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Review Article

Parasternal Intercostal Nerve Blocks in Patients Undergoing Cardiac Surgery: Evidence Update and Technical Considerations

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In the Enhanced Recovery After Surgery era, parasternal intercostal nerve block has been proposed to improve pain control and reduce opioid use in patients undergoing cardiac surgery. However current literature has reported conflicting evidence about the effect of this multimodal pain management, as procedural variations might pose a significant bias on outcomes evaluation. In this setting, the infiltration of the parasternal plane into 2 intercostal spaces, second and fifth, with a local anesthetic spread under or above the costal plane with ultrasound guidance, seem to be standardized in theory, but significant differences might be observed in clinical practice. This narrative review summarizes and defines the optimal techniques for parasternal plane blocks in patients undergoing cardiac surgery with full median sternotomy, considering both pectointercostal fascial block and transversus thoracic plane block. A total of 10 randomized trials have been published, in adjunct to observational studies, which are heterogeneous in terms of techniques, methods, and outcomes. Parasternal block has been shown to reduce perioperative opioid consumption and provide a more favorable analgesic profile, with reduced postoperative opioid-related side effects. A trend toward reduced intensive care unit stay or duration of mechanical ventilation should be confirmed by adequately powered randomized trials or registry studies. Differences in operative technique might impact outcomes and, therefore, standardization of the procedure plays a pivotal role before reporting specific outcomes. Parasternal plane blocks might significantly improve outcomes of cardiac surgery with full median sternotomy, and should be introduced comprehensively in Enhanced Recovery After Surgery protocols.

Key Words: cardiac surgery; cardiopulmonary bypass; parasternal block; multimodal, ERAS

LIBERAL NARCOTIC THERAPY allows hemodynamic stability in cardiac anesthesia, but results in significant side effects such as hyperalgesia, gastrointestinal alterations, prolonged mechanical ventilation, and respiratory depression that might negatively impact short-term outcomes.[1,2] Therefore, recent guidelines for perioperative care in cardiac surgery recommend multimodal pain management to decrease opioid use, and Enhanced Recovery After Surgery (ERAS) protocols have been shown to ensure early tracheal extubation and shorter duration of intensive care unit and hospital stays.[1] Parasternal intercostal nerve block has been proposed to improve pain control and reduce opioid use in patients undergoing cardiac surgery requiring sternotomy and/or cardiopulmonary bypass, and this might significantly improve the results of current ERAS protocols.[1,3] However current literature has reported conflicting evidence about the effect of this multimodal pain management, as procedural variations might pose a significant bias on outcomes evaluation. This narrative review summarizes and defines the optimal technique for parasternal intercostal nerve block in patients undergoing cardiac surgery with full median sternotomy.

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Methods

Electronic searches were performed of Ovid Medline and PubMed from their inception to March 2022. To improve sensitivity, the terms "cardiac surgery" or "sternotomy" and "parasternal"/"parasternal block"/"parasternal intercostal nerve block" were used either as key words or medical subject heading terms. The reference lists of all the retrieved articles then were reviewed using inclusion/exclusion criteria. Eligible literature for the present review included those in which patients underwent any cardiac surgery procedure with parasternal intercostal nerve block, using full median sternotomy as the surgical approach. When duplicate studies were identified with increased follow-up lengths or accumulating numbers of patients, only the most complete reports were selected for assessment at each time interval. All of the publications were limited to those involving human subjects. Case reports, abstracts, editorials, and reviews were excluded. English language restriction was imposed. Additional articles were retrieved by manually searching the reference lists from the extracted papers. The outcomes of interest included opioid consumption and quantification of postoperative pain.

Study Selection Criteria

Opinion articles, reviews, animal studies, and reports with duplication data have been excluded. The Patients, Intervention, Comparator, Outcomes, Study design (PICOS) study design was used for inclusion/exclusion criteria (Table 1). Studies were included if they were randomized controlled trials or observational studies dealing with patients undergoing cardiac surgery with the use of parasternal block and reported at least 1 outcome of interest. To identify eligible studies, a 2-step selection process was applied. Three reviewers (L.S., A. N., and F.C.) checked eligibility criteria and selected the studies for inclusion in the review. Three researchers (L.S., A.N., and F.C.) independently screened the records for inclusion and were blinded to each other's decisions. Disagreements between individual judgments were resolved by consensus and consultation with senior authors. Studies were excluded if they did not meet all criteria.

Table 1
PICOS Criteria for Inclusion and Exclusion of Studies Into the Review

Parameter	Inclusion Criteria	Exclusion Criteria
Patients	Patients undergoing cardiac surgery Full median sternotomy	Minimally invasive procedures
Intervention	Parasternal block	-
Comparator	Standard protocols	-
Outcomes	Opioid use Intensive care unit stay Duration of mechanical ventilation Postoperative complications (as described by single studies)	-
Study design	RCTs Observational studies Case series Letters publishing original data	Repeat publications of the same analysis or dataset Conference abstracts Editorials and opinion pieces Books or grey literature Restrictions: English language

Abbreviation: PICOS, Patients, Intervention, Comparator, Outcomes, Study design;RCT, randomized controlled trials.

