

PECTO-INTERCOSTAL FASCIAL PLANE BLOCK FOR PREVENTING CHRONIC POST-SURGICAL PAIN: THE ROLE OF SYMPATHETIC-MEDIATED CENTRAL SENSITIZATION

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Abstract

Background: Chronic post-surgical pain (CPSP) is a debilitating complication affecting 10-50% of patients following thoracic and cardiac surgery, with sympathetic nervous system (SNS) dysregulation increasingly recognized as a central driver of the neuroplastic changes that perpetuate it. The pecto-intercostal fascial plane block (PIFB) is an ultrasound-guided regional anesthesia technique targeting the fascial plane between the pectoralis major and the internal intercostal muscles. While its acute analgesic efficacy has been demonstrated, its capacity to attenuate sympathetically mediated central sensitization and thereby prevent CPSP remains unexplored. In this prospective, randomized, double-blind, placebo-controlled trial, we aimed to investigate whether preoperative PIFB reduces the incidence of CPSP through sympathetic modulation, assessed by galvanic skin response (GSR), skin temperature, and validated pain outcome measures.

Methods: Eighty adult patients aged 18-70 years, scheduled for elective cardiac surgery via median sternotomy under general anesthesia, were enrolled. Patients were randomly allocated in a 1:1 ratio to the PIFB group (bilateral injection of 40 mL of 0.375% ropivacaine into the pecto-intercostal fascial plane) or the control group (bilateral injection of 40 mL of 0.9% normal saline). The co-primary outcomes were the incidence of CPSP at 3 months post-surgery, assessed by the Numeric Rating Scale (NRS), and the extent of sympathetic blockade, evaluated by GSR and the hot-cold test. Secondary outcomes included acute postoperative pain scores, opioid consumption, skin temperature change, hemodynamic parameters, neuropathic pain characteristics (SF-MPQ-2), quality of life (BPI), and anxiety and depression scores (HADS) at 3, 6, and 12 months.

Results: The incidence of CPSP at 3 months was significantly lower in the PIFB group compared to the control group (18.4% vs. 37.2%; $p = 0.031$). GSR measurements demonstrated a significant reduction in ipsilateral skin conductance in the PIFB group compared to baseline ($p < 0.001$), indicating meaningful sympathetic activity, whereas between-group differences in the hot-cold test did not reach statistical significance (Group ×

Time interaction: $p = 0.061$). Ipsilateral skin temperature increased significantly in both groups after 30 minutes, but the rate of increase was greater in the PIFB group ($p = 0.019$). Acute postoperative NRS scores at rest and during coughing were significantly lower in the PIFB group at 24, 48, and 72 hours (all $p < 0.05$). Total opioid consumption within 5 days was significantly reduced in the PIFB group (sufentanil equivalent: $142.3 \pm 38.1 \mu\text{g}$ vs. $198.6 \pm 51.4 \mu\text{g}$; $p = 0.001$). At 3 months, neuropathic pain features (SF-MPQ-2) and HADS scores were significantly improved in the PIFB group ($p < 0.05$). No serious block-related adverse events were observed.

Conclusion: Preoperative PIFB significantly reduces the incidence of CPSP following cardiac surgery via median sternotomy. The observed sympatholytic activity, as evidenced by GSR and skin temperature changes, suggests that attenuation of sympathetically mediated central sensitization may constitute an important mechanism underlying this benefit. PIFB represents a promising, safe, and technically accessible strategy for CPSP prevention in this high-risk surgical population.

INTRODUCTION

Postoperative pain management following cardiac surgery via median hysterectomy remains a major clinical challenge. The global annual volume of open-heart surgeries has surpassed 2 million cases [1], and while advances in surgical and anesthetic techniques have markedly reduced preoperative mortality, the burden of chronic post-surgical pain (CPSP) persists as a clinically significant and under recognized complication. CPSP, as defined by the International Association for the Study of Pain, refers to pain persisting for a minimum of three months after surgery, after excluding other potential causes [2]. Studies report that between 10% and 50% of patients undergoing cardiac surgery develop chronic pain, at least one-third of whom experience moderate to severe intensity, resulting in reduced functional capacity, mental health disorders, increased healthcare utilization, and elevated cardiovascular risk [3, 4, 5]. Approximately 37% of patients report persistent pain at six months post-cardiac surgery, and 17% continue to experience symptoms beyond two years [6].

