th} percentile). Chi-square Test, Student's t-test. *: Mann–Whitney U test; †: p<0.05 (significant values are in italics and bold). CABG: Coronary artery bypass graft; COPD: Chronic obstructive pulmonary disease; ICU: Intensive care unit.

noglycan buildup, and regional hypoxia causing muscular spasms are the causes of the relationship between hypothyroidism and the emergence of chronic pain.[11,12]

The likelihood of developing chronic pain is higher in patients with preoperative chronic pain, particularly those taking opioids and describing angina before surgery.[7] Although a theoretical link has been proposed, it is unclear whether preexisting pain syndromes due to genetic predispositions or other risk factors confer a greater risk of chronic pain or whether the presence of chronic pain before surgery is causally related to postoperative pain through central sensitization and other mechanisms.[13] In our study, findings for the presence of pre-

operative angina were consistent with those documented in the literature. Patients with a previous diagnosis of chronic pain syndrome were removed from the study.

In the WREST -E study, it was found that the incidence of chronic sternal or chest pain increases in obese patients with large chest circumferences.[9] According to a different study, obesity, which is linked to a larger chest circumference in both men and women, increases the likelihood of chronic pain following sternotomy.[7] In the present study, chronic neuropathic patients were compared in terms of BMI, and no considerable difference was found.

Although the impact of the type of surgical intervention is unclear, the requirement for urgent surgical intervention is one of the strongest predictors of the development of chronic pain.[8] Emergency surgery may be connected with greater local tissue trauma due to the more rapid incision, sternotomy, and cannulation strategies. This may increase the development of chronic pain. Although clinical studies on the occurrence of chronic pain after other emergency methods can be observed in the literature, limited data are available because emergency procedures are typically excluded from studies examining risk factors for chronic pain after sternotomy. Further studies including analysis of emergency cardiac surgery are required to characterize this risk.[8,13] When comparing the two groups, our study observed no significant difference in the type and urgency of the procedure.

Brachial plexus injury following median sternotomy primarily influences C8-T1 nerve roots and is related to pain, dysesthesia, and motor deficit in the hand. In most patients, symptoms resolve within 1 week; however, approximately 1% of patients may develop permanent pain or sensory deficit.[14] No brachial plexopathy was found in our patients included in the study.

The incidence of chronic pain is higher in patients who need resternotomy during hospitalization following surgery.[8] The development of chronic pain is most likely exacerbated by repeated tissue trauma and inflammatory reactions related to resternotomy. Despite these observations, a history of sternotomy did not associate with a higher risk of chronic pain following subsequent surgery. The incidence of chronic pain seems to increase in patients with sternal wound infection.[10,12] Wound complications such as infection, mediastinitis, keloid formation, and wound dehiscence have been related to the development of chronic pain after sternotomy.[12] In this research, no difference was observed between the two groups when the presence of resternotomy was analyzed, but our patients included in the study were not investigated for the development of sternal wound infection, so the findings could not be evaluated.

A retrospective study demonstrated an increase in the development of chronic pain after IMA graft removal. Additional tissue trauma was correlated with an increase in acute pain after surgery due to intercostal nerve injury, damage from retraction, and more extensive use of electrocautery.[15] In our study, no considerable difference was observed between the two groups in the use of IMA graft.

It may result from saphenous nerve injury, surgical intervention, trauma, or postoperative subcutaneous suture compression.[16] Chronic leg pain has been described as primarily neuropathic and frequently manifesting as anterior leg dysesthesia in a large case series in the literature. In this case series, it was noted that female patients reported a greater rate of chronic leg pain and its incidence was 8%. They observed that mild or moderate pain severity did not influence their quality of life.[7] Seven patients in this study were found to have chronic neuropathic pain in the saphenous region following saphenous graft removal.

Patients may consider chronic pain after cardiac surgery as "normal" or "to be expected." Therefore, many patients do not report symptoms to their surgeon or cardiologist, which can result in delayed or incorrect diagnosis and treatment. As we observed in the study, a very small percentage of patients taking analgesics.

The present study has several limitations. In this retrospective cohort of patients who had open-heart surgery between 2020 and 2022, the longest follow-up period after surgery is 2 years and cannot be assessed in terms of long-term results. Because of the retrospective design, some clinical information could only be incompletely obtained from patient records and the hospital information system. The evaluation of minimally invasive treatments was inadequate as a result of only including open-heart surgery patients who received sternotomies. Furthermore, the lack of comparison of surgical procedures such as off-pump coronary bypass is among the shortcomings of our study. Another drawback of our study is that wound infections in the early postoperative period were not assessed in individuals with chronic neuropathic pain.

According to the findings of the present study, the incidence of chronic neuropathic pain was estimated to be 14.7%, and it was shown that the presence of DM, preoperative angina, and the long hospital stay might be factors contributing to the development of chronic neuropathic pain.

Patients should be informed and closely monitored for the development of chronic and neuropathic pain after cardiac surgery. Diagnosis and treatment of chronic discomfort should be interdisciplinary, considering the patient's quality of life and functionality.

Disclosures

Ethics Committee Approval: The study was approved by The Katip Çelebi University Non-interventionalClinical Research Ethics Committee (Date: 24/11/2022, No: 0528).

Informed Consent: Written informed consent was obtained from all patients.

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Research Article

Systemic Immune-Inflammation Index Predicts Acute Kidney Injury after Cardiac Surgery: A Retrospective Observational Study

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ABSTRACT

Objectives: Inflammation plays an essential role in the development of postoperative acute kidney injury (AKI) in patients receiving cardiac surgery. The study aims to examine the predictive value of the systemic immune-inflammation index (SII), a new biomarker reflecting systemic inflammation, in the development of AKI following cardiac surgery in patients who had coronary artery bypass grafting (CABG).

Methods: Patients who received CABG operation in 2022 were retrospectively examined. The incidence of AKI 7 days postsurgery using Kidney Disease Improving Global Outcomes criteria was the primary outcome. The patients were classified into the AKI (n=160) and non-AKI groups (n=424). Patients were compared in terms of basic clinical features, operative characteristics, postoperative variables, and hematological indices derived from preoperative complete blood count analysis. The ability of SII to predict AKI was assessed using receiver-operating characteristic (ROC) curve analysis. Multivariate logistic regression analysis was used to determine the independent relationship between the development of SII and AKI.

Results: In this investigation, the incidence of AKI was 25.6%. eGFR, serum albumin, and hemoglobin were significantly lower in the AKI group, whereas body mass index, hypertension, serum creatinine, neutrophil–lymphocyte ratio, platelet–lymphocyte ratio, and SII were significantly greater. The preoperative SII cutoff of 651.7 predicted AKI with 65.0% sensitivity and 64.9% specificity. The area under the ROC curve was 0.718 (95% confidence interval 0.676–0.760).

Conclusion: Preoperative SII may be a simple, inexpensive, and useful prognostic biomarker in predicting postoperative AKI in patients undergoing CABG.

Keywords: Acute kidney injury, coronary artery bypass grafting, systemic immune-inflammation index

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Introduction

Acute kidney injury (AKI) after cardiac surgery is one of the most frequent and significant complications found in patients undergoing open heart surgery. High mortality and morbidity are linked to AKI.[1,2] It has been revealed that the incidence of AKI after cardiovascular surgery is 5%–42%, and the incidence of renal replacement therapy (RRT) is 2%–8%.[3-5] There is no developed treatment for AKI after cardiovascular surgery An opportunity to create early identification and intervention techniques to improve outcomes may arise from an accurate assessment of AKI. Various risk-scoring models with independent risk factors have been created in previous studies to increase AKI predictability.[4-7] Due to the inconsistent risk factors found in this research or the expensive price of new biomarkers, there is still a need to discover a clinically meaningful and affordable risk factor for AKI.

Atherosclerosis is a major contributor to coronary artery disease and is highly linked with an ongoing inflammatory response.[8,9] The role of direct inflammatory injury in addition to intraoperative ischemia-reperfusion injury, endothelial cell dysfunction, and apoptosis in the pathogenesis of AKI is well known.[10,11] However, there are limited studies investigating the impact of inflammation due to preoperative ath-

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erosclerosis and other comorbid conditions on postoperative complications in patients who will be operated on for coronary artery bypass grafting (CABG). The neutrophil×platelet/lymphocyte ratio-based systemic immune-inflammation index (SII), which combines three inflammatory peripheral cell counts to take patients' inflammatory and immunological status into account, was recently developed.[12,13] This index has been reported to have a predictive value for mortality in patients with cardiovascular disease, including coronary artery disease and acute coronary syndrome.[14,15] In cardiac surgery, preoperative SII value has been linked with major negative outcomes such as postoperative atrial fibrillation (AF), prolonged mechanical ventilation, intra-aortic balloon pump (IABP) requirement, and mortality.[16-18] However, the literature on the usefulness of preoperative SII in predicting the occurrence of AKI after cardiac surgery, particularly in patients undergoing isolated CABG, is limited. As a result, this study mainly aimed to examine the predictive accuracy of SII for the formation of AKI in patients receiving CABG.

Methods

Ankara City Hospital's local ethics committee approval (approval no: E1-22-2983, date: 19.10.2022) was obtained for the study. The records of 660 patients who had cardiopulmonary bypass (CPB) during CABG in our hospital's operating theater for cardiovascular surgery between January 2022 and December 2022 were then retrospectively examined. Patients with preoperative evidence of acute or chronic infection, patients with systemic inflammatory or autoimmune dysfunction, patients with dialysis-dependent chronic kidney disease (CKD), patients with recurrent cardiac surgery, patients who need preoperative or postoperative IABP/extracorporeal membrane oxygenation (ECMO), and patients who were reoperated and/or died due to bleeding revision in the first week were removed from the study (Fig. 1). The files of the remaining 624 patients had the baseline complete blood count needed for inflammatory indices and all available clinical data. For the post hoc analysis, these patients were deemed fully evaluable. The need for informed consent was waived for this retrospective study. All procedures were conducted to the Declaration of Helsinki.

Patients' age, gender, body mass index (BMI), comorbidities, left ventricular ejection fraction, and preoperative laboratory data (blood urea, serum creatinine [sCr], determined glomerular filtration rate [eGFR], blood glucose level, glycosylated hemoglobin [HbA1c]), hemoglobin, neutrophils, lymphocytes, platelets, and C-reactive protein (CRP) were noted. Neutrophil–lymphocyte ratio (NLR), platelet–lymphocyte ratio (PLR), and SII (neutrophil×platelet/lymphocyte) values were determined. In the intraoperative period,

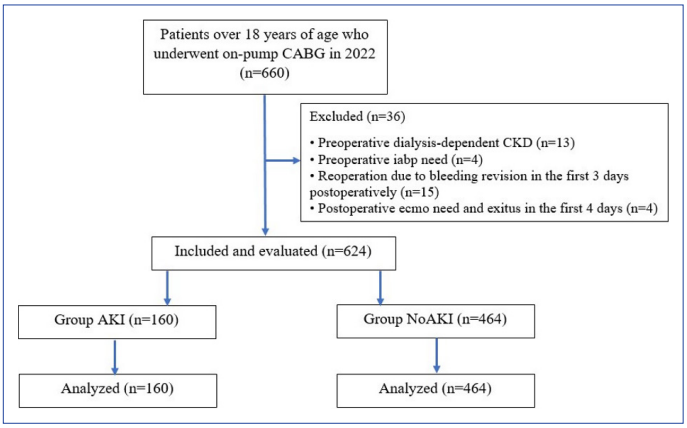

Figure 1. Flowchart of the patients.

CABG: coronary artery bypass grafting; CKD: chronic kidney disease; iabp, intra-aortic balloon pump; AKI: acute kidney injury; ECMO: extracorporeal membrane oxygenation.

cross clamp (CC), CPB, operation times, totally infused intravenous fluid (excluding blood product), blood and blood products, amount of urine, and need for diuretic and inotropic agents were recorded. The Kidney Disease Improving Global Outcomes (KDIGO) criteria, which classify AKI based on the highest change in sCr from preoperative baseline levels, were used to characterize the incidence of AKI.[19] All patients who met the KDIGO requirement for stages 1, 2, and 3 were considered to have AKI. A new requirement for dialysis following surgery is known as RRT. Postoperative result variables included extubation time, length of hospital and intensive care unit (ICU) stay, postoperative complications (AF, cerebrovascular accident), the requirement for erythrocyte suspension, and 30-day mortality.

Statistical Analysis

The IBM SPSS.25.0 software was employed for all dates examined. Categorical variables were defined as frequencies and percentages and analyzed with the Chi-squared test or Fisher's exact test. Continuous variables were presented as mean±SD (standard deviation) or medians (interquartile range) and to examine the differences between the two groups, the normality test (Kolmogorov–Smirnov) Mann–Whitney U test or Student's t-test were employed. To gather information on systemic inflammatory indices' capacity to predict AKI, a receiver-operating characteristic (ROC) curve was created. The area under the curve (AUC) was used to evaluate the ROC curve. Youden's index (J=sensitivity+specificity−1) was used to determine the most appropriate cutoff value. A model for multivariate logistic regression analysis was developed using factors that showed statistical significance in univariate logistic regression to identify the predictors of AKI. To prevent multicollinearity, NLR, PLR, neutrophil, lymphocyte, and platelet were excluded from

the multivariate logistic regression model. The Hosmer–Lemeshow test was employed for model fit. p<0.05 was considered significant in all comparisons. The sample size was established by the number of cases between the given dates, and posthoc power analysis was done using the total number of patients. After the study was completed, SII (measurement with the difference between groups) values were used for power analysis. According to this; Power analysis was conducted with G*Power 3.1.9.7 statistical package program; n=624 (n1=160, n2=464), α=0.05, effect size (d)=0.3; power=93% was observed.

Results

The data of 624 patients included in the study were examined retrospectively. The patients were classified into two groups patients who developed AKI (all patients with KDIGO stages 1, 2, and 3, Group AKI) and patients who did not develop AKI (Group NoAKI). According to KDIGO criteria, stage 1 AKI was found in 134 patients in Group AKI within the first 7 days postoperatively, stage 2 in 21 patients, and stage 3 in 5 patients. RRT was required in 4 patients. The incidence of AKI in this investigation was 25.6% (n=160). There was no statistical difference between the groups in terms of age, gender, ejection fraction, and comorbidities (diabetes, hyperlipidemia, chronic obstructive pulmonary disease, and previous cerebrovascular disease) (p:>0.05). Hypertension rate and BMI were statistically considerably lower in the AKI group (p:0.047, p:0.002, respectively). sCr, blood urea, NLR, PLR, and SII values were observed to be statistically significantly greater in the AKI group (p:0.004, p:<0.001, p:<0.001, p:<0.001, p:<0.001, respectively) (Table 1). Albumin, eGFR, hemoglobin, and lymphocyte levels were statistically significantly lower in the AKI group (p:<0.001, p:<0.001, p:0.002, p:<0.001, respectively) (Table 1).

Table 1. Baseline characteristics and laboratory data

	NoAKI (n=464) Mean±SD	AKI (n=160) Mean±SD	p*
Gender (M), n(%)	380 (81.9)	127 (79.4)	0.481
Age (year)	60.49±9.4	62.13±8.0	0.051
BMI (kg/m^2)	28.25±3.4	29.29±3.66	**0.002**
EF (%)	52.99±6.8	52.07±7.2	0.162
Hypertension, n(%)	165 (35.6)	71 (44.4)	**0.047**
Diabetes, n(%)	182 (39.2)	64 (40.0)	0.863
Hyperlipidemia, n(%)	108 (23.3)	36 (22.5)	0.841
COPD, n(%)	51 (11.0)	20 (12.5)	0.604
Cerebrovascular disease, n(%)	19 (4.1)	6 (3.8)	0.848
Baseline laboratory data			
	Median (IQR)	**Median (IQR)**	
Serum creatinine (mg/dL)	0.90 (0.8–1.0)	0.94 (0.8–1.1)	**0.004**
Blood urea (mg/dL)	34.00 (28.0–41.0)	38.0 (32.0–45.0)	**<0.001**
eGFR (ml/min/1.73 m^2)	88.00 (75.0–99.0)	80.00 (66.0–95.0)	**<0.001**
Blood glucose level (mg/dL)	111.00 (93.0–154.5)	120.00 (101.5–156.5)	0.065
HbA1c (%)	7.00 (6.0–9.1)	7.05 (6.0–8.3)	0.728
Serum albumin (g/dL)	43.00 (40.0–45.0)	41.00 (38.0–44.0)	**<0.001**
CRP (mg/dL)	3.2 (1.5–7.6)	3.8 (1.9–9.0)	0.785
Hemoglobin (g/dL)	14.00 (12.9–14.9)	13.60 (12.0–14.6)	**0.002**
Neutrophil (10^3/µL)	4.93 (4.0–6.0)	4.76 (3.9–5.9)	0.402
Lymphocyte (10^3/µL)	2.18 (1.7–2.7)	1.60 (1.3–1.84)	**<0.001**
Platelet (10^3/µL)	243.00 (204.5–286.0)	259.50 (212.5–309.0)	0.051
NLR	2.25 (1.7–2.9)	2.99 (2.4–3.7)	**<0.001**
PLR	112.26 (86.7–142.5)	155.46 (132.1–199.9)	**<0.001**
SII	541.17 (388.5–758.8)	747.18 (577.9–1043.2)	**<0.001**

COPD: chronic obstructive pulmonary disease; SD: standard deviation; BMI: body mass ındex; EF: ejection fraction; CRP: C-reactive protein; eGFR: estimated glomerular filtration rate; Hb: hemoglobin; NLR: neutrophil–lymphocyte ratio; PLR: platelet–lymphocyte ratio; SII: systemic immune-inflammation index.

*Bold values indicated p:<0.05, The independent samples t-test was used for continuous variables (mean±SD), the Mann–Whitney U test was used for continuous variables (median, IQR), and the Chi-square test was performed for categorical variables (n, %).

In the intraoperative period, the mean duration of CPB-packed red blood cell (pRBC) transfusion, and the proportion of patients in need of dobutamine and diuretics were observed to be statistically significantly higher in the AKI group. The proportion of patients in Group AKI who required only a pRBC transfusion during the postoperative phase was found to be statistically greater (p: 0.041) (Table 2).

We employed preoperative SII, NLR, and, PLR values for ROC analysis. The optimal value of the SII level in identifying AKI was 651.37 with a sensitivity of 65.0% and a specificity of 64.9%. Notably, the SII's AUC value (0.760) for detecting AKI was substantially greater than the NLR's and the PLR's combined AUC values (AUC: 0.556 vs. AUC: 0.554, respectively, Fig. 2).

A model was developed for multivariate regression analysis from the parameters reported to be potential risk factors for AKI in univariate logistic regression analysis (Table 3). According to the findings of multivariate logistic regression analysis, there was a higher risk of AKI in patients with BMI ≥ 30 kg/m2 (1.7 times), patients with preoperative sCr > 1.3 mg/dL (2.3 times), patients with preoperative serum albumin < 4 g/dL (1.9 times), in patients who require pRBC transfusion

Table 2. Intraoperative and postoperative variables

	No AKI (n=464) Mean±SD	**AKI (n=160) Mean±SD**	**p***
Intraoperative Period			
Duration of CC (dk)	63.20±18.8	64.72±18.4	0.373
Duration of CPB (dk)	100.05±25.9	107.96±28.6	**0.002**
Duration of operation (dk)	312.21±48.7	320.47±37.2	0.051
pRBC transfusion, n (%)			
0 unit	359 (77.4)	96 (60.0)	
1–3 units	101 (21.8)	60 (37.5)	**<0.001**
4–6 units	4 (0.9)	4 (2.5)	
FFP transfusion, n(%)			
0 unit	405 (87.3)	131 (81.9)	
1–3 units	57 (12.3)	26 (16.3)	0.086
4–6 units	2 (0.4)	3 (1.9)	
PC transfusion, n(%)			
0 unit	462 (99.6)	158 (98.8)	0.263
1 unit	2 (0.4)	2 (1.3)	
Total intravenous fluid (ml)	1607.03±537.7	1559.17±429.5	0.382
Total urine output (ml)	915.11±498.5	958.26±461.8	0.392
Dopamine, n(%)	86 (18.5)	39 (24.4)	0.111
Dobutamine, n(%)	29 (6.3)	20 (12.5)	**0.011**
Steradine, n(%)	7 (1.5)	4 (2.5)	0.411
Adrenalin, n(%)	4 (0.9)	4 (2.5)	0.112
Diuretic, n(%)	50 (10.8)	32 (20.0)	**0.003**
Postraoperative Period			
	Median (IQR)	**Median (IQR)**	
CVD SVD, n(%)	30 (6.5)	9 (5.6)	0.705
AF, n(%)	52 (11.2)	17 (10.6)	0.840
pRBC transfusion, n(%)	150 (32.3)	66 (41.3)	**0.041**
Extubation time (>12 h), n(%)	8 (1.7)	2 (1.3)	0.680
ICU stay (h)	24 (20–24)	24 (22–48)	0.800
Hospital stay (day)	7 (6–12)	7 (6–12)	0.343
Mortalite, n(%)	6 (1.3)	2 (1.3)	0.967

SD: standard deviation; CC: cross clamp; CPB: cardiopulmonary bypass; pRBC: packed red blood cell; FFP: fresh frozen plasma; CVD: cerebrovascular diseases; AF: atrial fibrillation; PC: platelet concentrate.

