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RESEARCH ARTICLE

Potential Role of Erector Spinae Plane Block on Neutrophil-Lymphocyte Ratio in Cardiac Surgery Patients

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ABSTRACT

Objectives: In cardiac surgery, a successful erector spinae plane (ESP) block has been demonstrated within the scope of multimodal analgesic approach. This study aimed to comparatively evaluate the effect of ESP block used in cardiac surgery on neutrophil-lymphocyte ratio (NLR).

Methods: Patients who underwent an ESP block and conventional analgesia technique for coronary artery bypass grafting surgery were retrospectively compared. Postoperative pain scores, analgesic consumption, extubation times, and intensive care unit (ICU) and hospital stays were recorded with patient and operative data. As the study's primary outcome, NLR values were calculated from the hemogram as an indicator of inflammation during the preoperative period and 3 days postoperatively.

Results: A total of 97 patients who underwent coronary artery bypass graft surgery with cardiopulmonary bypass were investigated. The highest pain score (p=0.016), total opioid (p=0.008) and acetaminophen (p=0.009) consumption, extubation (p=0.024), and ICU stay (p=0.045) in the first 24 h after extubation were significantly lower in the ESP group. NLR (p=0.019, p=0.046, and p=0.038, respectively) was significantly lower in the ESP group in the first 3 days.

Conclusion: In addition to being associated with less opioid use in the first 24 h in the postoperative pain management of cardiac surgery, ESP block reduces NLR 3 days postoperatively.

Keywords: Cardiac surgery, erector spinae plane block, neutrophil lymphocyte ratio

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Introduction

Perioperative pain management plays a crucial role in the management of patients undergoing cardiac surgery. In cardiac surgery, owing to surgical manipulation such as sternotomy, sternal retraction, internal mammary artery removal, and chest tube placement, pain is described as moderate to severe. Inadequate pain management results in hemodynamic deterioration associated with systemic complications such as atelectasis, pneumonia, and stasis of bronchial secretions (pulmonary); increased oxygen consumption and tachycardia (cardiovascular); muscle weakness (musculoskeletal system); and increased neurohormonal response.[1] Multimodal opioid-sparing pain management plans are strongly recommended by the Society for Advanced Post-Surgical recovery guidelines for perioperative cardiac surgical care (class I recommendation).[2] These include regional analgesia and intravenous (IV) and oral analgesics. Opioids can induce nausea, vomiting, pruritus, and respiratory depression when used only for analgesia.

An acute inflammatory response is also triggered by factors that cause postoperative pain (repeated surgical tissue trauma, bone fracture and dislocation, arterial dissection, tissue retraction, and vein removal). Inflammation and pain are interrelated, as the local release of proinflammatory mediators leads to peripheral sensitization, leading to increased pain. Host immunity and inflammatory states can be evaluated using serum markers such as neutrophils, lymphocytes, and platelets. Serum markers

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such as the neutrophil/lymphocyte ratio (NLR) have become invaluable owing to their noninvasive nature, simplicity, and predictability.[3]

Regional anesthesia techniques not only facilitate patient rehabilitation due to pain palliation but also modulate the inflammatory response as a result of surgical injury with various mechanisms at different levels.[4,5] Erector spinae plane (ESP) block is a myofascial plane block in which a local anesthetic is injected in the plane between the spina muscle or the transverse process.[6] Based on available evidence, in postoperative pain management in cardiac surgery, many studies elucidate that ESP block is associated with improved postoperative analgesia, has less opioid requirement, and affords faster recovery.[7–11] However, no literature exists exploring the effects of ESP block on surgery-induced inflammation. This study aimed to investigate the effects of ESP block employed for postoperative analgesia in cardiac surgery on surgery-induced inflammation using NLR.

Methods

After ethics committee approval (ethical no: E1-22-2982, 19.10.2022), patients who underwent on-pump coronary artery bypass graft (CABG) performed in the cardiovascular operating room between 01.01.2022 and 30.03.2022 were included in the study. Patient records from the hospital archive and hospital information systems were retrospectively searched. Emergency operations; recurrent cardiac surgery; combined cardiac surgery procedures; patients with preoperative requirement for intraaortic balloon pump or high inotropic support, with primary pulmonary hypertension, and with ejection fraction <40%; patients with systemic inflammatory or autoimmune disease, liver disease, malignancy, and chronic kidney disease were excluded from study. All procedures were performed in accordance with the Declaration of Helsinki guidelines.

