

The effect of pectointercostal fascial block on stress response in open heart surgery

ABSTRACT

Background: Activation of the hypothalamus–pituitary–adrenal (HPA) axis and inflammatory processes are common forms of stress response. The increased stress response is associated with a higher chance of complications. Open hearth surgery is one of the procedures with a high-stress response. Pectointercostal fascial block (PIFB), as a new pain management option in sternotomy, has the potential to modulate the stress response.

Objective: To determine the effect of PIFB on stress response in open heart surgery.

Methods: This study was a Randomized Controlled Trial on 40 open heart surgery. Patients were divided into two groups, control (20 patients) and PIFB (20 patients). Primary parameters included basal and postoperative TNF- α , basal and post sternotomy ACTH, and basal, 0, and 24 hours postoperative NLR. Secondary parameters include the amount of opioid use, length of the post-operative ventilator, length of ICU stay, and Numeric Rating Scale (NRS) 6, 12, 24, and 48 hours postoperative.

Results: The PIFB group had a decrease in ACTH levels with an average change that was not significantly different from the control group (-57.71 ± 68.03 vs. -129.78 ± 140.98). The PIFB group had an average change in TNF α levels and an average increase in NLR 0 hours postoperative that was not significantly lower than the control group (TNF α : -0.52 ± 1.31 vs. 0.54 ± 1.76 ; NLR: 12.80 ± 3.51 vs. 14.82 ± 4.23). PIFB significantly reduced the amount of opioid use during surgery, NRS at 6, 12, and 24 hours, and the length of post-operative ventilator use ($P < 0.05$, CI: 95%).

Conclusion: PIFB has a good role in reducing the stress response of open heart surgery and producing good clinical outcomes.

Key words: Open hearth surgery, pectointercostal fascial block, stress response

Background

Open hearth surgery is a highly stressful procedure. The

stress response is a defense mechanism of the body to create homeostasis condition. The stress response due to

Access this article online	
Website: https://journals.lww.com/sjan	Quick Response Code 
DOI: 10.4103/sja.sja_349_23	

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

How to cite this article: Fadhlurrahman AF, Setiawan P, Sumartono C, Perdhana F, Husain TA. The effect of pectointercostal fascial block on stress response in open heart surgery. Saudi J Anaesth 2024;18:70-6.

AHMAD FEZA FADHLURRAHMAN^{1,2}, PHILIA SETIAWAN³, CHRISTIJOGO SUMARTONO⁴, FAJAR PERDHANA³, TEUKU ASWIN HUSAIN³

¹Department of Anesthesiology and Intensive Therapy, Medical Faculty of Airlangga University, Surabaya, ²Department of Anesthesiology and Intensive Therapy, Faculty of Medicine, Brawijaya University, Dr. Saiful Anwar General Hospital, Malang,

³Division of Cardiovascular and Thoracic Anesthesia, Department of Anesthesiology and Intensive Therapy, Faculty of Medicine, Airlangga University, Dr. Soetomo General Hospital, ⁴Division of Regional Anesthesia, Department of Anesthesiology and Intensive Therapy, Faculty of Medicine, Airlangga University, Dr. Soetomo General Hospital, Surabaya, Indonesia

Address for correspondence: Dr. Ahmad Feza Fadhlurrahman, Department of Anesthesiology and Intensive Therapy, Faculty of Medicine, Brawijaya University, Dr. Saiful Anwar General Hospital, Malang, Indonesia.
 Bunga Camalia Street No.11 Malang, East Java, Indonesia.
 E-mail: fezafadhlurrahman@ub.ac.id

Submitted: 27-Apr-2023, **Revised:** 19-May-2023, **Accepted:** 04-Jun-2023, **Published:** 02-Jan-2024

surgery can be found as a metabolic response by activation of neuroendocrine and immune response (inflammation). The duration and area of surgery (more invasive surgery) will increase the stress response. Sufficient treatment is required to avoid excessive stress responses that result in hemodynamic instability, increased myocardial oxygen demand, Systemic Inflammatory Response Syndrome (SIRS), hypercatabolism, and organ dysfunction.^[1-3]