*Bold values indicated p:<0.05. The independent samples t-test was used for continuous variables (mean±SD), the Mann–Whitney U test was used for continuous variables (median, IQR), and the Chi-square test was performed for categorical variables (n, %).

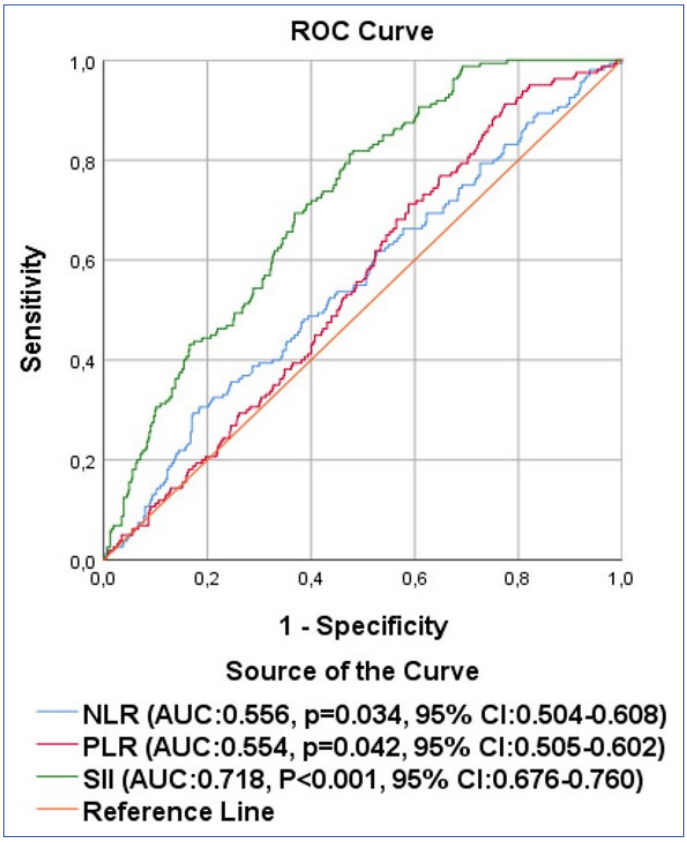

Figure 2. ROC curve analysis to establish the predictive value of SII, NLR, and PLR for AKI.

ROC: receiver-operating feature; AUC: area under the curve; NLR: neutrophil–lymphocyte ratio; PLR: platelet–lymphocyte ratio; SII: systemic immune-inflammation index.

during surgery (1.8 times), who need intraoperative diuretics (1.8 times), in patients with CPB time > 120 min (1.7 times), patients with preoperative SII > 651.37 (3.3 times) (p:<0.05).

Discussion

In this retrospective study, it was revealed that preoperative SII value may be a significant and independent predictor of postoperative AKI in patients receiving isolated CABG. However, obesity, preoperative creatinine elevation, hypoalbuminemia, intraoperative pRBC transfusion, diuretic requirement, and long CPB duration were validated as independent risk factors among other predictive risk factors in previous studies. Moreover, compared to NLR and PLR, the preoperative SII value demonstrated a better effective discrimination ability for AKI. Postcardiovascular surgery AKI is an independent risk factor that increases cost and morbidity and in-hospital mortality.[1,2] However, positive results can be attained if therapeutic interventions are undertaken within 24–48 h.[20] Thus, early risk factor identification by anesthesiologists and surgeons is crucial to lowering mortality and improving prognosis in patients with AKI.

Inflammation has been associated with many diseases, including chronic heart failure, cancer, metabolic problem, and cardiovascular disease.[21-23] In patients with coronary artery disease, atherosclerosis is now recognized not only as a cholesterol disorder accumulating on the vessel walls but also as a continuous, dynamic, and inflammatory process in the vascular system.[8,9] It has been demonstrated that endothelial damage and occlusive intravascular platelet aggregation contribute to the pathophysiology of atherosclerosis and acute coronary syndrome.[24] This platelet activation adheres to the endothelium during the coronary artery disease process, releasing a variety of proinflammatory cytokines. Moreover, it leads to neutrophil adhesion. Inflammatory mediators are secreted by neutrophils, which can control inflammatory respons-

Table 3. Univariate and multivariate logistic regression

	Univariate			Multivariate		
	p	OR	%95 CI	p	OR	%95 CI
BMI ≥ 30 kg/m²	**0.012**	1.676	1.122–2.503	0.013	1.757	1.127–2.741
Hypertension	0.048	1.446	1.003–2.083			
Preoperative hemoglobin ≤ 10 g/dL	0.019	3.436	1.226–9.633			
Preoperative blood urea ≥ 40 mg/dL	0.005	2.077	1.241–3.474			
Preoperative sCr > 1.3 mg/dL	**<0.001**	2.713	1.598–4.608	0.006	2.303	1.278–4.151
Preoperative eGFR < 90 ml/min/1.73 m²	0.004	1.721	1.185–2.501			
Preoperative serum albumin < 4 g/dL	**<0.001**	2.095	1.439–3.051	0.002	1.929	1.276–2.916
Preoperative SII > 651.37	**<0.001**	3.397	2.331–4.950	<0.001	3.345	2.251–4.973
pRBC transfusion during surgery	**<0.001**	2.279	1.553–3.346	0.004	1.839	1.209–2.796
Intraoperative dobutamin use	0.013	2.143	1.175–3.907			
Intraoperative furosemid use	**0.003**	2.070	1.273–3.365	0.030	1.800	1.057–3.062
CPB time > 120 min	**0.003**	1.906	1.238–2.936	0.029	1.706	1.055–2.759

OR: odds ratio; CI: confidence interval; BMI: body mass index; sCr: serum creatinine; pRBC: packed red blood cells; CPB: cardiopulmonary bypass; eGFR: estimated glomerular filtration rate; SII: systemic immune-inflammation index.

es. They may also demonstrate vigorous chemotaxis and phagocytosis. An increased neutrophil count shows an overactivated inflammatory response. Lymphocytes play a major role in specialized immunity. Inflammation and reduced lymphocyte count are two characteristics of weakened immunity. Hematological parameters such as neutrophils, platelets, and lymphocytes acquired from the complete blood count are potential markers of this inflammation. For instance, NLR is an indicator of critical stenosis and has been linked with both the severity and plaque morphology of coronary atherosclerotic disease.[25] Similar to NLR, PLR has also been shown to be a reliable indicator of advanced atherosclerosis.[26] For these reasons, coronary artery patients are operated on with varying degrees of inflammatory load, depending on the severity of the disease. As a result, we sought to assess preoperative inflammation and determine the prognostic value of AKI, one of the problems that follow heart surgery that is frequently reported.

In this study, SII was employed as a measure of systemic inflammatory response for AKI. In a noninvasive, widely accessible full blood count, SII is easily collected. It is an innovative inflammatory biomarker that combines neutrophil, lymphocyte, and platelet counts to represent the overall inflammatory state of the body. The predictive value of this indicator has been investigated in studies on a variety of disorders. It was initially investigated for poor outcomes in cancer patients.[27,28] Subsequently, the predictive accuracy of SII for mortality in chronic heart failure cases was demonstrated.[29] Similar findings have been made with coronary artery patients who have received the percutaneous coronary intervention, showing it to be an independent predictor for significant cardiovascular events, including abrupt cardiac death.[30] There are also studies analyzing the association between preoperative SII and postoperative complications in patients undergoing cardiac surgery. In a study performed on patients operated on for acute type A aortic dissection, it was found that preoperative SII was predictive for predicting postoperative multiorgan failure and 30-day mortality.[18] In another study, preoperative SII in patients who received on-pump CABG; has been linked to longer postoperative mechanical ventilation and ICU stay, AF, increased requirement for inotropic support, IABP support, and other infections other than sepsis.[17] To our knowledge, our study is the first to assess SII particularly in predicting AKI after CABG and isolated showed that SII was independently associated with AKI in patients undergoing CABG. According to our multivariate analysis result, we revealed that the risk of AKI increased 3.3 times with a cutoff value of SII>651.37 (65.0% sensitivity, 64.9% specificity).

It has been demonstrated that preoperative NLR elevation is determinative for both postoperative AKI and RRT requirements.[31] However, in patients receiving CABG, a high preoperative NLR was linked to poor baseline renal function.[32] Similar to NLR, preoperative PLR can be used as an independent indicator of AKI following cardiac surgery.[33] In comparison to either of these markers alone, SII can more accurately reflect the body's immunological and inflammatory condition.[34] Furthermore, several previous studies have contrasted the prognostic importance of the index with its components, including NLR or PLR. For instance, SII values have been demonstrated to predict postoperative AF more efficiently than NLR or PLR in patients undergoing isolated CABG.[16] Remarkably, we also discovered in our study that SII has a higher AUC for AKI compared to the AUC of NLR or PLR. This could be justified by the idea that calculating SII by adding platelet count to the NLR would simultaneously assess the aggregation route and the inflammatory pathway.[35,36]

In addition to SII, our study also showed that obesity, preoperative creatinine elevation, hypoalbuminemia, intraoperative pRBC transfusion, diuretic need, and prolonged CPB duration may all be risk factors for postoperative AKI. The secondary findings of our study are mostly consistent with previous studies analyzing risk factors for cardiac surgery-related AKI.[4,37-39] Adding preoperative SII to these risk factors may also enhance the selection of high-risk patients. The patient's risk for AKI can help doctors prepare for intraoperative and postoperative follow-up/management. In the high-risk patient group, such prevention of intraoperative nephrotoxic agents, optimization of intravascular volume, improvement perfusion during CPB, and prophylactic renal protective measures like mannitol/fenoldopam can be taken. Moreover, RRT can be initiated early or anti-inflammatory medication can be used, albeit there isn't enough evidence to support either one yet.[20,40]

Limitations

This research has several limitations. First, it was a single-center retrospective analysis. Some patients were excluded because of missing variables. The correlation between AKI and SII was found using spot laboratory data. Unfortunately, data on postoperative SII were not obtained. Inflammation caused by the CPB pump can cause bias. These results will need to be confirmed by a larger sample size prospective research.

In conclusion, the risk stratification method in cardiac surgery cohorts should adequately address the inflammatory profile of patients. As a simple, easily calculable, and reproducible inflammatory marker, SII is independently associated with an elevated risk of AKI in patients receiving CABG.

Disclosures

Ethics Committee Approval: Ankara City Hospital's local ethics committee approval (approval no: E1-22-2983, date: 19.10.2022) was obtained for the study.

Informed Consent: Written informed consent was obtained from all patients.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

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Research Article

Enhanced Recovery In Cardiac Surgical Patients With Low Left Ventricular Ejection Fraction: A Controlled Before-and-After Study

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ABSTRACT

Objectives: The application of Enhanced Recovery After Surgery (ERAS) in cardiac surgery has been increasing in recent years. The goal of this controlled before-and-after study is to compare the postoperative follow-up periods of patients who had low left ventricular ejection fraction and were operated on for coronary artery bypass grafting using the ERAS protocol and the standard protocol (CABG).

Methods: Controlled before-and-after study. A single hospital-based study. Perioperative data from 50 consecutive patients who used the standard protocol (preERAS) were matched with data from 50 consecutive patients in the prospective group (postERAS) which consisted of 50 consecutive patients. Patients with low left ventricular ejection fraction were detected in both groups.

Results: Patient demographics, operation and cross-clamp durations, cross-clamp and CPB, amount of perioperative bleeding, time of extubation, length of stay in the intensive care unit and hospital, and complications were all recorded and compared between groups. The time of extubation was statistically significantly earlier in the posters group (7.2±2.2 h vs. 10.9±6.0 h, p=0.001). Perioperative blood loss was statistically significantly lower in the postERAS group than in the preERAS group (359±56.9 vs. 392±75.8 cc respectively, p=0.028). The patients under posters protocol stayed statistically importantly lower in the intensive care unit (2.1±0.5 days vs. 2.4±0.8 days, respectively p=0.002).

Conclusion: The ERAS pathway was found to be feasible in patients and was associated with shorter extubation time, less perioperative bleeding, and a shorter stay in the intensive care unit and hospital.

Keywords: Cardiac anesthesia, enhanced recovery after surgery, perioperative care, outcomes

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Introduction

The aim of Enhanced Recovery After Surgery (ERAS) is to return the patients to their normal functional state as soon as possible. It has been demonstrated that ERAS reduces hospital stay duration, increases patient satisfaction, and lowers hospital costs.[1] The practice of ERAS has substantially increased in the recent few years in cardiac surgery.[2] However, in cardiovascular surgery, this patient-centered rehabilitation program was reported to be insufficient.[3] ERAS practices in cardiac surgery differ from the other surgical disciplines. The nature of cardiac surgery is one reason for this. Cardiopulmonary bypass is performed on the patients. They require higher volume replacement. Furthermore, postoperative bleeding and hemodynamic instability are more common. Also, these patients often have extensive medical comorbidities.[4]

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There have been reports of ERAS protocols regarding cardiac surgery. However, there has been a lack of proof or consensus for various components. Among these is carbohydrate or clear liquids administration until two hours before anesthesia and chlorhexidine-alcohol-based skin preparation.[5]

Gregory et al.[6] reported the main concepts of cardiac ERAS but added that there were lots of things to be done. Furthermore, the need for additional research was discussed to accurately determine the true nature of the alleged benefits of ERAS. Post-coronary artery bypass grafting complications were reported to occur more frequently in patients with low left ventricular ejection fraction.[7] However, there is insufficient data on the use of ERAS in cardiac surgery patients with low left ventricular ejection fraction.

The purpose of this study is to compare the postoperative follow-up periods of patients who underwent coronary artery bypass grafting using the ERAS protocol and patients who used the standard protocol (CABG). The authors hypothesize that the extubation time of the patients with low ejection fraction could be shortened by ERAS. The goal is to reduce the length of stay in the intensive care unit and the hospital, as well as to prevent complications.

Methods

This study has been approved by the Ethics Committee of our university under protocol number: KUGOKAEK 2017/369. Before patient enrollment, the study was registered at www.clinicaltrials.gov under the registration number: NCT03799965. This study was enrolled in our university hospital as a single center, controlled before-and-after study. PostERAS patients provided informed consent to participate in the study. Our study was conducted following the Declaration of Helsinki.

Study Design and Patient Enrollment

Two hundred and five patients planned to be operated on for CABG were evaluated. Data on 100 patients who participated in the ERAS Cardiac program were collected prospectively. Patients' demographics, comorbidities, and history of surgical procedures were recorded. The following parameters were monitored intraoperatively: operation duration, cross-clamp time, Cardiopulmonary Bypass (CPB) time, and amount of bleeding. The amount of drainage, time of extubation, duration of stay in the intensive care unit and hospital, re-exploration, and complication rates were recorded in the postoperative period.

The study included patients over the age of 18 who had elective CABG under CPB and were rated as ASA 3-4. Patients younger than 18 years, patients who refused to be included in the study, and patients who operated emergently were excluded.

As the control group, 100 patients who had previously been evaluated in the perioperative period and had not used the ERAS protocol were included. The data regarding these patients were scanned and recorded retrospectively. The historical data collection took place between January and December of 2017. Data on patients on the ERAS pathway were collected prospectively between January 2018 and December 2018. The steps of ERAS were summarized in Table 1. Then, patients with low LVEF were determined in both groups. Patients with borderline ejection fraction were assessed using the definitions from the ACCF/AHA Guideline for the Management of Heart Failure.[8] Patients without an LVEF value between 41% and 49% were excluded (Fig. 1). Real-time, volumetric echocardiography was used to estimate the patients' LVEF.[9]

patient's demographic data (age, height, weight, BMI), an indication of operation, operation duration, presence of a complication, CPB and aortic cross-clamp durations, and surgery type were all recorded. The patients, New York Heart Association functional status, additive Euro-SCORE, and preoperative left ventricular ejection fraction were also recorded. Medical history, and comorbidity history,

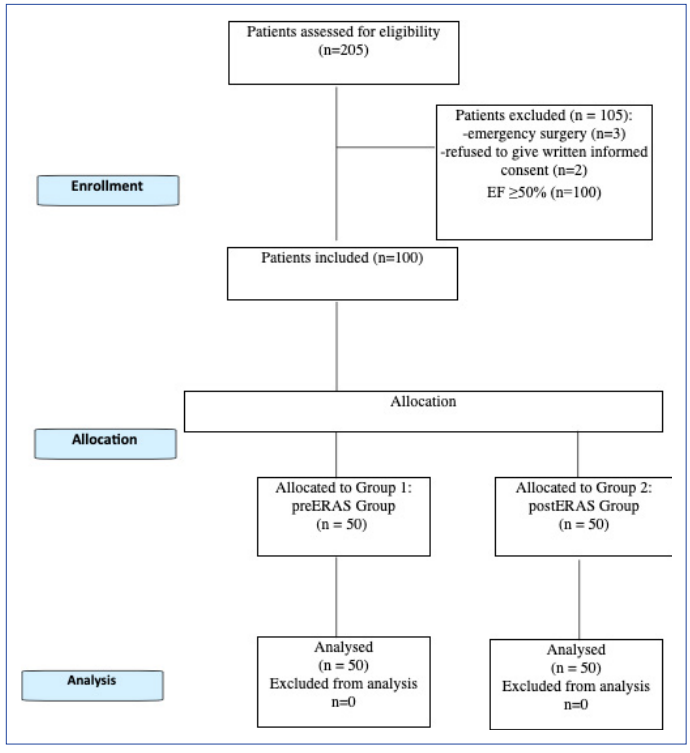

Figure 1. Flow Diagram.

Table 1. Cardiac ERAS pathway

Preoperative pathway	Informing the patient about the protocol details
	Smoking cessation at least 4 weeks ago
	cessation of alcohol at least 4 weeks ago
	Evaluation of the preoperative nutritional status.
	Recommending protein-rich nutrition for patients at least one week before the operation.
	Nutritional support if deemed necessary
	Giving information about the preoperative respiratory exercises.
	(30 deep breaths using the Triflo II once per hour)
	Drinking clear fluid two hours before surgery
	Preoperative 400 ml of oral carbohydrate loading until 2–4 hours
	Keeping patients nil per os for 6 hours
	Long-acting sedative drug use is not recommended for premedication.
	Anxiolytic agents are not given unless necessary
	No bowel preparation before surgery
	Surgical antibiotic prophylaxis within 1 hour.
	(30 mg/kg of cefazolin by intravenous)
Intraoperative pathway	Pulmonary artery catheter not used.
	liquid loading after induction.
	(Keeping CVP between 6 and 15 mmHg)
	Using protective lung ventilation strategies based on ideal body weight
	Perioperative blood transfusion: The transfusion threshold is <7.2 g/dL
	Tranexamic acid: A bolus of 20 mg/kg, followed by an infusion of 2 mg/kg/h until sternal closure
Postoperative pathway	Extubation of patients at postoperative 6th hour
	Early postoperative mobilization: Mobilization on a chair on the same day after surgery
	Urinary catheter withdrawal when urine output is >0.5 mL/h for 6 hours
	Central venous line removed at discharge from ICU
	Chest tubes were removed when collecting <100 mL of blood in 8 h without routine chest x-ray after drain removal
	Multimodal analgesia protocol: asetaminofen, tramadol, gabapentine, dexametadone
	Discontinuation of opioid infusions after extubation
	IV ondansetron postoperatively first 48 h

including hypertension, acquired myocardial infarction, hypercholesterolemia, and chronic obstructive pulmonary disease, were all elicited and documented. The time of removal of Foley sound, prophylaxis for thromboembolism, the presence of nausea/vomiting, drugs administered, the time of first defecation, the need for postoperative analgesics, the initiation of oral nutrition, the time of first mobilization, the duration of stay in the intensive care unit and hospital, the presence of a postoperative complication, the need for hospital readmission, and the rate of re-exploration were all recorded.

The criteria for discharge were determined as follows: no need for inotropes, no arrhythmia problems, easy mobilization, tolerability of normal regimen, the sufficiency of oral analgesics, normal urine output, absence of any finding of intestinal obstruction, and gas discharge. Both the patients under the ERAS protocol and control group were operated on by the same cardiac surgeons.

Anesthetic Management

As soon as the patient was taken to the operating room, a 16 G iv cannula was used to gain vascular access, and an intravenous normal saline infusion was started. Radial artery catheterization under local anesthesia was performed and continuous follow-up of arterial blood pressure was made with the transducer. The core body temperature was continuously measured using a non-invasive, single-use zero-heat flux thermometer.[10,11] Five lead ECG monitoring was applied. A pulse oximeter and a bispectral index monitor were used to keep BIS values between 40 and 60.

