Heart Surgery Forum 2024; 27(3): E222–E229
doi: 10.59958/hsf.6885

Article

Adherence to the Enhanced Recovery After Surgery in Cardiac Surgery Patients: A Randomized Clinical Trial

Shirin Hosseini[1], Saeid Hosseini[2], Zahra Vahdat Shariatpanahi[1,*], Majid Maleki[3], Fereydoon Noohi[3], Ziya Totonchi[4]

[1]Department of Clinical Nutrition and Dietetics, Faculty of Nutrition and Food Technology, Shahid Beheshti University of Medical Sciences, 1981619573 Tehran, Iran
[2]Heart Valve Disease Research Center, Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, 1995614331 Tehran, Iran
[3]Cardiovascular Intervention Research Center, Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, 1995614331 Tehran, Iran
[4]Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, 1995614331 Tehran, Iran
*Correspondence: nutritiondata@yahoo.com (Zahra Vahdat Shariatpanahi)

Submitted: 29 September 2023 Revised: 26 December 2023 Accepted: 10 January 2024 Published: 3 March 2024

Abstract

Background: Improving patients' outcomes using enhanced recovery after surgery (ERAS) during the surgical period has significant economic savings and increases organizational productivity. We evaluated the effects of ERAS protocol on outcomes including high sensitive-C-reactive protein (hs-CRP), hospitalization, intensive care unit (ICU) stay, feeding tolerance and pain score of cardiac surgical patients. **Methods**: A total of 260 patients were randomly assigned to the ERAS and control groups according to stratified block randomization. Fasting time in the ERAS group reduced from the conventional 12 h to 6 h with light meals. Also, on the day of the operation, 2 hours before the surgery, they received 250 mL of oral carbohydrate solution containing 25 g glucose. The control group received conventional standard care. Serum hs-CRP was measured before and after the operation. **Results**: Out of 260 participants, 107 patients received protocolized care (ERAS group), and 103 patients received conventional standard care. Recommendations to follow the ERAS resulted in a significant reduction in hs-CRP relative to the control group ($p = 0.001$). Complaints about thirst, hunger, anxiety, and pain were significantly less in the intervention group than the control group (All p-values = 0.001). In addition, the length of hospitalization, ICU stay, ventilation time, and first mobility were significantly shorter in the ERAS group (All p-values = 0.001). Besides, the first postoperative meal started earlier in the intervention group than the control group (p = 0.001). **Conclusion**: ERAS approach can lead to improvement in postoperative inflammation, thirst, hunger, anxiety, pain, duration of hospitalization, duration of ICU stay, first mobility, and ventilation time.

Keywords

hospitalization; carbohydrate loading; cardiac surgical procedure; C-reactive protein; critical care

Introduction

Improving the quality of care at various stages of surgery with an advanced recovery protocol reduces the risk of surgical complications. Enhanced recovery after surgery (ERAS) refers to a set of care protocols before, during and after surgery that are designed to reduce physiological and psychological stress in patients and achieve rapid recovery. The evidence for ERAS interventions in patients post-surgery has been critically assessed in several review articles and meta-analyses and Cochrane Database Systematic Reviews [1,2]. The key principles of the ERAS protocol include preoperative counselling, avoidance of perioperative fasting, preoperative nutrition and carbohydrate loading up to 2 hours preoperatively, standardized anesthetic regimen and early mobilization [2].

The ERAS protocol has been widely used in various surgical procedures; however, there is inconsistent data on the use of ERAS in cardiac surgery [3]. High mortality and surgical complications, along with high costs in cardiac surgery, have made cardiac surgery patients an appropriate case for ERAS strategies [4]. Adherence to ERAS prior to cardiac surgery has been shown to result in lower cardiac enzymes, shorter duration of ventilator support and intensive care unit (ICU) stay, less need for vasopressors and inotropic agents, and fewer complications such as serious arrhythmias [5,6]. Due to the variety of methods used in cardiac surgery and the specific characteristics of patients, it is difficult to implement universal advanced recovery guidelines for cardiac surgery [4].

