



# Efficacy of bilateral PECS II block in postoperative analgesia for ultrafast track pediatric cardiac anesthesia

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## ABSTRACT

**Background:** Effective analgesia after cardiac surgery contributes to fast recovery, and discharge from the critical care unit. Aim: This study was conducted to evaluate PECS II block for controlling post-sternotomy pain in pediatric population in ultrafast track cardiac surgery.

**Methods:** In this double-blind, randomized control trial, 40 children, 1–5 years old, underwent cardiac surgery via median sternotomy, Group (A) control: Analgesics were administered intravenously. Group (B): received 0.25% bupivacaine at 0.5 ml/kg divided equally to both sides for PECS block.

**Results:** PECS group had lower median Modified Objective Pain Score (MOPS) immediately, two, four, and 6 h postoperatively. PECS group had lower median fentanyl utilization by 35% than the control group with median utilization of 2.72 (95% CI 2.490–2.960) mic/kg/in the first 24 hours in contrast to 4.17 (95% CI 3.834–4.516) mic/kg/in the first 24 hours in the control group ( $P < 0.001$ ). First rescue analgesia was later in PECS group compared to the control group with median time (7 hours) and (2 hours), respectively. Furthermore, Pediatric Anesthesia Emergence Agitation (PAED) score was lower in the intervention group with median 9.5 and 12 in the control group ( $P < 0.001$ ). PECS group had shorter ICU stay than the control group ( $P < 0.05$ ), with mean ICU stay 52 hours (95% CI 43.522–62.378) compared to 80.40 hours (95% CI 64.310–96.490).

**Conclusion:** PECS block is an efficient technique that can be implemented as an integral part of fast-track cardiac surgery.

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## KEYWORDS

PECS; pediatric cardiac anesthesia; sternotomy; regional; fascial blocks

## 1. Background

According to the government of Egypt, the proportion of the population below the national poverty line elevated from 16.7% in 1999/2000 to 32.5% in 2017/2018 [1]. More than 130 dollars per capita was spent on health care in 2018, representing less than 5% of the country's GDP. To save money on healthcare, fast-track anesthesia has evolved into ultra-fast track anesthesia (UFTA), which is defined as extubation within 1 hour of surgery in the operating theater. UFTA is expected to reduce postoperative complications, improve hemodynamics, and reduce the length of stay in the ICU [2]. Anesthesia management, such as anesthesia technique, anesthetic drugs, body temperature control, and multimodal perioperative analgesia is the primary focus of UFTA [3]. Optimized analgesia in cardiac patients augments rapid recovery, mobilization, and early discharge from the Intensive Care Unit (ICU) [4].

For many years, thoracic epidural and paravertebral blocks have been the focus of clinical research. Performing deep nerve blocks is troublesome, due to expected complications, such as epidural hematomas

and spinal cord injury [5]. An innovative regional analgesic technique called the Pectoral Nerve Blocks (PECS) that relies on injection of local anesthetic (LA) between the muscles of the chest wall to anesthetize nerves that run in the fascial planes. PECS I and PECS II (modified PECS I) are interfacial blocks that were developed by Blanco et al. who provided an ultrasound description of PECS block [6].

## 2. Methods

### 2.1. Ethical approval and trial registration

The protocol of this study is registered in the Pan African Clinical Trial Registry ([www.pactr.org](http://www.pactr.org)) database ID No. (PACTR202111605483298) after obtaining the approval of the Faculty of Medicine, Ethics Committee of Ain Shams University, approval number (FMASU R 178/2021).

For each patient, the legal guardian (the father according to Egyptian law) and his mother were informed about the whole study process and details with expected complications before obtaining an informed written consent to enroll his child in the study with his right to withdraw at any time.

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We agree that all copyright ownership is transferable to the Egyptian journal of Anesthesia when the manuscript is accepted for publication. We certify that the submitted article will not constitute "Redundant Publication". This study is not previously published nor submitted elsewhere, not currently under consideration for publication in another journal and the methods employed respect the Helsinki Declaration of 1975, as revised in 1983.

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## 2.2. Randomization and group allocation

In this double-blind, randomized control trial, 40 children of both sexes, between 1 and 5 years of age, underwent cardiac surgical procedures via midline sternotomy, as described in the flow diagram (Figure 1). Patients with past history of allergy to local anesthesia, previous surgery, patients whose parents or surgeon refused, patients with known coagulopathy, preoperative critically ill, urgent operations, patients who did not meet the extubation criteria at the end of surgery, or if they were reintubated in the intensive care unit (ICU) for any reason were excluded from the study.