Several approaches can modulate the stress response during surgery, including the selection of surgical techniques, pharmacological approaches through intravenous and inhalation, and adequate pain management.^[1] Pain can produce a significant stress response and affect the patient's recovery process. Systemic opioids are still the most common pain management in open heart surgery patients. A high-dose opioid is considered effective in reducing pain levels and stress responses in open heart surgery. However, several adverse effects may arise.^[4,5]

Pectoral-intercostal fascial block (PIFB), a relatively new modality in open heart surgery, is promising for creating optimal analgesia in open heart surgery. PIFB is one of the peripheral nerve block techniques and provides analgesia in the anteromedial region of the chest wall.^[6] Previous studies have shown the effectiveness of PIFB in creating optimal analgesia and accelerating postoperative patient recovery.^[6-8] This study aims to evaluate the effect of PIFB on the stress response that occurs in open heart surgery patients and its implications for postoperative clinical conditions.

Methods

This study was approved by the ethics committee of Dr. Soetomo Hospital Surabaya with number 0413/KEPK/IV/2022. All subjects were well informed and signed a form of consent to participate in the study.

This study is a prospective experimental randomized controlled trial (RCT). Patients were divided into two groups: the control group (using opioid-based analgesia/ $n = 20$) and the treatment group (using preemptive PIFB and continuous opioids/ $n = 20$). The inclusion criteria include all open heart surgery patients with a sternotomy approach, aged 18–70 years, and using a CPB machine. Exclusion criteria included refusal from patients and families, allergy to local anesthetics, patients with urgent or emergency procedures, patients with preoperative inotropic or vasoactive drug support, patients with a diagnosis of sepsis or in immunosuppressed conditions, patients with CPB time more than 180 minutes and or aortic cross-clamp time more than 120 minutes.

Randomization and blinding

Sample allocation using simple randomization using an enveloped lottery containing the initial paper. Patients who receive K letter will be treated as a control group and P will be treated as a treatment group. At the time of the study, subjects and observers did not know about the status of the intervention. Observations were made by observers who did not know whether the patient belonged to the control or treatment groups.

Anesthesia and surgery

Before induction, all routine monitors such as pulse oximetry, noninvasive blood pressure, electrocardiography, and BIS (bispectral index) were installed. Small doses of sedative and analgesic agents were administered during the installation of a large bore infusion line and invasive arterial blood pressure. Anesthesia induction was performed using 0.05 mg/kg of midazolam, fentanyl 2–3 mcg/kg, propofol 1–2 mg/kg, and rocuronium 0.8 mg/kg. After intubation, CVC, core temperature, and end-tidal carbon dioxide were installed. Maintenance of anesthesia was performed with O₂ and 1 MAC of sevoflurane, continuous fentanyl 0.5 mcg/kg/hr, and rocuronium 0.4 mg/kg/hr. BIS values were maintained between 45–60 in all patients. After surgery, patients were admitted to the ICU.

PIFB

After induction, PIFB was performed using linear probe-ultrasound guide [Figure 1]. 10 mL of 0.375% Ropivacaine (dilute with normal saline) was administered through 25 G spinal needle on the fascial plane between the musculus pectoralis major and musculus intercostalis in the parasternal region (1–2 cm lateral parallel from the edge of the sternum) at four points, as high as ICS 2 right and left and ICS 5 right and left with total volume 40 mL and maximal dose 3 mg/kg bw.

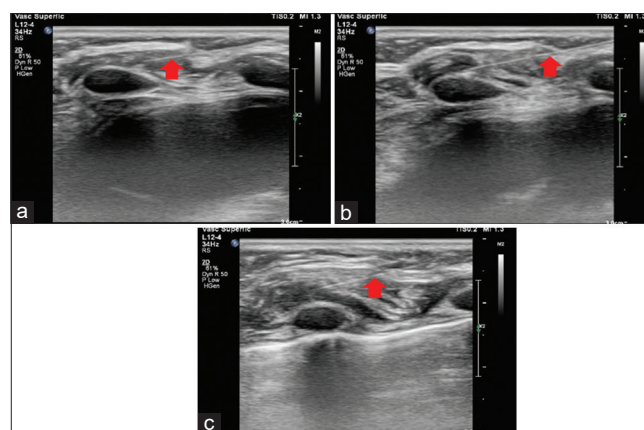


Figure 1: PIFB with ultrasound guidance. (a) the needle points to the target block (b) injection of local anesthetic at the target block, (c) spread of local anesthetic in the fascia plane between m. pectoralis major and m. external intercostalis. Red arrow: needle

