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Original study

Superficial Serratus Anterior Plane Block for Minimal Invasive Cardiac Surgery: a single-center randomized controlled trial

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Abstract

Introduction: **Multimodal pain management with serratus anterior plane block (SAPB) in minimal invasive cardiac surgery (MICS) may potentially reduce pain scores and opioid consumption. However, randomized controlled trials investigating the efficacy of a superficial SAPB are missing.**
Design: **Monocentric, prospective, outcome-assessor blinded randomized-controlled trial performed at the General Hospital Maria Middelares, Ghent, Belgium.**
Methods: **80 patients scheduled for mitral valve surgery (MVS) via port-access, aortic valve replacement via right anterior thoracotomy (AVR-RAT) and minimal invasive direct coronary artery bypass (MIDCAB) surgery were randomized to a superficial SAPB (42 patients) or to routine analgesia (38 patients). In the SAPB group, a single-shot block was performed with 1.25 mg.kg-1 levobupivacaine 0.25% between the latissimus dorsi and serratus anterior muscle. The primary outcome was static pain intensity measured by Numeric Rating Scale (NRS) 12 hours after extubation. Secondary outcomes were static pain intensity measured by NRS at 2, 4, 6 and 24 hours after extubation, cumulative opioid consumption, incidence of postoperative nausea and vomiting (PONV), time to extubation, ICU and hospital length of stay and the amount of carbon dioxide measured by arterial partial pressure (PaCO2).**
Results: **There was no treatment effect on static pain intensity at 12 hours after extubation (mean difference 0.238 [95% CI: -0.70 – 1.19; p = 0.78]). There was no treatment effect on static pain intensity on the other predefined timepoints nor on the cumulative opioid consumption during the first 48 postoperative hours (mean difference 0.10 mg [95% CI: -2.65 – 2.83; p = 0.911]) nor any of the other secondary outcomes. Looking at each surgical intervention separately, the results show a decrement in static pain intensity (mean difference -1.71 [95% CI: -2.94 – -0.40; p = 0.021]) for patients undergoing MIDCAB surgery at 6 hours post extubation.**
Conclusions: **In our setup, the effect of a single-shot superficial SAPB could not improve static pain intensity scores at 12 hours after extubation compared to a control group receiving standard intravenous opioid analgesia in a mixed group of minimal invasive cardiac surgical patients. Subsequently, the single-shot superficial SAPB could not reduce the cumulative opioid consumption in the first 48 postoperative hours. However, patients undergoing MIDCAB surgery may potentially benefit from this technique.**

Keywords: **Superficial serratus anterior plane block, minimal invasive cardiac surgery, multimodal pain management, fascial plane block.**

Trial registration and Ethics Committee approval: This prospective, randomized controlled trial was performed at the Department of Anaesthesia, Intensive Care & Pain Medicine at the General Hospital Maria Middelares, Ghent, Belgium, from October 2021 to March 2023. The study protocol (B0172021000006) was approved by the Institutional Ethics Committee (Buitenring Sint-Denijs 30, 9000 Ghent; Chairman P. Germonpré, MD, PhD) on 15th October 2021 and registered on ClinicalTrials.gov (NCT05107453) before the first patient was enrolled.

Introduction

Analgesia in cardiac surgery is historically based on large doses of intravenous opioids. Contemporary practice is rapidly changing due to "Enhanced Recovery After Cardiac Surgery (ERACS)" protocols with recommendations to implement multimodal opioid-sparing analgesic regimens for the treatment of postoperative pain[1]. Also, the opioid crisis, caused by widespread opioid abuse, has made clinical practitioners reconsider their perioperative practice in an attempt to reduce the use of opioids after surgery. Regional anaesthesia can be an integral part of this strategy, given its potential benefits on various patient-centred outcomes, improved perioperative analgesia and decreased opioid usage after surgery[2-4]. In particular, the emergence of truncal fascial plane blocks (FPB) has further broadened the application of regional anaesthesia in thoracic and cardiac surgery but requires further research to establish their true value and role in clinical care[5]. Several FPB techniques have been described for cardiac analgesia, including parasternal intercostal plane (PIP) block, interpectoral-pectoserratus plane (formerly known as PECS II) block, serratus anterior plane block (SAPB) and erector spinae plane block (ESPB)[6].