Patients who met all the study's inclusion criteria were randomly allocated by their national number to either group (A) or group (B) of 20 patients each.

**Group (A) control:** Analgesics were administered intravenously to control.

**Group (B) PECS:** was given 0.25% bupivacaine injection below pectoralis minor muscle and above serratus anterior (PECS II block) in volume of 0.5 ml/kg divided equally to both sides (0.25 ml/Kg on each side).

Blocks were given by the first author according to a closed opaque envelop given to him in the file of the patient without attendance of any of the other authors. Postoperative data were recorded by ICU residents and nurses (not involved in the study) in ICU sheets. Then data were collected in the next morning,

during ICU round, by the last author who was blind to the patient's group (i.e., whether the child received block or not) in absence of the first author.

## 2.3. Sample size

After reviewing the results of a previous study (Kaushal et al., 2019) [78], but using another technique (i.e., bilateral erector spinae plane (ESP) block) of pediatric patients presenting for cardiac surgery via midline sternotomy, the sample size was calculated using the PASS 11 programme, with power set to 95% and alpha error set at 5%. The means of pain score by MOPS assessment at 6 hours postoperatively was lower in patients who received ESP block than those with no block [(3.2 ± 0.48 versus 3.97 ± 0.71, respectively)]. Consequently, a sample size of 40 pediatric patients (20 patients in each group) was sufficient to achieve the study objective.

## 2.4. Randomization

After obtaining consent to be enrolled in the current study in the preoperative visit, patients were randomly allocated in a ratio of (1:1) in a double-blinded manner using a computer-based algorithm based on their national ID number. A senior anesthesiologist expert

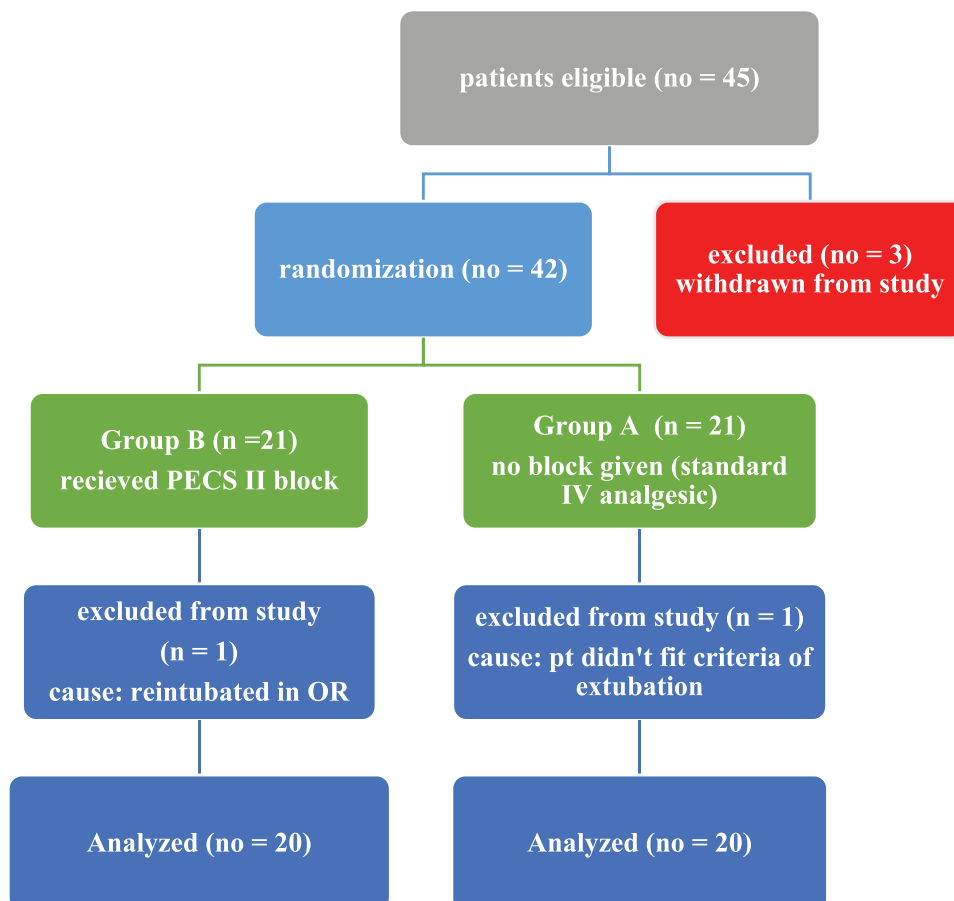


Figure 1. Flowchart demonstrating patient allocation.

who was not involved in the study administered the block according to the sealed envelope he received, to provide either PECS or no block (control group).