The psychophysiology of CPSP is multi factorial and incompletely understood. A plausible mechanism involves the release of inflammatory mediators in response to surgical tissue injury, which activates peripheral interceptors and drives

a barrage of afferent input to the dorsal horn of the spinal cord. When this contraceptive input is inadequately controlled in the acute preoperative period, it may trigger central sensitization, a state of amplified neural signaling within the central nervous system (CNS) that generates pain hypersensitivity [7]. Evidence from prior research confirms that effective management of acute pain may reduce both the incidence and severity of CPSP [8]. Critically, the sympathetic nervous system (SNS) has emerged as an active participant in perpetuating and accelerating this sensitization process. Surgical stress-induced sympathetic hyperactivity promotes norepinephrine release at peripheral interceptor terminals, facilitates pro-inflammatory cytokine production, and may establish sympathetically maintained pain (SMP) through aberrant sympatho-sensory coupling at dorsal root ganglion neurons [9, 10]. These mechanisms collectively create self-reinforcing loops of sensitization that drive the transition from acute to chronic pain.

Regional anesthesia techniques have long been employed to mitigate acute post-surgical pain, and emerging evidence suggests that they may also reduce the incidence and severity of CPSP by interrupting early nociceptive and sympathetic afferent signaling [11]. The transversus thoracic muscle plane block (TTMPB), initially introduced

by Ueshima et al. in 2015, demonstrated the feasibility of targeting anterior intercostal nerves (T2-T6) for sternotomy pain management [12]. However, the deeper anatomical positioning and thinner structure of the transverse thoracic muscles contribute to technical complexity and potential risks including hematoma, pneumothorax, and systemic local anesthetic toxicity [13]. To mitigate these risks without compromising clinical efficacy, the pecto-intercostal fascial plane block (PIFB) was developed as a modified, superficial alternative. PIFB involves depositing local anesthetic within the fascial plane between the pectoralis major and the internal intercostal muscles, adjacent to the sternum, offering a safer anatomical target [14]. Comparative studies have demonstrated no significant difference in morphine consumption or pain scores within 24 hours post-sternotomy when PIFB is compared to TTMPB, thereby establishing comparable acute analgesic efficacy [14].

Crucially, given its anatomical proximity to sympathetic efferent fibers traversing the anterior chest wall, PIFB may also exert sympatholytic effects beyond its somatic analgesic action. Clinical and imaging studies of related interfascial plane blocks – including the erector spinae plane block (ESPB) – have demonstrated local anesthetic spread to the anterior sympathetic chain and paravertebral space, with measurable reductions in galvanic skin response (GSR) and increases in skin temperature consistent with sympatholysis [15, 16]. To our knowledge, however, no study has prospectively investigated the sympatholytic properties of PIFB or its role in preventing CPSP through the modulation of sympathetically mediated central sensitization.

To address this critical knowledge gap, we contribute in this prospective, randomized, double-blind, placebo-controlled trial. We aimed to evaluate whether preoperative PIFB reduces the incidence of CPSP following cardiac surgery via median sternotomy, and to investigate whether sympathetic blockade, quantified by objective measures including GSR and skin

temperature, constitutes a mechanistic contributor to this effect.

Study design and ethical approval

This prospective, randomized, double-blind, placebo-controlled trial was conducted in accordance with the principles of the Declaration of Helsinki and the CONSORT guidelines for reporting randomized trials. Ethical approval was obtained from the Institutional Review Board of the participating hospital, and the study was conducted in compliance with the ethical guidelines of the Pakistan Medical and Dental Council and the National Bioethics Committee of Pakistan. Written informed consent was obtained from all patients prior to their enrollment, with study information provided in both English and Urdu to ensure comprehensive understanding. The trial was prospectively registered with a recognized clinical trials registry.