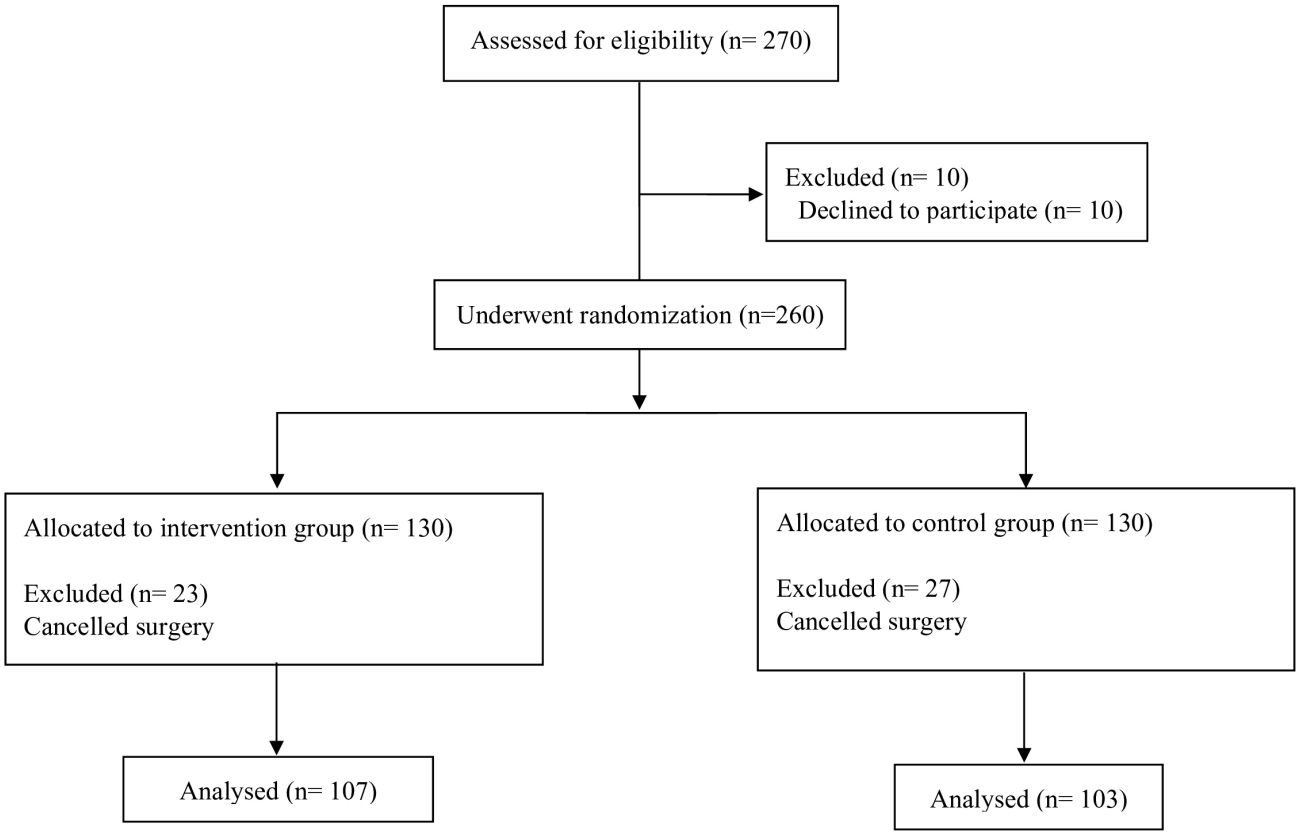

Fig. 1. Patients flow diagram.

Improving patients' outcomes and using advanced recovery components during the surgical period has significant economic savings and increases organizational productivity. Since this protocol has not been implicated in patients with cardiac surgery in Iran, we evaluated the effects of ERAS protocol [6] on outcomes including serum high sensitive-C-reactive protein (hs-CRP) level, length of stay in the ICU and hospital, feeding tolerance and pain score in cardiac surgery patients.

Materials and Methods

Study Design and Subjects

This prospective randomized controlled clinical trial, was conducted from April 2019 to September 2019 in a university hospital, recruiting adult subjects scheduled for elective valvular heart repair/replacement surgery or Coronary artery bypass graft (CABG) surgery. Written informed consent was obtained from participants before intervention. This study was registered in the Iranian Registry of Clinical Trials (IRCT20200114046131N1). The protocol was approved by the related institutional ethics committee (IR.RHC.REC.1397.042) and the work has been reported in line with Consolidated Standards of Reporting Trials (CONSORT) Guidelines. Also, it was done in accordance with the Declaration of Helsinki of the World Medical Association. Patients were included if they were $\geq$18 years of age, had a body mass index (BMI) of 18.5–30 kg/m^2 and were receiving elective heart surgery. The exclusion criteria were as follows: emergent surgery; a New York Heart Association (NYHA) class of heart function of IV; a history of stroke; high creatinine levels; non-normal liver function tests; severe mental disorder; a history of alcohol and drug abuse and patient refusal.

Randomization and Masking

The study sample size was calculated based on the primary outcome and α = 0.05, β = 0.01. Based on the findings reported by Li *et al*. [3], the minimum sample size estimated for each group was 100 with a power (1–β) of 90% and α = 0.05 for a parallel interventional study with two-tailed testing to detect a 1.5-days difference in the duration of hospitalization.

