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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,

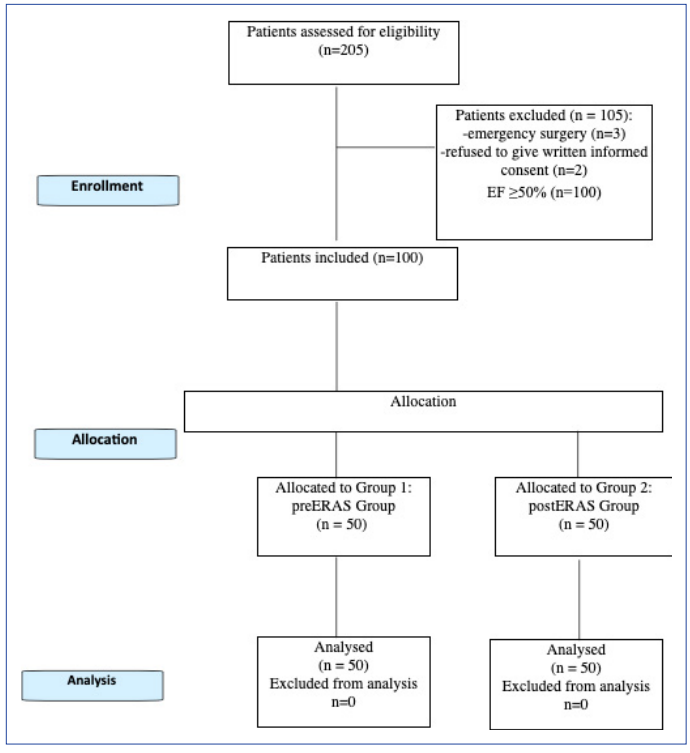

Figure 1. Flow Diagram.

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-

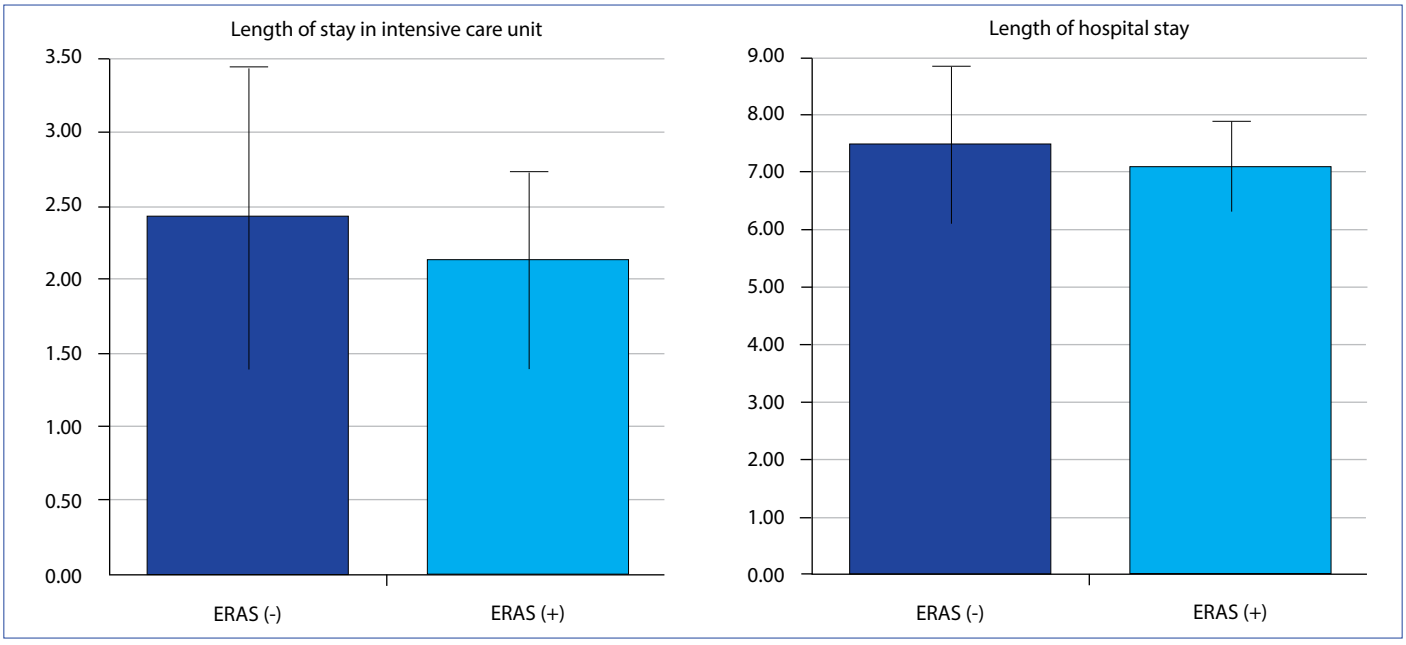

Figure 2. Comparison of pre eras and postERAS groups' length of stay in hospital and intensive care unit.

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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