The serratus anterior plane block (SAPB) has already proven its efficacy in thoracic surgery[7] and its application is now expanded to minimal invasive cardiac surgery (MICS). A systematic review and a recent meta-analysis showed that the SAPB reduces both pain scores and opioid consumption in thoracic surgery in comparison to systemic analgesia in the first 12-24h after surgery[7,8]. Importantly, a SAPB appears to be safe as there were no reported complications or hemodynamic compromises[8]. With a SAPB, the goal is to achieve complete sensory loss of the anterolateral hemithorax via blockade of the lateral cutaneous branches of the thoracic intercostal nerves (T2- T12). The SAPB is an ultrasound guided locoregional technique which is administered at the midaxillary level of the fourth and fifth rib. The block can be placed either below or superficial to the serratus anterior muscle. The spread is influenced by the administered volume of local anaesthetic (LA)[6,9].

Since the original article by Blanco et al. in 2013[9], only a couple of randomized-controlled trials (RCTs) aimed to investigate the effects of SAPB in MICS with beneficial effects on postoperative pain scores and reduced opioid consumption[10-12]. Although the pilot study by Blanco already mentioned that a superficial SAPB could be more effective than a deep SAPB, the aforementioned studies investigated the effects of a deep SAPB. Randomized controlled trials investigating the efficacy of a superficial SAPB in MICS are lacking. To our knowledge, this is the first RCT that aims to investigate the postoperative analgesic effects of a single-shot, superficial SAPB in MICS as part of a multimodal pain management protocol compared to a control group with standard intravenous opioid analgesia. We therefore hypothesized that a superficial SAPB improves static pain intensity scores at 12 hours after extubation, measured by numeric rating scale (NRS) in patients undergoing MICS.

Materials and methods

This prospective, randomized controlled trial was performed at the Department of Anaesthesia, Intensive Care & Pain Medicine at the General Hospital Maria Middelares, Ghent, Belgium, from October 2021 to March 2023. The study protocol (B0172021000006) was approved by the Institutional Ethics Committee (Buitenring Sint-Denijs 30, 9000 Ghent; Chairman P. Germonpré, MD, PhD) on 15th October 2021 and registered on ClinicalTrials.gov (NCT05107453) before the first patient was enrolled.

We enrolled adult patients aged 18 years and older scheduled for mitral valve surgery (MVS) via port-access, aortic valve replacement via right anterior thoracotomy (AVR-RAT) and minimal invasive direct coronary artery bypass (MIDCAB) surgery. We excluded reoperations, emergent surgeries, and procedures requiring a sternotomy; a complete list of exclusion criteria is presented in supplementary Table 1. With written informed consent, patients were randomized 1:1 without stratification to either a superficial SAPB (treatment) or routine analgesia (control) based on a computer-generated list.

All patients received their anaesthetic management as stated by the local institutional standard operating procedure (SOP). General anaesthesia was initiated by and maintained with target-controlled infusions (TCI) of propofol and remifentanil, guided by Bispectral Index (BiS) between 40 to 60. After loss of consciousness, 0.8 mg.kg-1 rocuronium was administered for neuromuscular blockade. Subjects received dexamethasone 5 mg and tranexamic acid 2 g. We used standard invasive monitors and single-lung ventilation to facilitate the surgical approach. Surgery was facilitated by cardiopulmonary bypass (CPB) with femoral arterial and venous cannulation strategy for MVS and MIDCAB; CPB with central arterial and femoral venous cannulation strategy facilitated the AVR-RAT procedures. For MVS, surgical approach used a 5-6 cm thoracotomy incision in the fourth intercostal space in the right midaxillary line augmented by stab incisions for

the thoracoscopic ports. For AVR-RAT, surgical approach used a 4-6 cm thoracotomy incision over the medial aspect of the second or third intercostal space. For the MIDCAB procedure, surgical approach used a 4- to 7-cm anterolateral thoracotomy in the fifth intercostal space. Incisions in the subxyphoid and seventh intercostal spaces grant access to facilitate exposure of all coronary artery territories[13].