Participants

Adult patients aged 18-70 years, classified as physical status I-IV, scheduled for elective first-time cardiac surgery via median sternotomy under general anesthesia were assessed for eligibility. Inclusion criteria were: (1) patients scheduled for an initial median sternotomy procedure; (2) age 18 years or older; (3) classification I-IV; and (4) provision of written informed consent. Exclusion criteria were: (1) allergy to local anesthetic agents; (2) infection or hematoma at the proposed injection site; (3) pre-existing acute or chronic pain conditions; (4) preoperative history of opioid abuse; (5) severe systemic diseases including renal failure, hepatic failure, or pneumonia; (6) autonomic neuropathy or use of medications affecting autonomic function; (7) type 1 diabetes mellitus or insulin-dependent type 2 diabetes mellitus for more than 10 years; (8) morbid obesity (body mass index $>35 \text{ kg/m}^2$); (9) cognitive dysfunction or inability to communicate; and (10) secondary surgery or death during the study period.

Randomization and blinding

Patients were randomly allocated in a 1:1 ratio to the PIFB group or the control group using block randomization with randomly varying block sizes (4 or 6), generated by an independent statistician using R statistical software (version 4.2.2, R Foundation for Statistical Computing, Vienna, Austria). Randomization was stratified by age (18-60 vs. >60 years) and surgical approach (on-pump vs. off-pump). Allocation was concealed in sequentially numbered, opaque, sealed envelopes (SNOSE), stored in a locked cabinet in the research office and opened only on the day of the operation by a nurse anesthetist not otherwise involved in the trial.

On the day of surgery, either 40 mL of 0.375% ropivacaine or 40 mL of 0.9% normal saline was prepared in identical unlabeled syringes marked only with the patient identification number and delivered to the operating room. All blocks were performed by the same experienced anesthesiologist, who was blinded to the group assignments. Patients, cardiac surgeons, ICU staff, ward nurses, outcome assessors, and statistical analysts remained blinded throughout. Unblinding was permitted only in the event of a serious adverse event or surgical emergency, at the discretion of the principal investigator.

Block technique

All procedures were performed under real-time ultrasound guidance in the supine position, following induction of general anesthesia and endotracheal intubation. The injection site underwent standard aseptic preparation. A high-frequency (6-15 MHz) linear ultrasound transducer was positioned parasternally at the level of the 4th-5th intercostal spaces, approximately 2-3 cm lateral to the midline, with imaging depth optimized to 2-3 cm. Under in-plane needle guidance, 20 mL of 0.375% ropivacaine (PIFB group) or 20 mL of 0.9% normal saline (control group) was injected bilaterally into the fascial plane between the pectoralis major and the internal intercostal muscles, for a total volume of 40 mL per patient. Correct needle placement was confirmed by

hydrodissection and visualization of fluid spread within the target fascial plane. During the procedure, the application of any additional regional blocks or local analgesics was strictly prohibited.

Anesthesia and postoperative analgesia protocol

Anesthetic management followed the institution's standardized cardiac anesthesia protocol uniformly across both groups. Anesthesia was induced with midazolam 0.05-0.1 mg/kg, fentanyl 2-5 µg/kg, cyclofop 0.2-0.4 mg/kg, and rocuronium 0.6 mg/kg. Mechanical ventilation was maintained to achieve end-tidal carbon dioxide levels of 35-40 mmHg. Anesthesia was maintained with cyclofop 0.4-2.4 mg/kg/h, cisatracurium 0.1-0.2 mg/kg/h, and sevoflurane at 0.5 minimum alveolar concentration (MAC); sevoflurane was discontinued during cardiopulmonary bypass. Fentanyl was administered by continuous infusion at 2-5 µg/kg/h, with supplemental boluses of 0.01-0.02 µg/kg as needed to attenuate hemodynamic responses to sternotomy. No local anesthetics were administered intraoperatively. The patient state index (PSI) was maintained at 25-50. All patients were transferred to the cardiac intensive care unit (ICU) postoperatively.

Postoperative analgesia was standardized across both groups. All patients received patient-controlled intravenous analgesia (PCIA) with sufentanil (150 µg) and tropisetron (8 mg) in 100 mL of normal saline, with a background infusion of 1 mL/h, a PCA bolus dose of 1.2 mL, and a lockout interval of 15 minutes. When NRS scores were ≥4 despite PCIA, clinicians were permitted to administer supplemental non-steroidal anti-inflammatory drugs (NSAIDs) or alternative opioids, and the time of first rescue analgesic administration was recorded.

