Perioperative Effects of Epidural Anesthesia on Hemodynamics, Pain, and Pro-brain Natriuretic Peptide Levels in Vascular Surgery: A Prospective Randomized Study

Mehmet Ilker Sivacigil[1], Leyla Sivacigil[2], Lale Yuceyar[3], Hulya Erolcay[3]

[1]University of Health Sciences Türkiye, Istanbul Beyoglu Eye Training and Research Hospital, Clinic of Anesthesiology and Reanimation, Istanbul, Türkiye

[2]University of Health Sciences Türkiye, Taksim Training and Research Hospital, Clinic of Anesthesiology and Reanimation, Istanbul, Türkiye

[3]Istanbul University-Cerrahpasa Faculty of Medicine, Department of Anesthesiology and Reanimation, Istanbul, Türkiye

──────── **Abstract** ────────

Aim: Vascular surgery is among the surgical procedures associated with the highest cardiac morbidity and mortality because the surgical stress response is pronounced in individuals with cardiogenic risk factors. The aim of this study is to evaluate the effect of epidural anesthesia on the surgical stress response during major vascular surgery.

Methods: Two groups (epidural group (EG), n=15; control group, n=15) were formed in the cardiovascular surgery operating room by prospective randomization. Hemodynamic fluctuations and visual analog scale (VAS) pain scores were monitored. The primary endpoint was defined as the change in N-terminal-proBNP (NT-proBNP) levels on postoperative day two compared with preoperative measurements. Troponin-I, changes in blood flow, pain scores, and sevoflurane use were secondary endpoints.

Results: Sevoflurane consumption was lower in EG, whereas fluid volume was higher. ≥11 tachycardia attacks were more frequent in CG, and ≥11 decreases in mean arterial pressure were seen (33.3% vs. 0%; p=0.042). VAS was lower in favor of EG (Day-1: 4.33±0.98 vs. 5.27±0.70, p=0.011; Day-2: 1.67±1.13 vs. 2.13±0.64, p=0.041). No difference in NT-proBNP/troponin-I levels was observed between groups.

Conclusion: In vascular surgery, epidural anesthesia can reduce hemodynamic fluctuations and early postoperative pain while limiting the rise in NT-proBNP. Biomarker findings are hypothesis-generating owing to methodological constraints and necessitate validation through studies with larger sample sizes.

Keywords: Anesthesia, epidural, vascular surgical procedures, natriuretic peptide, brain, Troponin I, postoperative pain

Introduction

Vascular surgery is among the surgical procedures with the highest cardiac morbidity and mortality during the perioperative period (1-2). The main reason for poor prognosis in patients with cardiogenic risk factors is hemodynamic changes that develop due to surgical stress. Effective management of the surgical stress response is critical for maintaining hemodynamic stability (1,3). Specific biomarkers are needed to predict cardiac mortality and morbidity, especially in high-risk patient groups (4,5).

Natriuretic peptides are hormones involved in the regulation of blood pressure and blood volume. Pro-B-type natriuretic peptide (proBNP) is released into the circulation in response to increased ventricular wall stress and pressure load; therefore, it is sensitive to

detecting perioperative cardiac stress and the risk of adverse events (4,6). Cardiac troponin I (cTnI) is a specific marker of myocardial damage, and its increase is linearly associated with poor prognosis (5). Since N-terminal-proBNP (NT-proBNP) reflects hemodynamic load and cTnI reflects necrosis, evaluating these two markers together may allow for more comprehensive monitoring of cardiac risk associated with surgical stress (4,7). We hypothesized that epidural anesthesia, when added to general anesthesia for major vascular surgery, provides effective pain control in the perioperative and postoperative periods, partially suppresses the surgical stress response, and reduces cardiac risk by lowering myocardial oxygen demand through sympathetic blockade, peripheral vasodilation, and increased coronary and collateral blood flow (7,8). Based on this rationale, the primary endpoint was defined as the change in NT-proBNP levels from the day before surgery to the day after surgery. Troponin I, the number of blood-flow changes, and visual analog scale (VAS) pain scores were secondary endpoints.

Specifically, prospective randomized data assessing the potential influence of the dynamics of NT-proBNP and troponin-I in relation to hemodynamic variations and pain scores are limited. Few prospective studies have examined the effect of epidural anesthesia on the dynamics of cardiac biomarkers in patients undergoing vascular surgery (4,7,9). The aim of this study is to evaluate the effect of epidural anesthesia on the surgical stress response in major vascular surgery by measuring cardiac biomarkers, hemodynamic variables, and pain scores. This will enable the monitoring of the frequency of surgical stress responses and related cardiac complications in the perioperative and postoperative periods and will contribute to maintaining hemodynamic stability.