A total of 270 patients were evaluated consecutively for eligibility. Ten patients were excluded after the initial assessment because they declined to participate. Therefore, 260 eligible patients were randomized. Permuted block randomization was used with a block size of 2 and an allocation ratio of 1:1 based on a computer-generated random digit table.

Table 1. Characteristics of participants.

	Control (n = 103)	ERAS (n = 107)	*p*-values
Demographic characteristics			
Age (year)	57.7 ± 7.9	59.03 ± 7.8	0.221[1]
Female/sex	17 (16.5)	20 (18.7)	0.683[2]
BMI (kg/m^2)	24.6 ± 3.8	24.8 ± 3.4	0.688[1]
LV function (%)	47.1 ± 4	47.9 ± 4.7	0.186[1]
NHYA			
I I	69 (68.3)	67 (67.7)	0.511[2]
I I I	34 (31.7)	40 (32.3)	
Surgery type			
CABG	95 (92.2)	98 (91.6)	0.869[2]
Valve	8 (7.8)	9 (8.4)	
Surgical data			
CPB time (min)	81.2 ± 14.5	83.1 ± 16.7	0.380[1]
Cross clamp time (min)	79.3 ± 29.8	75.9 ± 26.9	0.386[1]
Duration operation (hour)	4.8 ± 1.03	4.9 ± 0.9	0.455[1]
Vasoactive Drug Support (hour)	3.2 ± 0.9	3.02 ± 0.6	0.088[1]

[1] Independent-Samples *T* test (means ± SE). [2] Chi-square or Fishers Exact Test (count, %). BMI, Body mass index; LV, left ventricular; NHYA, the New York Heart Association; CABG, coronary artery bypass grafting; CPB, cardiopulmonary bypass.

Preoperative Clinical Pathway

The patients in the ERAS group received psychological counselling and education by trained personnel a week before their surgery. They received preoperative counseling and an information pamphlet. They were advised for smoking and alcohol cessation. Nutrition screening was performed to check for malnutrition and interventions were advised as required.

After admission, the patients in the ERAS group followed the diet prescribed by a dietitian to standardize their caloric intake by 7 pm the night before their surgery. The fasting time was reduced from the conventional 12 h to 6 h with light meals. On the day of the surgery, 2 hours preoperatively, the patients received 250 mL of oral carbohydrate solution containing 25 g glucose (ERAS group). The patients in the control group followed the diet prescribed by a dietitian to standardize their caloric intake by 7 pm the night before the surgery too, but their fasting time was about 12 h. The control group did not receive any beverages.

Anemia was modified based on the guidelines developed by the European Association for Cardio-Thoracic Surgery (EACTS) and the European Association of Cardiothoracic Anesthesiology (EACTA) before surgery in both groups [7]. Prophylactic antibiotics were administered within 60 min of surgical incision.

Intraoperative Clinical Pathway

General anesthesia was induced for all the subjects participating in the study. Median sternotomy was performed for all the patients. Mild hypothermic cardiopulmonary bypass (CPB) with a uniform setting was utilized in all the patients. Also, for myocardial protection, Buckberg solution was used. Data on the duration of CPB, cross-clamp time, and operation time were collected in a predesigned form.

Postoperative Clinical Pathway

Postoperatively, patients in both groups received intravenous patient-controlled analgesia according to the hospital protocol. Ondansetron was used to reduce the risk of postoperative nausea and vomiting. In the ERAS group, urinary catheters and thoracic drainage tubes were removed as soon as possible on postoperative day 1 instead of on postoperative days 2 or 3, as was the case in the control group. The patients were encouraged to ambulate as soon as possible. In the ERAS group, oral fluid was commenced within 6 h of extubation, and a full diet was started on the first day after extubation in the intensive care unit (ICU). The patients in the control group received the conventional postoperative nutrition protocol. In the control group, the postoperative diet started after confirming the passage of flatus. The order was to start the diet from clear liquid diet to full liquid diet and then to proceed with normal diet.

Outcomes

The primary outcome was the duration of hospitalization; the secondary outcomes were hs-CRP and the length of ICU stay. During the postoperative follow-up visits, postoperative complications occurring within the first postoperative week were also recorded, including respiratory failure, new-onset atrial fibrillation, acute kidney injury

Table 2. Anesthetic variables of participants.