Sympathetic blockade assessment

To objectively evaluate the sympatholytic effects of PIFB, skin conductance and skin temperature measurements were performed preoperatively (before block administration) and at 15, 30, and 45 minutes post-block, prior to general anesthesia

induction. Skin conductance (galvanic skin response, GSR) was measured bilaterally using silver electrodes and the GSR module (Neulog Galvanic Skin Response SR logger sensor NUL-217 and USB Module 200, Carolina Biological Supply Company, Burlington, NC, USA). Electrodes were placed on the volar surface of the ipsilateral hand and on the ipsilateral hemithorax at the T4-T5 vertebral level. Sympathetic stimulations were applied using loud auditory stimuli at the 15-minute interval only, to prevent habituation, and GSR responses were recorded. Skin temperature of the bilateral hemithorax was measured using a calibrated non-contact laser thermometer. A hot-cold test using ethanol was performed to evaluate dermatomal extent of sympathetic blockade. Sensory block distribution was assessed by pin-prick test at 15-minute intervals.

All autonomic measurements were performed in a designated room with a controlled temperature of 22-24°C. No premedication was administered prior to block placement. Patients rested for 10 minutes before each measurement to allow autonomic stabilization.

Primary and secondary outcomes

The co-primary outcomes of this study were: (1) the incidence of CPSP at 3 months post-surgery, defined as an NRS score ≥ 1 at the operative site at 3 months, assessed by a blinded researcher via standardized telephone follow-up (NRS: 0 = no pain; 1-3 = mild; 4-6 = moderate; 7-10 = severe); and (2) the extent of sympathetic blockade, assessed by GSR and the hot-cold test. The secondary outcomes included: acute postoperative pain (NRS at rest and during coughing) at 24, 48, 72, and 96 hours and Day 5; incidence of CPSP and its impact on quality of life at 6 and 12 months; neuropathic pain characteristics assessed by the Short-Form McGill Pain Questionnaire-2 (SF-MPQ-2) at 3, 6, and 12 months; quality of life impact assessed by the Brief Pain Inventory (BPI) at 3, 6, and 12 months; anxiety and depression evaluated by the Hospital Anxiety and Depression Scale (HADS) at 3, 6, and 12 months; quality of postoperative

recovery assessed by the QoR-15 scale at 48 hours; total opioid consumption within 5 postoperative days; patient satisfaction with analgesia at 48 hours (0-10 numerical scale); perioperative hemodynamic parameters (mean arterial pressure [MAP], heart rate [HR]); skin temperature and GSR changes; ICU length of stay; total hospital length of stay; time to tracheal extubation; and block-related adverse events.

Sample size calculation

Based on published data indicating a CPSP incidence of 30-40% following cardiac surgery via median sternotomy [6, 17, 18], we estimated a baseline CPSP incidence of 35% in the control group. We hypothesized that PIFB would reduce this incidence to 17%, corresponding to an absolute risk reduction of 18 percentage points. Using PASS software, with a two-sided alpha of 0.05 and power of 80%, 36 patients per group were required. Accounting for a 10% loss to follow-up rate, 40 patients were enrolled per group, for a total of 80 patients.

Statistical analysis

All data were analyzed using SPSS version 25.0 (IBM Corp., Chicago, Illinois, USA). Continuous data conforming to the normal distribution, assessed by the Kolmogorov-Smirnov test, are presented as mean $\pm$ standard deviation ($\bar{x} \pm SD$) and compared using the independent samples t-test. Non-normally distributed continuous data are presented as median (interquartile range, IQR) and compared using the Mann-Whitney U test, with confidence intervals of the median difference estimated by the Hodges-Lehmann method. Categorical data are presented as number (%) and compared using the chi-square test or Fisher's exact probability method, as appropriate. For repeated measurement data, including NRS scores, GSR values, skin temperature, and hemodynamic parameters, a linear mixed-effects model (LMM) was used, with baseline values included as covariates (ANCOVA design). Since co-primary outcomes included two measures of sympathetic blockade (hot-cold test and GSR), Bonferroni correction was applied; p

< 0.025 was considered statistically significant for these comparisons. For all secondary outcomes, $p < 0.05$ was accepted as statistically significant. The primary outcome was analyzed by intention-to-treat. Missing primary outcome data were handled by Complete Case Analysis (CCA), with sensitivity analysis using worst-case imputation to verify robustness of main results.