Clinical and biochemical parameters

The primary outcomes in this study are ACTH levels (basal pre-incision and 10 minutes post-incision), TNF- α (basal pre-incision and post-surgery), and NLR (basal pre-incision, 0 hours post-surgery and 24 hours post-surgery). Blood samples will be centrifuged at 3000 rpm for 15 minutes and stored in a -80°C freezer. TNF- α examination was performed using the ELISA method with the Human TNF- α ELISA Kit Elabscience reagent. ACTH examination was performed using the ELISA method with the Human ACTH Kit Elabscience reagent. The NLR examination was conducted at the Central Laboratory of Soetomo Hospital Surabaya.

Secondary outcomes include the amount of opioid use (operating room and 24 hours in ICU), the length of post-operative ventilator use, and the degree of postoperative pain at hours 6, 12, 24, and 48 using a numeric rating scale (NRS) 1–10.

Statistical analysis

Statistical analysis was performed using descriptive and inferential statistical analysis. Descriptive analysis was used to describe the research data. Continuous data were displayed as mean and standard deviation (SD), while qualitative data were displayed as frequency and percentage. Inferential statistical analysis was used to compare means between groups.

The normality test of continuous data was conducted using the Shapiro-Wilk test. The differences between groups were assessed using a paired two-sample *t*-test on data with normal distribution or the Wilcoxon–Mann–Whitney test on data with non-normal distribution. Type I error (α) was 0.05 with a 95% confidence interval, and type II error (β) was 0.2 with 80% power. A probability value of less than 5% was considered insignificant.

Results

This study was performed on 40 study samples (20 control groups and 20 PIFB groups). Demographic characteristics data between the two groups showed no significant difference [Table 1].

There was no significant difference in the average changes in TNF α , ACTH, or NLR levels ($P > 0.05$) between the two groups [Figure 2]. The PIFB group had lower average changes in TNF α levels than the control group (-0.52 ± 1.31 ($-1.83 - 0.79$) vs. 0.54 ± 1.76 ($-1.22 - 2.30$)). The average change in postoperative NLR of the treatment group was lower than the control (12.80 ± 3.51 ($9.29 - 16.31$) vs. 14.82 ± 4.23 ($10.59 - 19.05$)). In comparison, the average change in ACTH of the control group decreased more than

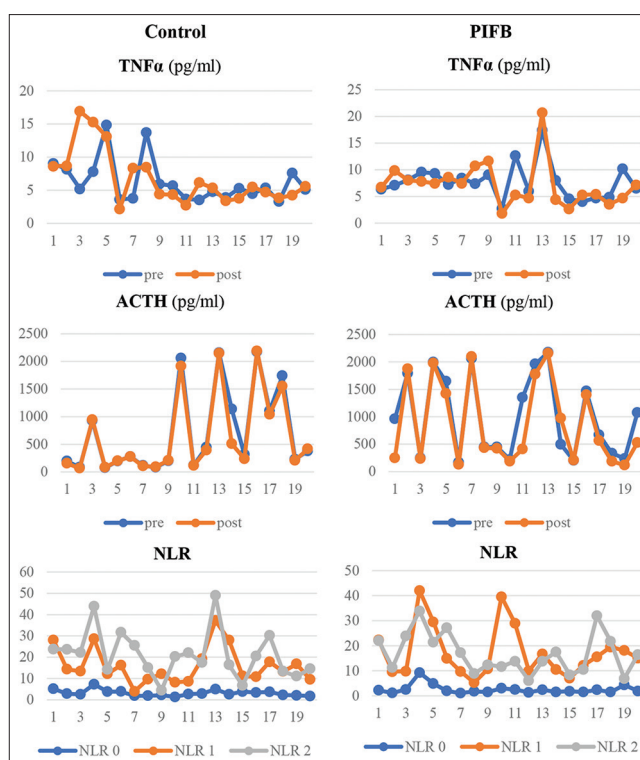


Figure 2: Primary parameters between groups

control group (-129.78 ± 140.98 ($-270.76 - 11.20$) vs. -57.71 ± 68.03 ($-125.74 - 10.32$)) [Figure 3 and Table 2].