Induction of anesthesia was made with fentanyl 1–2 μg/kg, midazolam 0.02 mg/kg, and propofol 1–2 mg/kg. Target-controlled infusions of fentanil for analgesia and propofol for hypnosis were used to provide total intravenous anesthesia. As a muscle-relaxing agent, rocuronium 1.0 mg/kg was given for tracheal intubation. A central venous catheter was inserted before the incision. Inotropes,

beta-blockers, and fluids were used to optimize preload, afterload, and miyokardialcontractility. Unfractionated heparin 300 IU/kg was administered before CPB.

Table 1 summarizes applications within the ERAS protocol. There was no subsequent continuous infusion of muscle relaxant. Train-of-Four monitoring was applied; muscle relaxant was readministered if 2–3 twitches were detected on the monitor. A multimodal protective lung ventilation management strategy was used to ventilate the patients. Within 1 hour of anesthesia and before surgical incision, 30 mg/kg cefazolin or cefuroxime was administered. Intravenous fluid was loaded following induction of anesthesia to maintain 6–15 mmHg of central venous pressure. A bolus of 20 mg/kg tranexamic acid was given, followed by an infusion of 2 mg/kg/h until the sternum was closed. Patients were transferred to the cardiovascular intensive care unit following the operation. Extubation was scheduled for 6 postoperative hours. Patient-controlled tramadol analgesia and acetaminophen with codeine were used to treat postoperative pain. Long-acting opioids were not used. Premedication with 0.1 mg/kg oral midazolam 1 hour before the patient entered the operating room was given to the control group patients who did not participate in the ERAS protocol.

Statistical Analysis

Average, standard deviation, median, minimum, maximum, frequency, and ratio values were used for the definitive statistics of data. The Kolmogorov-Simirnov test was used to determine the distribution of the variables. The T-test for independent sampling and the Mann-WHitney U test were used to analyze quantitative independent data if the Chi-square test conditions were not met, Fischer's exact test was used to analyze qualitative independent data.SPSS 22.0 program was used for statistical analysis.

Sample Size Calculation

With a target of a 30% reduction in extubation time and a standard effect size of 0.66, each group required 48 patients with 5% tolerance and 90% power. We included 50 patients in each group.

Results

205 patients were assessed for eligibility. Five patients were ruled out (Two patients declined to participate. Three patients underwent emergency aortic surgery). Following that, 100 patients with LVEFs ranging from 41% to 49% were excluded. The patients are grouped as preeras (Group 1) and ERAS (Group 2). Then, in both groups, patients with LVEFs of 41%–49% were excluded. The data from 100 patients were analyzed (Fig. 1).

The patients' average age was 60.9±9.2 years, their BMI was 28.5±3.4 and their LVEF was 43.6%±4.9% (Table 2). There was no statistically significant difference in age between the preERAS and postERAS groups among the demographic data compared (p=0.699, Table 3). In terms of BMI, there was no statistically significant difference between groups (p=0.241). While all of the patients in the ERAS protocol group had an ASA 3, only 1 patient in the preERAS group had an ASA 4. Mean LVEF was 43.9%±4.9% in the preeras group, while it was 43.2%±5.1% in the postERAS group (p=0.128).

The operation duration, CPB, and cross-clamp times did not differ statistically between groups (Table 3). The amount of perioperative bleeding in the postERAS group was statistically significantly lower than in the postERAS group (359±56.9 vs. 392±75.8 cc respectively, p=0.028). There was no statistically significant difference in the amount of postoperative tube drainage between the groups (p=0.177). Extubation time was statistically significantly reduced in the posters group (7.2±2.2 h vs. 10.9±6.0 h, p=0.001).

Postoperative bleeding occurred in 2 patients in the preERAS group, requiring re-exploration in one of them. Postoperative bleeding occurred in one patient in the postERAS group which did not require re-exploration. Patients undergoing the postERAS protocol spent statistically less time in the intensive care unit (2.1±0.5 vs. 2.4±0.8 days,

Table 2. Demographic data of the patients, intraoperative and postoperative data

	Min–Max	Median	Mean±s.s/n-%
Age	37–82	63	60.9±9.2
BMI	18–39	29	28.5±3.4
ASA			
III			99 (99.0%)
IV			1 (1.0%)
Ejection fraction (%)	25–49	45	43.6±4.9
Duration of Operation	3–6	4	4.3±0.8
Cross-Clamp	42–183	67	70.2±20.7
CPB Time	68–240	117	117.8±26.3
Preoperative Bleeding	250–600	400	375.5±68.7
Postoperative Drainage	200–750	300	334.5±76.1
Extubation Time	4–48	8	9.1±4.9
Complication			
(–)			97 (97.0%)
(+)			3 (3.0%)
Re-exploration			
(–)			99 (99.0%)
(+)			1 (1.0%)
length of stay in the ICU	2–5	2	2.3±0.7
length of hospital stay	7–12	7	7.3±0.8

Table 3. Outcome comparison of patients with or without ERAS program

	ERAS (-)		ERAS (+)		p
	Mean±s.s/n-%	Median	Mean±s.s/n-%	Median	
Age	61.2±8.1	62	60.5±10.3	63	0.699[δ]
BMI	27.9±3.0	29	29.0±3.6	29	0.241[m]
ASA					
III	49 (98.0%)		50 (100.0%)		0.315[k]
IV	1 (2.0%)		0 (0.0%)		
Ejection fraction (%)	43.9±4.9	45	43.2±5.1	45	0.128[m]
Duration of Operation	4.3±0.8	4	4.3±0.9	4	0.857[m]
Cross-Clamp	66.8±13.9	65	73.6±25.2	70.5	0.245[m]
CPB Time	112.9±20.4	115	122.7±30.5	117.5	0.065[δ]
Preoperative Bleeding	359.0±56.9	400	392±75.8	400	0.028[m]
Postoperative Drainage	330.0±86.3	300	339.0±64.9	350	0.177[m]
Extubation Time	10.9±6.0	10	7.2±2.2	7	0.001[m]
Complication					
(-)	48 (96.0%)		49 (98.0%)		0.558[k]
(+)	2 (4.0%)		1 (2.0%)		
Re-exploration					
(-)	49 (98.0%)		50 (100.0%)		0.315[k]
(+)	1 (2.0%)		0 (0.0%)		
Length of stay in ICU	2.4±0.8	2	2.1±0.5	2	0.002[m]
Length of hospital stay	7.5±1.0	7	7.1±0.5	7	0.001[m]

[m]Mann–Whitney u test/ [δ]Independent samples t-test/[k]Ki-kare test (Fischer test).

respectively, p=0.002). The duration of hospital stay in the postERAS group was found to be statistically significantly lower than in the postERAS group (7.1±0.5 vs. 7.5±1.0 days, respectively, p=0.001).

Discussion

In this controlled before-and-after study, patients with low LVEF who were scheduled for CABG were given the ERAS protocol. The values of the patients were compared with the preERAS group. The posters group had shorter extubation times, less perioperative bleeding, shorter stays in the intensive care unit and hospital, and lower complication rates.

ERAS pathways are designed to provide evidence-based, comprehensive, multidisciplinary perioperative care including best practices for preoperative, intraoperative, and postoperative management. It has been popular in cardiac surgical practice in recent years. However, the heterogeneity of the data obtained from the studies makes a difficult conclusion in ERAS protocols difficult.

The first step is to choose the right team for the creation of the cardiac ERAS program. Team members who trust one another should work together toward a common goal. In this context, we began by giving information to our cardiac surgeons. We stated what we should do following our patient's best interests. We made our plan to positively affect patient outcomes with precautions through common consensus meetings. However, we concentrated on patients with low LVEF, who have high complication rates after CABG. Even though this patient population is unique, no studies on the effectiveness of ERAS practices on this patient population have been conducted.

In their prospective observational trial, Fleming et al.[12] evaluated the ERAS protocols on a population of CABG and valve surgery patients. In this study, ERAS reduced bundle pain scores and complication rates. However, no difference could be discovered regarding the duration of hospital stay. Complication occurred in one patient in the postERAS group, whereas three patients in the preERAS group were complicated. Moreover, there were no patients reexplored in the postERAS group, where one patient was revised in the control group. The statistical insignificance of these values was discovered to be related to the sample size. Both the duration of stay in the ICU and the hospital were reduced in the posters group. Mortality and length of hospital stay were found to be correlated in a correlation analysis involving 26 hospitals.[13] Zaouter et al.[14] sought the effects of ERAS on the results of robotic endoscopic coronary ar-

tery bypass graft surgery patients. In line with our findings, they reported a reduction in the length of stay both in the ICU and the hospital. In addition, they also reported a reduction in the amount of transfusion. Extubation on the operating table was possible in these patients. Totonchi et al.[15] extubated all but two of their 100 adult patients undergoing noncomplex cardiac surgery in their randomized clinical trial. They advocated for extubation in the operating room using a combination of inhalational and intravenous anesthesia, as well as multiple anesthesia monitoring systems to provide adequate depth of anesthesia. The Society of Thoracic Surgeons stated that being able to extubate a patient within the first 6 hours after cardiac surgery was an indication of quality patient care.[16] The results of the studies on this issue are also controversial. A meta-analysis of 28 trials found no differences in mortality or major complications in patients undergoing "fast-track" cardiac surgery.[17] In another study y, patients extubated for 12 hours and patients extubated 6 hours after cardiac surgery had similar mortality, major complication rates, and hospital stays.[18] In a study of 459 cardiac surgery patients, when extubation times were reduced from 7.4 to 5.73 hours, the length of stay in the ICU was increased.[19] Moreover, there was no difference regarding the length of hospital stay. Grant et al.[20] found that an enhanced recovery program reduced time to extubation, floor length of stay, and hospital length of stay in a study of 451 patients (Fig. 2). No reintubation was reported but 62 patients were extubated in the operating theater in this study. CABG patients were sought in our study, and the patients were scheduled to be extubated as soon as possible. Our patients could be extubated an average of 7.4 hours after surgery, compared to 11.4 hours in the preERAS group, indicating a significant reduction. We consider that possible complications secondary to mechanical ventilation or prolonged sedation were prevented by early extubation.

Based on a systematic review and multidisciplinary consensus, the Society for Enhanced Recovery After Cardiac Surgery (ERAS Cardiac) recently published "Guidelines for Perioperative Care in Cardiac Surgery."[21] The standard use of high-dose opioids shifted to a more balanced approach to anesthesia, using lower doses of opioids, shorter-acting hypnotics, and earlier extubation.

Sola et al.[22] reported their experience with the application of ERAS on transcatheter aortic valve-implanted patients. They reported that using just one ERAS pathway would help to reduce perioperative risk and speed recovery. On the other hand, Williams et al.[23] sought the outcome of CABG patients under the ERAS program, similar to our study. PreERAS (489 patients) and postERAS (443 patients) cardiac groups were compared in this study; shorter hospital and ICU length of stay was discovered, similar to our study; and similar reintubation and ICU readmission rates were declared. In another study of 74 patients, the length of hospital stay was reported to be reduced, with the duration of hospital stay reduced from 5.4 to 4.1 days in ERAS patients.[24] The main advantage of our research was that it reflected the patient population of low LVEF who are prone to postoperative complications.

According to EACTS/EACTA guidelines,[25] PRBC should be used as a transfusion strategy based on the patient's clin-

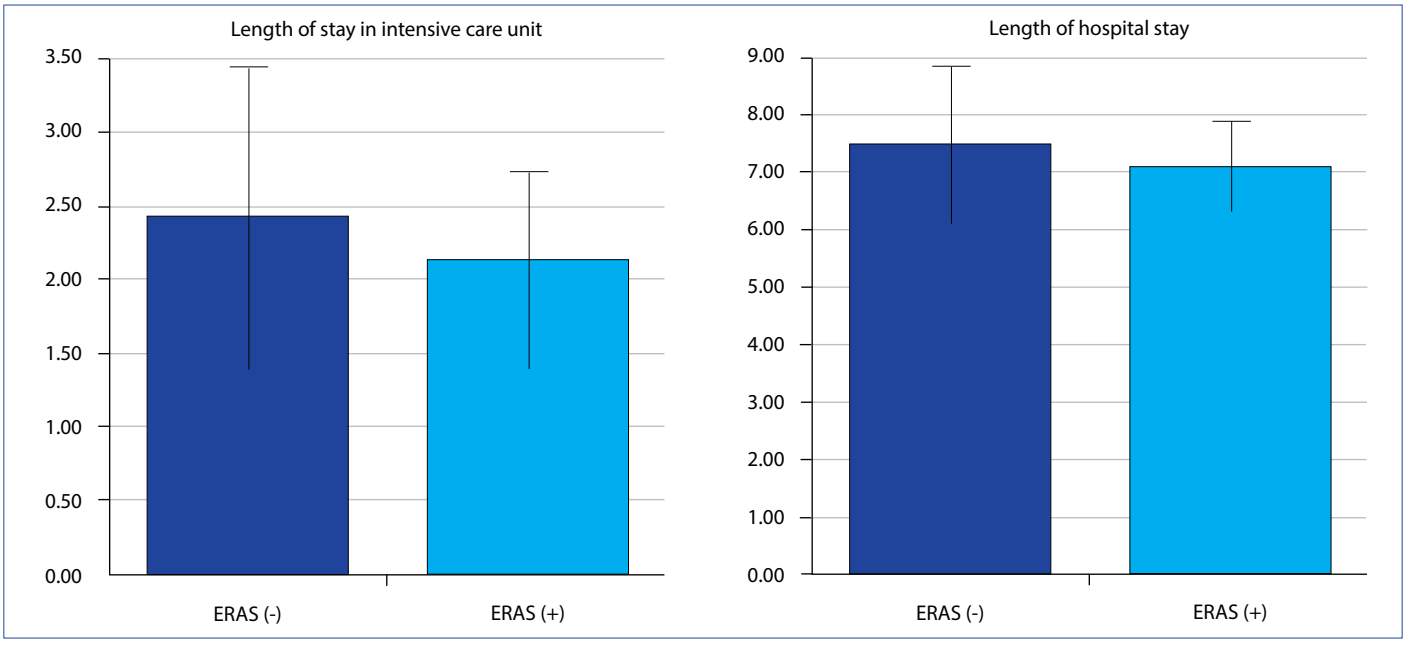

Figure 2. Comparison of pre eras and postERAS groups' length of stay in hospital and intensive care unit.

ical status rather than a fixed hemoglobin level threshold. For perioperative bleeding management in our study, we accepted a Hb level of 7–9 gr/dl as a base which was the suggestion of ESA.[26] One of the most important findings of our study was that the amount of bleeding during surgery was significantly reduced in postERAS patients. Tranexamic acid, which was recently approved for use in postERAS patients, was thought to be related to this outcome. Also, no complications regarding the use of tranexamic acid occurred in our study.

Our findings matched those of Zaouter et al.'s [27] in their study of ERAS outcomes in patients undergoing minimally invasive aortic valve replacement. The authors discovered shorter hospital stays, lower complication rates, and lower opioid consumption.

Limitations

The most important limitation of our study was that postoperative pain scores were not compared. This was due to the inaccessibility of preERAS patients' recorded visual analog scale values, which were scanned retrospectively. Therefore, these values were not included in the statistical analysis. Another limitation was the small sample size. We believe that a larger sample size study would significantly emphasize the importance of this issue.

The use of ERAS shortens the times required to extubate patients with low LVEF who are undergoing CABG surgery. admitted to Moreover, perioperative amount of bleeding can be reduced by cardiac ERAS protocol.

Disclosures

Ethics Committee Approval: This study has been approved by the Ethics Committee of our university under protocol number: KUGOKAEK 2017/369.

Informed Consent: Written informed consent was obtained from all patients.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

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Authorship Contributions: Concept – İ.Y.D., K.S., M.Y., Ç.D.; Design – İ.Y.D., Ç.D., M.Y., H.Ş., E.Y.; Supervision – İ.Y.D., E.Y., A.S., Ç.D.; Data collection &/or processing – İ.Y.D., H.Ş., Ç.D., K.T.S.; Analysis and/or interpretation – İ.Y.D., H.Ş., M.Y., A.S., K.S.; Literature search – İ.Y.D., Ç.D., H.Ş., R.Y., M.Y.; Writing – İ.Y.D.; Critical review – İ.Y.D., H.Ş., A.S., M.Y.

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Research Article

Ultrasound-Guided Rhomboid Intercostal Block for Analgesia After Cardiac Surgery: A New Indication for Novel Fascial Plane Block

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ABSTRACT

Objectives: Acute postoperative pain is a common complication after cardiac surgery. When not properly regulated, it may have a negative impact on clinical results. One of the novel fascial plane blocks that aims to blockade the lateral cutaneous branches of the thoracic intercostal nerves is the rhomboid intercostal block. In the literature, there is no research of rhomboid intercostal block in cardiac surgery, and a limited number of reports employing this block to analgesia for thoracotomy, scapulothoracic arthrodesis, and lung transplantation. In our research, we aimed to display a case series of bilateral rhomboid intercostal blocks employed as an element of multimodal analgesia in five consecutive patients who underwent cardiac surgery through a median sternotomy.

Methods: Five adult patients who had a rhomboid intercostal block for postoperative analgesia after cardiac surgery were investigated. Within the first 24 hours after surgery, cumulative morphine consumption and pain scores during rest and coughing were assessed.

Results: In the first 24 h after surgery, the median cumulative morphine intake was 4 mg (0–20 mg). Also, the patients' pain scores were less (NRS≤4) at all-time points. There were no opioid-related adverse events or block-related additions in any patient.

Conclusion: As part of multimodal analgesia, the rhomboid intercostal block was thought to help reduce opioid consumption as well as pain scores in cardiac surgery cases.

Keywords: Acute, cardiac, median sternotomy, nerve block, postoperative pain, surgical procedures, ultrasonography

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Introduction

Pain ranging from mild to severe can be experienced by up to 50% of patients after cardiac surgery.[1] Acute postoperative pain that is not properly managed can lead to chronic pain, lower quality of life and an increased risk of pulmonary complications.[2] Pain after cardiac surgery can be caused by sternotomy or thoracotomy incisions, chest retraction, internal mammary artery harvesting sternal wires, chest tubes, and visceral pain.[3] Recent improvements in ultrasound-guided fascial plane blocks, such as the erector spinae plane block (ESP), pectoral nerve blocks, and superficial and deep parasternal intercostal plane (PIP) blocks, have made them available to cardiac surgical patients. These blocks have been revealed to provide important analgesic benefits to the patients.[4]

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The rhomboid intercostal block (RIB) aims to block the lateral cutaneous branches of the thoracic intercostal nerves (Th3-9) and is one of the novel fascial plane blocks described for the first time by Elsharkawy et al.[5] It has been shown that RIB has been used effectively in the treatment of patients undergoing thoracotomy,[6] scapulothoracic arthrodesis,[7] and lung transplant process.[8]

Here, we report the use of RIB in five consecutive patients employed as an element of multimodal analgesia in those who underwent cardiac surgery through a median sternotomy. The patients were made aware of feasible risks, and they gave their consent to employ their clinical information.

Methods

RIB was performed during the preoperative period just prior to induction, as previously described.[5] Following standard monitoring (non-invasive blood pressure monitoring, five-lead electrocardiography, and pulse oxygen saturation) as recommended by the American Society of Anesthesiologists, the patients were positioned in a sitting position before an aseptic technique and ultrasound guidance were used. Through the adduction of the ipsilateral arm across the anterior thoracic wall, the lateral mobilization of the scapula was achieved. Then, at the T5 level on the oblique sagittal plane medial to the medial side of the scapula, a linear ultrasound probe (8–13 MHz, GE LOGIQ V1 US System, USA) was placed. After locating the trapezius, rhomboid, and intercostal muscles, as well as the pleura, thirty milliliters of 0.25% bupivacaine diluted to 0.25% was injected into the fascial plane between the rhomboid and intercostal muscles (Fig. 1). Concurrent with the injection, real-time visualization of the spread of local anesthetic (LA) in a craniocaudal direction was performed. The same process was performed on the contralateral side. Our institute's standard care protocols for cardiac anesthesia were followed during the perioperative period. Intravenous (IV) midazolam 0.05–0.1 mg/kg, fentanyl 2–5 μ/kg IV, pentothal 4–5 mg/kg IV, and rocuronium (1 mg/kg IV) were used for induction. Inhalation sevoflurane (MAC 1), O2/air (FIO2 0.40), and IV fentanyl infusion (2–5μ/kg/h) was employed to maintain anesthesia. The depth of anesthesia was kept between 40 and 60 bi-spectral index scores. At the end of the procedure, morphine 0.05 mg/kg was administered intravenously.

For the first twenty-four hours, each patient received 1 g/8h of acetaminophen, and patient-controlled analgesia (BodyGuard 575 pain management, UK) was initiated (bolus dosage, 20 μ/kg of morphine; lock-out period, 10 minutes; 4-h limit, 0.5 mg/kg). The pain was assessed using the numerical rating scale (NRS) at rest and coughing at extubation three, six, 12, 18, and 24 hours.