## 2.5. Anesthesia procedure

Preoperative anesthetic evaluations included complete history taking, comprehensive clinical examination, complete blood count (CBC), coagulation profile, as well as preoperative ECG, echocardiography, and chest X-ray.

After the patients arrived at the operating room, their identity was double-checked in preparation for surgery. Then intravenous catheter was secured, and preoperative sedation with 0.03 mg/kg midazolam was administered, then standard monitoring in the operating room, which included an electrocardiogram (ECG), radial arterial invasive blood pressure (IBP) line, pulse oximetry (SpO<sub>2</sub>), temperature, and end-tidal CO<sub>2</sub>.

After the establishment of the endotracheal tube, 5 Fr central venous lines were placed in the internal jugular vein or femoral vein using ultrasound guidance after standard induction of general anesthesia with 2 µg/kg fentanyl + 3-5 mg/kg thiopentone sodium + 0.5 mg/kg atracurium besylate with 1.0 percent - 1.5 percent isoflurane inhalation, 10 µg/kg/min atracurium infusion, and 0.5-1 µg/kg/hour fentanyl infusion used to maintain anesthesia.

## 2.6. Cardiopulmonary bypass technique

Surgical sterilization and draping were done followed by skin incision, sternotomy, and tissue dissection. Heparin sodium in a dose of 4 mg/kg was given intravenously and after 5 minutes activated clotting time (ACT) sampled targeting a level > 480 seconds. Aortic cannulation was done by surgeon followed by bi-caval venous cannulation and institution of cardiopulmonary bypass under mild hypothermia with core temperature between 32 and 34°C. Aortic cross clamp was applied and infusion of cold blood cardioplegia at a dose of 20 ml/kg/30 minutes (if needed as bidirectional Glenn was done without aortic cross clamp). After surgical completion, weaning of cardiopulmonary bypass was done with aid of inotropic support according to cardiopulmonary academy protocol and after decannulation protamine sulfate infusion was started at a ratio of 1:1 of given heparin dose, targeting baseline level of ACT. The last step was surgical hemostasis and closure, at this step patients of both groups received 15 mg/kg IV paracetamol and 0.25 mg/kg ketamine.

## 2.7. The procedure of PECS block

PECS II block was administered to group B after skin closure and wound dressing as follows: Following skin disinfection, a 5–10 MHz linear ultrasound probe (SonoSite Edge, Bothell, Washington) was placed at

the level of midclavicular line, and then moved laterally toward the axilla till three muscles appeared in the following order from superficial to deep: pectoralis major, pectoralis minor, and serratus anterior muscles, then a 20-gauge, 50-mm block needle was inserted in-plane approach craniocaudally. Bupivacaine 0.25% in a volume of 0.5 ml/Kg was prepared, divided equally to both sides (0.25 ml/Kg on each side) and injected into the fascial plane below the pectoralis minor and above serratus anterior muscle, with muscle detachment observed [7].

Patients in both groups were extubated after meeting the extubation criteria (consciousness, hemodynamic stability, peak inspiratory pressure (PIP) >20 cm H<sub>2</sub>O, no residual neuromuscular blockade, and acceptable arterial blood gas analysis), and those who did not meet the criteria were ruled out from the study.

## 2.8. Assessment of outcomes

Patients from both groups after admission to the ICU were managed according to the ICU protocol: standard monitoring, IV analgesic paracetamol 7.5 mg/kg Q 6 hr, and other standard management. An ICU nurse (who was not involved in the study) documented the Modified Objective Pain Score (MOPS) at 0, 2, 6, and 12 hours after surgery (Table 1).