	Control (n = 103)	ERAS (n = 107)	*p*-values
Premedication			
Alprazolam	40 (38.8)	64 (59.8)	0.002
Morphine	5 (4.9)	2 (1.8)	0.41
Both	58 (56.3)	41 (38.3)	0.009
Drug for pain during surgery			
Fentanyl	3 (2.9)	2 (1.9)	0.96
Sufentanyl	100 (97.1)	105 (98.1)	0.96
Indication of anesthesia			
Etomidate	3 (2.9)	0 (0.0)	0.11
Midazolam	100 (97.1)	107(100)	0.23
Muscle relax			
Cis-atracorium	19 (19.4)	21 (19.6)	0.83
Atracorium	84 (80.6)	86 (80.4)	0.83
Inotrope			
Norepinephrine	2 (11.1)	0 (0.0)	0.47
Dobutamine	0 (0.0)	2 (7.7)	0.51
Milrinone	2 (11.1)	6 (23.1)	0.30
Epinephrine	14 (77.8)	18 (69.2)	0.52

Calculated by Chi-square test or Fishers Exact Test and presented as count (%).

(AKI), stroke (new neurologic deficit), hospital-acquired infections or sepsis (including postoperative infections such as surgical site infections or respiratory tract infections) and death. In addition, postoperative pain scores at rest, nausea and vomiting and mobilization were collected from individual case report forms.

Sampling and Analysis

In the preoperative period, blood samples were taken before the surgery. After the operation, blood samples were taken one day after the patient's arrival in the ICU. Blood glucose was measured by glucose oxidase method kit (pars Azmoon, Iran). Serum hs-CRP and CPK-MB were measured after the operation and analyzed using a commercial ELISA kits (LDN, Germany and Delta, Iran). All the serum samples were permitted to clot while plasma samples were immediately centrifuged at 4 °C at 2010 g for 10 min. All the samples were stored in a –20 °C freezer for later batch analysis.

Assessment of Self-reported Discomfort

The patients rated their sense of pain on a visual analogue scale (VAS), and their nausea, hunger and thirst were also self-reported after surgery. The discomfort rated by the patients on the VAS (0, none or extremely light; 10, extremely severe) was evaluated by the investigator.

Statistical Analysis

Data analysis performed using SPSS software (version 21; IBM Corp., Chicago, IL, USA). In this study, *p*-value less than 0.05 considered as a statistically significant level. Frequency distribution, mean ± standard deviation reported based on the type of variable. Normality of data evaluated using Kolmogorov-Smirnov tests or Histogram Chart. Chi Square test or Fishers Exact Test was used to compare qualitative variables. Also, to compare the mean of quantitative variables between the groups, Student *T* test used. Paired *t*-test was applied for comparisons of variables before and after intervention. Finally, ANCOVA models used to eliminate the effect of confounders. Sample size was calculated based on primary outcome and $\alpha = 0.05$, $\beta = 0.01$.

Results

Fig. 1 shows the disposition of the patients throughout the study. The analyses were ultimately made on 210 patients (107 in the ERAS group and 103 in the control group). There was no significant difference between the two groups in terms of age, sex, body weight, height, body mass index (BMI), left ventricular (LV) function, the New York Heart Association (NHYA), type of cardiac surgery, and surgical data (Table 1).

Table 2 shows the data about the anesthetics used and the temperature of the operating room.

Table 3 summarizes the effects of the ERAS protocol on the biochemical findings of the patients. Recommendations to follow the ERAS resulted in a significantly lower increase in alkaline phosphatase (ALP) and total bilirubin relative to the control group (all *p*-values > 0.05). After surgery, one day after ICU admission, serum level of hs-CRP was significantly lower in the ERAS group com-

Table 3. Biochemical findings before and after surgery in patients who received either ERAS or usual care.

	Control (n = 103)		p-values[1]	ERAS (n = 107)		p-values[1]	p-values[2]
	before surgery	after surgery		before surgery	after surgery		
Hgb (g/dL)	13.02 ± 1.4	10.6 ± 1.9	<0.001	15.4 ± 1.5	10.9 ± 1.7	<0.001	0.308
Hct (%)	40.2 ± 3.8	35.5 ± 3.8	<0.001	41.04 ± 4.4	34.7 ± 5.1	<0.001	0.057
Na (mg/dL)	137.1 ± 16.8	135.7 ± 13.2	0.506	140.9 ± 2.1	139.03 ± 2.6	<0.001	0.282
K (mg/dL)	4.7 ± 2.1	4.6 ± 2.5	0.099	4.2 ± 0.3	4 ± 0.3	<0.001	0.935
FBS (mg/dL)	121.06 ± 2.29	144.52 ± 5.40	0.001	127.56 ± 3.22	133.53 ± 2.84	<0.001	0.002
Cr (mg/dL)	1.03 ± 0.16	0.96 ± 0.15	0.001	1.1 ± 0.28	1.06 ± 0.37	0.373	0.194
Uric Acid (mg/dL)	5.3 ± 1.3	5.3 ± 1.1	0.999	5.3 ± 1.9	4.9 ± 1.7	0.106	0.244
BUN (mg/dL)	14.7 ± 6.5	16.9 ± 4.3	0.004	16.1 ± 5.8	17.1 ± 7.2	0.264	0.611
SGOT (U/L)	21.6 ± 8.9	38.7 ± 9.5	<0.001	33.6 ± 6.9	40.1 ± 9.5	<0.001	0.584
SGPT (U/L)	24.8 ± 3.3	38.5 ± 3.5	<0.001	26.9 ± 7.8	32.1 ± 3.7	<0.001	0.043
ALP (U/L)	166.6 ± 24.4	210.1 ± 49.9	<0.001	164.9 ± 18.6	163.3 ± 15.7	0.497	0.001
Total Bilirubin (mg/dL)	0.8 ± 0.3	0.8 ± 0.1	0.999	0.8 ± 0.3	0.7 ± 0.2	0.004	0.007
CK-MB	21.1 ± 9	56.4 ± 7.9	<0.001	22.4 ± 7.1	54.1 ± 9.71	<0.001	0.061
Hs-CRP (mg/L)	4.6 ± 1.76	35 ± 14.8	<0.001	4.71 ± 1.5	23.2 ± 10.1	<0.001	<0.001

