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# Programmed intermittent bolus for erector spinae plane block versus intercostal nerve block in minimally invasive direct coronary artery bypass surgery: a randomized controlled trial

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## Abstract

**Objective** Continuous intercostal nerve block (ICNB) has been shown to offer effective pain relief after minimally invasive direct coronary artery bypass (MIDCAB). The erector spinae plane block (ESPB) could represent a viable alternative approach. This study aimed to compare the analgesic effect of programmed intermittent bolus (PIB) for ESPB to ICNB in patients undergoing MIDCAB.

**Methods** A prospective, open-label, randomized controlled trial was conducted. Eighty patients scheduled for MIDCAB were randomized into two groups ( $n=40$  per group). ESPB using a PIB injection was performed in the ESPB group, while ICNB was performed in the ICNB group. The primary outcome was numerical rating scale (NRS) pain scores at movement immediately after extubation. Secondary outcomes included the cumulative area under the curve (AUC) of the pain scores, perioperative analgesic consumption, adverse events and recovery data.

**Results** A total of 73 patients were included in the modified intention-to-treat analysis and 71 patients in the per-protocol analysis. There was no significant difference in numeric rating scale (NRS) scores at rest or movement between the two groups immediately after extubation, at 8, 24 and 48 h. The cumulative area under the curve (AUC) of the time NRS curve until 48 h after extubation and the necessity of rescue analgesics did not differ to a statistically significant degree between the two groups. Compared with the ICNB group, the ESPB group had significantly lower usage of intraoperative sufentanil ( $93.8 \pm 33.6$  vs.  $128.9 \pm 48.4$   $\mu\text{g}$ ;  $p=0.001$ ).

**Conclusions** Postoperative analgesic effect between ESPB and ICNB did not differ in patients after MIDCAB.

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**Trial registration** Chinese Clinical Trial Registry (ChiCTR1900022388, retrospectively registered on Apr 09, 2019).

**Keywords** Erector spinae plane block, Intercostal nerve block, Minimally invasive direct coronary artery bypass

## Introduction

Over the past two decades, the development of minimally invasive direct coronary artery bypass (MIDCAB) techniques has progressed significantly [1]. This technique has been primarily employed in low-risk patients with anterior lesions, especially those affecting the left anterior descending artery [2]. It is also used in high-risk patients who have contraindications to conventional bypass, such as the presence of extensive ascending aortic atheromatous or calcific changes that preclude safe aortic instrumentation [3]. With the development of surgical skills, an increasing number of multivessel grafting procedures are being performed using minimal-access techniques. The 2018 ESC/EACTS guidelines on myocardial revascularization [4] indicate that MIDCAB using the left internal mammary artery may offer an attractive alternative to conventional approaches for coronary artery bypass graft (CABG) surgery. Compared with conventional CABG, MIDCAB has been shown to be associated with reduced rates of wound infection, faster recovery, and decreased perioperative morbidity [5]. Patients still experience significant postoperative pain due to intercostal nerve injury and irritation caused by postoperative chest drainage tubes. Sympathetic stimulation induced by pain might increase the incidence of cardiovascular complications, as well as prolong intensive care unit (ICU) and hospital stays [6, 7]. Therefore, implementing effective pain management strategies after MIDCAB is important.

Conventional high-dose opioids carry the risks of respiratory depression, nausea, and vomiting [8, 9]. Increasing evidence supports the use of multimodal opioid-sparing approaches to effectively manage pain. Thoracic epidural analgesia (EA) [10] and paravertebral block (PVB) [11] are considered the most effective forms of regional anesthesia after thoracotomy, but their use following MIDCAB is controversial when heparin is used during surgery. Continuous intercostal nerve block (ICNB) has been shown to offer effective pain relief after MIDCAB [12]. The development of novel regional anesthesia techniques has greatly expanded the options for acute pain management.

Forero et al. [13] first described erector spinae plane block (ESPB) in 2016. The spread of local anesthetic to the paravertebral space following ESPB has been found in cadaveric studies conducted by Yang [14] and Adhikary [15], as well as in a magnetic resonance imaging study in healthy volunteers [16]. The visceral and somatic analgesic effects provided by the ESPB likely result from both transforaminal and epidural spread [17]. This regional anesthesia technique demonstrates a favorable clinical

safety profile and requires less technical expertise for implementation. Furthermore, the ESPB may represent a viable alternative anesthetic approach for cardiothoracic procedures, particularly in high-risk populations, including frail, obese patients and those with respiratory and/or hemodynamic issues [18]. Although previous findings demonstrated effective analgesia with ESPB following cardiothoracic surgery [19–21], its efficacy has not yet been compared with that of ICNB in the context of MIDCAB. The current study was designed to evaluate the analgesic effect of ESPB using a programmed intermittent bolus (PIB) regimen in comparison with that of ICNB in patients undergoing MIDCAB.