Rescue analgesia was given when MOPS score was ≥ 4 at rest, comprising 0.5 to 1 mcg/kg of fentanyl (With a maximum dose of 1 to 2 mcg/kg/dose each time and repeated at 30 to 60 minutes according to patients' response) to maintain MOPS < 4 [9].

**Primary outcome:** MOPS at 6 hours postoperative.

**Secondary outcomes:** Postoperative MOPS immediately after extubation, 2, 4, and 12 hours, total postoperative fentanyl consumption in the first 24 hours, Pediatric Anesthesia Emergence Delirium (PAED) score upon admission to the ICU (Table 2), time to first rescue analgesia (rescue analgesia given in case of breakthrough pain MOPS ≥ 4 in form of 0.5 mcg/kg fentanyl), the incidence of postoperative nausea and

**Table 1.** Modified Objective Pain Score (MOPS) [10].

Criteria	Finding	Points
Crying	none	0
	consolable	1
	not consolable	2
Movement	none	0
	restless	1
	thrashing	2
Agitation	asleep/calm	0
	mild	1
	hysterical	2
Posture	normal	0
	flexed	1
	holds injury site	2
Verbal	asleep/no complaint	0
	complains/cannot localize	1
	complains/can localize	2

**Table 2.** The Pediatric Anesthesia Emergence Delirium (PAED) scale [11].

Criteria	Not at all	Just a little	Quite a bit	Very much	Extremely
1. The child makes eye contact with the caregiver/parent	4	3	2	1	0
2. The child's actions are purposeful	4	3	2	1	0
3. The child is aware of his/her surroundings	4	3	2	1	0
4. The child is restless	0	1	2	3	4
5. The child is inconsolable	0	1	2	3	4

vomiting (PONV), extubation time in minutes, the requirement of reintubation in ICU, ICU stay, and length of hospital stay.

### 2.9. Statistical package and analysis

Values were presented as numbers and proportions or mean (95% confidence interval) for normally distributed data and as median and range for those following other distributions than normal. The distribution of qualitative variables among patient groups was compared by the chi-square test. Quantitative variables were checked for normality by the Shapiro–Wilk test. The means of normally distributed continuous variables were compared between groups using the unpaired t-test. Data following other distributions than normal were compared between groups by the Mann–Whitney test. All tests will be bilateral, and the level of significance was determined at a P-value of <0.05. Inferential statistics were performed by statistical software IBM-SPSS version 24

**Table 3.** Demographic data of both groups.

	control (Group A) n = 20	Pecs (Group B) n = 20	P-value
	mean (95% confidence interval)	mean (95% confidence interval)	
age (months)	17.05 (95% CI 12.3 to 21.8)	17.1 (95% CI 13.3 to 20.9)	0.987
weight (Kg)	10.2 (95% CI 8.39 to 12)	10.45 (95% CI 9.07 to 11.8)	0.831
height (cm)	74.15 (95% CI 69.7 to 78.6)	75 (95% CI 71.6 to 78.4)	0.769
body surface area (m <sup>2</sup> )	0.4531 (95% CI 0.4 to 0.506)	0.4631 (95% CI 0.421 to 0.506)	0.776

### 3. Results

The current study enrolled 40 patients (20 in each group). **Group A** (control) who received only systemic intravenous analgesic without any block and **Group B** (PECS) who received PECS II block in addition to standard intravenous analgesics.

Regarding demographic data, both groups were homogenous without statistical significance between groups regarding age, body weight, height, body surface area, and gender (Table 3). Seven patients were with down syndrome 4 in group A and 3 patients in group B. The surgical procedures conducted in both groups were ASD closure, VSD closure, PAVC repair, bidirectional Glenn, and Fallot tetralogy repair (Table 4, Table 5).

Regarding postoperative fentanyl consumption (Table 6), PECS block was decreased by 35% than the control group with a median utilization of 2.72 ug/kg/ first 24 hours in contrast to median fentanyl utilization in the control group 4.17 ug/kg/ first 24 hours (P-value <0.001).