[1] Calculated by Paired-Samples T test and presented as means ± SE. [2] Difference after surgery calculated by ANCOVA, adjusted for before surgery data. Hgb, Hemoglobin; Hct, Hematocrit; Na, Sodium; K, Potassium; FBS, Fasting blood sugar; Cr, Creatinine; BUN, Blood urea nitrogen; SGOT, glutamic-oxaloacetic transaminase; SGPT, glutamic-pyruvic transaminase; ALP, Alkaline phosphatase; CK-MB, Creatine kinase; Hs-CRP, high sensitive-C-reactive protein.

pared to the control group. Furthermore, the serum levels of glutamic-pyruvic transaminase (SGPT) and fasting blood sugar (FBS) decreased significantly in the ERAS group compared to the controls ($p < 0.05$).

Table 4 presents data on the patients' postoperative discomfort. Those who received ERAS had less complaints than the control group regarding thirst, hunger, anxiety, and pain (all p-values < 0.05). Regardless, there was no significant difference between the groups in terms of nausea and vomiting (all p-values > 0.05).

Tables 5,6 show the clinical characteristics of the participants in the recovery room and ICU. The patients in the intervention group experienced a shorter duration of hospitalization, length of stay in the ICU, ventilation time, and first mobility (all p-values < 0.05). In addition, the first meal after surgery was initiated sooner for patients who received the ERAS compared to the control protocol ($p < 0.05$).

Additionally, there was no significant difference between the two groups regarding postoperative outcomes such as stroke, acute kidney injury, atrial fibrillation, respiratory failure, infection, acute respiratory distress syndrome, myocardial infarction, unplanned reintubation, ICU readmission, and death (all p-values > 0.05).

Discussion

The present study showed that the ERAS approach results in improvements in postoperative thirst, hunger, anxiety, pain, duration of hospitalization, ICU stay, first mobility, and ventilation time. Furthermore, serum hs-CRP level decreased significantly more in the patients who received the ERAS protocol. The key pathway interventions in our study were preoperative patient education, nutrition counselling, reducing the fasting time before surgery and carbohydrate loading 2 hours before general anesthesia, postoperative nutrition intervention, early extubation, fast drainage and removal of the venous catheters, and early ambulation.

The ERAS protocol consisted of a group of evidence-based approaches that were implemented preoperatively to improve postoperative clinical and functional outcomes by diminishing surgical stress and enhancing postoperative recovery. During the 1990s, the 'fast-track' protocol was widely implemented in the context of cardiac surgery patients to improve postoperative outcomes [8]. Nevertheless, there is a major difference between the previous approach and the more comprehensive ERAS protocol. The 'fast-track' approach mainly focused on early extubation and shorter ICU stay through modifying the surgical and anesthetic technique (e.g., shorter-acting anesthetic medications and minimally-invasive incisions) [9]. In contrast to the 'fast-track' approach, the ERAS protocol incorporates more comprehensive preoperative optimizations to improve postoperative recovery. Furthermore, evidence demonstrates the higher beneficial effects of ERAS compared to the traditional approach regarding postoperative outcomes [10].

In this study, a reduction was observed in hs-CRP as a biomarker of inflammation, which is consistent with a previous systematic review [11]. Moreover, the implementation of ERAS protocols in various populations has also shown similar findings [12–14]. It has been reported that insulin resistance is associated with the accumulation

Table 4. Findings of major postoperative complications in patients who received either ERAS or usual care.