Materials and Methods

Compliance With Ethical Standards

The study was conducted in the Cardiovascular Surgery operating room and was approved by the Istanbul University-Cerrahpasa Faculty of Medicine Ethics Committee (approval no.: 43423, date: 01.12.2011), in accordance with the Declaration of Helsinki (10). All patients were provided with written and verbal information, and written consent was obtained. The supply of NT-proBNP and troponin I kits was provided by the Scientific Research Projects (BAP) Unit of Istanbul University-Cerrahpasa Faculty of Medicine University. Kits from Biomedica Slovakia and Diagnostic Automation Inc. were used for NT-proBNP and troponin I, respectively.

Study Design and Population

30 patients undergoing vascular surgery [American Society of Anesthesiologists (ASA) II-III] were randomly allocated to the study groups using a sealed opaque envelope randomization technique: the epidural group (EG), which received epidural anesthesia, and the control group (CG). Patient demographics (height, body weight, age, gender, and ASA status) were recorded. The randomization process and analysis sets are presented in Figure 1.

Exclusion Criteria

Liver dysfunction (alanine aminotransferase/aspartate aminotransferase >40), kidney failure, New York Heart Association (NYHA) IV heart failure, unstable angina, second-third degree atrioventricular (AV) block, pregnancy, glucocorticoid use, hyperthyroidism/hypothyroidism or thyroid hormone use, epidural contraindication (bleeding diathesis, hypovolemic shock, local infection, vertebral deformity, arthritis, osteoporosis, back pain, hypotension, increased intracranial pressure, previous laminectomy, drug allergy, back trauma, cauda equina syndrome).

Anesthesia Management and Monitoring

Following preoperative assessment, electrocardiography (ECG), peripheral oxygen saturation (SpO_2), and arterial blood pressure were monitored; an intravenous cannula and a urinary catheter were inserted; premedication with 0.03 mg·kg^{-1} midazolam was administered, and an appropriate crystalloid infusion was initiated. Invasive arterial pressure was continuously monitored with radial artery catheterization. During service follow-ups throughout the surgery, 20% increases or decreases in heart rate (HR) and mean arterial pressure (MAP) relative to reference values were recorded. HR <50 bpm (bradycardia), a 20% increase in HR (tachycardia), a 20% decrease in MAP (hypotension), and a 20% increase in MAP (hypertension) were considered. Standard algorithms were applied to manage hypotension, bradycardia, tachycardia, and hypertension (sevoflurane adjustment; 5 mL·kg^{-1} crystalloid bolus; 5 mg ephedrine; 0.5 mg atropine; 1 µg·kg^{-1} fentanyl).

For epidural anesthesia, 5-7 mg·kg^{-1} of balanced electrolyte solution was administered before catheter placement. The epidural catheter was inserted using the "loss of resistance" method at the L1-L2 or L2-L3 interspace; the block level was assessed using a pinprick after a 3-mL test dose of lidocaine. A preoperative 10-mL bolus of 0.5% bupivacaine +1 mg of morphine was administered epidurally.