**Table 4.** Gender, type of operation and preoperative risk scores of both groups.

	control (Group A) n = 20		Pecs (Group B) n = 20		Chi-Square	df	P-value
	n	% Within-group	n	% Within-group			
Gender							
Male	10	50.00%	9	45.00%	100	1	0.752
Female	10	50.00%	11	55.00%			
type of surgery					1.152	4	0.886
VSD	8	40%	6	30%			
Fallot tetralogy	5	25%	7	35%			
PAVC	2	10%	1	5%			
Bidirectional Glenn	3	15%	3	15%			
ADD	2	10%	3	15%			
associated congenital anomalies					0.173	1	0.677
Down S	4	20%	3	15%			
None	16	80%	17	85%			
Risk Adjustment for Congenital Heart Surgery (RACHS) score					0	4	1
category 1	3	15%	3	15%			
category 2	13	65%	13	65%			
category 3	4	20%	4	20%			
ASA physical status					0.95	4	0.62
II	2	10%	3	15%			
III	10	50%	7	35%			
IV	8	40%	10	50%			

**Table 5.** Intraoperative data for both groups.

	control (Group A) n = 20	Pecs (Group B)	T statistic	P-value
	mean (95% confidence interval)	mean (95% confidence interval)		
duration of surgery (hours)	3.625 (95% CI 3.309– 3.941)	4.1450 (95% CI 3.741– 4.549)	1.936	.060
CPB time (min)	56.85 (95% CI 42.918– 70.782)	61.80 (95% CI 46.572– 77.028)	−0.458	.649
aortic cross-clamp time (min)	32.65 (95% CI 22.429– 42.871)	33.25 (95% CI 22.486– 44.014)	−0.077	.938
intraoperative blood transfusion (ml/ kg)	12.10 (95% CI 11.602– 12.598)	11.95 (95% CI 11.674– 12.226)	0.5033	0.6176
intraoperative fentanyl (ug/kg)	3.10 (95% CI 2.756– 3.444)	3.40 (95% CI 2.912– 3.888)	0.960	0.343
time from the end of anesthesia till extubation (min)	17.75 (95% CI 15.733– 19.767)	15.75 (95% CI 13.992– 17.508)	1.4279	.161

The PECS block group had a shorter ICU stay than the control group, and a mean ICU stay of 52 hours (95% CI 43.522–62.378) in the PECS group and 80.40 hours (95% CI 64.310–96.490) in the control group (P-value <0.05) (Table 6).

The first call for rescue analgesia was later in the PECS group than in the control group with a median time in the control group of 2 hours when it was 7 hours in the PECS group. Also, postoperative agitation calculated by PAED score was lower in the intervention group with a median of 9.5 and 12 in the control group that was statistically significant with a P-value <0.001 (Table 7).

**Table 6.** Postoperative data of both groups.

	control (Group A) n = 20	Pecs (Group B) n = 20	T statistic	P-value
	mean (95% confidence interval)	mean (95% confidence interval)		
PO fentanyl 24 hr (ug/ kg)	4.1750 (95% CI 3.834–4.516)	2.7250 (95% CI 2.490–2.960)	6.685	< .001
ICU stay	80.40 (95% CI 64.310– 96.490)	52.95 (95% CI 43.522– 62.378)	2.8119	<0.05
hospital stay	6.60 (95% CI 5.752–7.448)	5.65 (95% CI 5.164–6.136)	1.85794	<0.05

**Table 7.** Time to first rescue analgesia call and PAED score for both groups.

	median	minimum	maximum	median	minimum	maximum	Mann-Whitney U	Z	P-value
time of first rescue analgesia (hr)	2	1	4	7	4	12	4	−5.288	<.001
PAED score on arrival	12	9	14	9.5	7	12	69.5	−3.625	<.001

Regarding MOPS PECS group had lower MOPS immediately (0 hour), 2, 4, and 6 hours postoperatively (Figure 2).

There was no statistically significant difference between the two groups regarding the incidence of complications, such as PONV, and respiratory complications (Table 8).

#### 4. Discussion

Pain is an undesirable side effect of surgery and requires prompt treatment. We have an ethical obligation to provide appropriate care that contributes to alleviating the severity of postoperative discomfort [12]. Perioperative pain has been shown to increase the risk of postoperative complications in patients undergoing open-heart procedures, including cardiac dysrhythmia, circulatory and pulmonary dysfunction, hypercoagulable state, and wound infection [13].