The PIFB group had significantly lower opioid use during surgery (5.12 ± 0.27 ($4.86 - 5.39$) vs. 7.32 ± 0.59 ($6.73 - 7.91$)) and significantly shorter ventilator usage postoperative duration (3.90 ± 1.44 ($2.46 - 5.34$) vs. 7.65 ± 1.71 ($5.94 - 9.36$)) than the control group. The NRS of the PIFB group was significantly lower than that of the control group at 6, 12, and 24 hours postoperatively ($P < 0.05$) [Figure 4 and Table 2].

Discussion

A stress response is one of the body defense mechanisms as a protective mechanism against homeostasis disruption. Adequate stress response management will affect the outcome of the surgery. An optimum pain management is one of the modalities to control the stress response in open heart surgery.^[1,2] Since being introduced by de la Torre in 2014 as a regional anesthetic for breast analgesia, PIFB has developed into a new analgesia alternative of sternotomy pain. Analgesic effects of PIFB are achieved by targeting the anterior branches of the intercostal nerves II–VI which innervate the sensory areas of the anteromedial chest wall. The local anesthetic, ropivacaine or bupivacaine, is placed in the fascial plane between the pectoralis major and externus intercostal muscles with ultrasound guidance.^[7,8] This

Table 1: Demographic characteristics data

Variable	Mean \pm t _{w/2} SE/Frequency (%)		Methods of Analysis	P
	Control (n=20)	PIFB (n=40)		
Age	54,6 \pm 4,7 yr	52,5 \pm 4,6 yr	Mann-Whitney Test	0,350
BMI	24,5 (23,2 – 25,9)	26,0 (24,2 – 27,8)	Mann-Whitney Test	0,218
EF	53,7 \pm 5,5 (48,2 – 59,2)	57,2 \pm 4,0 (53,2 – 61,2)	Mann-Whitney Test	0,255
Gender	M=14 (70%) F=6 (30%)	M=18 (90%) F=2 (10%)	Chi-Square Test	0,114
DM	Yes=5 (25%) No=15 (75%)	Yes=8 No=12	Chi-Square Test	0,500
HT	Yes=12 (60%) No=8 (40%)	Yes=8 (40%) No=12 (60%)	Chi-Square Test	0,206
CVA	Yes=3 (15%) No=17 (85%)	Yes=0 (0%) No=20 (100%)	Exact-Fisher Test	0,231
CPB Time	127,20 \pm 17,93	116,20 \pm 12,90	Two independent samples t-test	0,304
Xclamp Time	81,85 \pm 13,62	77,35 \pm 11,01	Two independent samples t-test	0,594
Surgery Time	363,45 \pm 26,98	357,25 \pm 19,88	Mann-Whitney Test	0,583
Lactate Change	1.6225 \pm 0,6039	1.4980 \pm 0,3764	Mann-Whitney Test	0,904