Retrospectively, intervention and control groups were created based on patients who underwent CABG between the specified dates by the same anesthesia and surgical team. An ultrasound-guided (PHILIPS Affiniti 50 color Doppler ultrasound device, Philips L12-5 50-mm linear array transducer) ESP block (bilateral, 20 mL 0.25% bupivacaine per side) was performed for the intervention group in the prone position prior to anesthesia induction by an experienced anesthesiologist. It was observed that a standard anesthesia technique and postoperative care protocol were applied to both groups, except for the ESP block, and analgesics were administered according to the reported pain score. Pain assessment was conducted using the visual analog scale (VAS, 10 as maximum pain and 0 as no pain) records available on the intensive care unit (ICU) observation sheet.

Demographic data (age, sex, height, and body weight), previous comorbidities, smoking status, and laboratory data including serum creatinine, albumin, estimated glomerular filtration rate, hemoglobin, neutrophil, lymphocyte, platelet, and C-reactive protein (CRP) parameters were recorded. Additionally, cardiopulmonary bypass (CPB), cross-clamp, and total procedure durations were recorded. Postoperative blood counts (hemoglobin, hematocrit, neutrophil, and lymphocyte value), amount of opioid and nonopioid analgesics, extubation time, length of hospital and ICU stay, and the patient's highest pain score reported daily were recorded. Required opioids were converted to oral morphine equivalents (OME) using the National Centers for Drug and Alcohol Research and Centers for Disease Control guidelines.[12,13]

Statistical Analysis

Descriptive statistics were presented as absolute numbers (n) and percentages (%) for categorical variables. Moreover, the median-interquartile range (25^{th}–75^{th} percentiles) was used for non-normally distributed data and the mean standard deviation for normally distributed data. Using the χ 2 test, categorical variables were compared. Continuous variables between with and without ESP block using the Mann–Whitney U test or independent samples t-test were compared, based on the Kolmogorov–Smirnov test for normality. For all analyses, statistical significance was set at $p<0.05$. Literature on the effect of ESP on the inflammatory response was limited. Hence, in this study, power analysis was conducted on 97 patients using the data obtained. NLR (1^{st} measurement with a difference between groups) values were used for power analysis after completion of the study. According to this, power analysis was performed using G* Power 3.1.9.7 statistical package program: n=97 (n1=55, n2=42), $\alpha=0.05$, and effect size (d)=0.76; power=93% was found.

Results

Within the specified 3-month period, it was determined that 118 patients underwent CABG operation. Among them, it was observed that 12 patients underwent off-pump CABG, and nine patients underwent reoperation secondary to postoperative bleeding. Preinduction ESP block (ESP group) was performed in 42 of the remaining 97 patients. The conventional group consisted of 55 patients (group C). Baseline demographic data, American Society of Anesthesiologists score, smoking status, comorbidities, number of bypassed grafts, procedure times, and preoperative laboratory data were similar between groups (Table 1).

The amount of opioids expressed in OME and total acetaminophen within the first 24 h after extubation was

Table 1. Basic demographic data, procedure times, and preoperative laboratory data

	Group C (n=55)		Group ESP (n=42)		p*
	n	%	n	%	
Gender (male)	44	80.0	34	81.0	0.907
Age (years), mean±SD	60.90±7.9		62.35±9.8		0.427
BMI (kg/m^2), mean±SD	28.76±4.2		28.08±4.1		0.432
ASA					
II	17	30.9	20	47.6	0.093
III	38	69.1	22	52.4	
Smoking status					
Never smoker	28	50.9	14	33.3	0.159
Former smoker	2	3.6	4	9.5	
Current smoker	25	45.5	24	57.1	
HT	35	63.6	26	61.9	0.861
DM	27	49.1	15	35.7	0.188
COPD	4	7.3	8	19.0	0.081
Stroke/TIA	3	5.5	3	7.1	0.732
LVEF (%), mean±SD	52.60±8.3		53.07±7.4		0.774
Number of grafts					
CABG×2	10	18.2	11	26.2	0.661
CABG×3	17	30.9	14	33.3	
CABG×4	23	41.8	15	35.7	
CABG×5	5	9.1	2	4.8	
CC time (min), mean±SD	74.65±26.6		69.15±19.9		0.266
CPB time (min), mean±SD	112.66±32.5		101.11±28.9		0.073
Procedure time (min), mean±SD	309.10±60.0		313.37±53.4		0.717
Preoperative laboratory data					
Hemoglobin (g/L), mean±SD	13.78±1.7		13.47±1.2		0.336
Serum creatinine (mg/dL), mean±SD	0.96±0.2		0.90±0.2		0.192
eGFR (ml/ min /1.73m^2), mean±SD	80.83±16.1		83.95±13.9		0.321
HbA1c (%), median (IQR)	6.70 (5.8–7.1)		5.90 (5.6–6.9)		0.052
CRP (mg/L), median (IQR)	2.0 (1.02–4.7)		2.19 (1.0–5.05)		0.686
Serum albumin (g/ dL), median (IQR)	42 (40–45)		42 (42–44)		0.176