	Control (n = 103)	ERAS (n = 107)	*p*-values
Thirst	100 (97.1)	53 (49.5)	<0.001[2]
Hunger	91 (88.3)	41 (38.3)	<0.001[2]
Anxiety	79 (76.7)	58 (54.2)	<0.001[2]
Nausea			
First day (yes)	24 (23.3)	36 (33.6)	0.100[2]
Second day (yes)	12 (11.6)	17 (15.9)	0.383[2]
Third day (yes)	3 (2.9)	5 (4.7)	0.763[2]
Vomiting			
First day (yes)	34 (33)	33 (30.8)	0.738[2]
Second day (yes)	15 (14.6)	8 (7.5)	0.107[2]
Third day (yes)	3 (2.9)	2 (1.9)	0.963[2]
Pain score	5.6 ± 1.3	4.8 ± 1.4	<0.001[1]

[1] Independent-Samples *T* test (means ± SE). [2] Chi-square or Fishers Exact Test (count, %).

Table 5. Postoperative clinical outcomes.

Variables	Control (n = 103)	ERAS (n = 107)	*p*-values[1]
ICU stay (hour)	92.6 ± 21.4	79.6 ± 12	<0.001
Hospitalization (day)	12.1 ± 3.3	10.5 ± 2.4	<0.001
Ventilation time (hour)	7.7 ± 2.1	5.5 ± 1.2	<0.001
First mobility (hour)	82.4 ± 28.4	43.9 ± 21.4	<0.001

[1] Calculated by Independent-Samples *T* test and presented as means ± SE. ICU, Intensive care unit.

of proinflammatory macrophages, subsequently leading to inflammation [15]. Moreover, preoperative carbohydrate loading was shown to improve postoperative insulin resistance [16]. Therefore, it can be concluded that reduction in postoperative insulin resistance by oral carbohydrate drinks may decrease postoperative inflammation [15].

In the present study, the clinical outcomes of patients after cardiac surgery, including thirst, hunger, anxiety, and pain, were improved following the ERAS protocol. Reducing the preoperative fasting period by providing oral carbohydrate drinks 2 hours before anesthesia induction has been shown to decrease anxiety, hunger, pain, and thirst [17].

Preoperative education and psychological counselling, which are an integral part of the ERAS protocol, were designed to alleviate individuals' anxiety and increase their compliance. It has also been hypothesized that insulin works to increase serotonin levels in the brain and thus regulate mood [18]. This mechanism can contribute to lower preoperative anxiety, thus improving the patients' psychological state in the preoperative period and thereby their postoperative anxiety.

Thirst before and after surgery has been suggested as the main influencing factor of patient discomfort, followed by hunger and anxiety [19]. Also, anxiety is directly related to the severity of postoperative pain. We found that the patients in the ERAS group experienced lower postoperative pain, which was paralleled with lower opioid administration. The reduction of early postoperative opioid use may have led to a reduced length of ICU stay and early mobilization [20]. The present study also demonstrated that the ERAS approach leads to earlier initiation of postoperative first meal in both liquid and solid forms. The patients in the ERAS group experienced lower pain, which resulted in early mobilization and subsequently improved the recovery of the physiological function of the gastrointestinal tract [21,22]. Additionally, the ERAS protocol includes postoperative physical therapy and rehabilitation exercise, which enable participants to resume their normal activities sooner and subsequently initiate their first postoperative meal in a shorter duration [20].

The recommendations to follow the ERAS guidelines resulted in a reduction in hospital and ICU stay, first mobility, and ventilation time. There is evidence regarding the association between inflammation and mortality, hospitalization, postoperative infection, and ventilation time [3,23]. It can therefore be conjectured that ERAS recommendations diminished the postoperative inflammatory status of the participants by providing oral carbohydrate loading and limiting preoperative fasting duration, which could have contributed to the lower duration of hospitalization, length of ICU stay, and shorter ventilation time. Higher postoperative pain can reduce mobility, increase the need for analgesics, and thus cause a longer hospital stay. Anxiety and pain are reported as a reason for reduced lengths of hospital stay [24,25].

Table 6. Postoperative eating delay for liquid and solid foods in patients who received either ERAS or usual care.

	Control (n = 103)	ERAS (n = 107)	*p*-values[1]
Hours before Start of liquids	10.5 ± 2.1	7.4 ± 1.4	<0.001
Hours before Start of solids	19.5 ± 3.7	11.5 ± 3.5	<0.001

[1] Calculated by Independent-Samples *T* test and presented as means ± SE.

We found a marked reduction in ALP, total bilirubin, and SGPT following the ERAS protocol. Although these changes were statistically significant, they were all within the normal range, which diminishes their clinical interpretation and applicability. These findings may indicate that liver function recovery was faster in the ERAS group compared to the controls [26], which could partly be related to preoperative oral carbohydrate loading, which can increase liver glycogen storage and subsequently accelerate liver function recovery [3].