Significant if P<0.05

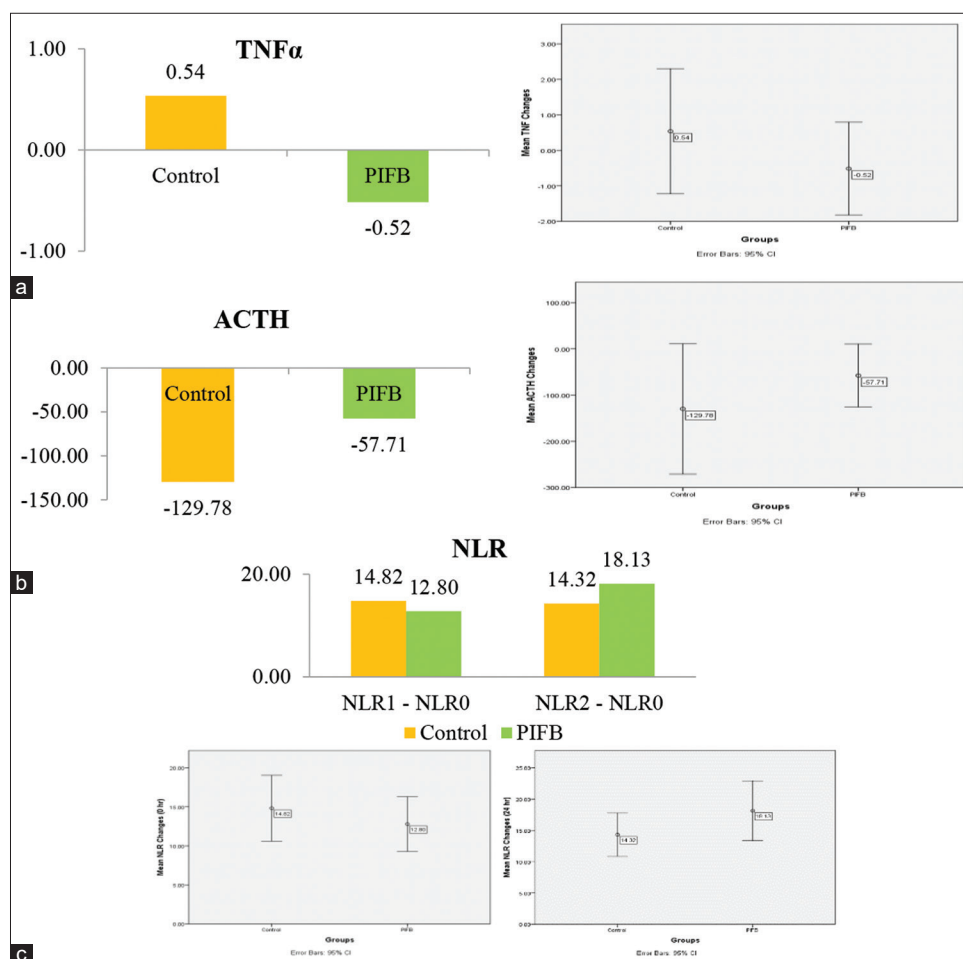


Figure 3: Comparison graph of the average changes in primary parameters between groups. (a) Graph and bar plot (95% CI) average changes in TNF α between groups; (b) Graph and bar plot (95% CI) average changes in ACTH between groups; (c) Graph and Bar Plot (95% CI) average changes in NLR between groups (NLR0:basal; NLR1: 0 hour postoperative; NLR2: 24 hour postoperative)

location is relatively safer from the possibility of vascular and pleural injuries during the procedure. A study from

Zhang *et al.*,^[9] on 108 open heart surgery patients with PIFB showed no complications associated with the PIFB

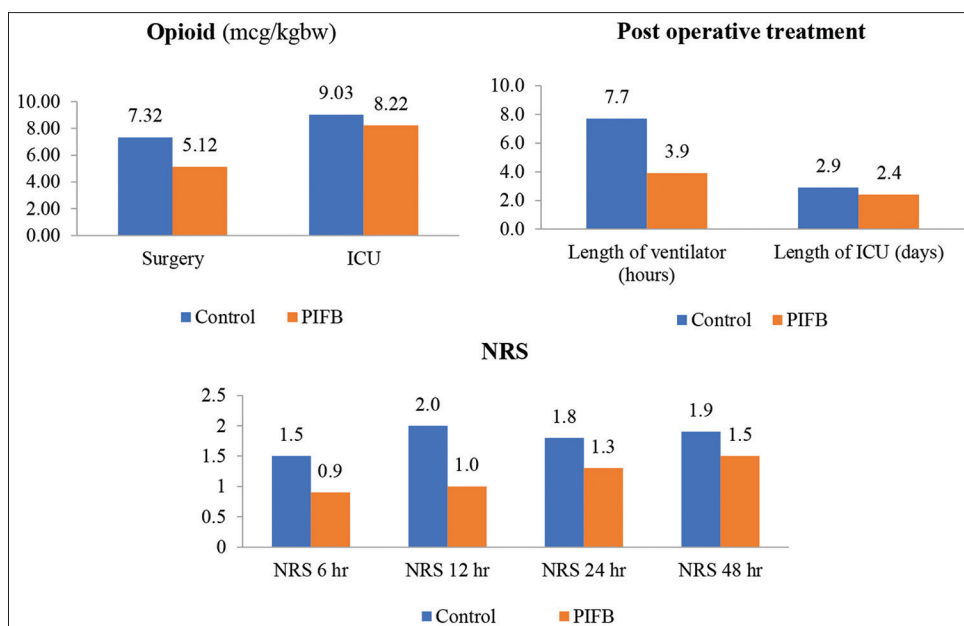


Figure 4: Comparison graph of the mean of secondary parameters between groups

Table 2: Recapitulation of the primary and secondary parameters comparison between two groups