Data Extraction and Quality Assessment

Three investigators (L.S., A.N., and F.C.) independently extracted data from all of the eligible studies using a standardized file. The data were retrieved only from the articles, and no attempt was made to get missing data from the authors. Any disagreement was solved by consensus.

Results

Postoperative local anesthetic administration in the intercostal space under direct vision by the surgeon ensures adequate delivery of drugs, minimizes bleeding complication, and inadvertent administration in blood vessels. Preincisional (preoperative) infiltration/nerve block with local anesthetic agents has been used in several surgical settings and has been shown recently to have comparable pain relief during the postoperative period after cardiac surgery through the sternotomy approach.[3]

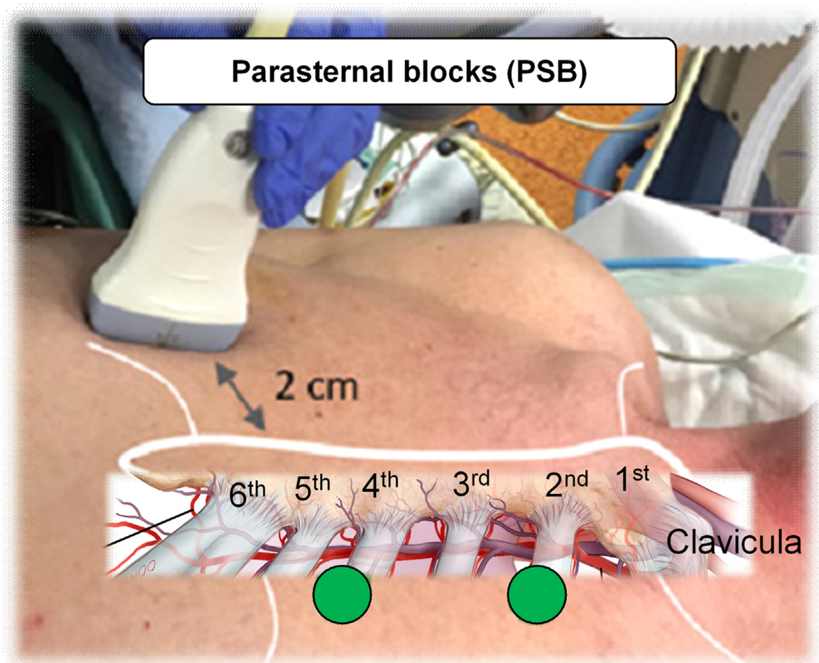
Definitions and Technical Details

Parasternal block was born as a blind technique used by surgeons after the closure of a sternal wound with metal wires, and immediately revealed adequate efficacy and safety profile. With the diffusion of ultrasound-guided anesthesia and the ERAS protocols, cardiac anesthesia developed. In the latest years, several authors tried to define the correct timing, dosage, and muscular plane to obtain better results with local anesthetic infiltration and to reduce adverse events correlated to accidental lesions of nearest vessels and organs (ie, mammary artery and lungs) (Fig 1).

Although blind infiltration was executed on each intercostal space from the second to the sixth and around drainage access ports without any indication about depth of injection and distance from vital structure, an ultrasound guarantees precision and safety, reducing the number of punctures that usually are suggested to be performed on the second and fifth or sixth intercostal spaces.

Many authors described several different techniques to obtain an effective parasternal block, revealing that the same locoregional anesthesia could be obtained by many ways of ultrasound visualization of the intercostal muscular plane and injection sites.

As previously described,[1,2,4-11] different planes of the parasternal region could be a target of locoregional anesthesia to produce effective pain control. The ultrasound visualization of parasternal osteomuscular structures, 2 cm lateral to the sternal



In-plane approach is recommended for administration of local anesthetic. Transverse approach might be useful to identify the trasversus thoracis muscle (deep to the intercostal muscle and superficial to the pleura).

A 6-to-13 MHz linear probe is placed at the level of first through fourth / fifth rib interspaces. Anesthetic is infiltrated from the 2nd to the 5th/6th intercostal space.

The internal mammary artery runs between internal intercostal and transversus thoracis muscles, 1.5 - 2.5 cm lateral to the border of the sternum. Nipple lane identify the fourth rib interspace.

Fig 1. Parasternal blocks: anatomic landmarks. PSB, parasternal blocks.

edge in the sagittal plane, reveals a sandwich composed from skin to lung of soft subcutaneous tissues, major pectoralis muscle, exterior intercostal muscles, interior intercostal muscles, internal mammary artery (when correctly visualized), transversus thoracic muscle, and pleura.

Modern anesthesia recognizes 2 functional planes that could be considered an adequate target of local infiltration for parasternal plane block (PSB): pectointercostal fascial block (PIFB), between the major pectoralis muscle and exterior intercostal muscle, and the transversus thoracic plane (TTP), a deeper block between the interior intercostal muscle and transverse thoracic muscles. Pectointercostal fascial block has been proposed as a simpler block because it is superficial and away from internal mammary arteries and pleura,[4,5,9] and is the one that generally is investigated in clinical studies due to high reproducibility and low risks.[4-9]

The current ultrasound-guided approach[4-9,12] is defined conventionally as the infiltration of the PSB plane on 2 intercostal spaces, second and fifth or sixth, with a local anesthetic spread under or above the costal plane. However, the access drainage ports down to the xyphoid process are not reached by local anesthetic and are usually the site of local infiltration.