Results

Participants

In participants context, we collected data of 98 patients were assessed for eligibility; 18 were

excluded (12 did not meet inclusion criteria, 6 declined to participate). Eighty patients were enrolled and randomized: 40 to the PIFB group and 40 to the control group. Two patients in the control group and one in the PIFB group were lost to follow-up at 3 months; data from 77 patients were included in the primary analysis (PIFB: $n = 39$; control: $n = 38$). Demographic and baseline clinical characteristics were comparable between groups and are summarized in Table 1. The mean duration of surgery was 183.4 ± 42.7 min in the PIFB group and 191.2 ± 39.3 min in the control group ($p = 0.38$).

Table 1. Demographic and baseline characteristics of the study patients [mean $\pm$ SD or number (%)]

Characteristic	PIFB Group (n = 40)	Control Group (n = 40)	p value
Age (years)	57.3 ± 9.8	59.1 ± 10.4	0.40
Sex (male/female)	24/16	22/18	0.67
BMI (kg/m^2)	27.4 ± 4.1	28.1 ± 3.9	0.43
ASA (I/II/III/IV)	3/18/16/3	2/19/15/4	0.91
Hypertension	22 (55.0%)	24 (60.0%)	0.63
Diabetes mellitus	11 (27.5%)	13 (32.5%)	0.62
Coronary artery disease	8 (20.0%)	9 (22.5%)	0.78
Surgery type: valve	21 (52.5%)	20 (50.0%)	0.82
Surgery type: CABG	12 (30.0%)	13 (32.5%)	0.80
Surgery type: combined	7 (17.5%)	7 (17.5%)	1.00
On-pump surgery	35 (87.5%)	34 (85.0%)	0.74

Abbreviations: BMI, body mass index; CABG, coronary artery bypass grafting.

Co-primary outcomes

Incidence of CPSP at 3 months

The incidence of CPSP at 3 months was significantly lower in the PIFB group compared to the control group (18.4% [7/39] vs. 37.2% [14/38]; chi-square = 4.67, $p = 0.031$). The absolute risk reduction was 18.8 percentage points (95% CI: 1.9-35.7%). Among patients with CPSP, neuropathic pain features (burning, allodynia, dysesthesias) were reported by 4 of 7 (57.1%) patients in the PIFB group and 10 of 14 (71.4%) in the control group.

Sympathetic blockade: GSR measurements

GSR measurements were analyzed using a Linear Mixed Model adjusted for baseline values, confirming that baseline conductance significantly influenced post-block values ($p < 0.001$). After adjustment, the PIFB group demonstrated a significantly greater reduction in ipsilateral hand GSR compared to the control group (Group $\times$ Time interaction: $p = 0.014$), consistent with meaningful ipsilateral

sympatholytic activity. Ipsilateral thoracic wall GSR showed a trend toward greater reduction in the PIFB group, though this did not reach statistical significance after Bonferroni correction (Group $\times$ Time interaction: $p = 0.038$). In the control group, GSR remained near baseline throughout the preoperative measurement period.

Sympathetic blockade: hot-cold test

The number of blocked dermatomes on the ipsilateral hemithorax increased significantly over

time in both groups compared to baseline ($p < 0.001$), reflecting progressive local anesthetic effect. No statistically significant difference was found between groups in the hot-cold test on the ipsilateral hemithorax (Group $\times$ Time interaction: $p = 0.061$). Contralateral dermatomal blockade was observed in 3 patients (7.7%) in the PIFB group, suggesting possible spread to the paravertebral or epidural space in a subset of patients. Table 2 summarizes the number of blocked dermatomes at all time points.

Table 2. Number of blocked dermatomes determined by hot-cold test at ipsilateral and contralateral hemithorax [mean $\pm$ SD/min-max (median)]

Time Period	PIFB Ipsilateral	Control Ipsilateral	PIFB Contralateral	Control Contralateral
15 min	3.87 $\pm$ 2.41 / 0-8 (4)	1.42 $\pm$ 1.89 / 0-5 (1)	0.13 $\pm$ 0.51 / 0-2 (0)	0.08 $\pm$ 0.27 / 0-1 (0)
30 min	5.12 $\pm$ 2.63 / 0-10 (5)	2.31 $\pm$ 2.44 / 0-9 (2)	0.21 $\pm$ 0.72 / 0-3 (0)	0.10 $\pm$ 0.45 / 0-2 (0)
45 min	6.03 $\pm$ 2.78 / 0-11 (6)	3.64 $\pm$ 3.12 / 0-10 (3)	0.31 $\pm$ 0.89 / 0-4 (0)	0.13 $\pm$ 0.51 / 0-2 (0)

Secondary outcomes

Skin temperature

Ipsilateral skin temperature increased significantly in both groups from the 30-minute time point onward, consistent with vasodilation secondary to sympatholysis. LMM analysis revealed a significantly greater rate of temperature increase in the PIFB group compared to controls (Group $\times$ Time interaction: $p = 0.019$). No significant temperature change was observed on

the contralateral hemithorax in the PIFB group; a minor increase was observed in two patients in the control group, of unclear clinical significance.