Pain Management

For the first 48 hours postoperatively, epidural patient-controlled analgesia (PCA) (100 mL of 0.05 bupivacaine +10 mg morphine; 6 mL·s^{-1} infusion, 4 mL bolus, 30 min lock) and IV-PCA (morphine 1 mg·mL^{-1}; 2 mg bolus; 15 min lock) were administered to the CG.
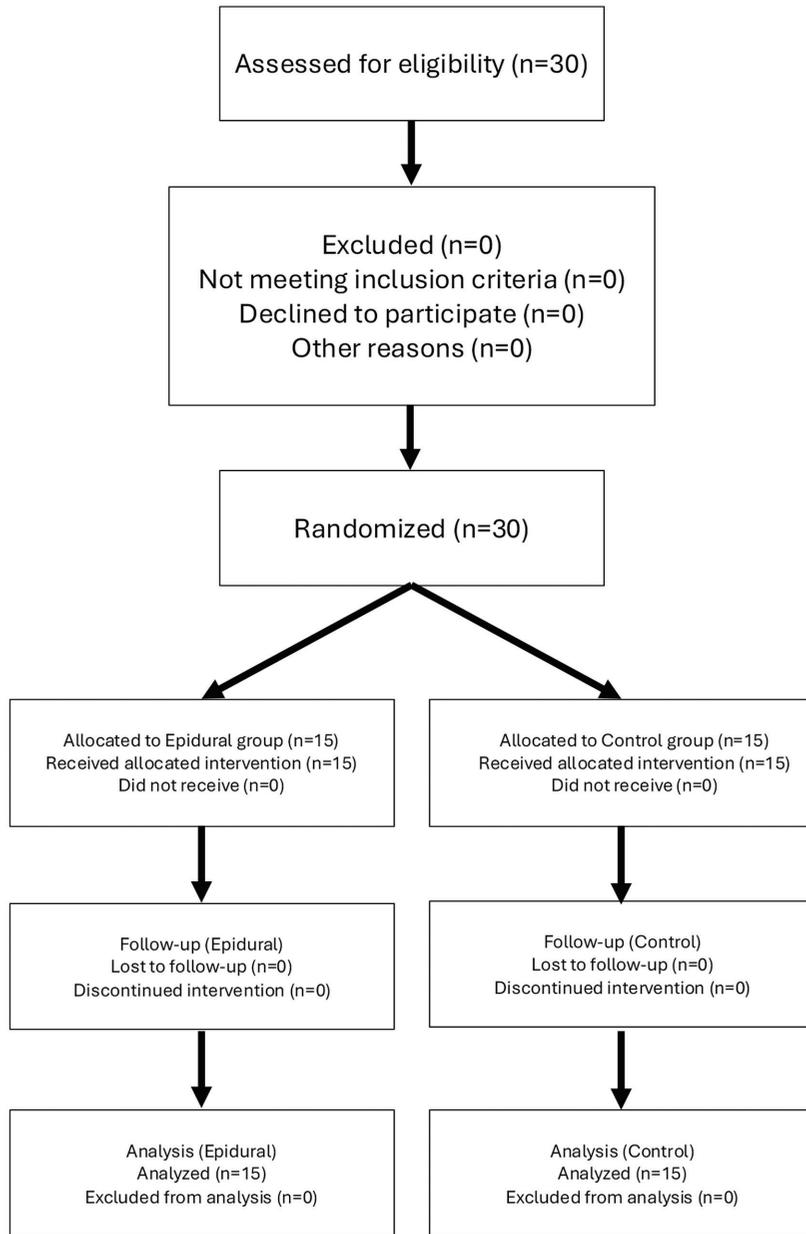
Figure 1. CONSORT flow diagram of patient enrollment, randomization, follow-up, and analysis

The main goal of this study was to determine how NT-proBNP levels changed on the second postoperative day compared with the day before surgery. High-sensitivity cardiac troponin (hs-cTn) was used to assess myocardial injury in the study. This study was conducted to evaluate myocardial injury in patients undergoing non-cardiac surgery. High-sensitivity cardiac troponin was used to assess myocardial injury. Myocardial injury after non-cardiac surgery (MINS) was defined as a postoperative hs-cTn value exceeding the 99th percentile upper reference limit in the absence of a non-ischemic cause, in accordance with the Fourth Universal Definition of Myocardial Infarction. Patients with NYHA class IV heart failure, unstable angina, and second- or third-degree AV block were excluded from the study. Troponin-I levels, number of hemodynamic fluctuations (HR/MAP criteria), VAS scores, and sevoflurane intake were the secondary endpoints. Follow-up and measurements: cardiac events were assessed on postoperative days 1 and 2, and pain was assessed using the VAS. Major adverse cardiac events (MACE), perioperative mortality, and perioperative MI were addressed through early clinical questioning and routine

assessments. In this study, clinical cardiac endpoints (e.g., MACE and mortality) were not systematically monitored as primary or secondary endpoints; instead, they were only addressed through early clinical questioning and routine assessments. Blood samples and ECGs were taken preoperatively, after extubation, and on the 1st and 2nd postoperative days. Plasma samples were centrifuged at 4000 rpm for 10 minutes and stored at -80 °C; NT-proBNP and troponin I measurements were performed after the patient enrollment was completed.

Statistical Analysis

Sample size was determined by one-way ANOVA based on pilot data (α=0.05, power =80%, effect size =0.5), which required at least 17 patients per group. Continuous variables were tested for normality and expressed as mean ± standard deviation or median (minimum-maximum), as appropriate. Categorical variables were presented as numbers and percentages. Between-group comparisons were performed using the independent samples t-test or Mann-Whitney U test, and categorical variables were analyzed using the chi-square or Fisher's exact test. Effect sizes were calculated using Cohen's d (0.2 small, 0.5 medium, and 0.8 large). Changes over time in MAP, HR and VAS were evaluated using the Friedman test with Bonferroni-corrected post-hoc comparisons. Correlations were assessed using Spearman's correlation coefficient. Analyses were conducted using NCSS 2007 and PASS 2008 software, and p<0.05 was considered statistically significant.