## Methods

The current study was a prospective randomized controlled trial (RCT) that was retrospectively registered at [www.chictr.org.cn](http://www.chictr.org.cn) (ChiCTR1900022388) on Apr 09, 2019. The experimental protocol was approved by the Institutional Ethics Committee of our Hospital (No. IRB00006761-M2018141, August 2018). The study ran from Sep 01, 2018 to Oct 01, 2019. We performed this study in accordance with Consolidated Standards of Reporting Trials (CONSORT) guidelines. All patients scheduled for MIDCAB were admitted to the department of cardiac surgery and screened for eligibility. We obtained written informed consent from all patients.

## Participants

We included patients who met the following criteria: (1) American Society of Anesthesiologists (ASA) status 2–3, (2) age 40–80 years, and (3) scheduled for MIDCAB. Exclusion criteria included (1) contraindications of nerve block (e.g., coagulation disorders, infection at the injection site), (2) inability to cooperate during the nerve block procedure (e.g., due to delirium or intellectual disability), (3) a history of spinal surgery or thoracic–spine abnormality, (4) known allergy to study drugs, (5) chronic consumption of opioids or other analgesics, and (6) refusal to participate.

## Randomization and blinding

Using a computer-generated random allocation sequence with a block size of 5, we randomly assigned the 80 patients into the two groups at a 1:1 allocation ratio. Group allocation numbers were concealed in sealed, opaque envelopes by the institutional statistician and were revealed to the anesthesia team 30 min before patients entered the operating room.

This was an open-label study. Since block time (before induction or not) and locations of catheters differed between the two groups, the anesthetists, surgeons and patients were not blinded to the protocol. For both groups, opaque adhesive tape was used to secure the nerve block catheters. In the intercostal nerve block group, the catheter was first extended posteriorly to the back and then advanced cephalad, whereas in the erector spinae block group, the catheter was directly advanced cephalad. In both groups, the catheter tips were secured at the shoulder and connected to the analgesia pump catheter connector. The nurses responsible for pain evaluation were blinded to group allocation.

### Intraoperative management

All participants received general anesthesia (GA) in accordance with our clinical routine and under standard ASA monitoring. Intraoperative monitoring included five-lead electrocardiography (ECG), pulse oximetry, invasive and non-invasive blood pressure (BP) and bispectral index (BIS) monitoring. We premedicated patients intravenously (i.v.) with midazolam (0.05 mg/kg). GA was induced using sufentanil (0.5 µg/kg) and propofol (1–2 mg/kg), and tracheal intubation with a 35–39 F left-side double-lumen tube was facilitated by rocuronium (0.6 mg/kg). Anesthesia was maintained with a combination of propofol (6–8 mg/kg/h), titrated to a BIS of 40–60 and a continuous infusion of sufentanil. One-lung ventilation was initiated with a tidal volume of 6–8 ml/kg and a respiratory rate of 12 bpm, and these parameters were adjusted to maintain an end-tidal CO<sub>2</sub> between 35 and 45 mmHg. Fluid management and infusion of vasoactive agents were guided by hemodynamic parameters.

The same team of surgeons performed all surgeries. A small, left anterior thoracotomy incision (5–6 cm) was made in the fifth intercostal space. Before the left internal mammary artery was clipped, the patient received unfractionated heparin (200 IU/kg) to achieve an activated clotting time (ACT) > 300 s. After coronary revascularization, protamine was administered to reverse the effects of heparin. A chest tube was inserted via the sixth intercostal space. Patients were transferred to the ICU of cardiac surgery, where they were extubated by physicians in accordance with the following criteria [22]: (1) hemodynamic stability with minimal vasopressor or inotropic support; (2) awake and able to follow commands; (3) adequate muscle strength and respiratory effort; (4) tidal volume > 6 ml/kg; (5) blood gases within normal ranges; (6) no significant metabolic acidosis; and (7) absence of significant mediastinal bleeding or coagulopathy.

### Postoperative analgesia

Before skin closure, all patients received butorphanol (1 mg) i.v. The ESPB or ICNB catheter was connected to

a Programmed Electronic Postoperative Analgesia Pump (Ai Peng Medical Technology Co Ltd, Jiangsu, China). We initiated a perineural analgesia regimen with a PIB of 0.2% ropivacaine (0.1 ml/kg/h) plus a patient-controlled bolus of 5 ml with a 30-min lockout period.

All patients underwent a multimodal analgesic regimen involving continuous infusion of dexmedetomidine (0.1 µg/kg/h) before extubation and butorphanol (1 mg every 6 h) up to 48 h post-extubation. The follow-up nurses assessed postoperative pain using the numeric rating scale (NRS; 11-point) at rest and movement. Rescue analgesia was provided with intramuscular morphine (5 mg) if NRS score ≥ 4/10. After 15 min, the patient would receive tramadol (100 mg) i.v. if re-evaluated NRS score ≥ 4/10.