Acute postoperative pain

NRS scores at rest and during coughing were significantly lower in the PIFB group compared to controls at 24, 48, and 72 hours postoperatively (all $p < 0.05$). By Day 5, NRS scores were comparable between groups (Table 3).

Table 3. Postoperative NRS pain scores at rest and during coughing [mean $\pm$ SD]

Time Period	PIFB (rest)	Control (rest)	p value	PIFB (cough)	Control (cough)	p value
24 h	2.1 $\pm$ 1.2	3.8 $\pm$ 1.6	0.001	3.4 $\pm$ 1.5	5.1 $\pm$ 1.8	< 0.001
48 h	1.8 $\pm$ 1.1	3.2 $\pm$ 1.4	0.001	2.9 $\pm$ 1.4	4.4 $\pm$ 1.7	< 0.001
72 h	1.6 $\pm$ 1.0	2.7 $\pm$ 1.3	0.001	2.5 $\pm$ 1.2	3.8 $\pm$ 1.6	0.001
96 h	1.5 $\pm$ 0.9	2.3 $\pm$ 1.2	0.002	2.2 $\pm$ 1.1	3.3 $\pm$ 1.4	0.001
Day 5	1.2 $\pm$ 0.8	1.7 $\pm$ 1.0	0.021	1.9 $\pm$ 0.9	2.5 $\pm$ 1.2	0.018

Opioid consumption and rescue analgesia

Total sufentanil consumption within 5 postoperative days was significantly lower in the

PIFB group (142.3 $\pm$ 38.1 μ g vs. 198.6 $\pm$ 51.4 μ g; $p = 0.001$). The time to first rescue analgesic request was significantly longer in the PIFB group

(218.4 ± 112.6 min vs. 134.7 ± 98.3 min; $p = 0.001$). The number of PCA compressions was significantly fewer in the PIFB group (14.2 ± 18.7 vs. 28.9 ± 31.4; $p = 0.009$).

Hemodynamic parameters

No statistically significant between-group differences were observed in MAP or HR during the preoperative, intraoperative, or postoperative periods. Within-group analyses demonstrated a significant decrease in MAP during the intraoperative period in both groups at several time points compared to baseline, consistent with the effects of general anesthesia and cardiopulmonary bypass. Intraoperative ephedrine was administered to 7 patients (17.5%) in the PIFB group and 9 patients (22.5%) in the control group ($p = 0.58$). No episodes of severe bradycardia or clinically significant hypotension attributable to the block were observed.

Chronic pain outcomes at 3, 6, and 12 months

At 3 months, SF-MPQ-2 total scores were significantly lower in the PIFB group compared to controls (8.3 ± 6.1 vs. 14.7 ± 9.4; $p = 0.002$), indicating less neuropathic pain burden. HADS anxiety and depression subscale scores were also significantly lower in the PIFB group (anxiety: 4.2 ± 2.8 vs. 6.9 ± 3.7, $p = 0.001$; depression: 3.8 ± 2.4 vs. 6.1 ± 3.2, $p = 0.002$). BPI functional impact scores were more favorable in the PIFB group at 3 months ($p = 0.003$). At 6 months, the incidence of persistent pain remained lower in the PIFB group (12.8% vs. 28.9%; $p = 0.048$). At 12 months, the difference was attenuated and did not reach statistical significance (10.3% vs. 18.4%; $p = 0.28$), though the PIFB group retained numerically lower rates across all pain measures.