At the end of surgery, acetaminophen 1 g, ondansetron 4 mg and a loading bolus of 0.1 mg.kg-1 piritramide were administered. As a part of the standard institutional analgesic regimen, local wound infiltration (LWI) with 20 ml levobupivacaine 0.25% was administered by the surgeon before wound closure along incision site and ports for trocars/chest tubes. Also, to avoid systemic hypothermia, forced-air warming was used at the end of the procedure. Patients in the SAPB group received the plane block after wound closure. The SAPB was administered in supine position under general anaesthesia. Local anaesthetic solution was levobupivacaine 0.25% (weight-based dosing at 1.25 mg.kg-1 with a maximum dose of 100 mg [40 ml]). A linear, high-frequency (3.4 - 12.6 MHz) ultrasound probe (Venue Fit™, GE HealthCare, Wauwatosa, WI, US) was moved to respectively the right mid-axillary region at the level of the 4th rib for MVS and AVR-RAT procedures and the left mid-axillary region at the level of the 5th rib for MIDCAB procedures. There, the plane between the latissimus dorsi and the serratus anterior muscle was identified. Using a 22-gauge, 50 mm SonoPlex® needle (Pajunk® GmbH, Geisingen, Germany), an in-plane injection of 1.25 mg.kg-1 levobupivacaine 0.25% was administered (see Figure 1). The quality of depicted anatomy and local anaesthetic spread was registered by the attending anaesthetist. To avoid local anaesthetic systemic toxicity (LAST), the total amount of levobupivacaine (SAPB+LWI) was restricted to 150 mg in order to remain below the toxic threshold of 3 mg.kg-1 levobupivacaine. The block was performed by a dedicated team of 3 anaesthetists trained in SAPB and with experience prior to the trial. The attending anaesthetist could not be blinded to treatment due to being part of the intraoperative anaesthetic management. All outcomes were assessed by blinded research personnel. For the duration of the study, patients, ICU nurses and attending intensivists were blinded to group allocation.

Patients were transferred to ICU on propofol sedation (1 – 3 mg.kg-1.h-1) and mechanical ventilation. Upon arrival on ICU, a chest X-ray was taken and propofol sedation was discontinued when the patient met the needed criteria for extubation (see supplementary Table 2). The postoperative analgesic regimen consisted of basic analgesia (acetaminophen 1 g every 6 hours) and predefined administrations of intravenous piritramide per 2 mg