The best description of PIFB and TTP has been done by Sepolvere et al.[4-9] An ultrasound linear probe must be positioned in the sagittal plane between 1.5 cm and 2.5 cm from the lateral sternal edge, second and fifth or sixth intercostal spaces must be identified, and then a smooth needle is introduced into the plane until it reaches the parasternal plane or transversus thoracic plane.[4,5,9]

Particular attention must be used approaching the internal mammary artery, as discussed by Sepolvere et al.[4,9], but it could be identified easily using the ultrasound Doppler on anechoic linear structures, or directly by Doppler, and then avoided during infiltration of TTP.[9]

Obviously, a deeper block increases theoretical risk of internal mammary artery injury, but this has not been demonstrated in the literature. Nowadays, the authors who suggested TTP block described some tricks to visualize and avoid internal mammary artery with the use of ultrasound guidance, but the superior efficacy and greater diffusion of TTP block has not been documented widely or adequately investigated in current literature.[4,9]

Figure 2 summarizes the current approaches for PIFB and TTP, highlighting echographic markers, technical tips, and potential confounders or complications.

Results From Clinical Studies

The results were consistent for the predicted efficacy of locoregional anesthesia in reducing intra- and postoperative opioids and somesthetic and neuropathic pain in the first 24-hour postoperative period. Some more randomized clinical

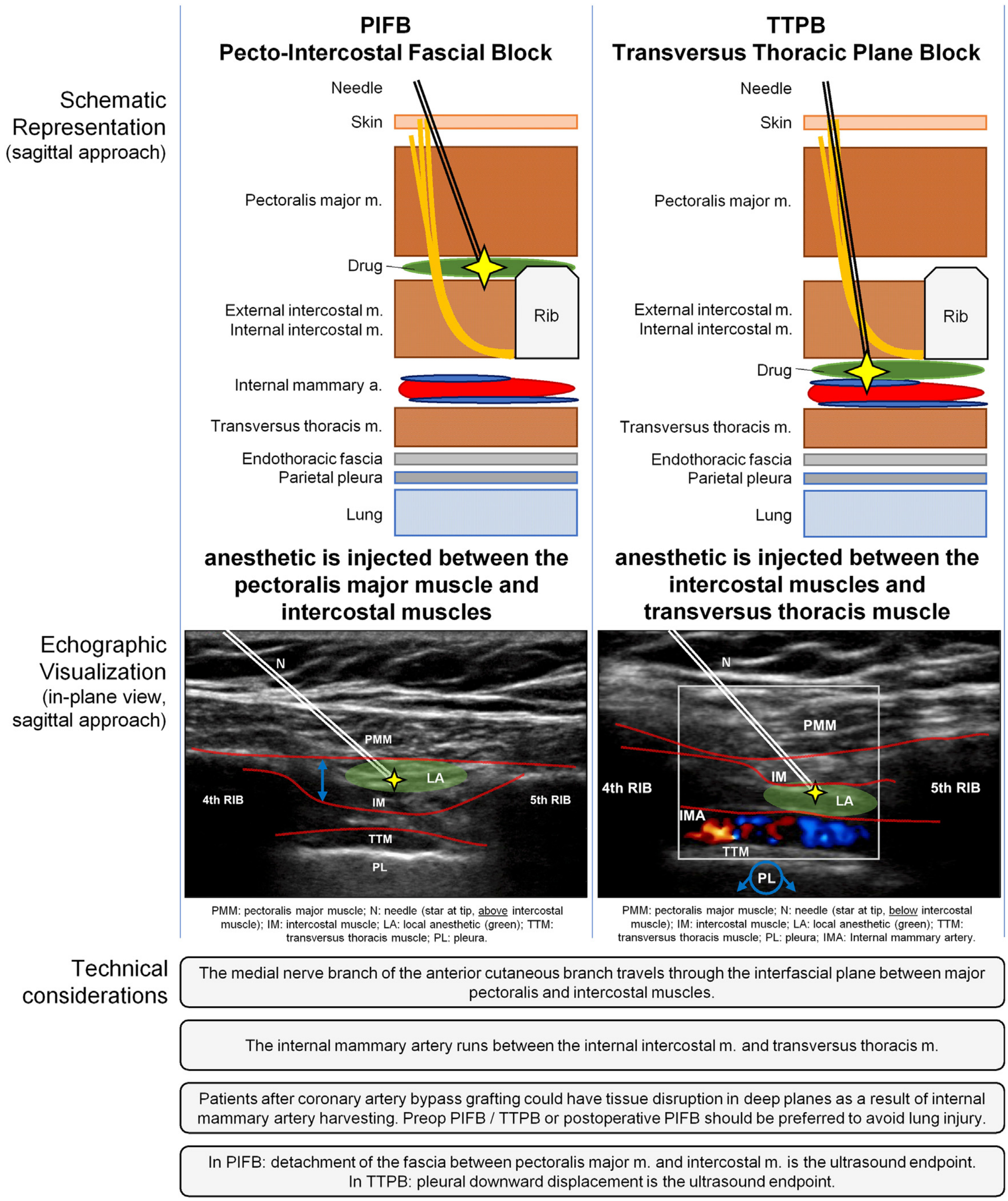


Fig 2. Parasternal blocks (pectointercostal fascial block and transversus thoracic plane block, sagittal approach): differences, technical considerations, and echographic markers. PIFB, pectointercostal fascial block; TTPB, transversus thoracic plane block.

trials (RCTs) should sustain the hypothesis that locoregional anesthesia with bilateral parasternal block should become a consolidated practice in management of postoperative pain after median sternal access surgery.[1-3,13-20] Also, the term "parasternal intercostal plane block" is not unambiguous, as different techniques with slightly different approaches have been described throughout the literature, and an alternative ultrasound approach could be used.