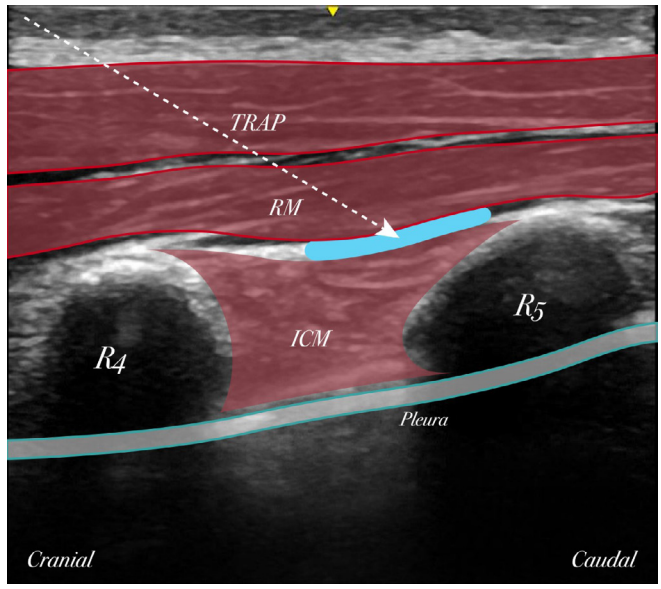

Figure 1. The schematic illustration of where to inject a local anesthetic when using an ultrasound-guided rhomboid intercostal block. The arrow indicates the direction of the needle where to inject a local anesthetic. Blue -the highlighted area is the desired spread of local anesthetic.

TRAP: trapezius muscle; RM: rhomboid muscle; ICM: intercostal muscle.

Statistical Methods

Continuous variables were presented as median (minimum-maximum) values, while categorical data were represented as absolute frequencies and percentages. SPSS Version 24 software (IBM, Armonk, NY, USA) was used.

Results

Table 1 presents the demographic information and surgical attribute of the patients. In the first 24 h after surgery, the median number of morphine employed was 4 mg (0 to 20 mg). Furthermore, patients had low pain scores (NRS≤4) at all-time points (Table 2). Neither opioid-related adverse events nor block-related problems were found in any patient.

Discussion

We present a case series of five patients undergoing open cardiac surgery who had bilateral RIB. The RIB was effective for pain scores and decreased postoperative 24-h morphine intake.

Due to the potential serious complications (epidural or spinal hematoma, hypotension, pneumothorax, etc.) of neuraxial techniques, there is a growing interest in fascial

Table 1. Patient demographic and surgical features

Gender, F/M	2/3
Age, years	55 (47–64)
BMI, kg/m^2	27.3 (21.5–29.8)
ASA, II/III	2/3
EF, %	55 (35–60)
Surgery type, CABG/AVR/ASD	3/1/1
Surgery time, min	305 (240–350)
By-pass time, min	122 (73–257)
Cross-clamp time, min	72 (25–200)
Extubation time, min	360 (240–420)
ICU discharge time, h	28 (24–76)

ASA: American Society of Anesthesiologists; ASD: Atrial Septal Defect; AVR: Aortic Valve Replacement; BMI: Body Mass Index; CABG: Coronary Artery Bypass Grafting; EF: Ejection fraction; ICU: Intensive Care Unit.

Table 2. NRS_{rest} and $NRS_{coughing}$ scores of patients at various time-points and cumulative morphine consumption

	Case 1	Case 2	Case 3	Case 4	Case 5
NRS_{rest}					
Extubation	2	2	3	0	0
3rd h	1	2	2	1	1
6th h	1	4	2	1	1
12th h	1	4	3	2	0
18th h	0	3	2	2	0
24th h	0	3	2	3	0
$NRS_{coughing}$					
Extubation	3	3	4	1	1
3rd h	2	3	3	1	2
6th h	2	5	3	2	2
12th h	2	4	4	4	0
18th h	1	4	3	4	0
24th h	0	4	2	4	0
Cumulative morphine consumption, first 24 h, mg	0	4.5	4	20	3.5

NRS: Numerical rating scale.

plane blocks in cardiac surgery (such as epidural, paravertebral, or intrathecal morphine). The ESP, superficial PIP, and deep PIP blocks have been suggested as effective methods of pain administration for patients undergoing cardiac surgery. Even Although the exact mechanism of action in the ESP block is unknown, the LA is expected to spreads to the paravertebral area and blocks the dorsal and ventral branches of the spinal nerve as well as the sympathetic ganglion. The literature, however, is divided into the absolute spread of LAs to nerve structures other than the dorsal ramus.[9] Moreover, the superficial PIP block, a relatively new fascial plane block, blocks the thoracic nerves' anterior cutaneous branches (Th2-6). Although studies have demonstrated its analgesic effect in cardiac surgery, given the mechanism of action, it is reasonable to expect that the superficial PIP block would be insufficient for managing pain caused by sources other than the sternotomy incision. Because the ESP and shallow PIP blocks only offer a small amount of analgesic coverage, new blocks will inevitably take the lead in heart surgery.

Despite reports that the RIB provides analgesia in the hemithorax and that cadaver studies show a good spread in the craniocaudal and anteroposterior directions, its effectiveness in cardiac surgery is unknown. The RIB's distal and more superficial implementation, as opposed to the RIB block, will make the application easier. In contrast, the issue of inconsistent LA spread found in the ESP block will be removed. While the real-time spread of LA was found in all patients in our research, sono-anatomically, landmarks were defined relatively easily. This proposes that RIB will be a more attractive alternative in cardiac surgery. Our case report has a limitation in that we did not assess the sensory distribution. We are also presently conducting a randomized controlled trial to investigate the analgesic efficacy of RIB after cardiac surgery.

In conclusion, this case series suggests that using the RIB as part of a multimodal analgesia treatment may help lower the amount of opioid intake as well as pain scores. More randomized controlled trials need to be conducted in their entirety.

Disclosures

Informed Consent: Written informed consent was obtained from all patients.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

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Authorship Contributions: Concept – B.D.; Design – S.M.Y., S.T.; Supervision – D.K., A.D.C.; Materials – C.K.; Data collection &/or processing – B.D., C.K.; Analysis and/or interpretation – S.M.Y., S.T., A.D.C., D.K.; Literature research – B.D., C.K., S.T.; Writing – B.D., S.M.Y., S.T.; Critical review – A.D.C., D.K.

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Research Article

Evaluation of Healthcare-associated Nosocomial Infections in the Pediatric Cardiovascular Surgery Intensive Care Unit in Türkiye (2012–2021)

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ABSTRACT

Objectives: The study evaluated the 10-year healthcare-associated infections (HCAI) data in the pediatric cardiovascular surgery intensive care unit (PCVS-ICU).

Methods: The electronic data of 106 patients with HCAI between 2012 and 2021 were retrospectively analyzed for the infection sites, isolated microorganisms, and antibiotic resistance.

Results: 3617 patients with 29155 patient days in our 12-bedded PCVS-ICU were evaluated. There were 64 HCAIs during 2012–2016, comprised of 17 (26.5%) bloodstream infections (BSI), 16 (25%) pneumonia, 13 (20.3%) urinary tract infections (UTI), 8 (12.5%) ventilator-associated pneumonia (VAP), 7 (11.1%) surgical site infection (SSI), and 3 (4.6%) soft-tissue infection (STI). In contrast, 42 HCAIs were observed in 2017–2021, which included 17 (40.4%) BSI, 10 (23.8%) pneumonia, 7 (16.6%) VIP, 4 (9.6%) UTI, 3 (7.2%) SSI, and 1 (2.4%) STI. The most common pathogen was the ***Candida*** species. The ventilator usage rate was 2.8 per 8635 ventilator days and 0.42 per 6439 ventilator days in the first and second five years, respectively. The rate of central venous catheter (CVC) use was 2.04 and 0.96 in the first and second five years, respectively.

Conclusion: The most common HCAI was BSI, and the most common isolated pathogen was ***Candida*** species within ten years in our PCVS-ICU. The infection rate, CVC, and UC usage rates were decreased, with an increased compliance rate on hand hygiene in the second five years, indicating strict adherence to infection control measures.

Keywords: Cardiovascular surgery, healthcare-associated infections, pediatric intensive care

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Introduction

Healthcare-associated infection (HCAI) is a significant cause of morbidity and mortality in hospitalized children. It is also responsible for prolonged hospital stays and increased costs.[1] The incidence of HCAIs varies significantly between countries, regions, and hospitals, which are associated with the causal microorganisms in the hospital, the healthcare team, and a variety of interactions among patients themselves.[2] As innate and acquired immunity are suppressed, and natural physical defenses such as skin integrity, cough reflex, and gastric motility are impaired, the susceptibility to HCAIs increases in pediatric intensive care unit patients.[3] The most common nosocomial infection in pediatric intensive care units is bloodstream infections (BSI), followed by pneumonia and urinary tract infections (UTI).[4,5]

The major HCAI pathogens in neonatal intensive care units comprised Gram-negative bacteria (GNB) such as *Klebsiella pneumonia* and *Escherichia coli*, Gram-positive bacteria such as *Staphylococcus aureus* and Coagulase-negative staphylococci (CNS).[6]

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HCAI rates in pediatric intensive care units (PICUs) in Türkiye ranged from 2.9% to 43.9%.[7] Due to the limited information available for HCAIs in the PCVS-ICU, we analyzed 10-year data on the frequency, infection sites, microorganisms grown in cultures, and antibiotic resistance registered in the hospital infection control surveillance system.

Methods

This study retrospectively analyzed the electronic data of 117 patients with HCAI in the PCV-ICU of the Kartal Koşuyolu Research and Training Hospital, Türkiye, from 2012 to 2021, according to the criteria of the Centers for Disease Control and Prevention (CDC), 2015 and the National Nosocomial Infections Surveillance Network (UHESA), 2017.

The following definitions and formulas were used to calculate healthcare-associated infection rates:

The number of hospitalized days refers to the total number of days of all patients hospitalized in the PICU during a year.

Invasive device day is the total number of days of exposure of a PICU patient to an invasive device during a year.

Healthcare-associated infection rate: Number of healthcare-associated infections/number of hospitalized patients)×100

Healthcare-associated infection frequency density (incidence): Number of healthcare-associated infections / patient days)×1000

Invasive device usage rate: Number of invasive device days/Patient days

Invasive device-related healthcare-associated infection rate (per 1000 catheter-days): (Invasive device-related SBIs/Invasive device days)×1000

Invasive device-associated healthcare-associated infection rate (%) (per 100 patients): Number of FNAIS/ Number of inpatients×100

Culture on blood, urine, sputum, wound site, and endotracheal aspirate was conducted weekly in the patients receiving catheter and ventilator therapy to exclude the infection. We transported the samples immediately after collection to the microbiology laboratory using special transport bags. Then the samples were cultivated onto the sheep blood agar, chocolate agar, and eosin methylene blue agar. The plates were incubated for 24–48 hours at 35°C±2°C. Additionally, gram staining was performed for all samples. Antibiotic susceptibility test results were evaluated according to the recommendations of the Clinical and Laboratory Standards Institute (CLSI-2015) and the European Committee on Antimicrobial Susceptibility Testing in 2018–2019. Vitek II (BioMerieux, France) system was used for the species identification of isolates in the clinical microbiology culture laboratory.

The study was approved by the ethical committee of Kartal Koşuyolu Research and Training Hospital.

Results

This study assessed 3617 patients with 29155 patient days, between 2012–2021, in 12-bedded PCVS-ICU. Of 64 HCAIs, including 17 (26.5%) BSI, 16 (25.0%) pneumonia, 13 (20.3%) UTI, 8 (12.5%) VAP, 7 (11.1%) SSI, and 3 (4.6%) STI, were detected during 2012–2016. Besides, 42 HCAIs were detected during 2017–2021, including 17 (40.4%) BSI, 10 (23.8%) pneumonia, 7 (16.6%) VIP, 4 (9.6%) UTI, 3 (7.2%) SSI, and 1 (2.4%) STI (Table 1).

The rate of HAI and incidence rate in the first five years were 3.47% and 4.54, respectively, vs. 2.26% and 2.65 in the second five years, respectively. In the first five years, the ventilator usage rate was 2.8 per 8635 ventilator days vs. 0.42 per 6439 ventilator days in the second five years.

Similarly, the CVC rate was 2.04 with a CVC use rate of 0.96 in the first five years vs. 1.8 CVC rate and 0.62 CVC use rate in the second five years. Moreover, the urinary catheter rate and the urinary catheter use rate were 0.8 and 0.91 in the first five years, vs. 0.73 ad 0.94 in the second five years, respectively.

The identified microorganisms in the first five years were *Candida albicans* (n=24), *Klebsiella pneumonia* (n=20), which were ESBL resistance (71%) and carbapenem resistance (50%), *Acinetobacter baummanii* (n=9) which showed carbapenem resistance (100%), *Pseudomonas aeruginous* (n=9) which showed carbapenem resistance (100%), and coagulase-negative staphylococci (n=5). No isolates showed colistin resistance.

In the second five years, the most common isolated pathogens were *Candida albicans* (n=41), *Klebsiella pneumonia* (n=21) which were ESBL resistance (65%), carbapenem resistance (75%), and colistin resistance (60%), *Stenomonas maltophilia* (n=20), *Acinetobacter baummanii* (n=7) which were carbapenem resistance (50%), colistin resistance (70%), *Pseudomonas aeruginosa* (n=7) which showed carbapenem resistance (100%), colistin resistance (100%) and coagulase-negative staphylococci (n=2) (Table 2).

Regarding antibiotic resistance, colistin resistance was not observed in GNB within the first five years, but it increased markedly in the second five years. Similarly, as for the carbapenem resistance, pan-resistant strains increased in the second five years. Meanwhile, hand hygiene compliance rates of the health care provider increased steadily from 77% to 86% from 2012 to 2017 and 83% to 94% from 2018 to 2021 (Table 3).

Discussion

HCAI is an important indicator of healthcare quality in developed and developing countries. Children are at higher risk

Table 1. Distribution of healthcare-associated infection (HAI) types (2012–2021)

Types of HAIs	Years																			
	2012		2013		2014		2015		2016		2017		2018		2019		2020		2021		Total	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
BSI	7	36.8	5	20	1	14.2	1	20	3	37.5	9	64.2	1	16.7	1	20	1	20	7	50	36	33.3
Pneumonia	6	31.5	6	24	2	28.4	1	20	1	12.5	0	0	2	33.3	1	20	2	40	5	35.7	26	24
VAP	4	21	2	8	2	28.4	0	0	0	0	5	35.8	0	0	1	20	1	20	0	0	15	13.8
SSTI	0	0	2	8	1	14.2	0	0	1	12.5	0	0	0	0	1	20	0	0	0	0	5	4.6
UTI	2	10.5	5	20	1	14.2	2	40	3	37.5	0	0	2	33.3	1	20	1	20	0	0	17	16
SSI	0	0	5	20	0	0	1	20	0	0	0	0	1	16.7	0	0	0	0	2	14.3	9	8.3
Total	19		25		7		5		8		14		6		5		5		14		108	

BSI: blood stream infection; VAP: ventilator-associated pneumonia; SSTI: skin and soft-tissue infection; UTI: urinary tract infection; SSI: surgical site infection.

Table 2. Distribution of the pathogens antibiotic susceptibility patterns between 2012 and 2021

Pathogens of HAIs	2012		2013		2014		2015		2016		2017		2018		2019		2020		2021	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Total (n=194)	19		20		20		14		16		20		24		25		24		12	
Klebsiella pneumoniae (n=41)	4	21	5	25	6	30	0	0	5	31.2	4	25	2	8.3	7	28	5	20.8	3	25
Pseudomonas aeruginosa (n=23)	6	31	4	20	3	15	3	21.4	0	0	1	5	3	12.5	1	4	2	8.3	0	0
Acinetobacter baumanii (n=16)	3	15.7	2	10	3	15	0	0	1	6.2	2	10	2	8.3	0	0	3	12.5	0	0
Candida spp (n=41)	2	10.5	3	15	1	5	3	21.4	7	43.7	5	20	4	16.6	7	28	9	37.5	0	0
Candida albicans (n=24)	4	21	4	20	3	15	1	7.1	1	6.2	0	0	3	12.5	2	8	1	4.1	5	41.6
CoNS (n=7)	0	0	1	5	2	10	2	14.2	2	12.4	0	0	0	0	0	0	0	0	0	0
Escherichia coli (n=5)	0	0	2	10	0	0	2	14.2	0	0	0	0	0	0	0	0	0	0	1	8.3
Enterococcus faecium (n=6)	0	0	0	0	0	0	0	0	0	0	0	0	3	12.5	3	12	0	0	0	0
Enterococcus faecalis (n=2)	0	0	0	0	0	0	0	0	0	0	1	5	0	0	1	4	0	0	0	0
Enterobacter cloacae (n=2)	0	0	0	0	1	5	0	0	1	6.2	0	0	0	0	0	0	0	0	0	0
Stenotrophomonas maltophilia (n=23)	0	0	0	0	1	5	2	14.2	0	0	7	35	6	25	0	0	4	16.6	3	25
Serratia marcesens (n=5)	0	0	0	0	0	0	1	7.1	0	0	0	0	1	4.1	3	12	0	0	0	0
Ralstonia picketti (n=29)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	8	0	0	0	0

İn some clinical samples more than one agent was isolated. HAI: Healthcare-associated infection; CoNS: Coagulase-Negative Staphylococcus

Table 3. Hand hygiene practices of the health care providers (2012–2021)

	Years									
	2012 %	2013 %	2014 %	2015 %	2016 %	2017 %	2018 %	2019 %	2020 %	2021 %
Hand hygiene	77	78	81	86	86	83	91	81	91	94

than adults regarding HCAIs due to vascular access problems, frequent drug administration requirements, and the need for more frequent nurse care in PICUs.[8] Studies have shown that the HCAI rates in PICU range from 3.6% to 20% worldwide.[9] These rates in Türkiye differ from 2.9% to 43.9% in the pediatric ICUs[7] and from 3.2% to 42.3% in the neonatal ICUs.[10] In our study, the HCAI rate was 3.47% in the first five years and 2.26% in the second five years. Although our rates are low compared to world data, it was noticeable that there was a 1.21% decrease in the second five years.

A study conducted in the PICU in the USA reported that the most common HCAI was BSI (41.3%), followed by VAP (22.7%).[11] Maoulainine et al.[12] reported that 79.6% of HCAIs were ESBL-producing GNB, and the most common

pathogen was *K. pneumoniae* (39.7%). Another study reported that the most common microorganisms isolated were GNB (79.8%), in which *Klebsiella pneumonia* was the most common pathogen (n=22, 29.3%). Consistent with the literature, we found GNB as the most common cause of HCAI in our PCVS-ICU, i.e., 73.6% of 76 isolates in the first five years, in which *K. pneumoniae* was the most common (26%). The second most common organism was *Candida spp*. (26.3%). In the second five years, of the 94 isolates, 69% were GNB, which included *Candida spp*. (31%).[13,14]

In a prospective study conducted in Spain, bacteremia was the most common HCAI in the PICU, followed by respiratory tract infections and UTIs. In their study, the most common pathogens were Coagulase-negative *Staphylococci, Pseudomonas aeruginosa,* and *E. coli*.[15] On the other hand, the most common HCAI pathogens in our PCVS-ICU were P. aeruginosa in pneumonia (might or might not be associated with ventilation support), *Stenotrophomonas (Xanthomonas) maltophilia* in bacteremia, and *E. coli* in UTI.

During the first five years of the study, colistin resistance was not observed, but carbapenem resistance was high. In contrast, colistin resistance was 100%, and pan-resistant carbapenem strains were observed in the second five years. As our hospital is a tertiary referral center for pediatric CVS, most admitted patients undergo surgery to correct complex cardiac pathologies with an increased tendency to prolonged hospital stays, mechanical ventilation, and HCAIs. Moreover, most of these operated children had syndromes or accompanying respiratory, neurologic, or gastrointestinal health problems. The use of broad-spectrum antibiotics as empirical treatment in these patients might lead to increased antibiotic resistance.

In many studies conducted with *S. maltophilia*, most isolates were from ICU patients.[16] Nosocomial infections caused by *S. maltophilia* are mostly defined as lung infections, urinary system infections, catheter-related infections, bacteremia, and sepsis.[17,18]

In hospitals, these bacteria can be isolated from central venous or arterial monitors, dialysis machines, disinfectant and hand washing solutions, deionized water, nebulizers, ventilation systems, tap water, shower heads, and the hands of healthcare personnel.[19]

In this study, 5% of the pathogens isolated in the first five years were *S. maltophilia*. However, it increased to 50% in the second five years, probably from the medical materials used. Moreover, the increase in hospital care-associated pneumonia cases in the second five years might be due to COVID-19.