*: The independent samples t-test and Mann–Whitney U test were used for continuous variables; the χ^2 was performed for categorical variables (n, %). ESP: Erector spinae plane; SD: Standard deviation; BMI: Body mass index; ASA: American Society of Anesthesiologists; HT: Hypertension; DM: Diabetes mellitus; COPD: Chronic pulmonary disease; TIA: Transient ischemic attack; LVEF: Left ventricular ejection fraction; CABG: Coronary artery bypass graft; CC: Cross-clamp; CPB: Cardiopulmonary bypass; eGFR: Estimated glomerular filtration rate; IQR: Interquartile range; CRP: C-reactive protein.

found to be significantly lower in the ESP group (p=0.008 and p=0.009, respectively). Likewise, the highest pain score reported in the same period was found to be significantly lower in the ESP group (p=0.016). In the ongoing days (24–48 h and 48–72 h), no difference was found for the highest pain score, opioid, and acetaminophen requirement in the groups (Table 2). While extubation time (median 420.0 versus 469.8 min, p=0.024) and ICU stay (median 20.5 versus 25 h, p=0.045) were shorter in the ESP group, hospital stay duration was similar (Fig. 1).

In the preoperative period, the NLR values were not different between the groups (p>0.05). These values peaked on the first day in the postoperative period and decreased in the next 2 days. The NLR values were found to be higher in all three measurement periods compared to the preoperative period, and these values were found to be significantly higher in the conventional group (p=0.019, p=0.046, and p=0.038, for NLR respectively, Table 2).

Discussion

In our study, the effects of USG-guided bilateral ESP block on surgery-induced inflammation were examined using NLR. It was found that NLR was significantly lower in the ESP group for three postoperative days. Also, the fact that the

Table 2. Analgesic consumption, pain scores, and neutrophil-lymphocyte ratio values

	Group C (n=55)	Group ESP (n=42)	p*
24 hours after extubation			
OME (mg), mean±SD	40.90±15.7	31.66±17.6	**0.008**
Acetaminophen (mg), mean±SD	1909.09±1058.8	1428.57±547.4	**0.009**
Highest reported pain score (VAS), median (IQR)	6 (5–7)	5 (4–7)	**0.016**
24-48th post extubation hours			
OME (mg), mean±SD	16.18±8.8	16.60±11.5	0.837
Acetaminophen (mg), mean±SD	689.09±558.16	685.71±572.0	0.977
Highest reported pain score (VAS), median (IQR)	3 (2–4)	2 (2–3)	0.674
Post extubation 48-72th hours			
OME (mg), mean±SD	11.45±8.1	9.04±6.7	0.124
Acetaminophen (mg), mean±SD	418.18±315.6	464.28±256.4	0.442
Highest reported pain score (VAS), median (IQR)	2 (1–3)	2 (1–2)	0.206
Preoperative NLR, mean±SD	2.72±1.0	2.96±1.1	0.465
PO 0th day NLR, mean±SD	21.54±10.7	17.22±7.3	**0.019**
PO 1st day NLR, mean±SD	10.98±6.8	8.92±3.0	**0.046**
PO 2nd day NLR, mean±SD	8.06±4.4	6.48±3.01	**0.038**

*: The independent samples t-test and Mann–Whitney U test were used for continuous variables. ESP: Erector spinae plane; OME: Oral morphine equivalent; SD: Standard deviation; VAS: Visual analog scale; IQR: Interquartile range; NLR: Neutrophil-lymphocyte ratio; PO: Postoperative.