A total of 10 randomized trials have been published about this topic (Table 2). Intraoperative data and operative details have been summarized in Table 3. Parasternal intercostal nerve block was introduced into the anesthesia scenario in 2005 by McDonald et al.[13] when they described blind postoperative parasternal block executed by a surgeon with levobupivacaine, and evaluated its efficacy and safety in a placebo-controlled double-blind randomized trial, recruiting 17 patients. Even if it was a small series, they evidenced a significant benefit in terms of postoperative analgesia requiring less opioid consumption in the first 4 hours after surgery and no rescue doses of analgesics compared with placebo, with total morphine use in 24 hours of 20.8 ± 6.2 mg versus 33.2 ± 10.9 mg, and 0 patients

Table 2
Baseline Characteristics and Study Outcomes of Randomized Trials

Study	Population	Baseline Characteristics, Control Group	Baseline Characteristics, Treatment Group	Comparison	Main Outcomes Related to the Use of Parasternal Block
Bousquet et al. 2021[2]	Patients 58-71 y old undergoing cardiac surgery	Placebo = 10 Age: 65 ± 6 BMI: 25.8 ± 5.5	Ropivacaine = 10 65 ± 6 23 ± 4	A total of 20 mL of a ropivacaine 2 mg/mL via parasternal and bilateral ESPB	Decreased use of morphine at 24 h (12 ± 8 *v* 43.5 ± 8) and at 72 h (30 ± 20 *v* 115 ± 60) No differences in VAS scores and ICU stay
McDonald et al. 2005[13]	Patients 18-80 y old undergoing cardiac surgery with or without CPB	Placebo = 9 Sex (m/f): 8/1 Age: 64 ± 11 BMI: 28.1 ± 4.2	Levobupivacaine = 8 8/0 61 ± 9 29.7 ± 1.9	54 mL of 0.25% LB via parasternal block	Decreased use of morphine (20.8 ± 6.2 *v* 33.2 ± 10.9), improved pO_2 at extubation. No differences in VAS scores
Barr et al. 2007[14]	Patients 40-80 y old undergoing cardiac surgery with or without CPB, no emergency	Placebo = 45 Sex (m/f): 35/8 Age: 60 ± 15 BSA: 1.9 (1.8-2.0)	Ropivacaine = 43 34/11 62 ± 18 1.9 (1.9-2.0)	0.75% ropivacaine via parasternal intercostal block or Saline before closure of sternal wound	Decreased use of morphine at 12 h (12 *v* 23.2) and at 24 h (18.8 mg *v* 23.7 mg); NRS score halved
Baki et al. 2016[15]	Patients 40-75 y old undergoing coronary artery bypass graft surgery with or without CPB, no emergency	Placebo = 41 Sex (m/f): 32/9 Age: 60.22 ± 13.27	Levobupivacaine = 40 31/9 64.18 ± 10.46	25 mL of levobupivacaine via parasternal intercostal block	Decreased tramadol consumption in the first 24 hours halving opioid requirement; simultaneous reduction in VAS scores
Padala et al. 2020[3]	Patients 20-50 y old undergoing cardiac surgery with or without CPB, no emergency	Preoperative = 43 Sex (m/f): 18/25 Age: 39.27 ± 12.64 BMI: 22.64 ± 4.10	Postoperative = 41 18/23 35.34 ± 11.33 21.63 ± 3.80	4 mL of 0.25% bupivacaine via parasternal block	Decreased intraoperative opioids consumption; no differences in total opioids requirement and VAS scores in the first 24 postoperative hours
Vilvanathan et al. 2021[17]	Patients 18-90 y old undergoing cardiac surgery with or without CPB, no emergency	Placebo = 45 Sex (m/f): 32/9 Age: 60.22 ± 13.27	Levobupivacaine = 45 31/9 64.18 ± 10.46	TTPB	Reduction in NRS scores at rest and during breathing exercise; reduced intraoperative fentanyl and postoperative rescue analgesic consumption for the first 12 h
Bloc et al. 2021[16]	Patients 18-80 y old undergoing cardiac coronary artery bypass graft surgery	Placebo = 17 Sex (m/f): 14/3 Age: 68.50 ± 10.00 BMI: 26.5 ± 3.3	Ropivacaine = 18 14/4 69.3 ± 7.80 BMI: 25.3 ± 3.8	Ropivacaine injection 0.25% via parasternal block	Decreased maximum concentrations of remifentanil and propofol required to avoid hypertension/tachycardia during sternotomy (from skin incision to sternal retractor setup) without increasing side effects. Decreased proinflammatory response
Kumar et al. 2021[18]	Patients 18-80 y old undergoing cardiac surgery with or without CPB, no emergency	Placebo = 20 Sex (m/f): 13/7 Age: 46.25 ± 14.47	Ropivacaine = 20 11/9 51.25 ± 15.86	Ropivacaine injection 0.25% via parasternal block	Decreased opioid consumption in the first 24 hours, reduced postoperative pain at 12 and 24 h at rest and 3, 6, 12, and 24 h during cough
Khera et al. 2021[20]	Patients 18-80 y old undergoing cardiac surgery with or without CPB, no emergency	Placebo = 40 Sex (m/f): 34/6 Age: 65.7 ± 9.86 BMI: 28.92 ± 4.84	Bupivacaine = 40 Sex (m/f): 27/13 Age: 65.78 ± 8.73 BMI: 28.57 ± 5.10	Bupivacaine injection 0.25% via parasternal block	No differences in primary endpoint. Reduced NRS at third and fourth postoperative day; no differences in postoperative delirium incidence
Kaya et al. 2021[19]	Patients 21-77 y old undergoing cardiac surgery with or without CPB, no emergency	Placebo = 20 Sex (m/f): 12/8 Age: 62 ± 8 BMI: 26.16	Bupivacaine = 19 Sex (m/f): 14/5 Age: 60 ± 7 BMI: 29.55	Bupivacaine injection 0.25% via parasternal block	Different time to first rescue dose of analgesic (280 minutes in TTPB group *v* 660 min in PIFB). Similar opioid consumption, postoperative NRS and ICU stay
Zhang et al. 2021[21]	Patients 18-80 y old undergoing cardiac surgery with or without CPB, no emergency	Placebo = 49 Sex (m/f): 21/28 Age: 45.6 ± 19.8 BMI: 21.3 ± 3.8	Bupivacaine = 49 Sex (m/f): 23/26 Age: 47.5 ± 18.9 BMI: 22.1 ± 3.5	20 mL of 0.4% ropivacaine was injected to this plane in 2 locations, over second and fourth ribs	Discordant results compared with all other studies. Worse outcome in PIFB with respect to normal saline infiltration, with higher dosages of intraoperative and postoperative opioids, that led to longer extubation time and ICU length of stay