### ICNB group

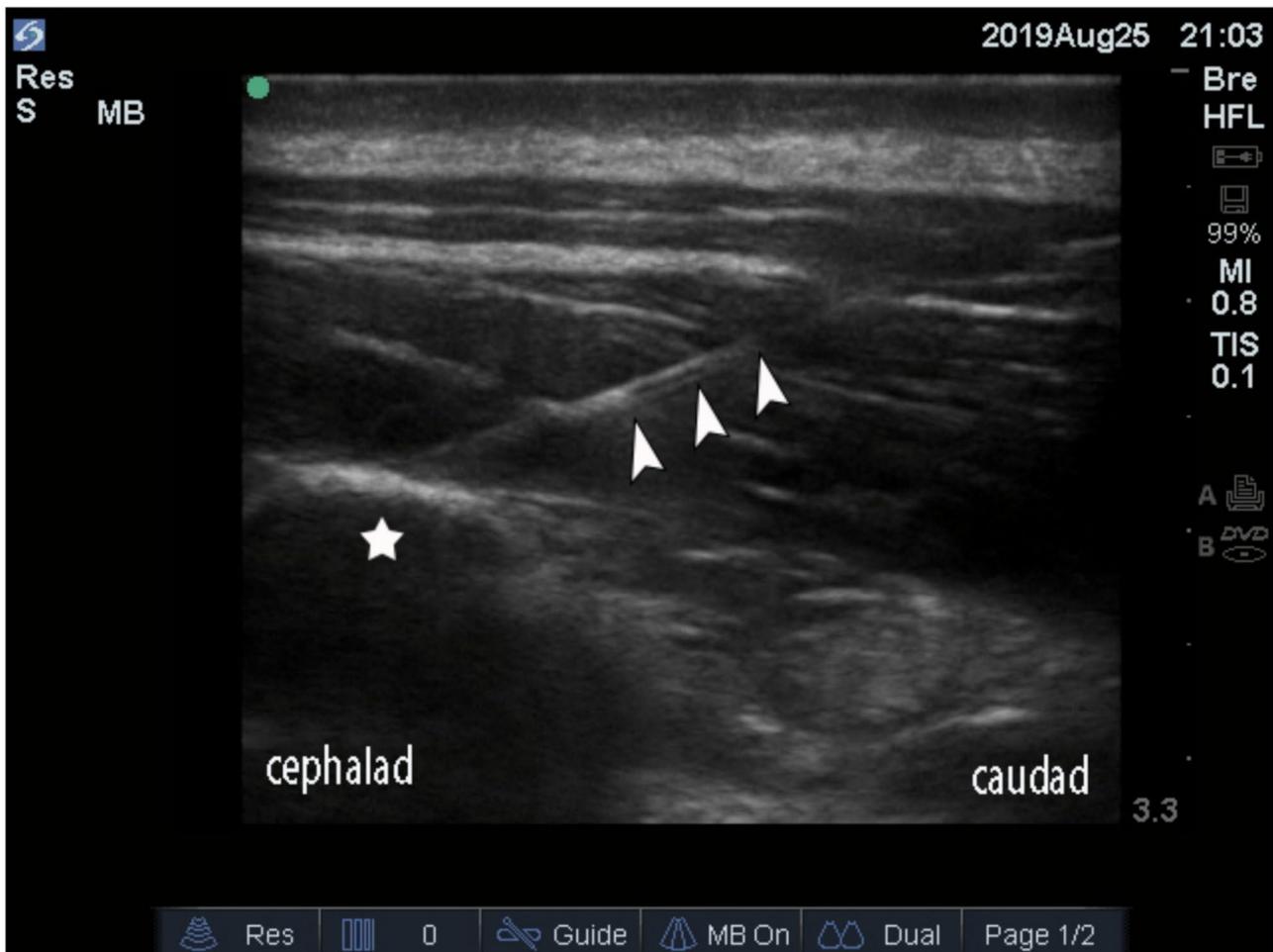
At the end of the operation, just before chest closure, the surgeon injected 0.5% ropivacaine into the fourth to seventh intercostal spaces, 5 ml at each interspace. A catheter (Stimuplex D, B Braun Melsungen AG, Tochigi, Japan) was inserted into the fifth intercostal space by experienced surgeons.

### ESPB group

Two experienced attending anesthetists performed all blocks. Ultrasound (US) guided ESPB was performed before anesthesia induction as per the method described by Forero [23] and Ueshima [24]. A linear probe (6–13 MHz, Xporte US; Fujifilm Sonosite, Bothell, WA, USA) was placed longitudinal at the level of the T5 spinous process and then moved laterally. An 80-mm 22-gauge Stimuplex D block needle was inserted in plane until the tip contacted the T5 transverse process. Then, the anesthetists injected 20 ml of 0.5% ropivacaine and inserted a Stimuplex D catheter (Fig. 1).

### Outcomes

The NRS score at movement immediately after extubation was assessed as the primary outcome. Secondary outcome measures included the NRS score at rest and movement at 8, 24, and 48 h after extubation; the cumulative area under the curve (AUC) of the time–NRS curve, intraoperative opioid consumption; and analgesic requirements during the first 48 h post-extubation. We calculated the oral morphine milligram equivalent (MME) of each opioid prescription by multiplying the opioid dose by a conversion factor [25]. Secondary outcome measures also included recovery data and adverse events (AEs). Recovery data included mechanical ventilation (MV) time, time to first flatus, time to first feeding, time to first ambulation, indwelling time of urethral catheter and length of hospital stay. Opioid- or block-related AEs were recorded, such as nausea and vomiting,



**Fig. 1** Ultrasonographic images of the catheter in the erector spinae plane block (ESPB) group. The arrowheads indicate the catheter, and the asterisk indicates the transverse process

pruritus, bleeding or hematoma, drug leakage or accidental catheter removal. Postoperative AEs included new-onset atrial fibrillation, pneumonia, and delirium.