Variable	Mean \pm t _{a/2} SE		P
	Control (n=20)	Treatment (n=20)	
Changes in TNF α	0.54 \pm 1.76	-0.52 \pm 1.31	0.715 ^b
Changes in ACTH	-129.78 \pm 140.98	-57.71 \pm 68.03	0.140 ^b
Changes in NLR (0 hours postoperative)	14.82 \pm 4.23	12.80 \pm 3.51	0.445 ^b
Changes in NLR (24 hours postoperative)	14.32 \pm 3.46	18.13 \pm 4.77	0.184 ^a
Opioids During Surgery	7.32 \pm 0.59	5.12 \pm 0.27	0.000 ^b
Opioids ICU	9.03 \pm 0.86	8.22 \pm 0.86	0.168 ^a
NRS 6 hours	1.50 \pm 0.28	0.90 \pm 0.43	0.018 ^b
NRS 12 hours	1.95 \pm 0.56	1.00 \pm 0.37	0.004 ^b
NRS 24 hours	1.80 \pm 0.42	1.30 \pm 0.27	0.022 ^b
NRS 48 hours	1.85 \pm 0.44	1.45 \pm 0.24	0.120 ^b
Duration Postoperative Ventilator usage	7.65 \pm 1.71	3.90 \pm 1.44	0.001 ^b
Duration ICU	2.90 \pm 0.52	2.40 \pm 0.28	0.183 ^b

^aTwo independent samples t-test. ^bMann-Whitney test. Significant if $P < 0.05$

procedure performed. PIFB is a relatively simple, safe, and effective block.^[7]

In general, the stress response can be found as a metabolic response through neuroendocrine activation (HPA axis) and an immune response (an inflammatory process).^[11,2] This study uses the ACTH levels to analyze neuroendocrine activation. TNF- α and NLR levels as a parameter of activation of the inflammatory process and its correlation with postoperative clinical conditions. Neuroendocrine activation involves the action of the HPA, where ACTH is one of the “main links” of the pathway.^[10] The amount of ACTH hormone in plasma is regulated in the HPA axis through a feedforward-feedback relationship between the pituitary and adrenal.^[11] Circulating half-life time of ACTH lasts about 7-12 minutes. In studies of healthy subjects, the onset of fast feedback of cortisol to ACTH

occurs at an average of 4 min after cortisol secretion (range 0–9 min) and an average of 11.5 minutes after Corticotrophin Releasing Hormone (CRH) secretion (range 9–15 min). This study used 10 min to evaluate the ACTH response to the sternotomy as a stressor.^[11,12]

The absence of an increase in ACTH level post-sternotomy in both groups indicates the effectiveness of the analgesic regimen in blocking the pain pathway. Opioids work predominantly at the modulatory and perceptual levels, while PIFB as a peripheral nerve block works predominantly at the transmission level.^[13] The comparison between the two groups found no significant difference ($P > 0.05$), indicating that analgesia management with PIFB has no significant difference from opioid-based analgesia management. PIFB can provide optimal analgesia against the stressor of sternotomy.

The inflammatory response in open heart surgery might be caused by surgical trauma, transfusion of blood products, hypothermia management, or CPB.^[14,15] Inflammatory responses can be indicated by the production of proinflammatory cytokines. This study used TNF- α and NLR levels to evaluate the inflammatory response.

Increased TNF- α levels in the postoperative period strongly correlate with increased complications. However, from several previous studies, there is a dynamic change in TNF- α levels during open heart surgery especially those performed with CPB. Sethi *et al.*'s study involving 167 congenital heart disease patients with pediatric and adult age ranges showed a significant increase in TNF- α levels after open heart surgery using CPB machines. Relatively different results were shown in Brancaccio *et al.*'s study of 20 open-heart surgery patients in the pediatric population. Postoperative TNF- α levels were significantly lower than pre-CPB levels. A hemofilter is thought to be one of the causes of the decrease in TNF- α levels during running CPB.^[16-18] Although no statistically significant differences were found between groups, the lower value of changes in TNF- α in the treatment group indicates one role of PIFB in modulating the inflammatory response.