During the COVID-19 pandemic, hand hygiene rates have increased, and additional measures such as restriction of intensive care visits, more protective measures such as masks and visors, and more frequent cleaning of the unit have been implemented by the health care providers.

In many epidemic investigations, the causes of the epidemic were related to the insufficient personnel or the acceptance of patients above capacity and the low level of hand hygiene compliance.[20,21] The prevalence of HCAIS decreased with increased compliance with hand hygiene in health professionals.[22,23] Although compliance with hand hygiene is the easiest, cheapest, and most effective method in preventing HCAIs, studies have shown that hand hygiene compliance rates remain about 30%–60%, and some do not exceed 50%.[24]

In our study, hand hygiene rates increased markedly (77%–86% from 2012 to 2017 and 83%–94% from 2018 to 2021) owing to training and awareness during the COVID-19 pandemic.

The Institute for Healthcare Improvement has developed the concept of a "care package" to provide the best possible multidisciplinary care for patients. Care packages should always apply to patients of all conditions and be evidence-based.[25] With the care package, it is important to reassure healthcare workers that they are part of the team and that zero infection is possible. In the hospital, care packages (ventilator-associated pneumonia care package, urinary catheter-related urinary system infection care package, and central venous catheter-related bloodstream infection care package) created by the infection control team according to the institution profile are used.

Covering the dressing of the central catheter with a semi-permeable and transparent dressing ensures that the catheter entry site can be observed, preventing frequent dressing changes. The care packages we apply in our hospital include basic components about field cleaning, catheter application procedure, and care, and their application is ensured. As a result, infection rates have decreased with the implementation of care packages in our hospital.

The care packages applied in infection control are an application that includes all these steps: education of healthcare workers, provision of care, evaluation, and recording of data for success in the fight against infection. Infection control section management, personnel training, procedural control, compliance, and calculation of surveillance are of great importance in the reliable implementation of care packages.[26]

After the training given before the application and the feedback in the field, the infections decreased shortly after the implementation of the care packages in our study. We attributed this to increased attention to the issue of infection control and strict adherence to infection control measures.

Serious measures are required to ensure infection control in the ICU. However, despite all efforts and precautions, the infection can still be observed. Factors such as inadequate personnel per patient, a high number of chronic patients who need to be hospitalized for a long time, and the inadequacy of physical facilities increase the number of HCAIs. We think that the increased compliance with all infection control measures, from hand hygiene to unit hygiene, is effective in the decrease in infection rates in this period. Infection control measures should be applied meticulously, and personnel training and infection frequency should be reviewed regularly. Awareness of HCAIs should be increased by conducting regional and multicenter current studies on pediatric surgery intensive care units.

Disclosures

Ethics Committee Approval: The study was approved by The Kartal Koşuyolu High Specialization Training and Research Hospital Clinical Research Ethics Committee (Date: 22/03/2022, No: 2022/6/578).

Informed Consent: Written informed consent was obtained from all patients.

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Research Article

Single-Center Outcomes of Vacuum-Assisted Closure Therapy for Mediastinitis After Pediatric Cardiac Surgery

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ABSTRACT

Objectives: Vacuum-assisted closure therapy is useful in treating mediastinitis, which is related to high mortality and morbidity rates after cardiac surgery. This study aimed to present our experience with vacuum-assisted closure therapy in mediastinitis after pediat-ric cardiac surgery.

Methods: This retrospective review included 10 patients who underwent vacuum-assisted closure therapy for mediastinitis in a single institution from 2020 to 2022. Pa-tients with wound discharge or abscess, sternal dehiscence, fever, and positive wound culture were considered to have medi-astinitis. The vacuum sponge was cut at the appro-priate size for the mediastinal defect and the skin edges were approximated with prolene sutures. The vacuuming continuously started at −50 mm Hg.

Results: Six (60%) patients were female and the median age during therapy was 1.9 months (range: 0.1–54 months). Five (50%) patients were neonates. The median duration of vacuum-assisted closure therapy was 14.5 days (range: 4–78). The median duration to obtain negative mediastinal culture was 14.5 days (range: 6–76). The sternum could be closed without difficulty in all patients except one who died due to low cardiac output. Hospital mortality occurred in 3 (30%) patients who needed extracorporeal membrane oxygenation support postoperatively. The median duration of follow-up was 10 months (range: 2–28).

Conclusion: Mediastinitis is an important problem associated with high morbidity and mortality rates after pediatric cardiac surgery. Data suggest that vacuum-assisted closure therapy can safely treat mediastinal infections without recurrence.

Keywords: Congenital heart disease, mediastinitis, pediatric cardiac surgery, vacuum-assisted closure

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Introduction

The treatment for deep sternal wound infection and medi-astinitis after pediatric cardiac surgery remained associated with a high risk of morbidity and mortality rates.[1,2] Median sternotomy is the usual approach in pediatric cardiac surgery, and mediastinitis after ster-notomy affects approximately 1% of children.[3,4] Additionally, the incidence of mediasti-nitis seems higher, especially in neonate patients.[5] Open chest and delayed sternal clo-sure techniques have a high risk of mediastinal infections.[6]

Mediastinitis provokes several problems, including prolonged hospital stay, prolonged antibiotic use, and increased healthcare costs.[6] Surgical debridement, drainage and irri-gation, antibiotic therapy, and direct or secondary closure with a pectoral muscle flap are the recommended treatment techniques for treating deep sternal wound infections.[7,8] However, the best treatment option still has no consensus.

A subatmospheric pressure with vacuum-assisted closure (VAC) system in chronic wound care was first used in 1997.[9] The VAC system advances wound healing by ex-tract-

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ing localized edema, develops vascular circulation, and improves granular tissue for-mation.[10,11] This report aims to present our experience of managing children with VAC therapy after cardiac surgery.

Methods

This study retrospectively reviewed the medical records of 10 consecutive patients who underwent VAC therapy for mediastinitis after congenital cardiac surgery from January 2020 to January 2022. Patients with wound discharge or abscess, sternal dehiscence, fe-ver, and positive wound culture were considered to have mediastinitis. The suspected pa-tients were diagnosed using computed tomography. Patients who had wound infections without mediastinitis were excluded from the study. Data were retrospectively collected from the patient's previous hospital records. Our study (numbered E-28001928-604.01.01-330) was approved by the institution on November 29, 2022, and was con-ducted following the principles of the Declaration of Helsinki.

Collected data included patient demographic characteristics, preoperative cardiac patholo-gy diagnosis, type of operations, and use of extracorporeal membrane oxygenation (ECMO) support, as shown in Table 1. Additionally, the type of microorganisms, the antibiotics used, the presence of delayed sternal closure, the number of VAC changes, and the duration are shown in Table 2.

Surgical Technique

Antibiotic treatment was started in all patients according to antibiograms before VAC treatment. Mediastinal or deep wound culture samples were obtained from all patients before starting the VAC application. The VAC sponge was cut at the appropriate size and depth for the wound geometry and placed in the mediastinal defect after careful hemosta-sis. Prolene sutures were used to approximate the skin edges to prevent the VAC sponge from overflowing and eroding the skin. The sponge was covered with a transparent ad-herent drape, and the VAC system was attached to it by making a hole in the drape. This drape was cut as small as possible so that it would not erode the healthy skin. The VAC system began to continuously vacuum the wound at −50 mm Hg. The VAC sponge was changed every 72/96 h. Two culture samples were taken from the mediastinum at each system change. A smaller sponge was inserted as the wound got smaller at each VAC change (Fig. 1). The VAC system was terminated and the chest cavity was closed when wound healing was observed and the culture was negative.

Statistical Analysis

Continuous variables were reported as median±range. Categorical variables were reported as n(%). IBM Statistical Package for the Social Sciences Statistics Software version 21 (SPSS Inc., Chicago, IL, USA) was used for statistical analyses.

Table 1. Demographic characteristics and operative data of patients

Patient	Age (month)	Weight (kg)	Sex	Preoperative diagnosis	Previous op-eration	Last operation	Postop events
1	3	3.5	M	TGA	ASO	Supralvalvar AS repair	ECMO
2	54	15	M	IAA+VSD+RV hypo-plasia	Bilateral PA banding, Com-prehensive stage 2 opera-tion	SVC Graft inter-position for SVC occlusion	
3	3	6	F	Pulmonary artery sling	Pulmonary artery sling repair	Tracheoplasty	ECMO
4	14	7.5	M	TGA+VSD+PS	MBT shunt	Rastelli operation	ECMO
5	0.8	2.7	M	Supracardiac TAPVD	Supracardiac TAPVD repair	Right PV reanastomosis	
6	0.2	2.8	F	HLHS		Norwood proce-dure	
7	60	12.5	F	TOF	MBT shunt	TOF repair	Revision for bleeding
8	0.1	3.1	F	Arcus hypo-plasia+VSD	Arcus recon-struction+PAB	Supravalvar AS repair	ECMO
9	0.2	3.4	F	IAA+VSD		Arcus reconstruc-tion+PAB	Revision for bleeding
10	0.2	3	F	Arcus hypo-plasia+VSD		Arcus reconstruc-tion+PAB	ECMO (twice)

AS: aortic stenosis; ASO: arterial switch operation; ECMO: extracorporeal membrane oxygenation; HLHS: hypoplastic left heart syndrome; MBT: modified Blalock-Taussig; PA: pulmonary artery; PAB: pulmonary artery banding; PS: pulmonary stenosis; RV: right ventricle; TAPVD: total anomalous pulmonary venous drainage; TGA: transposition of great arteries; TOF: tetralogy of Fallot; VSD: ventricular septal defect.

Table 2. Microbiological data of patients

Microorganism	Antibiotics	Delayed sternal closure	Number of VAC changes	Time VAC (day)
Acinetobacter baumannii, Klebsiella oxytoca	Colimycin, piperasilin/ tazobactam	yes	26	78
Klebsiella pneumonia	Colimycin, meropenem, vancomycin	yes	8	35
Escheria coli	Linezolid, meropenem	yes	5	15
Klebsiella pneumonia	Colimycin, meropenem	yes	3	8
Candida albicans	Anidulafungin, meropenem	yes	5	14
Klebsiella pneumonia	Ertapenem, vancomycin, meropenem	yes	3	8
Staphylococcus epidermid-is	Vancomycin, amikacin	yes	2	4
Enterobacter aerogenes	Ciprofloxacin, vancomy-cin, meropenem	yes	2	6
Serratia marcescens, Klebsiella pneumonia	Fluconazole, colimycin, meropenem, vancomycin	yes	17	51
Sterile	Vancomycin, meropenem	yes	12	35

VAC: vacuum-assisted closure.

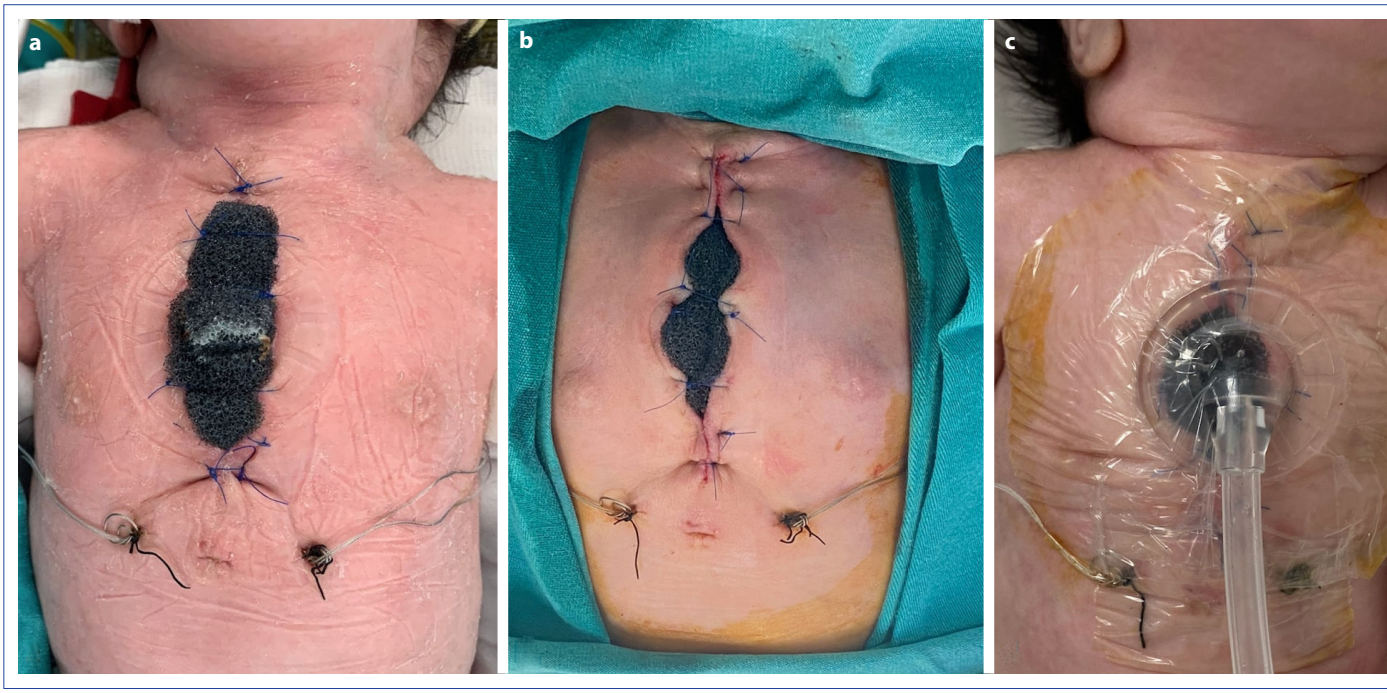

Figure 1. The image shows the placement of the VAC sponge with prolene sutures **(a)**. The images show the inserted smaller sponge at each VAC exchange as the wound granulation is present **(b, c)**.

Results

During our study, 10 patients, including 6 females and 4 males, with mediastinitis after pediatric cardiac surgery were treated with VAC therapy. The median age of the patients was 1.9 months (range: 0.1–54 months) and the median weight was 3.45 kg (range: 3–15 kg). Of the patients, five were neonates, three were infants, and two were children.

The primary diagnosis included interrupted aortic arch (IAA) and ventricular septal defect (VSD) in two patients, aortic arch hypoplasia and VSD in two patients, hypoplastic left heart syndrome (HLHS) in one patient, transposition of the great arteries (TGA) in one patient, supracardiac total anomalous pulmonary venous drainage (TAPVD) in one patient, TGA, VSD, and pulmonary stenosis (PS) in one patient, pulmonary artery sling in one patient, and tetralogy of the Fallot (TOF) in one patient. Functional biventricle and single ventricle were observed in 8 and 2 patients, respectively.

Seven (70%) patients were not operated on for the first time, and cardiac surgery was performed after redo sternotomy. It was the second operation of six patients, while the fourth operation of one. The sternum was left open in the early postoperative period due to myocardial dysfunction or edema in 9 (90%) patients. Central veno-arte-

rial ECMO support after cardiac surgery was required in 5 (50%) patients, and one of them needed ECMO twice. The median ECMO support duration was 6 days (range: 2–12 days). Sur-gical revision was required in two patients due to bleeding.

VAC therapy was applied after a median of 10 days (range: 1–27 days) from the cardiac surgery. The median VAC therapy duration was 14.5 days (range: 4–78), and the median change of VAC therapy was five times (range: 2–26). *Klebsiella pneumonia (n=3), Acinetobacter baumannii (n=1), Escherichia coli (n=1), Candida albicans (n=1), Staphylococcus epidermidis (n=1), Enterobacter aerogenes (n=1), and Serratia marcescens (n=1)* were obtained from the mediastinum cultures. Only one patient had sterile culture despite the wound abscess and the sternal dehiscence. Antibiotic treatments were changed by the infectious diseases specialist following the culture antibiogram. The median dura-tion to obtain negative mediastinal culture was 14.5 days (range: 6–76). The sternum could be closed without difficulty in all patients except one after VAC treatment, and no revision was required. The sternum could not be closed due to significant myocardial edema in this patient, who died due to sepsis.

Hospital mortality occurred in 3 (30%) patients. One of them, who underwent a Rastelli procedure for TGA-VSD-PS, required ECMO support caused by low cardiac output syndrome (LCOS). This patient had *Klebsiella pneumonia* mediastinitis and died due to sepsis despite the VAC therapy on postoperative day 30. This patient was the only patient whose sternum could not be closed after the VAC therapy. Another patient, who under-went aortic arch reconstruction and pulmonary banding operations for aortic arch hypo-plasia and VSD, required a second operation due to supravalvar aortic stenosis. This pa-tient needed ECMO support after the second operation and died due to multiorgan failure on postoperative day 125. The last patient, who underwent aortic arch reconstruction and pulmonary banding operations for aortic arch hypoplasia and large VSD, underwent extracorporeal cardiopulmonary resuscitation due to sudden cardiac arrest. This patient re-quired ECMO again caused by low cardiac output despite weaning from ECMO. This patient died because of septic shock on postoperative day 77. The median duration of in-tensive care unit (ICU) and hospital stay postoperatively were 96 days (range: 30–510) and 98.5 days (range: 10–510), respectively.

The median duration of follow-up was 10 months (range: 2–28) in the surviving patients.

One patient died after hospital discharge and the other one died after being transferred to another ICU, thus the overall mortality occurred in 5 (50%) patients. The first patient un-derwent a total repair operation for TOF and died after 5 months from hospital discharge due to right heart failure and LCOS at another center. The second patient underwent pul-monary sling repair and tracheoplasty operations (twice) and was transferred to the gen-eral pediatric ICU after 510 days of cardiac ICU hospitalization and died due to respirato-ry distress and sepsis although tracheal patency was demonstrated in bronchoscopy con-trols. This patient and three patients who died in the early postoperative period needed ECMO support in the postoperative period.

Discussion

Herein, we present our experience with 10 patients with mediastinitis treated with VAC. Our management in patients who develop mediastinitis after cardiac surgery mainly aimed to obtain a wound or mediastinal culture, extend antibiotherapy, and start mediastinal VAC treatment. Their antibiotic therapies were changed after the consultation with the infectious diseases specialist according to the culture results.

Mediastinitis and sternal wound problems may develop after pediatric cardiac surgery especially in low-weight neonates due to biochemical and nutritional imbalances, long cardiopulmonary bypass times, myocardial edema, low cardiac output syndromes, and central ECMO application.[2,12] Additionally, the age and weight of patients and re-exploration for postoperative bleeding are important in the course of infection.[6,13] The risk of mediastinitis increases with these factors.[13] The VAC system guards the medias-tinum or wound against contamination and supports blood circulation and tissue granula-tion. Moreover, VAC therapy reduces bacterial cell count and intercepts tissue fluid reten-tion.[14] This technology has been used in the last two decades for wound closure in chil-dren and neonates with sternal problems after cardiac surgery.[4,15] Herein, we used the VAC system in neonates, infants, and children to achieve sternal closure in mediastinitis.

Diagnostic criteria for mediastinitis differ from institution to institution and among clini-cians.[16] Wound microbiological cultures demonstrate a wide variety of organisms such as *Klebsiella pneumonia*, *Escherichia coli*, *Acinetobacter baumannii, Serratia mar-cescens, Staphylococcus aureus, Staphylococcus epidermidis, coagulase-negative Staphy-lococcus, enterococcus species, Pseudomonas aeruginosa, Proteus vulgaris, and Corynebacterium*.[16] Most of these microorganisms in our study were acquired from wound cultures, except for one patient. Additionally, VAC treatment was applied in this patient because of sternal dehiscence and abscess.

Surgical debridement, drainage and irrigation, and direct or secondary closure with a pec-toral muscle flap are the traditional surgical treatment strategies for mediastinitis.[6] We did not prefer any of these methods, especially because they are ineffective in neonates.[6] Half of our patients were neonates and the results of VAC therapy, especially in neonates, have been very successful in the literature.[6,12] We think that approximating the wound edges with prolene sutures, small dressings, and smaller sponges as the granulation in-creases are important in terms of VAC time shortening and wound healing acceleration. The sternum and wound site of all patients were closed except for one, and they did not need a muscle flap, and with no wound problems in their follow-up.

Empirical antibiotic therapy given preoperatively for prophylaxis is an effective way of dealing with postsurgical wound infections. However, empirical treatments cannot isolate every microorganism, especially resistant strains.[6] Children undergoing complex cardiac surgery are often given many antibiotics in the postoperative course and are at increased risk of infection by resistant and fungal pathogens. Our study indicated the effectiveness of our mediastinitis treatment strategy with the VAC system against fungal and resistant microorganisms.