#### Statistical analysis

We calculated sample size using PASS (NCSS Statistical Software, LLC, Kaysville, UT, USA). Based on the results from a pilot observation of 12 patients, the mean and standard deviation (MD, SD) of NRS scores at movement immediately after extubation were respectively 3.8 and 0.8 in the ESPB group and 3.1 and 1.2 in the ICNB group. Given an anticipated dropout rate of 10%, we calculated that a total sample size of 80 patients (40 per group) would provide 80% power to reject the null hypothesis of equal means when the mean difference was  $-0.7$  with SD of 1.2 for the ICNB group and 0.8 for the ESPB group at a two-sided  $\alpha$  of 0.05.

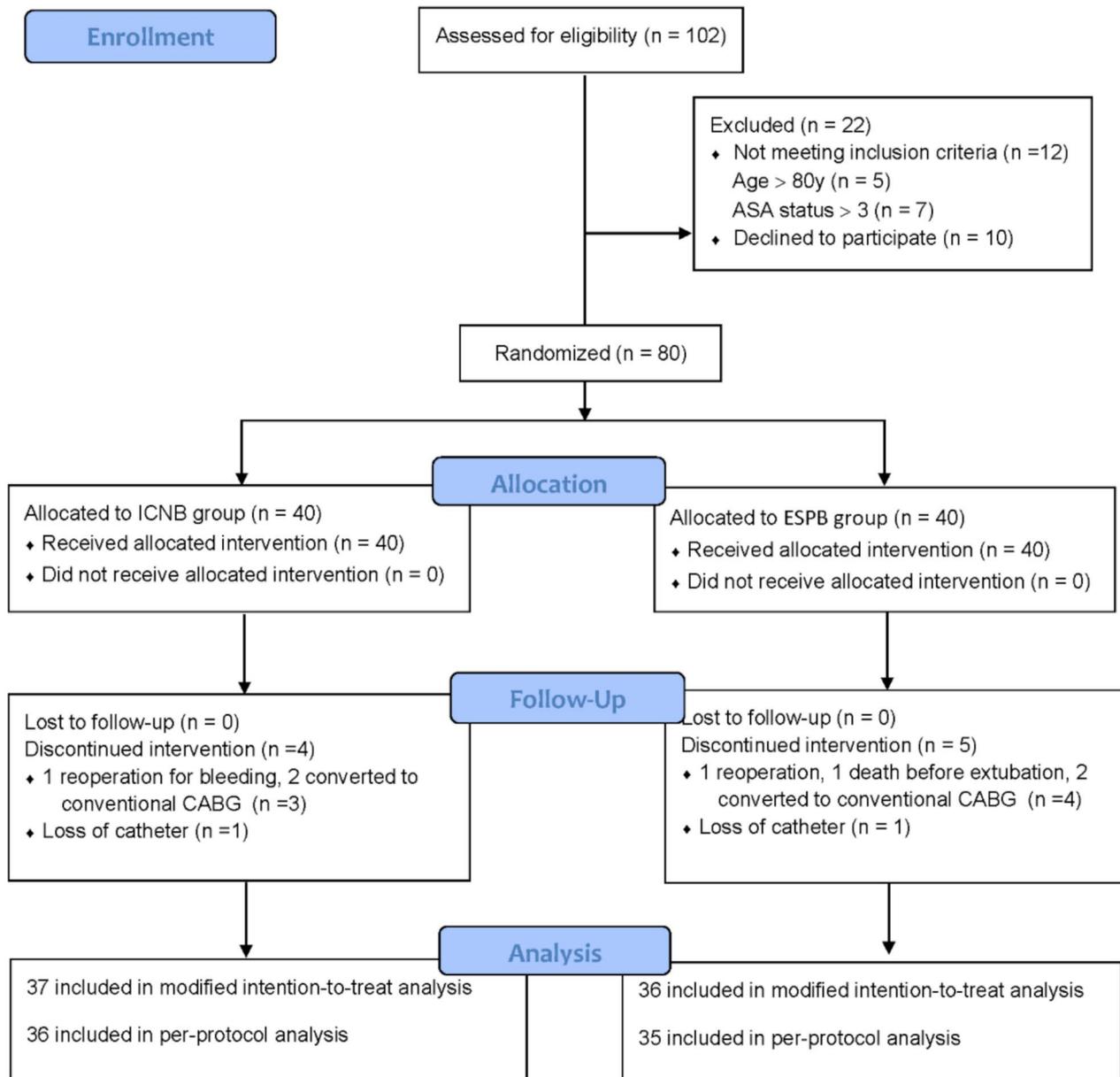
An independent statistician performed all statistical analyses using SPSS version 22.0 (IBM Corp., Armonk, NY, USA) and OriginPro version 8.1 (OriginLab Corp., Northampton, MA, USA) with the significance level set