On the other hand, the NLR level indicates the relationship between innate and adaptive immune responses and is a suitable parameter for inflammatory conditions. NLR is a visible parameter to assess because it is obtained from routine examinations. Silberman *et al.*'s retrospective study of 3,027 open-heart surgery patients showed that an increase in NLR values would be accompanied by an increase in the likelihood of complications, even mortality, regardless of the essential characteristics of the patient.^[19,20] In this study, the average change in NLR level postoperatively (0 hours postoperatively) in the treatment group was lower than in the control group, although there was no significant difference ($P > 0.05$).

The role of local anesthesia in trauma is through the blockade of nociceptive input to the inflammatory surge that occurs. Local anesthesia blocks the pain transmission pathway through type C and A delta nerve fibers and also inhibits substance P activity due to bradykinin stimulation which can produce neuroinflammatory conditions. Local anesthesia also plays a role in reducing the overall systemic inflammation level.^[21,22] In addition, systemic absorption of local anesthetic can also be one of the anti-inflammatory mechanisms of peripheral nerve block. The anti-inflammatory properties of local anesthetics come from the ability to modulate the inflammatory cascade that occurs, especially its role in the immune system.^[21]

Besides its role in the biochemical parameters of the stress response, PIFB is also expected to directly impact patients' postoperative recovery conditions. Several previous studies have shown positive results. An RCT study by Zhang *et al.*^[9] on 108 open-heart surgery, patients showed an excellent role of PIFB in the recovery process. Optimal pain management and low rates of postoperative complications could reduce the length of ICU and hospital stay in the group of patients with PIFB compared to controls.^[23] The same thing was also obtained in this study. The clinical parameters of the treatment group, including postoperative pain level and duration of ventilator use, had significantly lower values than the control group ($P < 0.05$).

The differences between clinical and biochemical parameters of the stress response cannot be fully explained. This condition was also found in previous studies. Its role influences the good outcomes of clinical parameters of PIFB in modulating neurogenic inflammation, and the condition does not have a strong correlation with the biochemical parameters of the stress response.^[21] PIFB also modulates the inflammatory responses in open heart surgery.

Limitations in this study included the study personnel allocation. PIFB is performed by different anesthesiologists. To minimize bias between operators, the standard was carried out through ultrasound parameters. The operator performing the block must be able to see that the needle tip is in the correct position and evaluate the spread of the local anesthetic. In addition, the basal condition of preoperative patients associated with inflammatory conditions and hormonal disturbances needs to be further evaluated.

Conclusion

Preemptive PIFB produces stress response modulation as good as opioid-based but with better clinical outcomes, including opioid use, postoperative pain level, and ventilator duration. PIFB can be considered in multimodal analgesia management in open heart surgery to provide fast-track or early recovery after open heart surgery programs.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Cusack B, Buggy DJ. Anaesthesia, analgesia, and the surgical stress response. *BJA Educ* 2020;20:321–8.