Abbreviations: BMI, body mass index; BSA, body surface area; CPB, cardiopulmonary bypass; ESPB, erector spinae plane block; ICU, intensive care unit; LB, levobupivacaine; NRS, Numerical Rating Scale; PIFB, pectointercostal fascial block; TTP, transversus thoracic plane block; VAS, visual analog scale.

requiring rescue doses versus 4 patients in the placebo group.[13] Moreover, alveolar-arterial oxygen gradient and pH values were better in the parasternal block group, although it did not influence time to tracheal extubation and Mini Mental State Examination, with an improvement of near 30 mmHg in alveolar gradient (from 198 *v* 227) compared with the placebo group. Levobupivacaine blood concentrations were recorded and no adverse events of Local Anesthetics Toxicity Syndrome have been reported.[13]

One year later, Barr et al. published results from a randomized, controlled, double-blinded trial on 88 patients undergoing cardiac surgery. They demonstrated that the Numeric Pain Rating Scale (NRS) was halved in the ropivacaine group compared with the normal saline one, and with a contemporary reduction of morphine consumption at 12 and 24 hours (12 mg *v* 23.2 mg and 18.8 mg *v* 23.7 mg).[14]

Ten years later, Baki et al. uselessly tried to correlate blind postoperative parasternal block with levobupivacaine for prevention of chronic neuropathic sternal pain in a randomized trial with 81 patients.[15] However, they demonstrated that bilateral parasternal block effectively reduced total tramadol consumption in the first 24 hours, halving opioid requirement (125.7 ± 28.9 mg *v* 213.17 ± 61.25 mg of tramadol), with a simultaneous reduction in Visual Analog Score (VAS) at any time.[15] Previous studies have linked these results to shortening the intensive care unit (ICU) stay measured in hours, but in the authors' experience, 5 hours of ICU stay could be attributed to several center-specific internal procedures and are not enough to determine an impact on postoperative course. Unfortunately, no correlation was demonstrated between postoperative bilateral parasternal block and chronic neuropathic pain, even if they used and suggested a specific tool such as the Leeds Assessment Neuropathic Symptoms and Signs pain scale questionnaire.[15] In these series, no differences in time of mechanical ventilation were demonstrated.[13-15]

In a randomized trial on 84 patients, Padala et al. demonstrated different analgesic profiles between preoperative and postoperative parasternal intercostal sound-guided block obtained with bupivacaine 0.25%. They effectively revealed that preoperative sound-guided parasternal block reduced intraoperative opioids consumption but did not affect total opioids requirement for the first 24 postoperative hours and VAS score for the same period, with a medium value of 25 mm[3]. Unfortunately, 2 groups significantly differed for cardiopulmonary bypass duration and total time of surgery, and it likely determined prolonged mechanical ventilation of the preoperative parasternal block group. No data were collected about the ICU stay.[3] The authors contributed to defineing importance of preoperative parasternal intercostal sound-guided block to maintain hemodynamic stability and prevent heartbeat fluctuation during cardiac surgery, improving anesthesia management.[3]