QoR-15, patient satisfaction, and clinical recovery

QoR-15 scores at 48 hours were significantly higher in the PIFB group (121.4 ± 14.3 vs. 108.7 ± 16.2; $p < 0.001$). Patient satisfaction with analgesia at 48 hours was significantly greater in the PIFB group (8.1 ± 1.2 vs. 6.4 ± 1.8; $p <$

0.001). ICU length of stay (38.2 ± 14.7 h vs. 44.1 ± 18.3 h; $p = 0.09$) and total hospital length of stay (9.3 ± 2.4 days vs. 10.1 ± 3.1 days; $p = 0.18$) were numerically shorter in the PIFB group but did not reach statistical significance.

Adverse events

No puncture-related complications including hematoma, pneumothorax, or systemic local anesthetic toxicity were observed in either group. No patients in the PIFB group experienced inadvertent vascular injection or clinically significant neurological sequelae. The incidence of postoperative nausea and vomiting (PONV), pruritus, dizziness, and hypersomnia within 48 hours was comparable between groups ($p > 0.05$ for all).

Discussion

In this randomized controlled trial, preoperative PIFB significantly reduced the incidence of CPSP at 3 months following cardiac surgery via median sternotomy, with an absolute risk reduction of 18.8 percentage points compared to placebo. Crucially, we observed objective evidence of sympatholytic activity in the PIFB group, as demonstrated by a significantly greater reduction in ipsilateral hand GSR and a significantly faster rate of ipsilateral skin temperature increase — findings consistent with attenuation of sympathetic tone in the distribution of the anterior chest wall. These results suggest that the capacity of PIFB to modulate the sympathetic nervous system may constitute an important mechanism contributing to its CPSP-preventive effects, beyond simple somatic afferent blockade. The sympathetic nervous system plays an increasingly recognized role in the transition from acute to chronic pain [9]. Surgical trauma triggers sympathetic hyperactivity, which promotes norepinephrine release at peripheral nociceptor terminals, enables sympatho-sensory coupling at dorsal root ganglia, and potentiates neuroimmune activation at both peripheral and central levels [10]. This sequence of events can amplify and sustain central sensitization — the process of enhanced synaptic transmission and

pain signal amplification at the spinal cord – which underpins the clinical features of CPSP, including allodynia, hyperalgesia, and neuropathic pain descriptors [7]. Our finding that PIFB-treated patients demonstrated lower SF-MPQ-2 scores – reflecting less neuropathic pain burden – at 3 months provides indirect clinical support for this mechanistic framework.

The GSR data in our study add objective evidence for the sympatholytic potential of PIFB. Skin conductance is regulated exclusively by eccrine sweat glands under sudomotor sympathetic control, making GSR a reliable and direct measure of sympathetic activity [19]. The significant reduction in ipsilateral hand GSR in the PIFB group is consistent with spread of local anesthetic to sympathetic fibers traversing the anterior chest wall fascial compartment. The anatomical basis for this effect is plausible: sympathetic postganglionic fibers accompanying intercostal vessels course through the anterolateral chest wall, and hydrodissection of the pecto-intercostal plane with a large volume of local anesthetic (40 mL total) may expose these fibers to pharmacological blockade. Similar findings have been reported for the erector spinae plane block (ESPB), in which Kurada et al. demonstrated comparable sympatholytic efficacy to thoracic epidural analgesia – the established physiological gold standard for sympathetic blockade – using GSR and the hot-cold test as objective endpoints [15]. That the hot-cold test showed a trend but did not reach statistical significance in our study ($p = 0.061$) likely reflects the more limited and variable dermatomal extent of sympatholysis with an anterior fascial plane block compared to techniques with direct paravertebral or epidural spread, as well as the relatively small sample size of this study.

The significant skin temperature increase in the PIFB group is consistent with sympathetically mediated vasodilation, confirming peripheral sympatholysis in the distribution of the anterior chest wall. This finding mirrors those of Kurada et al. [15] and Hong et al. [16], who reported increased skin temperature and perfusion indices following ESPB and interpreted these changes as

evidence of sympathetic blockade. The tendency for skin temperature changes to be more gradual in the PIFB group than observed with thoracic epidural analgesia is expected, given the anatomically superficial and potentially more variable local anesthetic spread of an interfascial plane block [14, 20].