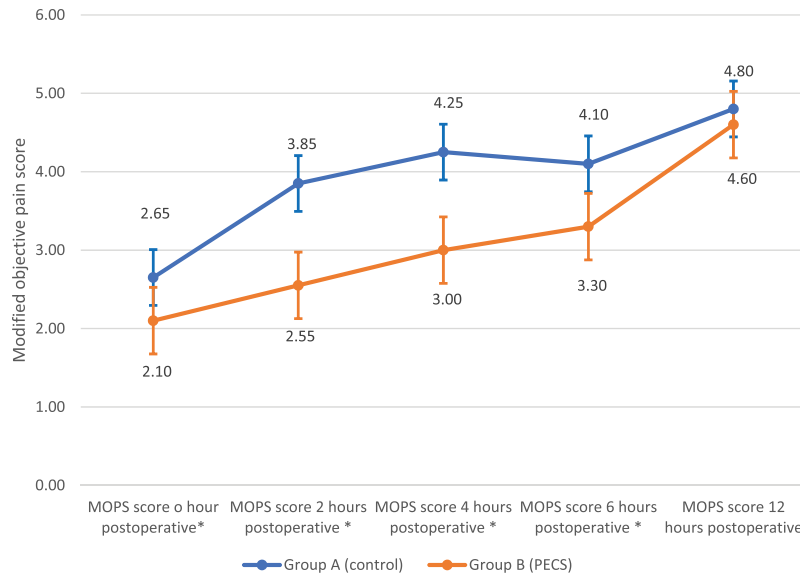
The first postoperative day following adult heart surgery is the most painful and gradually subsides later. Cardiopulmonary bypass (CPB) triggers a systemic inflammatory response, which may intensify postoperative pain. Despite the availability of myriad and different pain score systems, each with a particular pediatric age group, it is difficult to quantify pediatric pain [14].

Systemic opioids have long been used to manage postoperative pain in children undergoing median sternotomy heart surgery [15]. The opioid dose used in pediatric heart surgery has been evolved, and higher doses of opioids have been found to reduce the stress response during surgery [16]. Opioid-induced side effects are more pronounced with high-dose opioids (opioid-based anesthesia) (nausea and vomiting, sedation, constipation, and immune depression). The effect of different fentanyl doses was investigated in RCT to evaluate stress response in congenital heart surgery. A dose of 25–50 mcg/kg fentanyl was recommended for balanced anesthesia to alleviate hemodynamic and metabolic stress. These lower doses do not completely suppress the stress response; nevertheless, they have been recently used to improve early recovery and extubation. Children who have undergone cardiac reoperations may develop chronic pain [17].

PECS II is a development of the PECS I block. The PECS II block has been demonstrated to be as effective in providing analgesia as the paravertebral block [18].

According to the current study, patients who received PECS II block seemed to have lower pain scores by MOPS during the first six hours after surgery than the





**Figure 2.** MOPS score at time intervals (\*) At time interval means that it is statistically significant difference by Mann Whitney test with p-value <0.05.

**Table 8.** Postoperative complications of both groups.

	control (Group A)		Pecs (Group B)		Chi-Square	df	P-value
	n	% Within-group	n	% Within-group			
patients need reintubation in ICU	2	10.00%	2	10.00%	0	1	1
patients developed postoperative respiratory complications	1	5.00%	0	0.00%	1.026	1	1
patients developed PONV	6	31.60%	4	20.00%	0.685	1	0.645

control group, which was reflected in postoperative fentanyl consumption and the first call for rescue analgesia.

Zhang et al. conducted an RCT on a group of 100 children aged 6–60 months undergoing cardiac surgery who were randomly assigned to receive bilateral transversus thoracis plane block (TTP group) or no nerve block. Up to 24 hours after extubation, the TTP group had a significantly lower MOPS than the control group, and the TTP group consumed significantly less fentanyl than the control group, with postoperative fentanyl consumption (ug/kg) in patients who underwent TTP block reaching  $1.48 \pm 0.43$  in contrast to  $3.98 \pm 1.21$  in the control group [19].