In 2021, Bloc et al. enrolled 35 patients in a randomized, controlled, double-blind trial that evaluated the efficacy of preincisional ultrasound-guided parasternal plane block in coronary artery bypass graft with sternotomy.[16] The authors significantly demonstrated reductions in remifentanil and propofol median maximum effect-site concentrations, with 4.2 ng/dL versus 7 ng/dL of remifentanil and 3.9 μg/dL versus 5 μg/dL of propofol. In this study, the minimum patient state index was significantly lower in the placebo group than in the parasternal one (11.7 *v* 18.3).[16] Interestingly, a significant reduction in proinflammatory cytokines released during cardiopulmonary bypass over the first postoperative week (interleukin [IL]-8, IL-18, IL-23, IL-33, and MCP-1) also has been shown.[16] Unfortunately, no details about postoperative outcomes were described by the authors.

Vilvanathan et al.[17] recruited 90 patients into 2 groups, one undergoing modified ultrasound-guided TTP block with levobupivacaine and the other enrolled in the hospital analgesic protocol with intravenous morphine.[17] They demonstrated a significant reduction in NRS pain score at rest and during breathing exercise together to a lower intraoperative fentanyl and postoperative rescue analgesic consumption for the first 12 hours, with rescue analgesics required by patients in the controlled group within 4 hours of tracheal extubation.[17] Vilvanathan also did not demonstrate any improvement in mechanical ventilation-free time for ICU stay, revealing that different analgesic management did not interfere with the recovery of mechanical respiratory function enough to obstruct extubation, unless a high-risk respiratory patient was evaluated[17] but this might have been related to the procedural differences between TTP block, which was used by the authors, and PIFB, which was described in other series.

Recently, a small case series on 10 patients was published by Bousquet et al.,[2] in which PSB was combined with erector spinae plane block and compared with 10 control cases. They demonstrated a significant reduction in morphine consumption but not in postoperative NRS. This small series revealed that combined locoregional infiltration sites could be feasible and safe.

Kumar et al.[18] compared PIFB to the placebo group in a double-blind randomized controlled trial, confirming the efficacy of locoregional anesthesia in reducing opioid consumption in the first 24 hours and reducing postoperative pain at 12 and 24 hours at rest, and 3, 6, 12, and 24hours during cough. These results in 2021 strengthened the recent evidence on the efficacy of PIFB and were echoed by other trials.

Kaya et al.[19] randomized 39 patients in a double-blind trial to evaluate efficacy and safety of TTP block compared to PIFB, and revealed that these techniques were overlapping for opioid consumption, postoperative NRS and ICU stay, and differed for the time to first rescue dose (280 minutes in the TTP block group *v* 660 minutes in the PIFB group). Maybe, a small sample size and a greater learning curve for TTP block, considering that is deeper than PIFB, could have generated this gap.

Khera et al.[20] published an interesting randomized double-blind controlled trial on management of cardiac surgery patients in the ICU with doubled administration of PIFB, at admission to the ICU, and on first postoperative day. They recruited a large sample size, with a total of 80 patients, and monitored intraoperative bispectral index to reveal differences in postoperative delirium. Unfortunately, they missed every endpoint, except for NRS on the third and fourth postoperative days, revealing no differences in postoperative delirium incidence.

The last RCT was led by Zhang et al.,[21] who enrolled 98 patients in a double-blind randomized controlled clinical trial to compare PIFB to normal saline infiltration performed at

Table 3
Intraoperative Data and Operative Details

Study	Design	Patients, Control Group (C)	Patients, Treatment Group (T)	Block type	Block Time	oMEDD, Intraoperative	oMEDD, at 24 h	Time to Extubation (min)	Surgery Time (min)
Bousquet et al. 2020[2]	OBS	10	10	PIFB + ESPB	PRE	C: 235 T: 130	C: 135.9 T: 36	C: 240 T: 300	C: 289 T: 216
McDonald et al. 2005[13]	RCT (DB)	9	8	PSB	POST	C: 68.6 T: 77.8	C: 189 T: 162	C: 38.1 T: 36.4	/
Vilvanathan et al. 2020[17]	RCT (DB)	45	45	TTP	PRE	C: 195.22 T: 135.12	C: 480 T: 240	C: 332 T: 323	/
Abadi et al. 2021[1]	OBS	53	53	PSB	POST	/	C: 149 T: 32	/	/
Padala et al. 2020[3]	RCT (SB)	41	43	PIFB	PRE vs POST	/	T: 81.6 (block), 92.4 (block + TENS)	T: 494 (block), 414 (block + TENS)	T: 334 (block), 292 (block + TENS)
Sepolvere et al. 2020[8]	OBS	-	5	PSB	PRE	0	0	/	/
Orzturk et al. 2015[23]	RCT	40	40	PIFB	POST	/	C: 157.2 T: 79.5 (block), 111 (block + TENS)	C: 217.8 T: 193.6 (block), 210.2 (block + TENS)	/
Baki et al. 2015[15]	RCT	41	40	PIFB	POST	/	C: 42 T: 25	C: 255 T: 231	/
Bloc et al. 2021[16]	RCT	17	18	PIFB	PRE	/	/	/	C: 212 ± 41 T: 209 ± 41
Kumar et al. 2021[18]	RCT	20	20	PIFB	POST	/	C: 15.3 T: 14.1	C: 384 T: 378	/
Khera et al. 2021[20]	RCT	40	40	PIFB	POST + 1POD	/	C: 49.1 T: 40.8	/	/
Kaya et al. 2021[19]	RCT	19	20	PIFB	PRE	/	T: 15 TENS: 15	T: 480 TENS: 397	/
Zhang et al. 2021[21]	RCT	49	49	PIFB	POST	C: 38 T: 59	C: 31 T: 54	C: 162 T: 582	/