at  $p$  value  $< 0.05$ . Outcome analyses were primarily performed in a modified intention-to-treat (mITT) population. For the primary outcome, analyses were conducted as per protocol (PP), excluding those subjects with protocol deviations (Fig. 2). We used the Kolmogorov–Smirnov test to assess the normality of data distribution. Continuous variables were presented as means (SDs) or medians (interquartile ranges [IQR]), while categorical variables were expressed as absolute frequencies (percentages). We compared perioperative measurements using Student's  $t$  test or the Mann–Whitney U test as appropriate for continuous variables and the  $\chi^2$  test for categorical variables. For pain scores, between-group differences at all time points postoperatively were analyzed using Mann–Whitney U test with Bonferroni correction (three time comparisons), and  $p$  value  $< 0.017$  was considered statistically significant. For secondary outcomes,  $p < 0.05$  was considered significant.



# CONSORT

TRANSPARENT REPORTING of TRIALS



**Fig. 2** Consolidated Standards of Reporting Trials flowchart. ESPB, erector spinae plane block. ICNB, intercostal nerve block

## Results

### Baseline patient characteristics and intraoperative data

The study flowchart is shown in Fig. 2. From September 2018 to May 2019, 102 patients were assessed for eligibility. After excluding 22 patients, we randomized the remaining 80 into two groups. Seven patients were

excluded after randomization and a total of 73 subjects was included in the final mITT population (for details, see Fig. 2). As shown in Table 1, the two groups were comparable in demographic and baseline clinical variables. The duration of surgery and the number of revascularizations did not differ between the groups.

**Table 1** Baseline characteristics of the study patients

	ICNB Group (n = 37)	ESPB Group (n = 36)	P-value
Age, y	61.5 ± 8.1	63.7 ± 6.7	0.216
Male, n (%)	24 (64.9)	25 (69.4)	0.804
BMI, n (%)			0.243
≤ 24 kg/m <sup>2</sup>	14 (37.8)	19 (52.8)	
> 24 kg/m <sup>2</sup>	23 (62.2)	17 (47.2)	
ASA, n (%)			0.778
II	9 (24.3)	7 (19.4)	
III	28 (75.7)	29 (80.6)	
Hypertension, n (%)	21 (56.8)	22 (61.1)	0.813
Diabetes mellitus, n (%)	14 (37.8)	14 (38.9)	1.000
Hypercholesterolemia, n (%)	13 (35.1)	9 (25.0)	0.446
Thrombotic diseases, n (%)	11 (29.7)	12 (33.3)	0.804
Length of surgery, min	229.5 ± 82.8	237.1 ± 79.0	0.688
No. of revascularizations, n (%)			0.597
1	21 (56.8)	23 (63.9)	
2	9 (24.3)	7 (19.4)	
3	5 (13.5)	5 (13.9)	
4	2 (5.4)	1 (2.8)	

Values are shown as mean ± SD or median (range) or number (%)

ASA indicates American Society of Anesthesiologists classification; BMI, body mass index

### Pain scores and analgesics

As shown in Table 2, in the mITT population, there was no significant between-group difference in the NRS score at movement immediately after extubation (median [IQR], 4.0 [2.0–5.0] vs. 3.0 [2.0–4.0];  $p > 0.017$ ). The PP analysis showed no significant difference in the NRS score at movement between the two groups immediately after extubation (median [IQR], 4.0 [2.0–5.0] vs. 3.0 [2.0–4.0];  $p > 0.017$ ). Use of intraoperative sufentanil was significantly lower in the ESPB than in the ICNB group ( $93.8 \pm 33.6$  vs.  $128.9 \pm 48.4$   $\mu\text{g}$ ;  $p = 0.001$ ). As shown in Table 2; Fig. 3, we found no statistically significant differences between the groups in the NRS score at rest and movement; or in necessity of rescue analgesics at 8, 24, and 48 h. The cumulative AUC of extubation-8 h, extubation-24 h, and extubation-48 h was not statistically different between the groups (Table 2; Fig. 4).

### Recovery data

Recovery data are shown in Table 3. No significant between-group difference was observed in the incidence of postoperative opioid-related AEs. Except for two cases of accidental catheter removal due to ineffective catheter fixation, no patients had block-related AEs. The MV time, time to first flatus, time to first feeding, time to first ambulation, indwelling time of urethral catheter, and length of hospital stay were comparable between the two groups.

### Discussion

In this study, no significant difference in pain scores, AUC of the time NRS curve until 48 h after extubation, necessity of rescue analgesics, or recovery data was found between the ESPB and ICNB groups. The clinical significance of our study is in demonstrating the comparable value of ESPB and ICNB as part of a multimodal analgesic protocol to acute pain control after MIDCAB.