Results

The study was conducted in a total of 30 cases undergoing vascular surgery in the operating room of Istanbul University Faculty of Medicine, Department of Cardiovascular Surgery (EG n=15; CG n=15) (Figure 1). The ages of the subjects ranged from 42 to 77 years (59.27±8.78). There was a significant age difference between the groups; the CG was older (EG 55.07±7.43; CG 63.47±8.17; p=0.006). There was no difference in BMI (EG 27.00±2.10; KG 27.67±1.91; p=0.372) and gender distribution (female EG 33.3%; CG 13.3%; p=0.390) (Table 1).

Anesthetic Consumption and Fluids

In the EG, sevoflurane consumption was significantly lower (56.40±13.99 mL vs. 67.40±14.32 mL; p=0.042). The intraoperative fluid volume administered was higher in the EG group (2586.67±1130.02 mL vs. 1870.00±296.29 mL; p=0.030) (Table 2).

Hemodynamic Variables

The rate of "≥11 times" for increased CAD was higher in the CG (EG 13.3%; CG 53.3%; p=0.020). The intergroup difference in MAP increase was not significant. No differences were found among the HR decrease categories. The rate of "≥11 times" occurrence in MAP was significantly higher in the CG group (EG 0%; CG 33.3%; p=0.042) (Table 3).

Table 1. Baseline demographic and anthropometric characteristics of the groups (epidural and control)			
	Epidural (n=15)	**Control (n=15)**	**p**
	Mean ± SD	**Mean ± SD**	
Age (years)	55.07±7.43	63.47±8.17	0.006*
BMI (kg/m²)	27.00±2.10	27.67±1.91	0.372
	n (%)	n (%)	
Gender†			0.390
Female	5 (33.3%)	2 (13.3%)	
Male	10 (66.7%)	13 (86.7%)	

*p<0.01. Data are presented as mean ± SD or n (%). Comparisons of age and BMI were made using the independent samples t-test (Mann-Whitney U if the assumption of normality was not met), and for gender†, the chi-square test (Fisher's exact test if necessary). Significance level was p<0.05
SD: Standard deviation, BMI: Body mass index (kg/m²)

Table 2. Sevoflurane consumption and total fluid volume during surgery (epidural and control)						
	Epidural (n=15) Mean ± SD	**Control (n=15) Mean ± SD**	**p**	**Mean difference (E-C)**	**Pooled SD**	**Cohen's d**
Sevoflurane consumption (mL)	56.40±13.99	67.40±14.32	0.042*	-11.00	14.16	-0.78
Fluid volume (mL)	2586.67±1130.02	1870.00±296.29	0.030*	716.67	826.05	0.87

*p<0.05. Data are presented as mean ± SD. Groups were compared using an independent samples t-test (Mann-Whitney U test when normality was not achieved). Significance level: p<0.05. Mean difference calculated as epidural minus control (E-C). Effect size interpreted according to Cohen's criteria (0.2= small, 0.5= moderate, 0.8= large)
SD: Standard deviation, mL:milliliters

Pain

Visual analog scale was lower in favor of the EG group on day 1 (EG 4.33±0.98; CG 5.27±0.70; p=0.011) and day 2 (EG 1.67±1.13; CG 2.13±0.64; p=0.041); the decrease from day 1 to day 2 was significant in both groups (p=0.001) (Table 4).

Biomarkers

No significant differences were found between groups for preoperative, post-extubation, and postoperative day 1 and day 2 measurements of proBNP and troponin I. This result shows that the primary endpoint does not differ significantly between the groups. In intra-time comparisons, no significant change in proBNP was observed in the EG, whereas a significant increase was detected in the CG after pre-operation (p=0.031), on the 1st postoperative day (p=0.016), and on the 2nd postoperative day (p=0.015). There was no significant effect of time on troponin I in either group (Tables 5 and 6). No significant difference was observed between preoperative NT-proBNP levels and postoperative day 2 levels (p>0.05). High-sensitivity cardiac troponin levels did not exceed the 99th percentile upper reference limit in any patient; therefore, no cases of MINS were identified. No MACE, perioperative myocardial infarction, or deaths were observed.