The most important detail of using VAC is adjusting the pressures. High negative pres-sure in the mediastinum can be a risk for direct cardiac structure or conduit compression and may decrease cardiac output, particularly in cases of severe mediastinitis and or cardi-ac dysfunction.[17,18] Thus, we prefer to use lower negative pressure (−50 mm Hg) in our study. VAC treatment can be performed with higher pressures in case of sternal closure because there will be no direct contact with cardiac structures. Filipelli et al.[12] conducted a study on six neonates who underwent VAC therapy for mediastinitis after cardiac sur-gery. They preferred high negative pressure (−125 mm Hg) because they applied a VAC system on the closed sternum. Conversely, some studies reported that low pressures re-cover the mediastinum, sternum, and wound as efficiently as high negative pressures without complications such as insufficient drainage or tissue damage.[3,19]

Literature reported various mortality rates after VAC therapy. Filippelli et al.[12] reported zero early mortality rate in six patients, Onan et al.[6] reported a 14% early mortality rate in 14 patients, and Aydin et al.[13] reported a 22% early mortality rate in nine patients.[6,12,13] We believe that mortality in this patient group is especially associated with primary cardiac pathology or cardiac functions. The early mortality rate was 30% in 10 patients in our study. All of these patients needed ECMO support during the postoperative period and were weaned from ECMO. One of our two patients who died during the follow-up period underwent ECMO support in the postoperative period. Thus, patients who needed ECMO support in the postoperative period accounted for 80% of our total mortality.

Hemodynamic parameters should be cautiously monitored in patients undergoing sternal VAC therapy.[17,18] Petzina et al.[17] reported that negative pressure on the chest decreases left ventricular end-diastolic volume, stroke volume, and so cardiac output. They suggest-ed that VAC compression damages the diastolic filling of the ventricles.[17] More nega-tive effects of this negative pressure can be seen, especially in operations, such as Rastelli and Fontan, where conduits are used.[20] Our study revealed no adverse hemodynamic effects of VAC treatment. However, the only patient whose chest could not be closed after VAC treatment was our patient who underwent a Rastelli operation. Therefore, more attention should be paid to hemodynamic parameters, especially in patients using conduits.

The major limitations of this study are the single-center, limited-patient, and retrospective design. Studies with multiple centers, more patients, and long-term outcomes are needed to demonstrate the VAC therapy outcomes.

In conclusion, mediastinitis is a rare but serious problem with increased mortality and morbidity rates after pediatric cardiac surgery. The VAC system is a confident treatment for mediastinitis and sternal wound problems after pediatric cardiac surgery. It provides high-quality and rapid healing of surgical wounds and can be safely applied in the treat-ment of mediastinitis after cardiac surgery.

Disclosures

Ethics Committee Approval: The study was approved by The instutitional Ethics Committee (Date: 29.11.2022, No: E-28001928-604.01.01).

Informed Consent: Written informed consent was obtained from all patients.

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Research Article

Difference Among Perioperative Factors Related to Ultra-Fast Track Extubation After Fontan Completion

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ABSTRACT

Objectives: The immediate extubation technique in patients undergoing a Fontan operation is commonly used to reduce the negative effects of positive-pressure ventilation on pulmonary blood flow and provide a hemodynamic advantage. This study aimed to determine the correlation between the perioperative characteristics of patients undergoing a Fontan operation and the success of fast track extubation.

Methods: Perioperative data from patients from all age groups undergoing a Fontan operation were retrospectively analyzed and correlated with their extubation time.

Results: A table extubation was performed on 72.7% of patients undergoing a Fontan operation. Age, presence of fenestration, conduit localization, heterotaxy, cross and bypass durations, and success of ultra-fast track extubation have no significant correlation.

Conclusion: Ultra-fast track extubation strategy facilitated the hemodynamic adaptation of patients to the Fontan circulation. However, the Fontan population has little variation in early extubation characteristics.

Keywords: Airway extubation, cardiac surgery, congenital heart diseases, fontan circulation

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Introduction

Interest in reducing the duration of mechanical ventilation following Fontan operations is growing. Mechanical ventilation-associated high thoracic pressure, decreased resultant systemic and pulmonary return, and increased central venous pressure are among the disadvantages of delayed extubation in patients undergoing a Fontan operation.[1,2] Avoiding these adverse effects is important, especially in single ventricle physiology, concerning hemodynamic stabilization. The Fontan circulation is distinguished by the passive blood flow through the pulmonary vascular bed caused by the venous pressure. Spontaneous breathing was shown to increase the venous return from the systemic circulation to the pulmonary arteries.[3-6] This is caused by the negative intrathoracic pressure created during physiologic inspiration that acts as a driving force for the systemic venous return and improves the pulmonary blood flow in patients with a single ventricle. The first report by Fontan hypothesized the theoretical importance of spontaneous breathing for the hemodynamics of patients with a single ventricle, which was later confirmed by other studies.[5] Thus, early extubation was suggested to provide a physiologic benefit in patients undergoing single ventricle palliation.[2]

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However, the prevailing use of an early extubation strategy and its impact on clinical outcomes remains unconfirmed.[7] Several studies have revealed that early extubation decreases hospital and intensive care unit (ICU) length of stay, improves hemodynamics, and minimizes postoperative complications, thereby reducing cost and resource utilization.[2,4,5,7] This suggests that an early re-introduction of the physiologic breathing mechanics avoids venous stasis and improves end-organ perfusion in patients undergoing a Fontan operation due to its support on the cardiac output. A fast-tracking protocol includes a rapid mechanical ventilation discontinuation, which can sometimes be accomplished in the operating room (OR) at the end of the procedure or shortly after ICU arrival.[3] Therefore, patients with a single ventricle stand as suitable candidates for implementing a postoperative fast track extubation strategy.

Methods

This study retrospectively included 22 patients operated on for Fontan completion from 2021 and 2022 in the cohort. The same surgical team operated on all patients. Patients who were transferred to the ICU under extracorporeal membrane oxygenation support and/or died were excluded from the analysis. The perioperative in-hospital data of patients were reviewed.

Each patient's anesthetic and surgical protocol was standardized across the cohort. Anesthesia was induced with propofol at 2 mg/kg, fentanyl at 1–2 mcg/kg, rocuronium at 0.6 mg/kg, and maintained with 0.8–1 MAC sevoflurane preoperatively. The depth of anesthesia was determined with Bispectral index monitoring.

Standard aortobicaval cannulation was performed for cardiopulmonary bypass setup with mild systemic hypothermia. Cardiac arrest was achieved with aortic cross-clamping if any in-chamber intervention was planned, such as valve repairs, atrial septectomy, and intra-extra cardiac approach, for Fontan completion. Del Nido cardioplegia was used to initiate the arrest, followed by blood cardioplegia for maintenance. A fenestration was created in all patients, except for one patient in Group 1, before completing the procedure. Unbalanced common atrioventricular (AV) valves were repaired via a valvuloplasty reinforced with a polytetrafluoroethylene strip over the superior and inferior bridging leaflets of the common valve.

Surgical correction was confirmed after completing the procedure using transesophageal echocardiography. Postoperative pain was controlled with a pre-extubation parasternal block with 0.5 ml/kg of bupivacaine in 0.25% concentration. Anesthesia was discontinued 20 min after the parasternal block administration. The effects of muscle relaxants were counteracted with sugammadex (2 mg/kg).

The following parameters were considered as indicators of successful on-table extubation: confirmed surgical repair of the defect with stable hemodynamics and no evidence of relevant hemorrhage; adequate spontaneous breathing; body temperature of 36°C; and appropriate blood gas analysis with a 40% fraction of inspired oxygen. The anesthesia team and the surgeon jointly decided on extubation in a personalized, case-based manner. Perfusions of 0.2–0.5 mcg/kg/h of dexmedetomidine and analgesic doses of 0.5–1 mcg/kg/h of fentanyl were started during the patients' ICU follow-up. Patients were given non-invasive respiratory support at 2 L/kg/min per protocol.

Statistical Analysis

The Statistical Package for the Social Sciences (IBM Inc., Armonk, NY) software was used for statistical analysis and table creation. Continuous data were represented as medians and interquartile ranges. The Mann-Whitney U and independent samples t-tests were used to compare continuous data between the two groups. Pearson's chi-square and Yate's continuity correction tests were used for categorical data comparison. A p-value of <0.05 was considered statistically significant.

Results

Data about the types of pathology are summarized in Table 1. The most common cardiac pathology among the cohort was an unbalanced AV canal followed by tricuspid atresia/pulmonary stenosis/atresia. Perioperative patient data are presented in Table 2. Patient characteristics, including age, sex, weight, and body surface area, were not significantly different between the two groups. Information regarding the previous Glenn operation, such as the time of operation, and the preoperative Glenn pressure, were not significantly different between the groups. Preoperative and postoperative echocardiographic patient data were

Table 1. Pathologies of patients

Diagnosis	Number of Patients
Tricuspid atresia-pulmonary stenosis/atresia	6
Intact ventricular septum-pulmonary atresia	1
Double inlet left ventricle-pulmonary stenosis	1
Unbalanced atrioventricular canal-pulmonary atresia/stenosis	7
Hypoplastic left heart syndrome	4
Transposition of great arteries-ventricular septal defect-pulmonary stenosis	1
Double inlet right ventricle-pulmonary atresia/stenosis	2

Table 2. Perioperative patient data

	Patients (22)	Patients extubated (16)	Patient unable to be extubated (6)	p
Age (months)	49.8 (59.7–42.02)	52.5 (60.9–41.9)	47.9 (53.2–40.4)	0.417
Sex		5 females; 11 males	3 females; 3 males	0.624
Weight (kg)	14.5 (17–13)	15.1 (17–13)	13.95 (16.5–12.5)	0.631
Body Surface Area	0.62 (0.71–0.58)	0.64 (0.73–0.58)	0.6 (0.71–0.57)	0.483
Age at Glenn Operation (months)	12.5 (20.25–12.5)	12.5 (18–7.25)	12.5 (27.5–5.75)	0.824
Glenn Pressure (mmHg)	13.5 (15.25–11)	13 (15.75–10.5)	14 (15.5–11)	0.934
Main ventricle		1 right; 6 left; 11 biventricular	2 right; 2 left; 2 biventricular	0.206
Preoperative AV valve insufficiency		Grade 0: 7 patients	Grade 0: 2patients	0.403
		Grade 1: 4 patients	Grade 1: 1 patient	
		Grade 2: 3 patients	Grade 2: 3 patients	
		Grade 3: 2 patients		
Antegrade flow to pulmonary artery		4 patients	3 patients	0.267
Pulmonary banding		2 patients	3 patients	0.1
Pulmonary atresia		11 patients	5 patients	0.369
Isomerism		Right ventricle: 4		
		Left ventricle: 1	All patients had normal atrial morphology	
Mc Goon Index	2.04 (2.32–1.7)	1.93 (2.32(1.67)	2.15 (2.32–1.98)	0.252
Cross Time	104 (129–79) (7 patients)	87 (121.25–77.5)	123 (–104)	0.289
Bypass Time	128 (174.25–108.5)	125 (168.25–105.5)	136 (185.25–116.25)	0.396
Fenestration Diameter	3.6 (4–3.6)	3.6 (4–3.6)	3.8 (4–3.6)	0.717
Postoperative AV valve insufficiency		Grade 0: 9 patients	Grade 0: 3 patients	0.633
		Grade 1: 7 patients	Grade 1: 3 patients	
Intensive care unit length of stay	1 (2–1)	1 (2–1)	1.5 (3.25–0.75)	0.607
Length of hospital stay	15 (22.5–10)	14.5 (22.75–1025)	15.5 (22.5–9.75)	1

compared between the groups. Our analysis revealed no statistically significant difference in the data about the pathology, such as the dominant ventricle, presence of a preoperative or postoperative atrioventricular (AV) valve insufficiency, antegrade flow to the pulmonary artery, and presence of pulmonary atresia. The distribution viewed considering the presence of a heterotaxy syndrome revealed five isomeric patients, including four right and one left, in the on-table extubation group while none in Group 2. The presence of arrhythmia was not statistically significantly different between the groups. Only one patient from each group had arrhythmia. The two patient groups have been homogenously distributed according to preoperative hemodynamics, including saturation, hemoglobin, hematocrit, white blood cell count, and C-reactive protein. Further, the postoperative hemodynamics of patients with the analysis of the same parameters did not yield a statistically significant difference between the groups. Additionally, the McGoon index was statistically insignificant concerning the likelihood of performing fast track extubation. The analysis of cross and bypass times revealed no significant difference between the groups. Pulmonary artery reconstruction was not significantly different between the groups, and reconstruction was performed on all the included patients in the cohort. Valve repairs were performed on four patients, of whom two had extracardiac conduits while the other two had intra-extracardiac conduits. Ultra-fast track extubation was performed on 67% of patients with extracardiac conduit while on 50% of patients with intra-extra cardiac Fontan. Our study revealed no correlation between extubated Fontan in the OR and shorter ICU or hospital stays.

Discussion

The feasibility of the fast-tracking strategy for all ages has been reported.[3] However, previous studies have mentioned that the early extubation strategy is less frequently practiced in younger patients undergoing a Fontan operation with more frequent needs of reintubation while early extubation is feasible in older patients regardless of the surgical complexity.[3,8] This association was not apparent in our analysis, which revealed no significant age difference between the on-table extubation group and the non-extubated group.

The use of fenestrations in the Fontan circuit has conflict-

ing evidence.[9,10] Patients undergoing a Fontan operation with non-fenestrated procedures were more likely to be extubated early.[7,10] Similarly, previous studies concluded that fenestration alone is insufficient to ensure optimal early postoperative hemodynamics.[6] Conversely, lack of fenestration was associated with an increased risk of extubation failure in a predictive model published for failed extubations in patients undergoing a Fontan operation.[11] Our study revealed that all patients, except one, had a fenestration, thereby eliminating this variability in our study. Notably, the mentioned patient lacking a fenestration was extubated on the operating table. This patient was a 10-year-old isomeric Kawashima patient with large arteriovenous malformations acting as an escape route, thereby favoring a non-fenestrated Fontan completion approach. Therefore, we believe that fenestrations are essential to avoid acute Fontan failure by acting as an escape route for high Fontan pressures brought on by abnormal pulmonary artery anatomy or increased pulmonary vascular resistance.[9]

Regarding the operation strategy, earlier extubation was more likely to be performed in patients undergoing a Fontan operation with extracardiac conduits.[7] Our study results were consistent with the literature. A higher percentage (73.6%) of patients with extracardiac Fontan was extubated in the OR compared to patients with intra-extra cardiac conduit (66%). This can be attributed to multiple factors. Firstly, our study performed a concomitant AV valve repair or an atrial septectomy in two of the patients with intra-extra cardiac conduits along with total cavopulmonary anastomosis completion. The other patient was isomeric, and an intra-extra cardiac conduit was chosen due to the mesocardiac localization of the inferior vena cava in this patient. Hence, these patients were operated on with aortic cross-clamping, and cardiac arrest with cardioplegia under hypothermic conditions. Thus, the total surgical times, as well as bypass durations, were expectedly longer, and the overall physiologic stress imposed by the operation was considerably increased as opposed to a non-cardiac arrest approach.

The literature revealed the association between longer cardiopulmonary bypass duration and prolonged mechanical ventilation following congenital heart surgery.[3] This is unsurprising because longer cardiopulmonary bypass (CPB) times are required for increasing surgical complexity and for unexpected surgical complications.[3] Moreover, longer CPB time is associated with an increased risk of inflammatory response syndrome with generalized edema, decreased respiratory compliance, acute lung injury, and coagulopathy.[3] Contradictorily, a previously published study revealed no correlation between bypass duration and length of mechanical ventilation, nor the length of hospital stay in patients undergoing a Fontan operation.[6] Our analysis reveals similar results. We found no correlation between shorter bypass duration and on-table extubation in patients undergoing a Fontan operation. This is because the bypass durations homogenously differed among the patients in our cohort and the prolongations were not extreme. However, we excessively prolonged bypass durations, thereby affecting the extubation success.

The impact of pulmonary artery size remains debatable in a Fontan operation.[12,13] Earlier studies demonstrated that decreased pulmonary artery indices negatively impact the early hemodynamics of patients undergoing a Fontan operation.[12,13] Conversely, the modifications made to the original Fontan operation since these earlier studies must be considered when viewing the impact of the pulmonary artery size on the single ventricle hemodynamics. More recent studies have revealed that reduced pulmonary artery size, as determined by the McGoon ratio, had no negative impact on the early postoperative outcomes of patients undergoing a Fontan operation.[12] Our analysis revealed similar results. We found no statistically significant correlation between the preoperative McGoon index and the success of fast track extubation in patients undergoing a Fontan operation.

Uncertainty persists over the ideal time for performing the bidirectional cavopulmonary anastomosis.[14,15] Early-age (3–6 months) bidirectional cavopulmonary anastomosis has been frequently used in many hospitals, particularly for infants with hypoplastic left heart syndrome, to maintain ventricular and atrioventricular valve function.[15,16] Several studies revealed that early bidirectional cavopulmonary anastomosis may be performed safely and effectively.[14-16] Therefore, a delay in stage 2 palliation may have a detrimental impact on cardiac function following Fontan completion.[14] The two groups in our cohort have no statistically significant difference in the age of the Glenn operation. Conversely, our patients were in late-stage 2 palliation following the literature because the median age at the Glenn operation was 12.5 months for both groups. This is because of the presence of patients with antegrade pulmonary artery flow in both groups which causes a delay in Fontan completion surgery.

The Fontan procedure has undergone numerous modifications since its introduction in 1971, which mirror advances in surgical and postoperative management, and is currently used to treat a broad spectrum of congenital heart diseases with a functional single ventricle.[5,17] Therefore, the highly varying patient characteristics and pathologies should be considered when assessing extubation success in patients

undergoing a Fontan operation. Heterotaxia remains an independent risk factor for morbidity following the Fontan operation despite the recent advancements in improving early and intermediate outcomes in patients.[17] Our study included four isomeric patients, including three right and one left. All of the isomeric patients were extubated in the OR.

Commonly, studies include selected and hemodynamically stable patients and unstable patients have longer mechanical ventilation times despite the encouraging results published regarding extubation in the OR in patients with Fontan completion.[5,18] Conversely, several authors have reported that early extubation is possible after total cavopulmonary connection in the majority of patients, including those who are hemodynamically unstable.[5,18] Furthermore, the extubation of unstable patients is associated with the stabilization of circulation.[18] This is a critical finding about the extubation strategy to be followed in unstable cases where transferring the patient to the ICU with mechanical ventilatory support is a common practice. None of the patients in our study required reintubation following extubations performed in the OR developed hemodynamic instability following extubation. Furthermore, 66.6% of the patients in Group 2 were extubated during the first 24 h postoperatively. Determining the exact reason for the delay in extubation is difficult because of the retrospective nature of the study. These patients did not have major differences in their perioperative parameters. Thus, we can only assume from the patient data that the oxygenation of patients was not interpreted as adequate, and the extubation was delayed until the unstable condition of the patient was resolved. This raises the question of whether the decision to proceed with ultra-fast track extubation can be made more flexible since fixed inclusion and exclusion criteria do not exist and the literature suggests extubation as a step taken in favor of patient stabilization. The consideration of unstable patients for fast track extubation could introduce a possible paradigm shift in the extubation strategy in patients with a single ventricle.

Previous studies have revealed a correlation between earlier extubation and shorter length of hospital or ICU stay following a Fontan operation.[6,18] Our study revealed no association between early extubation and hospital length of stay in our patient population. Extubation in the OR and the incidence of postoperative complications were previously reported as the two most significant indicators of the postoperative length of hospital stay.[19] This lack of association can be attributed in part to the presence of significant pleural effusions that may influence discharge times following the Fontan completion which may or may not be affected directly by early extubation.[7] Our study revealed pleural effusions in three patients, of whom two were from the group extubated in the OR. Thus, we could not reach a clear conclusion on this matter. Several studies have previously reported a lack of correlation between earlier extubation and shorter length of hospital stay, similar to our results.[4,7]

Greater flexibility has been given to cardiac anesthesiologists with the use of shorter-acting anesthetic drugs, combined with certain regional anesthesia techniques, regarding anesthetic regimens that allow this strategy during the planning of early extubation.[1,8] Pain management and sedation without respiratory depression become critical considerations for all practitioners involved, regardless of the timing of extubation in a patient.[3] The perioperative team's education and approach to early extubation and postoperative airway management is a critical component in allowing safe and successful early extubation of pediatric patients with cardiac diseases. Therefore, the success of fast track extubation in patients undergoing a Fontan operation should be viewed as multifactorial, and surgeons, anesthesiologists, and ICU specialists should closely collaborate.

This study has certain limitations. The main limitation was the small patient cohort and the retrospective design. Consequently, the study was confined to data from the medical records of patients and can only indicate correlations between variables instead of causality. The decision to proceed with on-table extubation was made using a patient-specific approach although the operative and anesthetic management of patients did not differ much between the groups.

Evidence to establish a causal relationship between early extubation and patient outcomes remains insufficient despite the increasing prevalence of early extubation strategies. Our study results reveal no clear association between perioperative variables and the success of ultra-fast track extubation. Therefore, prospective randomized trials are required to determine whether fast-tracking improves outcomes in children undergoing congenital heart surgery, as previously concluded. However, on-table extubation of patients undergoing a Fontan operation appears to be a feasible strategy.