NOTE. Study with all of the missing data about the outcomes of interests described in the table have been removed. The term parasternal block is used when no specific / uniquivocal description was made in the original publication and it was not possible to distinguish between pectointercostal fascial block and transversus thoracic plane block or significant overlap might exist.
Abbreviations: DB, double blind; ESPB, erector spinae plane block; OBS, observational study; oMEDD, oral morphine equivalent daily dose; PIFB, pectointercostal fascial block; PRE, preoperative block; PSB, parasternal block (not specified); POST, postoperative block; RCT, randomized controlled study; SB, single blind; TENS, transcutaneous electrical nerve stimulation; TTP, transversus thoracic plane block.

Table 4
Summary of Side Effects

Study	PaO_2-PaO_2 (Extubation)		Vomit		Itch		Nausea		Sedation	
	PSB	Control	PSB	Control	PSB	Control	PSB	Control	PSB	Control
McDonald et al. 2005[13]	198	227								
Vilvanathan et al. 2020[17]			1	8	3	13	2	10	2	11
Padala et al. 2020[3]			3	3	3	3	3	3	3	3
Kaya et al. 2021[19]							4	4		

NOTE. Study with all missing data about outcomes of interests described in table have been removed.
Abbreviation: PSB, parasternal block.

ICU admission. They had discordant results compared with all of the other studies; in fact, this RCT found worse outcomes in PIFB in respect to normal saline infiltration, with higher dosages of intraoperative and postoperative MMO, that led to longer extubation time and ICU length of stay, but obviously reduced parecoxib consumption, and, consequently, the postoperative NRS at rest and at cough was better in the PIFB group.[21] In the authors' opinion, in this RCT there was an evident bias, maybe related to intraoperative anesthesiologic management and postoperative randomization. However, the authors inserted biochemical outcomes that could have suggested that high, well-controlled, postoperative pain could reduce inflammatory and stress response significantly, even if the pain controll was not linked to intraoperative pain control, in particular blood glucose, blood insulin, "homeostasis model assessment: insulin resistance," and IL-6[21].

A comparison of the side effects had shown that PSB was associated with a reduced incidence of vomit, itch, nausea, and sedation (Table 4). The longitudinal evaluation of the VAS score has been performed in 5 studies only,[15,17-20] showing a significant and sustained reduction of the VAS score with PSB compared with a control group (Table 5).

Limitations and Future Directions

Unfortunately, this evidence could not have enough strength outside high-volume cardiac surgery to carry this technique out in daily clinical use. The authors pushed on safety and the opioid-sparing anesthesia invoked by the ERAS Society to obtain a wide spread, but it still proved to be difficult in feasibility because of its lack of ultrasound-guided locoregional anesthetic management in high-volume cardiac centers.

In fact, only McDonald et al.[13] demonstrated an efficacy on postoperative respiratory performance, even if their results were disconnected from clinical practice and their relevance could be the object of discussion, considering that postoperative pulmonary complications were been collected, and none of their data revealed the clinical impact of locoregional anesthesia for the prevention of such complications.[13]

Studies have failed to demonstrate the differences in Mini-Mental State Examination (MMSE) without parasternal block, maybe to reveal a better neurologic outcome associated with better or faster awareness and clarity of mind, but in practice, large cardiac centers have to fight frequent postoperative delirium, and no studies have tried to identify its incidence with and without locoregional anesthesia, most likely for a small number of enrolled patients.[13]

Half of the currently available RCTs excluded patients with low left ventricular ejection fraction for enrollment, and none stratified respiratory risk for selection; this could be a strong bias for the absence of statistically significant differences in pulmonary complications or hospital or ICU length of stay.

In a large meta-analysis published in 2022, Li et al.[22] observed similar results on opioid consumption and postoperative pain relief, with consistent data on postoperative NRS/VAS score, but they used a sufentanil equivalent to consolidate the data from different RCTs. This method has not been recommended by literature, but this, in fact, did not change the power of their results. However, the authors observed that previous studies have paid excessive attention to analysis of raw

Table 5
Pain Evaluation (VAS Scale) in the Postoperative Course

Study	VAS @ 1 h		VAS @ 4 h		VAS @ 8 h		VAS @ 12 h		VAS @ 18 h		VAS @ 24 h	
	PSB	Control	PSB	Control	PSB	Control	PSB	Control	PSB	Control	PSB	Control
Vilvanathan et al. 2020[17]	3.29	4.3	2.89	4.04	2.58	4.19	2.64	4.5	2.72	4.63	3.49	5.09
Baki et al. 2016[15]	2.2	5.4	1.5	4.5	1.7	4.2	1.6	3.5	/	/	1.4	2.6
Kumar et al. 2021[18]	0.5	0	1	0	2	0	3.5	1	/	/	/	/
Khera et al. 2021[20]	/	/	/	/	/	/	/	/	/	/	5.4	5.8
Kaya et al. 2021[19]	0	0	0	0	0	3	2	4	2	3	1	0.5

NOTE. Study with all missing data about outcomes of interests described in table have been removed.
Abbreviations: PSB, parasternal block; VAS, Visual Analog Score.