Table 3. Frequency of intraoperative hemodynamic fluctuations: heart rate (HR) and mean arterial pressure (MAP) changes (epidural and control)

Change	Frequency	Measure	Epidural (n=15)	Control (n=15)	p
Increase	None	HR	3 (20.0%)	1 (6.7%)	0.598
Increase	None	MAP	0 (0.0%)	0 (0.0%)	1.000
Increase	1-10 times	HR	10 (66.7%)	6 (40.0%)	0.143
Increase	1-10 times	MAP	14 (93.3%)	9 (60.0%)	0.080
Increase	≥11 times	HR	2 (13.3%)	8 (53.3%)	0.020*
Increase	≥11 times	MAP	1 (6.7%)	6 (40.0%)	0.080
Decrease	None	HR	2 (13.3%)	0 (0.0%)	0.483
Decrease	None	MAP	2 (13.3%)	0 (0.0%)	0.483
Decrease	1-10 times	HR	11 (73.4%)	10 (66.7%)	1.000
Decrease	1-10 times	MAP	13 (86.7%)	10 (66.7%)	0.390
Decrease	≥11 times	HR	2 (13.3%)	5 (33.3%)	0.390
Decrease	≥11 times	MAP	0 (0.0%)	5 (33.3%)	0.042*

*p<0.05. Data are presented as n (%). "Increase/decrease" indicates a ≥20% increase/decrease in the relevant parameter compared to baseline; "Frequency" rows indicate the number of events (None, 1-10 times, ≥11 times). Groups were compared using the chi-square test (Fisher's exact test if necessary); significance level is p<0.05

Table 4. Postoperative pain levels (VAS) - day 1 and day 2 comparisons (epidural vs. control)

VAS	Epidural (n=15) Mean ± SD (Median)	Control (n=15) Mean ± SD (Median)	p	Cohen's d (Epidural-Control)	Magnitude (|d|)
Day 1	4.33±0.98 (4.00)	5.27±0.70 (5.00)	0.011**	-1.1	Large
Day 2	1.67±1.13 (1.00)	2.13±0.64 (2.00)	0.041*	-0.5	Medium
Day 1/day 2;†	0.001***	0.001***	-	-	-

*p<0.05; **p<0.01; ***p<0.001. Data are presented as mean ± SD (median). For between-group (epidural vs. control) comparisons, an independent samples t-test (Mann-Whitney U test if normality was not achieved) was used. For within-group (day-1 vs. day-2) comparisons, a paired t-test (Wilcoxon signed-rank test if normality was not achieved) was used. Significance level p<0.05. Mean difference calculated as Epidural minus Control (E-C). Effect size interpreted according to Cohen's criteria (0.2= small, 0.5= moderate, 0.8= large)
VAS: Visual analog scale (0-10), SD: Standard deviation

Table 5. Comparison of cardiac biomarkers by time points: proBNP and Troponin-I (epidural and control)

Time point	Marker	Epidural (Mean ± SD (median)	Control (Mean ± SD (median)	p	Cohen's d (E-C)	Magnitude (|d|)
Pre-op	proBNP (pg/mL)	87.05±115.18 (48.79)	33.53±28.52 (40.38)	0.148	0.638	Medium
	Troponin-I (ng/mL)	0.91±1.42 (0.32)	1.00±1.66 (0.08)	0.967	-0.058	Trivial
Post-extubating	proBNP (pg/mL)	71.53±108.39 (37.02)	54.20±31.80 (57.93)	0.539	0.217	Small
	Troponin-I (ng/mL)	3.24±11.29 (0.01)	1.25±1.67 (0.62)	0.081	0.247	Small
Post-op day 1	proBNP (pg/mL)	42.26±29.05 (32.40)	60.61±47.11 (45.51)	0.389	-0.469	Small
	Troponin-I (ng/mL)	0.69±1.57 (0.08)	1.34±2.28 (0.56)	0.187	-0.332	Small
Post-op day 2	proBNP (pg/mL)	49.27±49.77 (32.95)	99.49±151.35 (52.66)	0.412	-0.446	Small
	Troponin-I (ng/mL)	2.03±5.13 (0.03)	1.01±1.44 (0.76)	0.461	0.271	Small

Data are presented as mean ± SD (median). An independent samples t-test (Mann-Whitney U when normality was not achieved) was used for comparisons between groups at each time point; p<0.05 was considered statistically significant. Mean difference calculated as Epidural minus Control (E-C).Effect size interpreted according to Cohen's criteria (0.2= small, 0.5= moderate, 0.8= large)
proBNP: N-terminal pro-B-type natriuretic peptide (pg/mL), Troponin-I (ng/mL), Pre-op: Before surgery, post-extubating = after extubating, Post-op day 1/2 = post-operative day 1/2; SD: Standard deviation

Table 6. Within-group comparisons over time: paired p-values for proBNP and Troponin-I (epidural and control)

Comparison time points	ProBNP epidural (p)	ProBNP control (p)	Troponin epidural (p)	Troponin control (p)
Pre-op vs. post-extubating	0.570	0.031*	0.575	0.180
Pre-op vs. post-op day 1	0.191	0.016*	0.790	0.594
Pre-op vs. post-op day 2	0.124	0.015*	0.477	0.683
Post-extubating vs. post-op day 1	0.427	0.570	0.594	0.657
Post-extubating vs. post-op day 2	0.820	0.460	0.859	0.865
Post-op day 1 vs. post-op day 2	0.460	0.307	0.722	0.917