Strengths and Limitations

The multidisciplinary nature of the ERAS protocol makes this method difficult to implement, and this difficulty may be associated with a reduced level of compliance. In our study, the ERAS protocol was implemented by multidisciplinary teams, including surgeons, cardiologists, anesthesiologist, clinical pharmacists, nutritionists, and nursing personnel from preoperative, intraoperative, and postoperative care stages, and showed improved outcomes in the patients. This may translate into a high level of compliance.

There are also several limitations to this study that warrant consideration. This study was a single-center intervention, and the generalizability of the findings is therefore minimized. Even though all the personnel involved in the intervention process were trained before the start of the study, there are potentially some unmeasured factors that may have influenced our findings, including interpersonnel variability, unit-level protocols, unique workforce structure, and local medication formulary. Furthermore, intraoperative surgical complications such as hemodynamic instability, bleeding, or other unforeseen events prevented all the points of the ERAS protocol from being used equally for all the patients. Furthermore, due to the nature of the study, complete blinding was not possible.

Conclusion

This study showed that cardiac surgery patients benefited from the implementation of the ERAS protocol and had better outcomes with this approach. Our study was performed on non-emergency patients. It is better to conduct future studies on emergency patients or on patients with comorbidities, as most elements of the ERAS protocol are applicable in these groups as well.

Availability of Data and Materials

Data will not be made available in a public repository as we have not obtained ethical clearance to share data publicly. However, on request from the corresponding author, data could be provided while maintaining anonymity.

Author Contributions

ShiH, ZVS, SaeH, MM, FN, and ZT contributed to the conception and design, acquisition and interpretation of data, verified the underlying data, and writing and editing of the manuscript, and all reviewed and approved the manuscript for submission. All authors contributed to editorial changes in the manuscript. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

The protocol was approved by the institutional ethics committee of Rajaie Cardiovascular, Medical and Research Center (approval number IR.RHC.REC.1397.042) and was registered on https://IRCT.ir with identity number IRCT20200114046131N1. Written informed consent was obtained from participants before intervention.

Acknowledgment

Our appreciation goes to all the patients who volunteered for this trial, and all those who gave their valuable help and support towards this study.

Funding

This research received no external funding.

Conflict of Interest

The authors declare no conflict of interest.

References

[1] Brown JK, Singh K, Dumitru R, Chan E, Kim MP. The Benefits of Enhanced Recovery After Surgery Programs and Their Application in Cardiothoracic Surgery. Methodist DeBakey Cardiovascular Journal. 2018; 14: 77–88.

[2] Oravec N, Arora RC, Bjorklund B, Gregora A, Monnin C, Duhamel TA, *et al*. Expanding enhanced recovery protocols for cardiac surgery to include the patient voice: a scoping review protocol. Systematic Reviews. 2021; 10: 22.

[3] Li M, Zhang J, Gan TJ, Qin G, Wang L, Zhu M, *et al*. Enhanced recovery after surgery pathway for patients undergoing cardiac surgery: a randomized clinical trial. European Journal of Cardiothoracic Surgery: Official Journal of the European Association for Cardio-thoracic Surgery. 2018; 54: 491–497.

[4] Williams JB, McConnell G, Allender JE, Woltz P, Kane K, Smith PK, *et al*. One-year results from the first US-based enhanced recovery after cardiac surgery (ERAS Cardiac) program. The Journal of Thoracic and Cardiovascular Surgery. 2019; 157: 1881–1888.

[5] Watt DG, McSorley ST, Horgan PG, McMillan DC. Enhanced Recovery After Surgery: Which Components, If Any, Impact on The Systemic Inflammatory Response Following Colorectal Surgery?: A Systematic Review. Medicine. 2015; 94: e1286.

[6] Engelman DT, Ben Ali W, Williams JB, Perrault LP, Reddy VS, Arora RC, *et al*. Guidelines for Perioperative Care in Cardiac Surgery: Enhanced Recovery After Surgery Society Recommendations. JAMA Surgery. 2019; 154: 755–766.

[7] Pagano D, Milojevic M, Meesters MI, Benedetto U, Bolliger D, von Heymann C, *et al*. 2017 EACTS/EACTA Guidelines on patient blood management for adult cardiac surgery. European Journal of Cardio-thoracic Surgery: Official Journal of the European Association for Cardio-thoracic Surgery. 2018; 53: 79–111.

[8] Krohn BG, Kay JH, Mendez MA, Zubiate P, Kay GL. Rapid sustained recovery after cardiac operations. The Journal of Thoracic and Cardiovascular Surgery. 1990; 100: 194–197.

[9] Bainbridge D, Cheng D. Current evidence on fast track cardiac recovery management. European Heart Journal Supplements. 2017; 19: A3–A7.