There is no consensus on a gold-standard analgesic strategy for MIDCAB. Traditional high-dose opioid-based analgesia after cardiac surgery is associated with undesirable side effects. Regional analgesia, including novel interfascial block technologies, might provide an opioid-sparing effect and thereby reduce opioid-related AEs. A retrospective cohort study of cardiac surgery via lateral mini-thoracotomy [26] indicated that continuous ESPB was associated with reduced in-hospital opioid consumption compared with a group that received no regional anesthesia, but this study included only 31 cases of MIDCAB. In a previous trial of 60 MIDCAB cases [21], compared with the sham block group, patients in the ESPB group had lower intraoperative fentanyl use and hydromorphone consumption. In contrast, Hoogma et al. [27] observed no clear association between ESPB and severity of pain or opioid consumption during the first 24 h after MIDCAB. In our study, ESPB was administered preoperatively, whereas ICNB was performed during surgical closure. This timing discrepancy likely accounts for the observed reduction in intraoperative opioid requirements within the ESPB group, rather than indicating the superiority of the regional technique itself.

**Table 2** Pain scores and analgesics

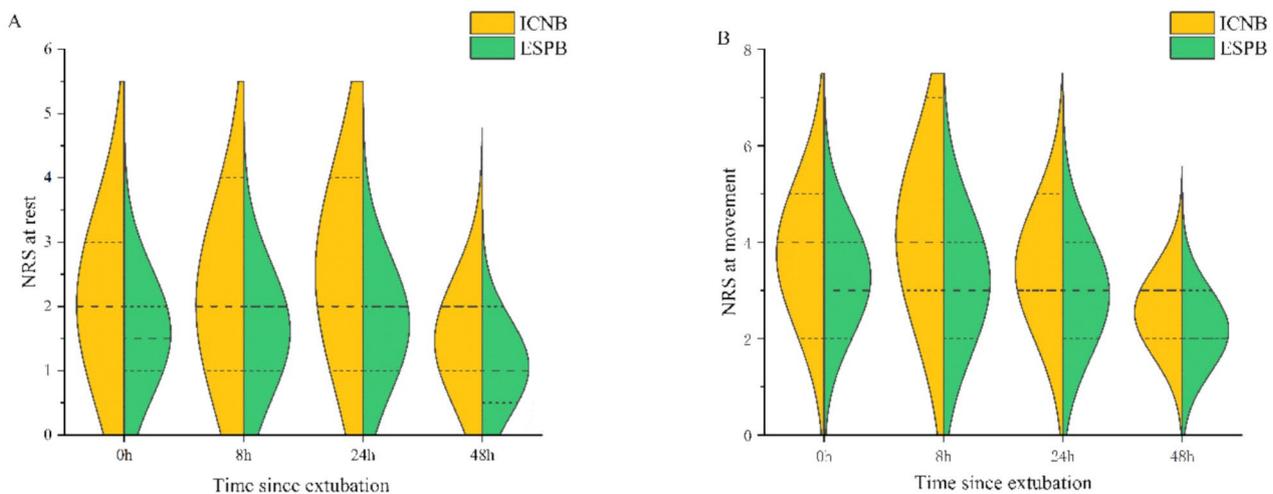
	ICNB Group (n = 37)	ESPB Group (n = 36)	P-value
Primary outcome (MoveNRS-extubation)			
Intention-to-treat analysis	4.0 (2.0, 5.0)	3.0 (2.0, 4.0)	0.162 <sup>a</sup>
Per-protocol analysis	4.0 (2.0, 5.0)	3.0 (2.0, 4.0)	0.088 <sup>a</sup>
Pain post-extubation (NRS)			
RestNRS-extubation	2.0 (0.0, 3.0)	1.5 (1.0, 2.0)	0.176 <sup>a</sup>
RestNRS-8 h	2.0 (0.5, 4.0)	2.0 (1.0, 2.0)	0.352 <sup>a</sup>
RestNRS-24 h	2.0 (1.0, 4.0)	2.0 (1.0, 2.0)	0.052 <sup>a</sup>
RestNRS-48 h	2.0 (1.0, 2.0)	1.0 (0.3, 2.0)	0.077 <sup>a</sup>
MoveNRS-8 h	4.0 (3.0, 7.0)	3.0 (2.0, 4.0)	0.038 <sup>a</sup>
MoveNRS-24 h	3.0 (3.0, 5.0)	3.0 (2.0, 4.0)	0.067 <sup>a</sup>
MoveNRS-48 h	3.0 (2.0, 3.0)	2.0 (2.0, 3.0)	0.060 <sup>a</sup>
Cumulative AUC at rest			
AUC-extubation-8 h	16.22 ± 10.58	12.78 ± 6.18	0.096 <sup>a</sup>
AUC-extubation-24 h	52.54 ± 33.47	39.44 ± 18.96	0.044 <sup>a</sup>
AUC-extubation-48 h	100.21 ± 61.92	72.78 ± 33.05	0.021 <sup>a</sup>
Cumulative AUC at movement			
AUC-extubation-8 h	31.56 ± 13.02	25.89 ± 10.54	0.045 <sup>a</sup>
AUC-extubation-24 h	92.11 ± 36.29	74.78 ± 29.52	0.029 <sup>a</sup>
AUC-extubation-48 h	163.78 ± 58.13	135.78 ± 48.19	0.028 <sup>a</sup>
Intraoperative sufentanil, µg	128.9 ± 48.4	93.8 ± 33.6	0.001*
Rescue analgesics post-extubation			
8 h, n (%)	17 (45.9)	8 (22.2)	0.048 <sup>a</sup>
8~24 h, n (%)	16 (43.2)	9 (25.0)	0.140 <sup>a</sup>
24~48 h, n (%)	8 (21.6)	3 (8.3)	0.190 <sup>a</sup>
Post-operative 48 h oral MME, mg	165 (150, 210)	150 (150, 165)	0.057