*p<0.05. The p-values in the table represent paired comparisons between the two specified time points within each group (epidural, control) (Pre-op ↔ Post-extubating; Pre-op ↔ Post-op Day-1/Day-2; etc.). Analysis was performed using a paired t-test (Wilcoxon signed-rank test when normality was not met); p<0.05 was considered significant.
proBNP: N-terminal pro-B-type natriuretic peptide, Pre-op: Pre-operative, post-extubating = post-extubating, Post-op day 1/2 = post-operative day 1/2

Discussion

In this study, proBNP and troponin-I levels were simultaneously evaluated in vascular surgery patients in the EG who underwent epidural anesthesia to investigate the secondary cardiac effects of epidural anesthesia on the surgical stress response. Current guidelines classify vascular surgery as high cardiac risk and recommend rigorous perioperative and early postoperative surveillance. Reducing the surgical stress response is essential for lowering morbidity and mortality by mitigating adverse effects on the hemodynamic, respiratory, and gastrointestinal systems (1,3).

Pro-B-type natriuretic peptide and troponin-I levels increase during cardiac stress or injury; even slight elevations in troponin have been associated with 30-day mortality (11,12). In vascular patients, elevated preoperative and early postoperative NT-proBNP levels predict MACE (12). This study indicated that the intergroup differences in NT-proBNP and troponin-I levels were not statistically significant; nevertheless, the observed "lesser increase"

in EG should be interpreted not as a conclusive effect but as a trend consistent with the prevailing literature. Consequently, the identification of a "vlesser increase" in the EG should be regarded not as conclusive evidence of an effect but as an observation that suggests trends and generates hypotheses. Data demonstrate that high thoracic epidural anesthesia (TEA) can reduce troponin release through its sympatholytic effect; furthermore, it is associated with attenuated changes in NT-proBNP following cardiac surgery (4-7).

At specific intervals, the CG exhibited significantly larger variations in hemodynamic parameters. Thoracic epidural anesthesia/epidural can improve hemodynamic stability by causing vasodilation and lowering HR and blood pressure through sympathetic blockade (13). This study found that tachycardia and hypertensive episodes were less frequent in the EG. Significantly lower VAS scores on postoperative days one and two in EG indicate effective analgesia, which reduces pain-induced sympathetic activation and cardiac strain. The literature supports the idea that epidural

analgesia may reduce VAS scores and opioid use and facilitate early ambulation, which could benefit cardiac function (14,15).

Possible mechanisms include suppression of the sympathetic stress response, reduced increases in catecholamines and cortisol, control of HR and afterload, decreased myocardial O_2 consumption, and coronary vasodilation. Furthermore, reduced opioid use and early mobilization resulting from effective analgesia have been considered factors that could explain the cardioprotective effects of the epidural approach (9). Recent evidence suggests that the incidence of postoperative myocardial infarction after noncardiac surgery may be reduced with epidural anesthesia, and specific studies have shown reductions in mortality rates (9,16).

When interpreting biomarkers, it is important to remember that troponin levels can increase slightly in low-risk individuals and can peak late. It is also important to remember that pre-analytical factors (such as storage and kit conditions) and false positives can affect the results (7). For NT-proBNP, pre-analytical factors such as age and gender effects and the timing and location of sampling are significant (17). A correlation has been observed between intraoperative fluid volume and lung USG B-lines in cesarean patients; however, BNP may not consistently exhibit a direct correlation with the administered fluid (8). Our study did not reveal a significant difference in NT-proBNP and troponin levels between the two groups; however, an increase in NT-proBNP levels was noted in the CG group in the within-group analysis. This observation should be interpreted in the context of the hypothesis that elevated sevoflurane consumption and greater hemodynamic fluctuations in the CG group may have contributed to increased proBNP levels. Research has also reported postoperative BNP elevation in studies comparing spinal and general anesthesia (18).

Pölzl et al. (19) found that high preoperative NT-proBNP levels were associated with 30-day and 5-year mortality in 6,938 patients undergoing cardiac surgery. A high NT-proBNP level at diagnosis and a preoperative NT-proBNP drop below 3000 ng/L were associated with more favorable perioperative outcomes and shorter lengths of stay in the intensive care unit (19). In our study, we found no significant difference in NT-proBNP levels between the groups. We did not include patients with advanced heart failure, advanced kidney failure, or high-grade cardiac arrhythmias in our research. This could explain the lack of a significant difference in NT-proBNP levels. NT-proBNP levels may demonstrate more pronounced differences in patients with advanced heart failure. In this respect, we believe that our study may provide insights for future research.