2. Iwasaki M, Edmondson M, Sakamoto A, Ma D. Anesthesia, surgical stress, and “long-term” outcomes. *Acta Anaesthesiol Taiwan* 2015;53:99–104.
3. Mauricio Del Rio J, Nicoara A, Swaminathan M. Neuroendocrine stress response: Implications for cardiac surgery-associated acute kidney injury. *Rom J Anaesth Intensive Care* 2017;24:57–63.
4. Gravlee GP, Shaw AD, Bartels K. Hensley’s practical approach to cardiothoracic anesthesia. 6th ed. Wolters Kluwer; 2019.
5. Kwanten LE, O’Brien B, Anwar S. Opioid-based anesthesia and analgesia for adult cardiac surgery: History and narrative review of the literature. *J Cardiothorac Vasc Anesth* 2017;33:808–16.
6. Chin KJ, Versyck B, Pawa A. Ultrasound-guided fascial plane blocks of the chest wall: A state-of-the-art review *Anaesthesia* 2021;76:110–26.
7. Liu V, Mariano ER, Prabhakar C. Pecto-intercostal fascial block for acute poststernotomy pain: A case report. *A A Pract* 2018;10:319–22.
8. Devarajan J, Balasubramanian S, Shariat AN, Bhatt HV. Regional analgesia for cardiac surgery. Part 2: Peripheral regional analgesia for cardiac surgery. *Semin Cardiothorac Vasc Anesth* 2021;25:265–79.
9. Zhang Y, Gong H, Zhan B. Effects of bilateral pecto-intercostal fascial block for perioperative pain management in patients undergoing open cardiac surgery: A prospective randomized study. *BMC Anesthesiol* 2021;21:175.
10. Rhodes ME. Stress: Neuroendocrinology and neurobiology. *Handbook of Stress*. 2nd ed. Elsevier; 2017.
11. Gibbison B, Spiga F, Walker JJ, Russell GM, Stevenson K, Kershaw Y, *et al.* Dynamic pituitary-adrenal interactions in response to cardiac surgery. *Crit Care Med* 2015;43:791-800.
12. Carroll BJ, Ritchie JC, Rogers H, Kim DK. Fast feedback inhibition of adrenocorticotropic hormone secretion by endogenous cortisol in humans. *Neuroendocrinology* 2019;109:299-309.
13. Zubrzycki M, Liebold A, Skrabal C, Reinelt H, Ziegler M, Perdas E, *et al.* Assessment and pathophysiology of pain in cardiac surgery. *J Pain Res* 2018;11:1599–611.
14. Corral-Velez V, Lopez-Delgado J, Betancur-Zambrano N, Lopez-Sune N, Rojas-Lora M, Torrado H, *et al.* The inflammatory response in cardiac surgery: An overview of the pathophysiology and clinical implications. *Inflamm Allergy Drug Targets*. 2015;13. doi: 10.2174/1871528114666150529120801.
15. Saracevic A, Medved I, Hrabric VS, Kozmar A, Bilic-Zulle L, Simundic AM. The association of systemic inflammatory markers with indicators of stress and cardiac necrosis in patients undergoing aortic valve replacement and revascularization surgeries. *Physiol Res* 2020;69:261-74.
16. Kazmierski J, Banys A, Latek J, Bourke J, Jaszewski R. Raised IL-2 and TNF- α concentrations are associated with postoperative delirium in patients undergoing coronary-artery bypass graft surgery. *Int Psychogeriatr* 2014;26:845-55.
17. Sethi BS, Kapoor PM, Chauhan S, Chowdhury UK, Kiran U, Choudhury M. Perioperative levels of tumor necrosis factor- α correlate with outcomes in children and adults with tetralogy of Fallot undergoing corrective surgery. *World J Pediatr Congenit Heart Surg* 2014;5:38-46.
18. Brancaccio G, Villa E, Girolami E, Michielon G, Feltri C, Mazzera E, *et al.* Inflammatory cytokines in pediatric cardiac surgery and variable effect of the hemofiltration process. *Perfusion* 2005;20:263-8.
19. Martins EC, Silvera L, Viegas K, Beck A, Junior GF, Cremonese RV, *et al.* Neutrophil-lymphocyte ratio in the early diagnosis of sepsis in an intensive care unit: A case-control study. *Razão neutrófilo-linfócito no diagnóstico precoce de sepse em unidade de terapia intensiva: Um estudo de caso-controle*. *Rev Bras Ter Intensiva* 2019;31:64–70.
20. Silberman S, Abu-Yunis U, Tauber R, Shavit L, Grenader T, Fink D, *et al.* Neutrophil-Lymphocyte ratio: Prognostic impact in heart surgery. Early outcomes and late survival. *Ann Thorac Surg* 2018;105:581-6.
21. Grosu I, Lavand’homme P. Continuous regional anesthesia and inflammation: A new target. *Minerva Anesthesiol* 2015;81:1001-9.
22. Zubrzycki M, Liebold A, Skrabal C, Reinelt H, Ziegler M, Perdas E, *et al.* Assessment and pathophysiology of pain in cardiac surgery. *J Pain Res* 2018;11:1599–611.
23. Kumar AK, Chauhan S, Bhoi D, Kaushal B. Pectointercostal Fascial Block (PIFB) as a novel technique for postoperative pain management in patients undergoing cardiac surgery. *J Cardiothorac Vasc Anesth* 2021;35:116-22.