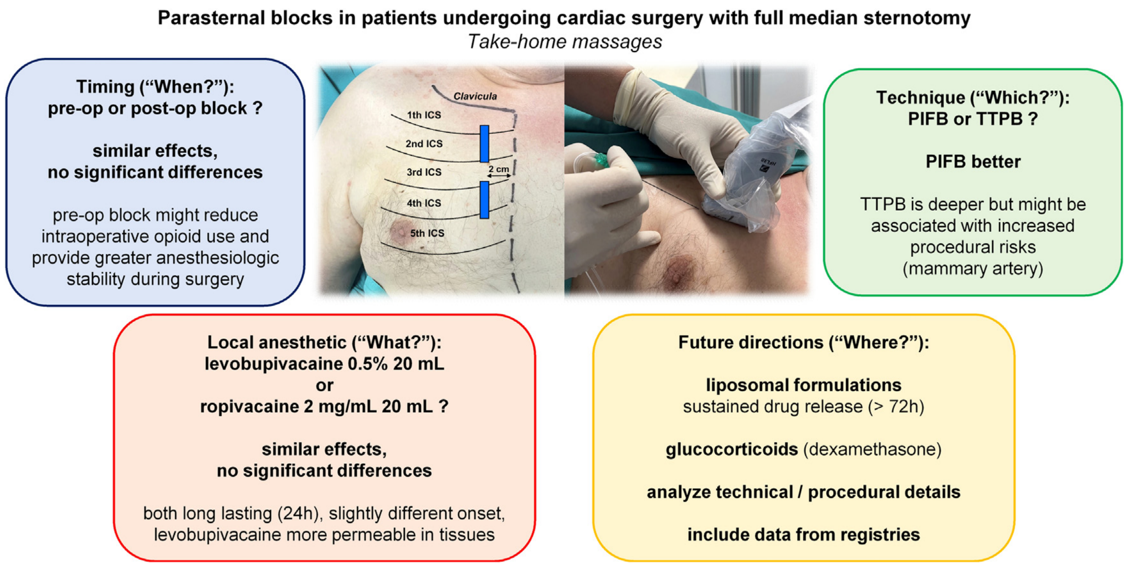


Fig 3. Parasternal blocks in patients undergoing cardiac surgery with full median sternotomy: take-home messages. The blue square indicates the position of the ultrasound probe. ICS, intercostal space; PIFB, pectointercostal fascial block; TTPB, transversus thoracic plane block.

data, like those on cognitive impairments that, in fact, revealed no differences in all of the RCTs analyzed, and only Vilvathan et al.[17] reported excessive sedation (Ramsey score >3) with no descriptive time of onset and offset, revealing a minor data lack. Moreover, excessive sedation also could depend on volatile agents and hypnotic drugs used for premedication or induction of anesthesia, by cerebral transient edema, or excessive hypnosis under general anesthesia, but no data of intraoperative bispectral index (or any other validated neurologic system) have been collected by studies thus far.

The authors agree with the considerations about ICU length of stay and total hospital stay, because differences in ICU and hospital discharge were not protocolled in each study, as they depended on a multimodal approach, that some authors cited as ERAS, that are highly heterogeneous among centers and in different periods within the same center. The need for a standardization of protocols and endpoints is warranted to produce comparable and reproducible results for future studies.

Also, the data from registries and nationwide databases are warranted to draw conclusions about the duration of ventilation, duration of ICU and hospital stay, pulmonary complications, and economic implications. Besides the approach on the sternal wound, chest tubes remain a significant source of postoperative pain and should receive a detailed scientific evaluation of analgesic techniques. A holistic approach to reduce postoperative pain is awaited in the future.

Conclusions

Ten RCTs, blind and ultrasound-guided, on PSB, achieves the first outcome of reduction of perioperative opioid consumption and, in general, better analgesic profile. Some RCTs also evidenced reductions in ICU stay or mechanical ventilation length, but these results have to be confirmed because they were discontinuous and center-specific, and the clinical analysis of respiratory function (that frequently prolonged ICU stay) could not be extrapolated by raw data published.

In fact, PSB showed an efficacy like other ultrasound-guided fascial blocks, and steadily reduced opioid consumption over a better analgesic effect in patients undergoing cardiac surgery with full median sternotomy (Fig 3). Nowadays, authors also must validate respiratory and neurologic protection of locoregional anesthesia in cardiac surgery. These reasons are strong enough to justify its wide use in sternotomy, but literature should identify the safest and best technique and the correct hypnotic and analgesic intraoperative management to reduce inflammatory response to cardiopulmonary bypass and time of weaning, especially in high respiratory- and cardiac-risk patients such as obese and critically ill cardiac patients, with a predictably long ICU length of stay.

Conflict of Interest

None.

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