Laferrière-Langlois et al. (20) examined 33,089 patients who underwent cardiac surgery with epidural anesthesia between 1966 and 2022. They compared the potential benefits of TEA during cardiac surgery in terms of mortality, atrial fibrillation, and pulmonary complications with the risk of epidural hematoma associated with intraoperative heparinization. Across all published studies, no cases of epidural hematoma were reported. The use of epidural anesthesia should be considered a safe treatment option in cardiac surgery (20).

Publications suggesting that epidural anesthesia reduces the perioperative stress response primarily concern thoracic epidural analgesia and cardiac surgery. From this perspective, it is not surprising that the effect of the lumbar epidural catheter used in our study on perioperative cardiac markers was less clearly demonstrated than that of a thoracic epidural catheter. This issue could be clarified by future studies with larger patient groups.

Pro-B-type natriuretic peptide has been widely recognized as a valuable biomarker for the assessment and prediction of cardiac dysfunction in both elective and emergency surgical populations. Elevated perioperative proBNP levels have been associated with increased cardiovascular morbidity and adverse outcomes. In the present study, we aimed to investigate the relationship between epidural analgesia and perioperative proBNP levels in patients undergoing elective vascular surgery and to evaluate its potential impact on cardiac stress and function.

Study Limitations

This study has several limitations that should be considered when interpreting the findings. First, the sample size was relatively small, which may have made it harder to find significant differences in cardiac biomarkers like NT-proBNP and troponin-I between the study groups. Consequently, the lack of statistically significant differences must be regarded with caution, as the study may lack sufficient power to identify minor biomarker variations. Moreover, only early postoperative biomarker levels were analyzed, and long-term clinical cardiac outcomes were not comprehensively evaluated. Additionally, the study cohort comprised solely patients undergoing significant vascular surgery, potentially constraining the applicability of the results to other surgical groups. Advanced cardiac imaging techniques were not utilized, consequently subtle perioperative cardiac alterations may not have been entirely documented. Subsequent investigations involving larger patient populations, diverse patient demographics, and extended postoperative monitoring durations may yield more thorough understanding of the correlation between epidural anesthesia and perioperative cardiac stress. Another limitation of this study is the considerable

age disparity noted between the study groups. Age is known to affect perioperative cardiac biomarkers like NT-proBNP, so this imbalance may have made it harder to understand biomarker results. Future prospective studies with larger sample sizes and more balanced baseline characteristics, incorporating both biomarker assessments and clinically meaningful cardiovascular outcomes, are required to further clarify the potential cardioprotective effects of epidural anesthesia.

Despite these limitations, the prospective randomized design and the comprehensive assessment of hemodynamic parameters, postoperative pain scores, and sequential biomarker measurements establish a hypothesis-generating framework for elucidating the potential impact of epidural anesthesia on the surgical stress response in patients undergoing significant vascular surgery. These findings should therefore be interpreted as hypothesis-generating and warrant confirmation in larger randomized studies evaluating both biomarkers and clinically relevant cardiovascular outcomes.

Conclusion

This study revealed no significant differences between the groups regarding NT-proBNP and troponin-I levels. Our findings suggest that epidural anesthesia during vascular surgery can attenuate increases in (NT-) proBNP and troponin-I and reduce hemodynamic fluctuations. The epidural approach, when applied to the appropriate patients and under safe conditions, may help attenuate changes in blood flow and reduce pain immediately after surgery. Biomarker findings are speculative owing to study constraints and require validation in larger studies that encompass clinical cardiac outcomes.

Ethics

Ethics Committee Approval: The study was conducted in the Cardiovascular Surgery operating room and was approved by the Istanbul University-Cerrahpasa Faculty of Medicine Ethics Committee (approval no.: 43423, date: 01.12.2011).

Informed Consent: Written informed consent was obtained from the responsible adult for each patient.

Footnotes

Authorship Contributions

Surgical and Medical Practices: M.I.S., Concept: M.I.S., L.Y., H.E., Design: M.I.S., L.Y., H.E., Data Collection or Processing: M.I.S., L.S., Analysis or Interpretation: M.I.S., Literature Search: M.I.S., L.S., Writing: M.I.S., L.S.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The supply of NT-proBNP and troponin I kits was supported by the Scientific Research Projects (BAP) Unit of İstanbul University-Cerrahpaşa Faculty of Medicine. NTproBNP levels were measured using kits from Biomedica (Slovakia), and troponin I levels were measured using kits from Diagnostic Automation Inc.