[10] Baxter R, Squiers J, Conner W, Kent M, Fann J, Lobdell K, *et al*. Enhanced Recovery After Surgery: A Narrative Review of its Application in Cardiac Surgery. The Annals of Thoracic Surgery. 2020; 109: 1937–1944.

[11] Noss C, Prusinkiewicz C, Nelson G, Patel PA, Augoustides JG, Gregory AJ. Enhanced Recovery for Cardiac Surgery. Journal of Cardiothoracic and Vascular Anesthesia. 2018; 32: 2760–2770.

[12] Jaloun HE, Lee IK, Kim MK, Sung NY, Turkistani SAA, Park SM, *et al*. Influence of the Enhanced Recovery After Surgery Protocol on Postoperative Inflammation and Short-term Postoperative Surgical Outcomes After Colorectal Cancer Surgery. Annals of Coloproctology. 2020; 36: 264–272.

[13] Wierdak M, Pisarska M, Kuśnierz-Cabala B, Kisielewski M, Major P, Witowski JS, *et al*. Use of inflammatory markers in the early detection of infectious complications after laparoscopic colorectal cancer surgery with the ERAS protocol. Wideochirurgia i Inne Techniki Maloinwazyjne = Videosurgery and other Miniinvasive Techniques. 2018; 13: 315–325.

[14] Gustafsson UO, Oppelstrup H, Thorell A, Nygren J, Ljungqvist O. Adherence to the ERAS protocol is Associated with 5-Year Survival After Colorectal Cancer Surgery: A Retrospective Cohort Study. World Journal of Surgery. 2016; 40: 1741–1747.

[15] Shimobayashi M, Albert V, Woelnerhanssen B, Frei IC, Weissenberger D, Meyer-Gerspach AC, *et al*. Insulin resistance causes inflammation in adipose tissue. The Journal of Clinical Investigation. 2018; 128: 1538–1550.

[16] Kotfis K, Jamioł-Milc D, Skonieczna-Żydecka K, Folwarski M, Stachowska E. The Effect of Preoperative Carbohydrate Loading on Clinical and Biochemical Outcomes after Cardiac Surgery: A Systematic Review and Meta-Analysis of Randomized Trials. Nutrients. 2020; 12: 3105.

[17] Evman S, Akoğlu H, Yıldızeli B, Batırel Fevzi H, Yüksel M. What is the optimal postoperative oral feeding timing protocol for thoracotomy patients? Prospective randomized clinical trial on postoperative complications. Turkish Journal of Thoracic and Cardiovascular Surgery. 2017; 25: 117–123.

[18] Martin H, Bullich S, Guiard BP, Fioramonti X. The impact of insulin on the serotonergic system and consequences on diabetes-associated mood disorders. Journal of Neuroendocrinology. 2021; 33: e12928.

[19] Madsen M, Brosnan J, Nagy VT. Perioperative thirst: a patient perspective. Journal of Perianesthesia Nursing: Official Journal of the American Society of PeriAnesthesia Nurses. 1998; 13: 225–228.

[20] Breuer JP, von Dossow V, von Heymann C, Griesbach M, von Schickfus M, Mackh E, *et al*. Preoperative oral carbohydrate administration to ASA III-IV patients undergoing elective cardiac surgery. Anesthesia and Analgesia. 2006; 103: 1099–1108.

[21] Kehlet H, Wilmore DW. Multimodal strategies to improve surgical outcome. American Journal of Surgery. 2002; 183: 630–641.

[22] Henriksen MG, Jensen MB, Hansen HV, Jespersen TW, Hessov I. Enforced mobilization, early oral feeding, and balanced analgesia improve convalescence after colorectal surgery. Nutrition (Burbank, Los Angeles County, Calif.). 2002; 18: 147–152.

[23] Esme H, Apilioğulları B, Keşli R, Yoldaş B, Bekçi T, Çalık M, *et al*. Evaluation of procalcitonin, interleukin 6, and tumor necrosis factor alpha levels as early markers of postoperative complications following major thoracic surgery. Turkish Journal of Thoracic and Cardiovascular Surgery. 2012; 20: 857–861.

[24] Tran S, Wolever TMS, Errett LE, Ahn H, Mazer CD, Keith M. Preoperative carbohydrate loading in patients undergoing coronary artery bypass or spinal surgery. Anesthesia and Analgesia. 2013; 117: 305–313.

[25] Morrison SR, Magaziner J, McLaughlin MA, Orosz G, Silberzweig SB, Koval KJ, *et al*. The impact of post-operative pain on outcomes following hip fracture. Pain. 2003; 103: 303–311.

[26] Zheng Y, Wang L, Wu F, Rong W, Liu Y, Zhang K, *et al*. Enhanced recovery after surgery strategy for cirrhosis patients undergoing hepatectomy: experience in a single research center. Annals of Surgical Treatment and Research. 2020; 98: 224–234.