ESP block reduced the postoperative opioid and acetaminophen consumption and significantly lowered pain scores in the first postoperative day after extubation was confirmed in our study. Additionally, our findings also revealed that the mechanical ventilation and ICU stay duration were significantly shorter in the ESP group. Complications such as infection, local anesthetic toxicity, pneumothorax, or hematoma that may be observed secondary to ESP block application were not noted in all patients. The results found in such a critical group of patients corroborated with previous studies showing that ESP block is a safe and effective technique for postoperative analgesia.[8,11,14]

Information regarding host immunity and inflammatory status can be obtained through the evaluation of neutrophil and lymphocyte counts and their ratios such as NLR obtained from the complete blood count. In cardiac surgery, neutrophilia and relative lymphopenia are used as prognostic markers for mortality.[15] A strong and statistically significant association between the first postoperative NLR value and 1-year mortality has been reported.[16] In parallel, patients with a 30-day mortality had a higher median NLR on the second postoperative day compared to patients without mortality.[17] Moreover, an increased NLR has been associated with the development of postoperative atrial fibrillation (AF) and acute kidney injury (AKI) after cardiac surgery.[16,18,19] The primary mechanism responsible for neutrophils is that stem cells increase neutrophil formation under the influence of growth factors.[20] Conversely, lymphocytopenia results from lymphocyte redistribution into the lymphatic organs due to the increase in catecholamine and cortisol levels and apoptosis.[21] Lymphocytes are mainly involved in specific immunity, and a decreased lymphocyte count is a feature of decreased immunity and is inversely proportional to inflammation. The combination of neutrophilia and lymphocytopenia in NLR increases the prognostic value compared to their individual effects, considering the complex nonlinear relationships between neutrophil and lymphocyte counts. These parameters obtained from routine blood tests have advantages in terms of cost-efficiency and time. When we examined the effect of ESP block and pain palliation on NLR in our study, we observed that the NLR values attained the highest levels in both groups in the first postoperative day and gradually decreased in the following periods. In all three measurement times, the NLR parameters were found to be significantly lower in the ESP group.

Surgical incision, dissection, nerve cut, stretching, or compression leads to perioperative pain. Some studies have revealed that acute postoperative pain can exacerbate this systemic inflammatory response and showed a positive correlation.[22,23] With peripheral inflammation induced by surgical trauma, some mediators, particularly interleukin-6 (IL-6), are released into the circulation and act on distant organs to stimulate the acute-phase response. This response induces acute-phase protein synthesis in the liver, neutrophil mobilization from the bone marrow,