References

1. Thompson A, Fleischmann KE, SmilowitzNR, et al. AHA/ACC/ACS/ASNC/HRS/SCA/SCCT/SCMR/SVM guideline for perioperative cardiovascular management for noncardiac surgery: a report of the American College of Cardiology/American Heart Association Joint committee on clinical practice guidelines. Circulation. 2024:150:e351-442.

2. Boghean A, Guțu C, Firescu D. Perioperative risk: short review of current approach in non cardiac surgery. J Cardiovasc Dev Dis. 2025;12:24.

3. Halvorsen S, Mehilli J, Cassese S, et al. 2022 ESC Guidelines on cardiovascular assessment and management of patients undergoing non-cardiac surgery. Eur Heart J. 2022;43:3826-924.

4. Jakobsen C-J, Kirkegaard H, Lindskov C, et al. Epidural anaesthesia reduce NT-proBNP after cardiac surgery. Eur J Anaesth. 2002;23:23.

5. Vascular Events In Noncardiac Surgery Patients Cohort Evaluation (VISION) Study Investigators; Devereaux PJ, Chan MT, Alonso-Coello P, et al. Association between postoperative troponin levels and 30-day mortality among patients undergoing noncardiac surgery. JAMA. 2012;307:2295-304.

6. Rodseth RN, Lurati Buse GA, Bolliger D, et al. The predictive ability of pre-operative B-type natriuretic peptide in vascular patients for major adverse cardiac events: an individual patient data meta-analysis. J Am Coll Cardiol. 2011;58:522-9.

7. Loick HM, Schmidt C, Van Aken H, et al. High thoracic epidural anesthesia, but not clonidine, attenuates the perioperative stress response via sympatholysis and reduces the release of troponin T in patients undergoing coronary artery bypass grafting. Anesth Analg. 1999;88:701-9.

8. Vetrugno L, Dogareschi T, Sassanelli R, et al. Thoracic ultrasound evaluation and B-type natriuretic peptide value in elective cesarean section under spinal anesthesia. Ultrasound J. 2020;12:10.

9. Hu Q, Yu X, Zhou T. Epidural analgesia during surgery and its relation to postoperative myocardial infarction: meta-analysis. Wideochir Inne Tech Maloinwazyjne. 2024;19:11-24.

10. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA. 2013;310:2191-4.

11. Sayed Masri SNN, Basri F, Yunus SN, Cheah SK. Cardiac troponin as a prognostic indicator for major adverse cardiac events in non-cardiac surgery: a narrative review. Diagnostics. 2025; 15:1061.

12. Choi JH, Cho DK, Song YB, et al. Preoperative NT-proBNP and CRP predict perioperative major cardiovascular events in non-cardiac surgery. Heart. 2010;96:56-62.

13. Li Y, Dong H, Tan S, Qian Y, Jin W. Effects of thoracic epidural anesthesia/analgesia on the stress response, pain relief, hospital

stay, and treatment costs of patients with esophageal carcinoma undergoing thoracic surgery: a single-center, randomized controlled trial. Medicine (Baltimore). 2019;98:e14362.

14. Hewson DW, Tedore TR, Hardman JG. Impact of spinal or epidural anaesthesia on perioperative outcomes in adult noncardiac surgery: a narrative review of recent evidence. Br J Anaesth. 2024;133:380-99.

15. Macrosson D, Beebeejaun A, Odor PM. A systematic review and meta-analysis of thoracic epidural analgesia versus other analgesic techniques in patients post-oesophagectomy. Perioper Med (Lond). 2024;13:80.

16. Landoni G, Isella F, Greco M, Zangrillo A, Royse CF. Benefits and risks of epidural analgesia in cardiac surgery. Br J Anaesth. 2015;115:25-32.

17. Clerico A, Del Ry S, Maffei S, Prontera C, Emdin M, Giannessi D. The circulating levels of cardiac natriuretic hormones in healthy adults: effects of age and sex. Clin Chem Lab Med. 2002;40:371-7.

18. Kurt N, Kaşıkçı MM, Pişkin Ö, Hancı V, Sakin M. Comparison of brain natriuretic peptide (BNP) levels in patients under general or spinal anesthesia. Haydarpasa Numune Med J. 2019;59:128-35.

19. Pölzl L, Lohmann R, Theurl F, et al. Prognostic implications of preoperative N-Terminal pro-B-type natriuretic peptide dynamics in patients undergoing cardiac surgery. JACC Adv. 2025;4:102096.

20. Laferrière-Langlois P, Jeffries S, Harutyunyan R, Hemmerling TM. Epidural catheterization in cardiac surgery: a systematic review and risk assessment of epidural hematoma. Ann Card Anaesth. 2024;27:111-20.