Disclosures

Ethics Committee Approval: The study was approved by The Koç University Ethics Committee (Date: 30/12/2022, No: 2022.484.IRB1.193).

Informed Consent: Written informed consent was obtained from all patients.

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Research Article

The Effect of CRP/Albumin, Platelet/Lymphocyte, SOFA, and APACHE II in Predicting Mortality in Covid-19 Patients in Intensive Care Unit

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ABSTRACT

Objectives: It is important to predict the prognosis during hospital admission of Covid-19 patients. The purpose of this study was to see how CRP/Albumin (CAR) and Platelet/Lymphocyte (PLR) ratios, obtained from patients in the intensive care unit (ICU) within the first 24 hours of their hospitalization with a Covid-19 diagnosis, predictmortality and how they correlated with acute physiology and chronic health evaluation (APACHE II) and sequential organ failure assessment (SOFA).

Methods: Using hospital records, records of 83 patients hospitalized in the ICU with a diagnosis of Covid-19 between 11.03.2020 and 01.01.2021 were retrospectively analyzed . Patients were divided into two groups discharged (Group I) and exits (ex) group (Group II). CAR and PLR were recorded during the first 24 hours of ICU admission, and APACHE II and SOFA scores were computed. The calculated CAR and PLR were correlated with APACHE II and SOFA scores and their association with mortality was investigated.

Results: SOFA, APACHE II, PLO, and age were higher, and albumin was lower in patients in the mortal course ($p<0.05$). ROC analysis revealed that APACHE II and SOFA scores could be employed to estimate mortality.

Conclusion: We believe that APACHE II and SOFA scores can be used to predict mortality in patients admitted to the ICU due to Covid-19, whereas CRP/Albumin and Platelet/Lymphocyte ratios cannot.

Keywords: APACHE II, Covid-19, CRP/Albumin Ratio, Mortality, Platelet/Lymphocyte Ratio.

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Introduction

The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes coronavirus disease (Covid-19) has caused an unprecedented global pandemic of unprecedented magnitude. Covid-19 can causes everything from a minor infection to a life-threatening situation. The prospective course of Covid-19 at the time of admission is difficult to predict at patient admission.[1-3]

Different risk scores were and developed to predict Covid-19 prognosis and plan appropriate treatment. These scores included demographic and radiologic characteristics,[4] physiologic,[5] and biochemical parameters,[6] as well as various combinations of these. To calculate these risk scores, it is necessary to allocate time for further evaluations, and examinations. There is also no particular scoring system for Covid-19 yet, although it has been revealed in several studies.[4,5]

The Acute Physiology and Chronic Health Evaluation II (APACHE II) and Sequential Organ Failure Assessment (SOFA) scores have long been used in intensive care units (ICUs). APACHE II is used to evaluate the prognosis and mortality of a patient.[6] SOFA evaluates organ dysfunction, morbidity, and mortality.[7] We believe that these two scoring systems can be used to predict mortality in Covid-19 patients, and we believe that more research should be done on this topic.

In a Covid-19 case, leukocytes, lymphocytes, and platelets decrease the.[18] Progressive lymphocytopenia indicates disease severity.[8] Several studies have shown that PLR can be used as an independent prognostic indicator in Covid-19 patients, both severe and non-severe.[8] Because CAR estimate the level of inflammation in two ways (increased CRP and decreased albumin), it may provide more information

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than only CRP and/or albumin alone.[9] CAR may also be a prognostic indicator for Covid-19 patients.

As a result, the purpose of this study was to assess the predictive power of CRP/Albumin ratio (CAR) and Platelet/Lymphocyte ratio (PLR), SOFA, and APACHE II scores in patients admitted to the ICU with Covid-19.

Methods

The study was planned retrospectively, and HNEAH - KAEK letter 2022/176-3860 was used to obtain ethics committee approval. The study included patients hospitalized in ICU between 11.03.2020 and 01.01.2021 in our hospital. The study included 83 older patients over the age of 18 , who had a positive Covid-19 PolymeraseChainReaction (PCR)test, were not diagnosed with t cancer, did not have any immunosuppressive disease, were not receiving immunosuppressive therapy, did not have the hematologic disease, and did not have the chronic liver disease. Patients under the age of 18 who had a negative Covid-19 PCR test, any malignancy that would affect the primary variables, immunosuppressive disease, receiving immunosuppressive therapy, and hematologic or chronic liver disease were excluded from the study.

The hospital system recorded age, gender, PCR positivity, date of ICU admission, type, and date of discharge from the ICU. Patients were divided into two groups according to the type of discharge from the ICU: discharged (Group I) and exits (Group II). Following, CAR, PLR, APACHE II, and SOFA scores were calculated by and analyzing the blood tests that were routinely taken during the first hospitalization to the ICU. The total APACHE II score the sum of three subscales, acute physiology score, age, and chronic health assessment. The highest score value is 71. Mortality rise from 25% a total score of 25 to 80% a score of 35 or higher. [10] A total of six organ systems are scored between 1 and 4 in the SOFA score. The evaluation is based on the total score. The total score between 6 and 24, with a higher score indicating worsening morbidity.[11]

Power Analysis

The TLO effect size between the study groups was found to be 0.56 [12] (alpha error probability=0.05) in the power analysis performed with the G*power 3.1 program related to our study; in the sample size analysis performed with the power value 0.80, the total number of samples required to be taken was found to be 83.

Statistical Methods

The SPSS 22 program was used for data analysis. The data were presented in the form of an arithmetic mean, standard deviation, median, range, frequency, and percentage distribution. The Kolmogorov–Smirnov test was used as a normal distribution test.The unpaired t-test was used to compare paired groups in the analysis of normally distributed data, the Mann–Whitney U test was used to compare paired groups of variables that did not show normal distribution, and the Chi Square test was used to evaluate qualitative data. The binary logistic regression test was used to determine the factors that influence mortality, and the Kaplan–Meier and LogRank analye were used to determine the effect of SOFA and APACHE II cut-off values on survival. Results were evaluated at the significance level of $p<0.05$.

Results

A total of 247 patients were analyzed from hospital records. 114 patients did not meet the inclusion criteria, and n 50 patients information was incomplete. Therefore, 164 analyzed patients could not be included in the study.The study included 83 patients, 25 of whom were discharged and 58 of whom passed. Sociodemographic characteristics of the patients according to group characteristics are given in Table 1.

Table 1. Demographic characteristics by group

Feature	Group X±SD or n (%)		p
	Discharged n: 25 (30.1)	Ex n: 58 (69.9)	
Age	58.48±16.68	72.71±9.692	<0.001*
Gender			
Female	6 (24.0)	16 (27.6)	0.945+
Male	19 (76.0)	42 (72.4)	
The time between PCR+ and ICU hospitalization (days)	6.64±3.32	5.78±4.17	0.170 ǂ
Duration of ICU stay (days)	12.04±9.43	12.84±7.28	0.219 ǂ
Total	25 (30.1)	58 (69.9)	

*Unpaired t-test ǂ Mann–Whitney U test+Chi Square test PCR: ICU: Intensive Care Unit; SD: Standard Deviation PCR: Polymerase Chain Reaction ICU: Intensive Care Unit.

It was found that albumin (p<0.001) was significantly lower, while SOFA (p<0.001), APACHE II (p<0.001), and TLO (p=0.034) were significantly higher in the ex-group (Table 2).

Age, Albumin, PLR, SOFA, APACHE II, and GCS variables were found to be significant in univariate tests, so a logistic regression analysis was performed to determine the factors affecting mortality. The variables age (p=0.893), Albumin (p=0.254), PLR (p=0.141), and GCS (p=0.978) were found to be statistically insignificant, whereas SOFA (p=0.042) and APACHE II (p=0.048) were found to be significant (Table 3).

Albumin, PLR, SOFA, APACHE II, and GCS variables used in a logistic regression analysis to determine the factors influencing mortality toby age. Albumin (p=0.142), PLR (p=0.150), and GCS (p=0.812) levels were found to be statistically insignificant,whereas SOFA (p=0.045) and APACHE II (p=0.049) levels were found to be significant (Table 3).

The ROC analysis revealed that the areas under the curve for APACHE II and SOFA scores were significant, whereas the areas under the curve for PLR and CAR were not (Table 4). The optimum cut-off value for mortality prediction was discovered to be 14 for APACHE II and 8 for SOFA score (Table 5).

Kaplan–Meier Survival Analyses were performed considering the recommended cut-off values for APACHE II and SOFA scores(Table 6, Table 7). The APACHE II of <14 group survival durations were statistically significantly longer than the APACHE II of >14 groups (LogRank:5.43 p=0.025) (Table 6 Fig. 1). There was no statistically significant difference in survival times between the SOFA groups (LogRank:3.07 p=0.080) (Table 7).

Discussion

According to our findings, hospitalization APACHE II and SOFA scores can be used to predict mortality in patients ad-

Table 3. Logistic regression analysis for mortality prediction

	OR 95% CI	p	OR 95% CI	p*
Age	1.01 (0.92–1.07)	0.893	-	-
Albumin	0.93 (0.75–1.08)	0.254	0.95 (0.89–1.02)	0.142
PLR	0.98 (0.93–1.02)	0.141	0.97 (0.99–1.03)	0.150
SOFA	2.18 (1.03–4.62)	0.042	1.08 (1.01–1.12)	0.045
APACHE II	1.19 (0.94–1.51)	0.048	1.04 (1.01–1.08)	0.049
GCS	0.99 (0.37–2.65)	0.978	0.97 (0.93–1.11)	0.812

*Adjusted Age; OR: Odds Ratio; CI: Confidence Interval; PLR: Platelet/Lymphocyte Rate; SOFA: Sequential Organ Failure Assessment; APACHE II: Acute Physiology and Chronic Health Evaluation; GCS: Glasgow Coma Scale.

Table 4. Areas under the ROC Curve in the differential mortality diagnosis

	AUC	SE	95% CI
CAR	0.606	0.0656	0.493 to 0.711
PLR	0.627	0.0644	0.514 to 0.731
SOFA	0.843	0.0425	0.746 to 0.913
APACHE II	0.865	0.0391	0.772 to 0.930

AUC: Areas Under Curve; SE: Standard Error; CI: Confidence Interval; CAR: CRP/Albumin Rate; PLR: Platelet/Lymphocyte Rate; SOFA: Sequential Organ Failure Assessment; APACHE II: Acute Physiology and Chronic Health Evaluation.

Table 5. Optimal values for APACHE II and SOFA score

	Cut-off	Sensitivity	Specificity	PPV	NPV	LR+
Apache II	14	0.966	0.640	0.851	0.937	2.683
SOFA	8	0.983	0.600	0.862	0.889	2.457

PPV: Positive Predictive Value; NPV: Negative Predictive Value; LR: Likelihood Ratio; Apache II: Acute Physiology and Chronic Health Evaluation; SOFA: Sequential Organ Failure Assessment.

Table 2. Comparison of biochemical values and scores by groups

	Discharged n: 25 (30.1)			Ex n: 58 (69.9)			
	M±SD	Median	Range	M±SD	Median	Range	p
CRP	14.52±8.34	13.90	29.50	19.98±21.22	15.30	127.20	0.336ǂ
Albumin	34.62±2.99	35.50	10.50	30.64±5.15	31.00	23.40	0.001*
CAR	0.42±0.26	0.40	1.07	0.67±0.71	0.48	3.95	0.128ǂ
Platelet	243.00±84.19	244.00	347.00	269.33±109.58	254.00	573.00	0.287*
Lymphocyte	0.76±0.46	0.69	2.27	0.67±0.40	0.60	2.19	0.297ǂ
PLR	416.66±301.2	356.00	1398.40	503.13±276.16	423.75	1197.0	0.034ǂ
SOFA	8.60±1.29	8.00	4.00	11.09±2.08	10.00	7.00	<0.001*
APACHE II	13.04±5.30	13.00	19.00	21.50±5.35	21.00	26.00	<0.001*

*Unpaired t-test ǂMann Whitney U test; M: Mean; SD: Standard Deviation; CRP: C Reactive Protein; CAR: CRP/Albumin Rate; PLR: Platelet/Lymphocyte Rate; SOFA: Sequential Organ Failure Assessment; APACHE II: Acute Physiology and Chronic Health Evaluation.

Table 6. Kaplan-Meier life analysis for APACHE II

	<14 APACHE II	>14 APACHE II	All Patients Group
Day 5	0.875	0.907	0.976
Day 10	0.875	0.735	0.833
Day 15	0.683	0.389	0.752
Day 30	0.683	0.203	0.426
Median±SE Lifetime	22.42±3.17	14.80±1.21	15.86±1.25
95% CI	16.20–28.64	12.42–17.18	13.42–18.31
LogRank: 5.43 p=0.025			

Apache II: Acute Physiology and Chronic Health Evaluation; CI: Confidence Interval.

Table 7. Kaplan–Meier life analysis for SOFA

	<8 SOFA	>8 SOFA	All Patients Group
Day 5	0.890	0.955	0.976
Day 10	0.890	0.746	0.833
Day 15	0.785	0.495	0.752
Day 30	0.785	0.218	0.426
Median±SE Lifetime	24.20±3.39	15.23±1.22	15.86±1.25
95% CI	17.54–30.86	12.83–17.63	13.42–18.31
LogRank:3.07 p=0.080			

SOFA: Sequential Organ Failure Assessment: CI: Confidence Interval.

mitted to the ICU due to Covid-19. We discovered that the optimum cut-off value for APACHE II was 14 and for SOFA score as 8, furthermore, TLO and CAR values not predict mortality in patients admitted to the ICU due to Covid-19.

Specific scoring systems may and in treatment selection, treatment success, and efficient, and effective use of available resources. Despite studies,[4,5] no specific scoring system Covid-19 mortality has been identified. SOFA and APACHE II scoring systems are commonly used in ICU. These scoring systems can and suggest the mortality of Covid-19 patients.

Ghaith et al.[13] and studied critical Covid-19 patients admitted to the ICU and discovered that mortality was higher (83%) in patients over the age of 60. Du et al.[14] also found that advanced age was associated with mortality in Covid-19 patients. In our study, we discovered that advanced age was associated with higher mortality in Covid-19 patients, as has been shown in other similar studies.[12,15-17]

Deligöz et al.[18] found that low albumin level is a risk factor for mortality, furthermore, they stated that low albumin levels are have been linked to a poor prognosis in various studies. In the study by Tseng et al.,[15] albumin was found

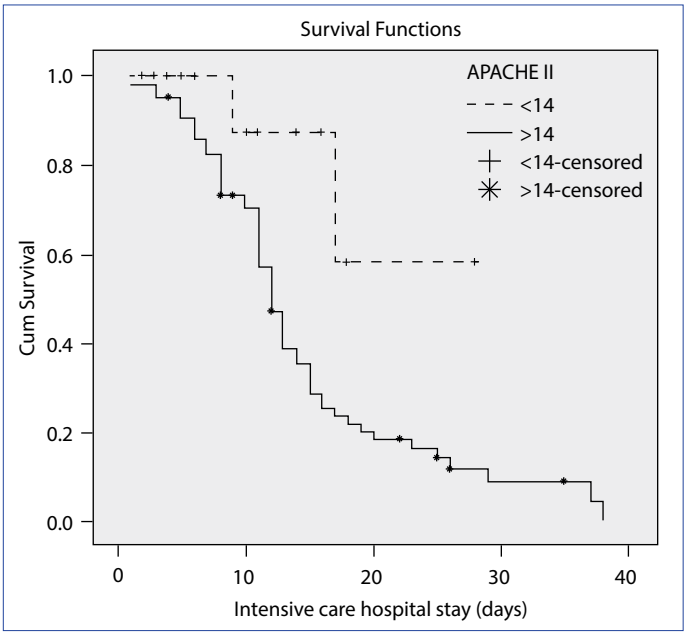

Figure 1. The relationship of APACHE II score with an intensive care life expectancy.

Apache II: Acute Physiology and Chronic Health Evaluation.

to be an important predictor of mortality. We discovered that Covid-19 patients with low albumin levels had a more fatal course.

In our study, PLR was significantly higher in the mortal group. This conclusion is supported by numerous studies. Korkmaz et al.[8] discovered that PLR was significant in predicting disease severity and prognosis in hospitalied Covid-19 patients. Uzundere et al.[17] also reported that PLR was a risk factor for mortality in patients with Covid-19 admitted to ICU.

Vicka et al.[19] compared the (SAPS) II, APACHE II, and SOFA scores and discovered that APACHE II had the best mortality prediction in Covid-19 patients hospitalied in the ICU. Vahedi et al.[7] showed that higher SOFA and APACHE II scores indicate higher mortality in ICU patients. Beigmohammadi et al.[20] discovered that APACHE II and SOFA scores were higher in Covid-19 patients who died. Discovered that SOFA and APACHE II scores at the time of ICU admission could be used to predict mortality in Covid-19 patients, similar to these studies. Bayrak et al.[16] found that an APACHE II score of >15 was linked with ICU mortality according to Kaplan–Meier curves and found that the APACHE II score predicted mortality. In our study, we discovered that APACHE II score greater than 14 on the Kaplan–Meier curve associated with ICU mortality.

Hocanlı et al.[21] discovered that CAR was statistically significantly higher in ICU patients than in ward patients and that this rate was associated with mortality. Another study

found that a high CAR at baseline was associated with 28-day mortality.[22] CAR was also found to be higher in the fatal group of Covid-19 patients by Özdemir et al.[9] Lucijanić et al.[23] and studied 2309 Covid-19 patients admitted to the ICU and discovered that high CAR values were associated with 30-day and post-discharge mortality. Kalabin et al.[24] used multivariate logistic regression analysis to examine CAR in the first 24 hours in Covid-19 patients (OR 1.21, 95% CI 0.96.–1.51, p=0.06) and discovered that CAR was not an independent predictor of mortality. We also found that CAR was not an independent predictor of mortality in our study.

Conclusion

We believe that APACHE II and SOFA scores can be used to predict mortality in patients admitted to the ICU due to Covid-19, whereas CRP/Albumin and Platelet/Lymphocyte ratios cannot.These results need to be supported by the results of other studies for clarity.

Disclosures

Ethics Committee Approval: The study was planned retrospectively, and HNEAH - KAEK letter 2022/176-3860 was used to obtain ethics committee approval. The study included patients hospitalized in ICU between 11.03.2020 and 01.01.2021 in our hospital.

Informed Consent: Written informed consent was obtained from all patients.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

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Authorship Contributions: Concept – Ü.T., Ö.D.; Design – Ü.T., Ö.D.; Supervision – Ö.D., O.E.; Fundings – Ü.T., Ö.D.; Materials – Ü.T., Ö.D.; Data collection &/or processing – Ü.T., Ö.D.; Analysis and/or interpretation – Ü.T., Ö.D.; Literature search – Ü.T., Ö.D.; Writing – Ö.D.; Critical review – Ö.D., O.E.

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Research Article

Comparing Total Parenteral Nutrition with Other Methods in Treating Chylotorax

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ABSTRACT

Objectives: This study aimed to examine the role of total parenteral nutrition in the treatment of chilotorax.

Methods: A total of 1149 patients who were operated for esophagus cancer were screened between 2010 and 2021. Of these patients, 49 were identified with chilorotax. Patients were divided into three groups. Some of these were treated surgically (first group) and through conventional approaches such as plorodesis, and somatostatin (second group). The only method of treatment used for the remaining patients was total parenteral feeding (third group). These three groups were statistically compared using clinical data to demonstrate that total parenteral nutrition is as effective as other treatments for chilotorax.

Results: A total of 1144 patients who received surgical treatment for esophageal cancer were analyzed. Chilotorax was used to diagnose 49 of these patients. Fewer deaths and complications occurred in the third group who were treated with just total parenteral nutrition. When the groups were compared using post hoc multiple comparison tests, based on the length of stay in the hospital after diagnosis and treatment initiation, it was discovered that; the average length of stay in the hospital in group 3 was less than the other two groups.

Conclusion: The use of total parenteral nutrition alone or in conjunction with surgical and another interventional processes in the treatment of chylothorax importantly reduces the risk of difficulties as well as the death rate. In all patients with chylothorax, parenteral nutrition should be included to the treatment protocol.

Keywords: Chylotoraks, esophagus cancer, parenteral nutrition

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Introduction

Chylothorax is a condition defined by the accumulation of lymphatic fluid in the intrathoracic area as a result of ductus thoracic integrity disruption. Its treatment is a significant clinical table because it raises therapy costs due to its possibility to cause morbidity and mortality and prolong hospital stays.[1] Malnutrition can result from the loss of chylous fluid, which is high in protein, fat, electrolytes, bicarbonate, lymphocytes, and fat-soluble vitamins in chylothorax. As a result, it is necessary to clarify the etiology and rapidly plan the treatment (Table 1). Treatment of the malnutrition clinic, in addition to removing the etiological cause, is critical for rapid and successful treatment. Because of the frequent complications of surgical treatment in a chylothorax and the requirement for optimal parenteral nutritional therapy, the significance of total parenteral nutrition (TPN) in the treatment of chylothorax is becoming clearer day by day. The purpose of this study was to evaluate the efficacy of TPN therapy in comparison to other chylotorax treatment options.