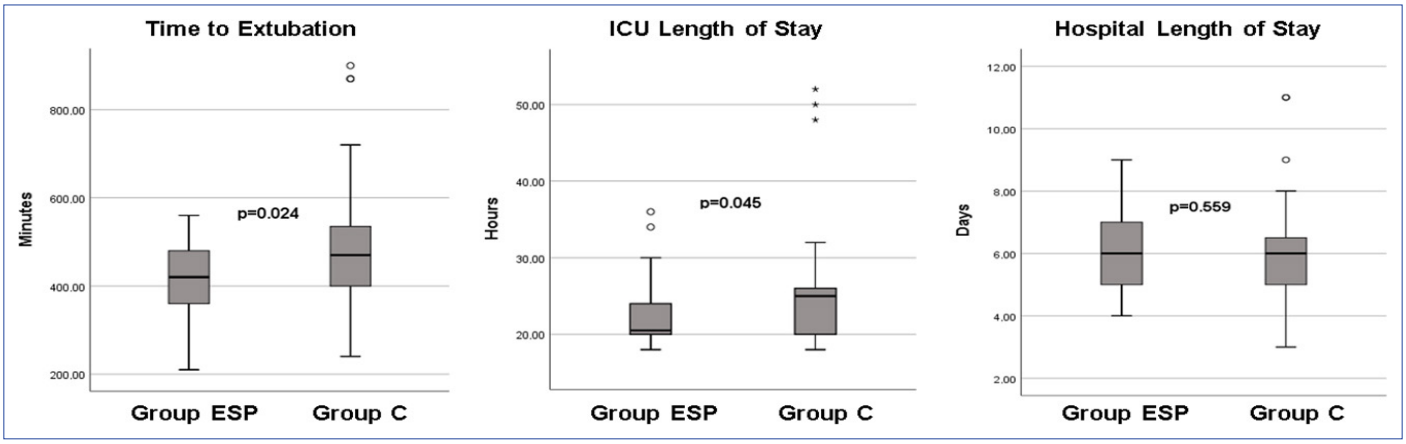

Figure 1. Extubation time and length of intensive care unit and hospital stay of the groups. The Mann–Whitney U test was used for the continuous variables (median, interquartile range [IQR]); the box plot represents data as median values (bold horizontal line) and IQR (box).
ICU: Intensive care unit; ESP: Erector spinae plane.

and altered T-lymphocyte differentiation.[4] Regional analgesia techniques block the transmission of nociceptive and inflammatory signals from the peripheral to the central nervous system and can prevent both peripheral and central pain sensitization, thus reducing postoperative pain sensation and inflammatory response following tissue injury.[5,24] In orthopedic surgeries, epidural block has been demonstrated to significantly reduce inflammatory mediators (IL-6 and CRP) and postoperative pain compared to patients treated with IV morphine.[22,25] Similarly, in cardiac surgery, ESP block employed as part of the ERAS program has been associated with lower postoperative CRP levels.[26] Our study contributes to the data supporting the use of ESP blocks in cardiac surgery patients, as it exhibited that ESP block is associated with lower inflammatory parameters and analgesic efficacy.

In addition to known surgical stress, CPB triggers the release of potent inflammatory mediators that elicit a major postoperative stress response that leads to a systemic inflammatory response-like syndrome.[27,28] Studies have revealed the relationship between inflammatory status, which is evaluated using NLR, and postoperative negative outcomes such as AF, delirium, and AKI in patients undergoing cardiac surgery.[16,29,30] Thus, the development of strategies to control the inflammatory response following cardiac surgery is currently the highlight of significant research efforts. Several techniques have been studied in clinical trials, including maintenance of hemodynamic stability, reducing CPB circuit exposure, and pharmacological and immunomodulatory agents. Others include minimized extracorporeal circulation system, off-pump coronary artery bypass surgery method, minimally invasive surgical technique, hemofiltration and leukocyte filter use during CPB, and some medical treatments.[31] However, while minimal extracorporeal circuits and leukocyte filter avoid most of the detrimental effects of standard CPB methods, these techniques warrant additional costs. Although ultrafiltration to remove liquid and low-molecular-weight substances from plasma has beneficial anti-inflammatory effects, especially in pediatric patients, hemofiltration seems to be less efficacious in adults.[31] Furthermore, not every patient is suitable for the off-pump or minimally invasive surgical technique. Corticosteroid use has not yet been fully elucidated because of its possible side effects and its net benefit has not yet been shown. Suggested medical treatments for anti-inflammation such as aprotinin, vitamins C and E, N-acetylcysteine, and mannitol do not have clear established effects. ESP block, aside from alleviating postoperative pain, can prevent inflammatory response induced by surgical stress. In our study, inflammatory parameters were lower in the ESP group and this decrease persisted for 3 days. This indicates that although the effect of local anesthetic administered with the ESP block has already expired, the initial anti-inflammatory effects of the block still continue. ESP block provides the clinical benefit of hitting two birds with one stone in cardiac surgery. In the postoperative period, two highly desirable conditions include quality analgesia and alleviation of the expected stress response. Admittedly, more studies are warranted to examine the effects on clinical outcomes.

One of the limitations of this study include the single-center, retrospective design. Another limitation is the lacking sensory test data determining the dermatomal distribution after the block. We deem that prospective studies with larger sample sizes are required to quantify inflammatory cytokines.

In conclusion, we believe that adding a preoperative ESP block to the strategies to alleviate the systemic inflammatory response after cardiac surgery will provide remarkable benefits. The fact that ESP block has exhibited inflammatory response reduction in addition to postoperative pain control may expand the indications for the block.

Disclosures

Ethics Committee Approval: The study was approved by The Ankara City Hospital No. 1 Clinical Research Ethics Committee (Date: 19/10/2022, No: E1-22-2982).

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

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

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