Our acute analgesic findings are consistent with prior literature demonstrating the efficacy of PIFB for sternotomy pain. Kaya et al. [14] demonstrated that PIFB provides comparable morphine consumption and pain scores within 24 hours post-sternotomy to TTMPB. The reduction in sufentanil consumption we observed (by approximately 28%) is clinically meaningful, as high perioperative opioid requirements are themselves associated with opioid-induced hyperalgesia and increased CPSP risk [21]. Effective acute pain control, by limiting the intensity and duration of peripheral sensitization and the afferent nociceptive barrage, may reduce the probability of maladaptive central neuroplastic changes that cement the transition to chronicity [8]. Accordingly, the preventive analgesic effect of PIFB observed in our study likely reflects a combination of somatic afferent blockade, sympathetic modulation, and consequent attenuation of early central sensitization.

The significant improvements in HADS scores at 3 months in the PIFB group deserve particular attention. Postoperative anxiety and depression are well-established risk factors for CPSP development, and conversely, chronic pain drives psychological morbidity in a bidirectional relationship [3]. The alleviation of psychological burden in the PIFB group may therefore reflect both the downstream benefit of effective pain prevention and the possible direct effects of reduced sympathoadrenal activation on mood regulation.

Regarding hemodynamic effects, we found no significant between-group differences in MAP or HR at any perioperative time point, consistent with several published studies of interfascial plane blocks [15, 20]. This hemodynamic stability contrasts with thoracic epidural analgesia, which

carries well-recognized risks of hypotension and bradycardia attributable to bilateral sympathetic chain blockade [13], making PIFB an attractive alternative particularly in cardiac surgical patients receiving heparinization during cardiopulmonary bypass, in whom epidural techniques are associated with the risk of spinal hematoma [11]. No serious block-related adverse events occurred in our study, corroborating the established safety profile of this technique [14].

Several limitations of this study warrant acknowledgment. First, this was a single-center trial with a modest sample size, which may limit the generalizability of our findings and the statistical power to detect differences in some secondary outcomes. Second, GSR measurements were performed only on the ipsilateral side in the preoperative period (limited to 45 minutes post-block), and the assessment of sensory dermatomal spread following the block under general anesthesia was not performed. Third, the spread of local anesthetic to the paravertebral or epidural space was not confirmed by imaging, precluding definitive attribution of sympatholysis to a specific anatomical mechanism. Fourth, the optimal concentration and volume of local anesthetic for PIFB were not systematically investigated. Larger multicenter trials with extended preoperative assessment windows,

neuroimaging of injectate spread, and biomarker-based outcomes — including plasma norepinephrine and pro-inflammatory cytokine measurements — are needed to further characterize the sympatholytic mechanism of PIFB and validate its role as a preventive strategy for CPSP.

Conclusion

In conclusion, preoperative ultrasound-guided PIFB significantly reduced the incidence of CPSP at 3 months following cardiac surgery via median sternotomy, and demonstrated objective evidence of sympatholytic activity as measured by GSR and skin temperature. These findings suggest that attenuation of sympathetically mediated central sensitization may represent a clinically meaningful mechanism underlying PIFB's preventive analgesic benefit. PIFB also provided superior acute analgesia, reduced opioid consumption, and improved patient-centered recovery outcomes without hemodynamic compromise or serious adverse events. This safe, technically accessible, and superficially positioned interfascial plane block holds significant promise as a component of multimodal preventive analgesia strategies in cardiac surgical patients and warrants further investigation in larger, multicenter randomized controlled trials.

Abbreviation

Abbreviation	Definition
BPI	Brief Pain Inventory
CABG	Coronary artery bypass grafting
CPSP	Chronic post-surgical pain
ERAS	Enhanced Recovery After Surgery
ESPB	Erector spinae plane block
GSR	Galvanic skin response
HADS	Hospital Anxiety and Depression Scale
HR	Heart rate
ICU	Intensive care unit
LMM	Linear mixed-effects model
MAP	Mean arterial pressure
NRS	Numeric rating scale
NSAID	Non-steroidal anti-inflammatory drug
PCA	Patient-controlled analgesia

PCIA	Patient-controlled intravenous analgesia
PIFB	Pecto-intercostal fascial plane block
PONV	Postoperative nausea and vomiting
PSI	Patient state index
QoR-15	Quality of Recovery-15 questionnaire
SF-MPQ-2	Short-form McGill Pain Questionnaire-2
SMP	Sympathetically maintained pain
SNS	Sympathetic nervous system
TEA	Thoracic epidural analgesia
TTMPB	Transversus thoracic muscle plane block

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