Values are shown as mean ± SD or median (range) or number (%)

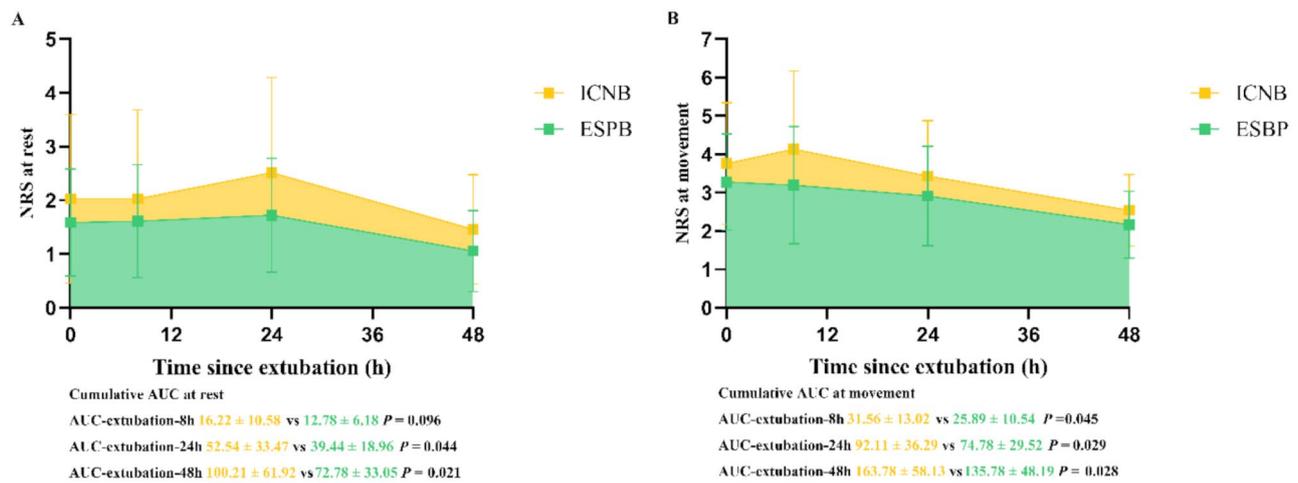
NRS, numeric rating scale. MME, morphine milligram equivalents. Post-operative oral MME was calculated from end of surgery to 48 h post-extubation

<sup>a</sup> Bonferroni correction with the significance level set at a p value < 0.017

\* p value < 0.05



**Fig. 3** A violin plot demonstrating postoperative NRS for pain at rest (A) and movement (B) following extubation. A violin plot shows the volume of the samples at each point by width and lines correspond to the 25th percentile, median, and 75th percentile. NRS, numeric rating scale



**Fig. 4** Comparisons of the overall postoperative analgesic efficacy as indicated by the cumulative AUC of the time-NRS curve. AUC, area under the curve

**Table 3** Recovery data

	ICNB Group (n = 37)	ESPB Group (n = 36)	P-value
Mechanical ventilation time (h)	12.6 ± 5.2	12.6 ± 5.9	0.977
Time to first feeding (h)	6.5 ± 1.8	6.9 ± 1.8	0.309
Time to first flatus (d)	1.9 ± 0.4	1.9 ± 0.6	0.616
Time to first ambulation (d)	2.7 ± 1.0	2.9 ± 0.8	0.337
Indwelling time of urethral catheter (d)	2.6 ± 1.0	2.8 ± 0.9	0.425
Hospital stay (d)	16.2 ± 5.6	17.6 ± 7.2	0.356
Adverse event			
Nausea and vomiting, n (%)	5 (13.5)	3 (8.3)	0.711
Atrial fibrillation, n (%)	7 (18.9)	4 (11.1)	0.515
Delirium, n (%)	1 (2.7)	2 (5.6)	0.615
Pneumonia, n (%)	1 (2.7)	1 (2.8)	1.000

Values are shown as mean ± SD or median (range) or number (%)

Time to first feeding; calculated from extubation. Time to first flatus (d), Time to first ambulation (d): calculated from post-operation

Few studies have compared postoperative pain scores between ESPB and ICNB. In Fiorelli's previous RCT of patients undergoing lung surgery via mini-thoracotomy [28], NRS scores were significantly lower in the ESPB group than in the ICNB group at all time points during the postoperative 48-h period. In a study of patients undergoing thoracoscopic surgery [29], no difference in pain scores was observed between ICNB and single-injection ESPB groups. In a previous study of thoracoscopic surgery [30], the analgesic efficacy of ESPB was non-inferior to that of single shot ICNB with intravenous analgesia. In our current study, no significant difference was found in NRS pain score between the two groups. The inconsistent results of these studies could be attributed to differences in procedures, concentrations of local anesthetic, single injection versus infusion, and a multi-modal analgesic regimen.