The Chinese journal of anesthesia published an article by Xu et al., who utilized the random number table method to divide 32 ASA physical status I or II pediatrics aged 4–15 years who underwent Nuss procedure under general anesthesia into two groups: Erector Spinae plane (ESP) block plus general anesthesia (group EG, n = 16) and general anesthesia (group G, n = 16). In the EG group, bilateral ESP blocks were performed after anesthesia induction. Both groups

received intravenous analgesia after surgery and sufentanil as background analgesia intraoperatively as well as fentanyl as rescue analgesia. FLACC scores were recorded at rest and during coughing at zero, 1, 6, 12, 24, and 48 hours after the operation. FLACC scores were significantly lower in the ESP group at rest within 12 hours of surgery and during coughing within 6 hours of surgery, less intraoperative use of sufentanil reduced postoperative requirement for fentanyl as well as ibuprofen. In addition, there was decreased incidence of hypoxemia, a shorter tracheal extubation time as well as a shorter duration in PACU (P < 0.05). Consequently, they concluded that ultrasound-guided bilateral ESP block could reduce opioid consumption in the perioperative period while improving analgesic efficacy and safety [20].

Monahan et al. conducted a systematic review and meta-analysis involving 605 participants. Patients who received regional block experienced significantly reduced pain levels at each measurement point. Other outcomes examined revealed no differences, such as mechanical ventilation hours, length of ICU stay, and length of hospital stay. No adverse outcomes associated with regional anesthetic procedures (e.g., hypopnea, LA drug toxicity, or neurologic complications) were detected in all trials [21].

According to an abstract published in the American Society of Anesthesiologists in 2018, researchers retrospectively analyzed 32 consecutive charts before November 2017. (PECS block cohort). These patients were then retrospectively matched with patients who had not received PECS blocks before November 2017 (Non-block cohort). The use of pectoral fascial blocks is associated with a significant reduction in opioid consumption intraoperatively, even though there was a non-significant difference in postoperative morphine equivalent consumption in the first 24 hours (24.5 mg

vs. 22.6 mg IV,  $P = 0.65$ ). However, when compared to the non-block cohort, the total intraoperative opioid dosage was substantially lower in the block cohort (44.1 mg vs. 67.7 mg IV morphine equivalents,  $P < 0.001$ ). Since the retrospective nature of this investigation, it is unclear whether institutional therapeutic policies influenced the findings [22].

Furthermore, patients who underwent PECS II block had a lower PAED score when they arrived in the ICU, which is an important factor to consider minimizing increased oxygen consumption and the risk of decannulation or inadvertent chest tube or surgical drain slippage.

Furthermore, more research is necessary to determine efficacy across a variety of patient populations. For example, patients presented for superior Cavo-pulmonary anastomosis (bidirectional Glenn) or total Cavo-pulmonary anastomosis (Fontan) have a significant benefit from fast-track cardiac surgery as extubation shortly after surgery augments venous return with negative intrathoracic pressure along with enhancing the flow to the passive pulmonary circulation arrangement [23].

In the case of sternotomy, it was evident that bilateral PECS II block was more effective than systemic analgesia alone, even though the anatomical explanation is unknown. The anterior branches of the intercostal nerves are distant away to be blocked by PECS block [24]. Nonetheless, they may induce analgesia by lowering pectoral or intercostal muscular spasms. The same conflict is present with erector spinae plane block, despite being commonly used in cardiac surgery, its mechanism of action is still undetermined [25].

The mechanism mediating the hypothesized efficiency of the PECS block is unknown, and its distribution does not include the anterior intercostal branches, which comprise the nerve supply to the sternotomy incision. To determine the mechanism of pain alleviation found in numerous trials including adults and children undergoing cardiac surgery through median sternotomy, further anatomical and radiological research is needed [26].

Even though an injection site in the PECS II block is more lateral than in the parasternal zone, local anesthetics tend to extend in all directions of the fascial plane, reaching the anterior intercostal cutaneous branches medially [6].

The theory of local anesthetic diffusion can be applied to any interfascial plane block; however, some types of interfascial planes may have a broader local anesthetic spread than others, according to Elsharkawy et al. In addition, the deep pectoral fascia is thinner and more mobile than fasciae from other anatomical sites, which could explain how easily local anesthesia diffuses throughout the thoracic wall; nevertheless, further research is needed to validate this concept [27].

The current study has limitations, including a small sample size, we believe that patients might require a rectus sheath block or its equivalent to reduce pain from the mediastinal tube, but a local anesthetic toxic dose was a limitation.

## 5. Conclusion

PECS block is an easy method to perform facial block with evident efficacy to reduce patient pain. However, further research is needed to implement the technique as part of multimodal analgesia in postoperative pediatric cardiac patients to attenuate patients' pain and reduce hospital stay as part of UFTA.

## Disclosure statement

No potential conflict of interest was reported by the author(s).

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