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Table 1. Etiology of the Clinical Course of Chylothorax

Etiology of Chylothorax
Congenital Causes
Ductus anomaly
Acquired Causes
Traumatic
Blunt trauma
Penetrating trauma
Surgical procedures
Nontraumatic
Malignancy
Infection
Idiopathic

Methods

Upper gastrointestinal system cancers are most common between 40. and 50. degrees east meridians and between 120. and 150. degrees east meridians worldwide.[2] In particular, esophageal cancers occur significantly more frequently in Persian regions than elsewhere in the world. Our research was carried out in the east of Türkiye, where upper gastrointestinal system cancers are the most common. As a result, surgical treatment of cancers, particularly esophageal cancers, is common, and surgical treatment complications are common. One of the most critical complications among these is chylothorax.[2] Patients who had undergone esophageal surgery and then developed chylothorax and applied to two centers in Van where surgical treatment of esophageal cancers is commonly performed were reviewed retrospectively and included in our study. In this research; 1144 patients who underwent surgical treatment for esophageal cancer, between January 2010 and June 2021, were evaluated. Patients with metastatic illness, liver and kidney failure, patients with extra metabolic illness, and patients undergoing surgical therapy for the second time, were removed from our research patient population. Among the remaining patients, 49 patients who developed chylothorax were included in the research and were split into three groups. Group 1; is the patients who had just surgical treatment, group 2; is the patients who had other treatment methods in addition to surgical treatment, and group 3; is the patients who receive just TPN treatment.

TPN was planned and overseen by the nutritional support unit of Van Education and Research Hospital, and all clinical information was recorded. A clinician, a pharmacist, a dietitian, two nurses, and a secretary make up the nutritional support team at our hospital, which is overseen by a doctor. The NRS 2002 (Nutritional risk screening) scale, which is advised by ESPEN, was used to determine and calculate the patients' nutritional needs (The European Society for Clinical Nutrition and Metabolism). The Harris–Benedict or Schofield equations were used to determine the patients' energy requirements. Patients have been found to have an average energy need of 50 kcal/kg/day. We employed solutions developed to provide 30% of total energy from lipids and 65%–70% from carbohydrates. It is aimed at providing 1.5 g/kg/day protein to the patients. Blood sugar, fluid, electrolyte, and mineral requirements of the patients were frequently monitored, and any deficiencies were treated with additional treatments as required. None of the patients was provided human albumin support.

Results

A total of 49 of 1144 esophageal cancer patients treated at the Ministry of Health Sciences University Van Education and Research Hospital and Yüzüncü Yıl University Faculty of Medicine Dursun Odabaş Medical Center experienced chylothorax due to ductus thoracic injury. The ethics committee of the Republic of Türkiye Ministry of Health Van Education and Research Hospital evaluated these patients retrospectively according to the ethics committee accepted dated 03.02.2022 and numbered 2022/78-11. Eight (3♂ 5♀) of the 49 patients, had only surgical treatment. While 21 patients (8♂ 13♀) had surgical treatment and extra treatment methods (TPN, somatostatin, talc, and pleurodesis, etc.), and 20 (7♂ 13♀) patients had only TPN and medical support. The patients were grouped demographically dependent on their age and gender (Table 2). Before the patients were diagnosed with chylothorax, the average amount of drainage fluid entering the thoracal tube was 850 cc/day, 770 cc/day, and 650 cc/day, respectively (Table 2). The mean daily drainage amounts in these patients were as follows after the drainage fluid turned chylous, the diagnosis of chylothorax was made as a result of the necessary laboratory tests, and the necessary treatment was initiated: 190 cc/day in group 1, 110 cc/day in group 2, and 260 cc/day in group 3 (Table 2). In patients who underwent only surgery, the following complications were noted: empyema in 2 (25%) patients, hemothorax in 4 (50%), bilateral pneumothorax in 5 (62%), atelectasis in 3 (37%), pneumonia in 7 (88%), thrombophlebitis in 1 (12%), hypoproteinemia in 9 (92%), and hyperglycemia in 1 (12%). Complications included empyema in 4 patients (19%), hemothorax in 7 (33%), pneumothorax in 15 (71%), atelectasis in 5 (23%), pneumonia in 12 (57%), thrombophlebitis in 1 (9%), hypoproteinemia in 3 (23%), hyperglycemia in 5 (19%). In the patients who had just TPN, the following complications were noted: empyema in 2 (5%), atelectasis in 2 (10%), pneumonia in 12 (35%), hypoproteinemia in 3 (18%), and hyperglycemia in 5 (25%) (Table 3, Figs. 1–2). Following

Table 2. Results

	Surgery	Surgery & Other Treatments	TPN
Sex	3♂ 5♀	8♂ 13♀	7♂ 13♀
Mean Age, years	66	73	71
Mean drainage in patients diagnosed but not receiving treatment, cc/day	850	770	650
Mean drainage in patients diagnosed and receiving treatment, cc/day	190	110	260
Number of complications	32	52	22
TPN, kcal/day	0	1400	2850
Mean blood albumin amount during the treatment, gr/day	2.4	2.9	3.1
Hospitalization after the treatment, day	22	25	19
Mortality (1 month) (in hospital)	2	7	1
Mortality (3 months)	1	4	2
Total Mortality	3	11	3

Table 3. Numerical Distribution of Complications

	Surgery	Surgery & Other	TPN
Empyema	2	4	2
Hemothorax	4	7	0
Pneumothorax	5	15	0
Atelectasis	3	5	2
Pneumonia	7	12	12
Thrombophlebitis	1	1	0
Hypoproteinemia	9	3	3
Hyperglycemia	1	5	5

chylothorax treatment, the hospitalization duration of the patients whose thoracostomy tubes were excluded and challenges were treated for group 1, group 2, and group 3 were recorded as 22, 25, and 19, respectively, while they were in the hospital (Table 2). These values were 1, 4, and 2 months after discharge, respectively (Table 2, Fig. 3).

Statistical Analysis

Cohen's T-test was used to determine the minimum number of samples, that is, for power analysis, following the hypothesis of our study research. The minimum number of samples required to achieve an 80% power value was determined to be 51. Our sample number was 49; therefore, it was very close to this value. The Chi-square test was employed in our research to compare the expected values with the discovered values. In this research, the Chi-square distribution table was research to calculate the approximate importance level (p-value) after calculating the degrees of freedom and Chi-square values. The p-value was calculated as an important value between 0.01 and 0.05 (i.e., 5%–1%). The analysis was performed using the one-way ANOVA test. Post hoc multiple comparison tests were added to find out which groups had important p-values.

Discussion

The ductus thoracicus is an extension of the cisterna chile that runs between the aorta and the azygos vein, in the chest and opens into the left jugular-subclavian venous junction (Fig. 4). Several more lymphaticovenous anastomoses are created by the ductus thoracicus with the vena

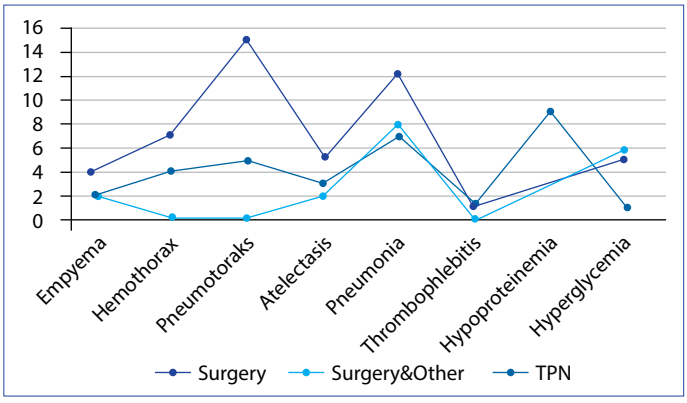

Figure 1. Numerical Distribution of Complications by Groups.

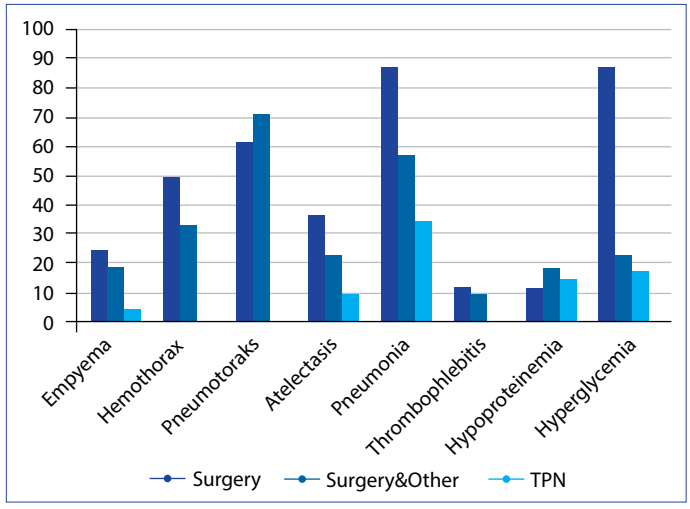

Figure 2. Percentage Distribution of Complications by Groups.

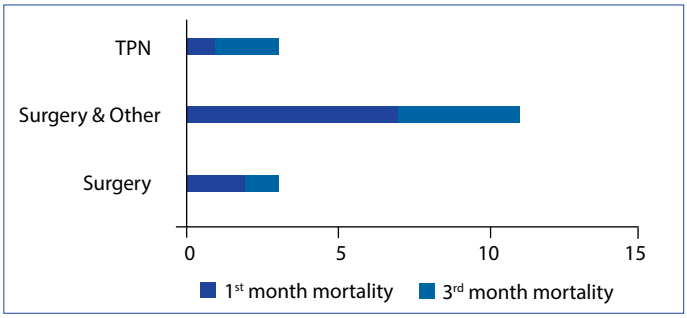

Figure 3. First month, third month, and total mortality numbers by groups.

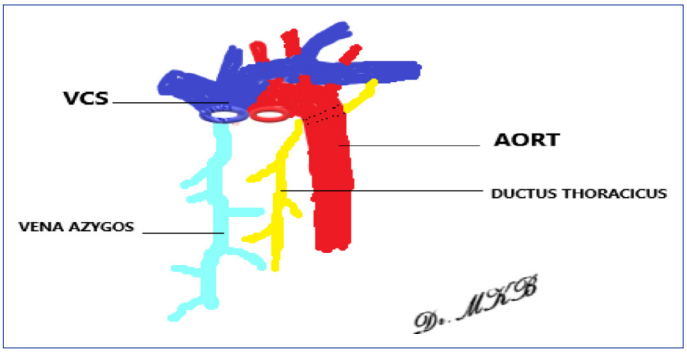

Figure 4. Anatomy of the ductus thoracicus.

azygos, intercostal, and lumbar veins. It also communicates with the right lymphatic duct on multiple occasions.[1]

The ductus thoracicus' primary function is to transport fats and return extravascular proteins to the blood. The lymphocyte is the most common cell type in lymphatic fluid, and the basal flow rate is 0.82–0.27 ml/kg/hour, depending on the meal and its fat content.[1,2] Approximately 60%–70% of digested lipids are absorbed by intestinal lymphatics and transmitted by the ductus thoracicus. Fatty acids with fewer than ten carbons are directly absorbed by the portal system, whereas fatty acids with more carbons are transported after being changed to chylomicrons in the lymphatics.[2]

While esophageal surgery, cardiovascular surgery, thoracic surgery, and mediastinal dissections for lung cancer may all play a role in the etiology of chylothorax. The etiology of the condition may also be influenced by nonsurgical factors such as certain infections or penetrating neck and thoracic trauma. Congenital causes, such as duct anomaly or idiopathic chylothorax, may also contribute to the ethiology.

Because chylothorax does not cause much pleural irritation, the clinical manifestation is dyspnea rather than pain and fever. This liquid is bacteriostatic because it contains lecithin and fatty acids.[3] The amount of effusion is also proportional to the clinical severity of breathlessness. On auscultation, there is a clear reduction in lung sounds on the side with effusion. Other clinical symptoms caused by immunodeficiency and malnutrition include weakness, dehydration, metabolic acidosis, and other clinical symptoms. Malnutrition caused by chylothorax can be discovered in 25%–50% of thoracic surgery patients.[3,4] Due to pleural effusion or mediastinal chyloma, a mediastinal radiopaque shadow appears on the chest X-ray. The ductus thoracicus can be imaged by lymphangiography and nuclear scintigraphy methods. These imaging methods, while showing the anatomy of the duct as well as the location of the leak, are rarely used as diagnostic methods. The examination of pleural fluid obtained via thoracentesis or tube thoracostomy supports the diagnosis. Pleural fluid with the appearance of milk is present in ~50% of chylothorax cases. This situation could be caused by poor nutritional habits and foods with variable lipid content. As a result, the appearance of effusional fluid may not always result in the correct diagnosis. This milk-like off-white liquid is also identified as chylous. In the chemical evaluation of this chylous fluid, the number of triglycerides was discovered to be greater than in other effusions, but the amounts of LDH, protein, and cholesterol were reported to be similar.[4] The triglyceride cholesterol ratio is >1, this ratio is <1 in nonchylous pleural effusions. If the triglyceride level is <50 mg/dl, the likelihood of chylothorax is 4%, whereas 98% of effusions with a triglyceride level > 110 mg/dl are chylous.[5] The total protein content of chylous effusion was pH 7.3–7.8, albumin 1.2–3.9 g/dl, globulin 1.1–3.6 g/dl, and total lipid 0.5–6 g/dl. The electrolyte values of chylous fluid were discovered to be about equal to those of plasma.[4,5] However, not every aspirate obtained via thoracentesis or tube thoracostomy that has a chylous consistency and appearance is a chylothorax. Pseudochylothoraxis a clinical condition caused by long-term pleural effusions that can be distinguished from chylothorax through chemical analysis. The following are the most significant diagnostic criteria: Microscopic examination revealed a higher cholesterol-triglyceride ratio, a higher lymphocyte ratio, and fat lobules stained with Sudan III.[5] Pseudochylothoraces are also high in lipids, but the main attribute of the effusion's lipid content is cholesterol rather than triglycerides. In chylothorax, the number of triglycerides is high.[6] Chylothorax was diagnosed in our study using clinical features, imaging, and laboratory tests. In the postoperative period, lymphatic fluid leakage from the thoracic duct occurs at a rate of 1%–4% after esophageal surgeries and 0.5%–2.5% after cardiac and thoracic surgeries.[7,8]

Chylothorax treatment can be performed medically, i.e., conservatively, interventionally, or surgically.[9] Because this procedure also provides a definitive diagnosis, the first step

in treatment is to drain the fluid that has accumulated in the pleural space. While thoracentesis is sometimes essential for this process, tube thoracostomy is frequently needed for chylous fluid drainage.[9] Only the patient group that received surgical treatment (group 1) was comprised of patients diagnosed at an early stage and treated using relatively more traditional treatment methods. Some reports state that drainage in the spontaneous closure of the duct is effective.[9] However, because the loss of lipid, fluid, electrolyte, and metabolite can harm the patient's clinic table until this effect occurs, it is recommended to be used in the early stages of chylothorax when protein and fat loss are not excessive.[10] Daily drainage can range from 2500 to 3000 cc, according to studies, but conservative treatment methods are generally considered successful if the drainage is ≤500 cc.[11] Some clinical studies reveal that somatostatin analogs can decrease or even completely stop chylous pleural effusion. These drugs are thought to work by decreasing intestinal blood flow and preventing lipid absorption.[1] As a result, the belief that somatostatin therapy must be supplemented with parenteral nutrition predominates.[1] In our study, group 2 patients received treatment in addition to surgery, while group 3 patients did not have surgery and received only TPN treatment. If there is an important decrease in drainage, that is, the daily drainage does not fall below 500 cc, or full lung expansion is not able due to inadequate drainage, a switch from conservative treatment to treatment with interventional procedures is needed.[12] The most commonly used interventional treatment methods are pleurodesis with povidone-iodine, fibrin glue or talc, tetracycline sclerotherapy, and fluoroscopic embolization to the duct using platinum micro coils.[13-15] Interventional treatment methods include pleuroperitoneal shunting and pleurectomy.[13] The surgical treatment aims to ligate the thoracic duct. This procedure can be performed using either thoracoscopic or open surgery.[13] It is suggested that the patient drink olive oil or employ dyes such as methylene blue or solvent black to help identify the duct before surgery.[13]

Parenteral nutrition in chylothorax can take the form of peripheral or central parenteral nutrition. Because the nutritional risk index in these patients is usually >84 due to hypercatabolism, parenteral nutrition can be started quickly. Another indication for TPN is the presence of severe lymphatic leakage in these patients. If nutrition is to be conducted peripherally, the osmolality of the provided product should not exceed 600 mOsm/L, and the calcium content should be applied with care.[16] The number of calories needed, the total amount of fluid to be provided to the patient, and the predicted duration of the parenteral nutrition support all affect whether the parenteral nutrition will be prescribed centrally or peripherally.[17] If parenteral nutrition is to be conducted via the central vein, the catheter entry site should be as far away from wounds, previous catheter entry sites, tracheostomy, or fistulas as possible from wounds, previous catheter entry sites, tracheostomy, or fistulas. The use of simultaneous ultrasonography during central venous catheterization can make the procedure easier and safer.[18] A treatment plan based on all of these recommendations was developed for the patients in our study who received only TPN.

When our research was examined demographically, no statistical difference was discovered between the groups in terms of gender and age. The intergroup p-value for gender and age were respectively calculated to be 0.08 ($p>0.05$) and 0.11 ($p>0.05$).

When the daily drainages from the thoracic cavity of all three groups were followed and recorded before starting treatment after the chylothorax diagnosis, there was no statistical difference between the three groups, and the p-value was calculated as 0.15 ($p>0.05$). When the thoracic tube drainages were compared between the start of treatment and the removal of the chest tube after diagnosis, group 2 drained approximately 190 cc per day, which was significantly less than the other groups. The p-value was reported to be 0.045 when the drainages were equated following treatment ($p<0.05$). The low number of drained chylous has been attributed to the aggressive use of surgical and nonsurgical treatment methods. However, it was found that aggressive treatment methods were employed, the risk of problems increased in this group, the length of hospital stay was prolonged, and the number and rate of death in the hospital were greater than in the other groups. Two had 52 complications, which was found to have significantly more complications than the other groups ($p=0.03$). Some of the complications were caused by surgical and interventional procedures, while others were caused by medical treatment methods used. No difference was discovered in terms of the risk and number of problems between the surgical treatment group and the only TPN-given group ($p=0.095$). In terms of early mortality, group 2 patients were found to be at a higher risk than the other groups ($p=0.015$). This is thought to be because infections cause patients to rapidly enter multi-organ failure, the catabolic process cannot recover quickly, and the complications of aggressive treatment methods are severe.

Following treatment initiation, patients' blood albumin levels were continuously monitored for nutritional monitoring. It was recorded that albumin values had similar rates. In this comparison, the significance value was discovered as $p=0.068$ ($p>0.05$). Because of the heavy catabolic pro-

cess and the long half-life and synthesis of albumin, it is thought that this result is not statistically significant.

When the total number of deaths during and after hospitalization was examined, group 3, which included 20 patients, had three deaths, which was discovered to be significantly different from the other groups. When the groups were equated in this way, the p-value was 0.009 ($p<0.05$), which was regarded as highly statistically important ($p<0.01$).

When the groups were examined based on the length of stay in the hospital following diagnosis and treatment initiation, it was discovered that group 3 had a 19-day average length of stay in the hospital. This was 22 days for group 1 and 25 days for group 2. The length of stay in the hospital was statistically importantly shorter in the group that got only TPN ($p=0.036$). In group 3, we believe that, in addition to the absence of invasive interventions and a lesser postsurgical recovery period following the discharge, full nutritional support allows patients to recover more quickly. This is because nutritional support promotes not only the rapid replacement of necessary metabolites but also the immune system. Therefore, we found that our study's primary hypothesis and goal were achieved and supported.

In conclusion, the use of TPN alone or in combination with surgical and other interventional procedures in the treatment of chylothorax significantly decreases the risk of complications as well as the death rate. The length of stay in the hospital of these patients was found to be statistically significantly lower in patients with chylothorax treated with only TPN, which was the primary goal of the study. It was determined that all patients with chylothorax should receive parenteral nutrition as part of their treatment plan.

Disclosures

Ethics Committee Approval: The ethics committee of the Republic of Türkiye Ministry of Health Van Education and Research Hospital evaluated these patients retrospectively according to the ethics committee accepted dated 03.02.2022 and numbered 2022/78-11.

Informed Consent: Written informed consent was obtained from all patients.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

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