Except for NRS and rescue analgesics, we chose the AUC of the time NRS curve as a secondary outcome. Unlike the means or medians of pain scores at specific

time points, the AUC reflects both the intensity and duration of pain. Recently, the AUC of the time NRS curve has been adopted as a primary or secondary outcome in several studies on postoperative analgesia of continuous ESPB [31, 32]. The cumulative AUC of pain scores is intended to provide an overall assessment of the pain experience over a specific period. In the clinical context, these results can assist in comparing the efficacy of different treatment modalities or interventions. For example, a lower cumulative AUC of pain scores might indicate a more effective treatment in reducing the overall burden of pain. In the current study, the cumulative AUC from extubation to 8 h, 24 h, and 48 h showed no statistically significant difference between the two groups, comparable analgesic efficacy between blocks within 48 h.

Application of regional anesthesia might play a pivotal role in facilitating patient recovery after cardiac surgery. Previous placebo-controlled studies on MIDCAB [21] and elective on-pump cardiac surgery with median sternotomy [33] demonstrated that, compared with a sham

block, ESPB was associated with decreased durations of MV and ICU stay. Krishna's study of elective on-pump surgery with median sternotomy [34] revealed that, compared to i.v. analgesics, ESPB was associated with earlier time to ambulation. A study by Fiorelli et al. [28] demonstrated that ESPB provided less respiratory muscle strength impairment than ICNB in patients undergoing lung surgery via mini-thoracotomy, but the duration of MV was not reported. In the current study of patients, no significant difference was observed in duration of postoperative MV between the two groups, and these results are valid only in patient undergoing mini-thoracotomy with antero-lateral approach. MV in our study was long lasting, partly because patients were extubated by physicians in ICU according to relatively strict criteria, and the fast-track strategy was not used during this period.

The 2022 ESAIC/ESRA guidelines classify the ESPB as a low-bleeding-risk procedure permissible for patients on antithrombotic therapy [35]. However, our study (registered in 2019) excluded patients with coagulation disorders. Implementing the updated guidelines enables the safe expansion of ESPB use to wider patient populations. While ESPB is generally safe as shown in our study, inadvertent hemodynamic instability, potentially due to epidural spread of local anesthetic, has been reported in frail patients [36]. Moreover, fascial blocks are volume-dependent nerve blocks. Local anesthetic systemic toxicity (LAST) has been reported in single-dose ESPB when large volumes of local anesthetics are used [37, 38] or continuous infusions in patients with cardiac/hepatic dysfunction [39]. Risk mitigation strategies might be considered such as lower LA concentrations, vigilant plasma drug monitoring in critically ill patients, and adjunct use to enhance analgesia when reducing LA doses. Dexmedetomidine [40], magnesium sulfate, and ketamine [41] have demonstrated efficacy as adjuvants to ESPB regimens in opioid-free anesthesia, particularly for vulnerable populations.

This study has several limitations. Firstly, due to the different connection areas of the patient-controlled analgesia pump, blinding patients to group allocations was not possible. However, the nurses responsible for assessing pain were blinded to the protocols, which enhanced the objectivity of evaluations. Second, age-related pharmacokinetic variations and ideal body weight (IBW)-based dosing are critical considerations for local anesthetic regimens. However, as our study was powered to detect clinically meaningful differences in the primary outcome, a post hoc age/IBW subgroup analyses were not performed due to limited participant numbers. Thirdly, ESPB was administered preoperatively whereas ICNB was performed postoperatively, introducing potential bias. The results demonstrated higher intraoperative opioid requirements associated with block administration

timing, supporting preoperative ICNB implementation in clinical practice.

## Conclusion

In conclusion, postoperative analgesic effect between ESPB and ICNB did not differ in patients after MIDCAB. Further studies could focus on refining dosing and infusion regimens of regional blocks to optimize analgesic effects.

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## Author contributions

Conceptualization and methodology: TW, XW, ML, YL; Formal analysis and investigation: TW, XW, ZY, JY, YJ, DY; All authors participated in revising the manuscript substantially; Writing, review and editing: ML and YL; Supervision: ML and YL.

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## Data availability

The raw data and materials used and/or analyzed during the current study will be available upon request from the corresponding authors.

## Declarations

### Ethics approval and consent to participate

This study was approved by the the Institutional Ethics Committee of Peking University Third Hospital (No. IRB00006761-M2018141). The study was retrospectively registered in the Chinese Clinical Trial Registry (identifier: ChiCTR1900022388) on Apr 09, 2019. The study was conducted in accordance with the Declaration of Helsinki. All participants provided informed consent to participate in the study.

### Consent for publication

Not applicable.

### Competing interests

The authors declare no competing interests.

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