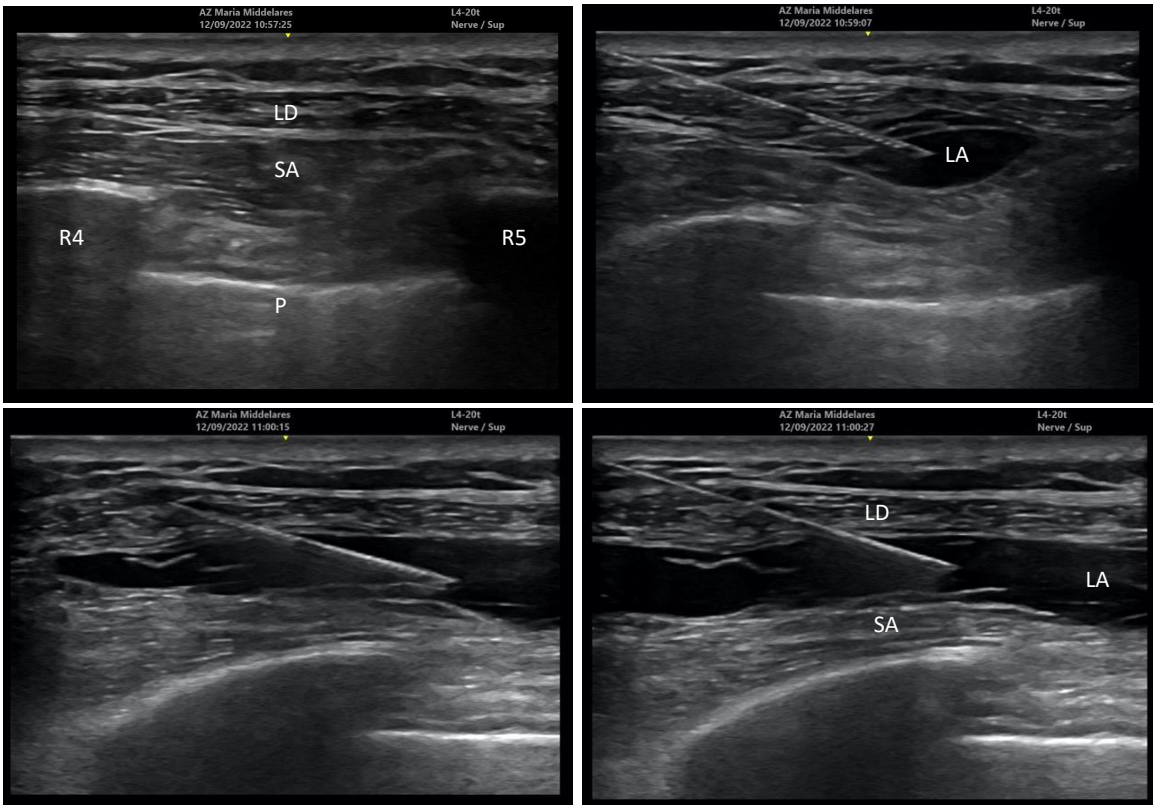

Fig. 1 — Ultrasound image with anatomy and local anaesthetic spread of superficial serratus anterior plane block. LD, Lattisimus dorsi muscle; SA, Serratus anterior muscle; R4, Rib 4; R5, Rib 5; P, Pleura; LA, Local anaesthetic.

triggered by NRS threshold ≥ 4 and titrated until NRS < 4 and ran until discharge from ICU.

Static pain intensity, measured by NRS each 2 hours starting from extubation up to 48 hours after extubation, was recorded by investigators blinded to group allocation. A ≥ 33% reduction in pain intensity difference was defined as a meaningful clinical important difference[14]. The primary outcome is static pain intensity, measured by NRS, at 12 hours after extubation. Secondary outcomes included (i) static pain intensity, measured by NRS, at 2, 4, 6 and 24 hours after extubation; (ii) cumulative opioid consumption in oral morphine equivalent dose (mg)[15]; (iii) the incidence of postoperative nausea and vomiting (PONV); (iv) time to extubation; (v) ICU and hospital length of stay (LoS); (vi) the arterial partial pressure of carbon dioxide (PaCO2). The incidence of PONV was scored (nausea: yes/no, vomiting: yes/no) every 2 hours and carbon dioxide levels (PaCO2) were sampled every 4 hours by arterial blood gas.

Statistical analysis

Based on the work of Farrar et al.[14], we hypothesized that the effect size in the study had to be a reduction of 35% in static pain intensity, measured by NRS, for the treatment group. Based on the study by Magoon et al.[10], we therefore estimated a sample size of 72 patients to detect a 35% reduction in pain intensity (measured by NRS) at 12 hours after extubation with 80% power with a 5% significance level. We increased the sample size to 80 patients, considering the possibility for dropouts.

Analysis of the primary outcome was based on an intention-to-treat approach, defined as inclusion of all randomised patients and no inclusion or exclusion criteria violation. The rate of missing data, which were all missing completely at random, did not override the 5% threshold for the primary and secondary outcome measures. Consecutively, no imputation method was applied.

In order to assess normality of data, the Shapiro-Wilks test in conjunction with histograms were used. Descriptive statistics are presented as mean ± standard deviation (SD) when normally distributed or as median (interquartile range (IQR)) when not normally distributed. Categorical data are presented as numbers or percentages. NRS values at different timepoints (2, 6, 12 and 24 hours after extubation) and cumulative piritramide dose were compared using a two-tailed independent Student t-test with a p value of < 0.05 defining statistical significance. For non-normally distributed variables, the Mann-Whitney U test was used with a p-value of 0.05 defining statistical significance. The corresponding 95% confidence interval (95% CI) was derived by bootstrapping. This similar procedure was applied to each numerical secondary outcome parameter. For binary outcomes, a chi-square test was used.

For exploratory reasons, we performed two subgroup analyses wherein we hypothesized that the surgical approach may influence the difference in treatment effect on the primary and secondary outcome measures. In the first analysis, we hypothesized that the difference in treatment effect could differ in each separate surgical approach (between groups comparison). In the second analysis, we hypothesized that per treatment arm the observed outcome differs per surgical approach (within groups comparison). For the subgroup analyses, the Kruskal-Wallis test was used with post-hoc pairwise comparisons with Bonferroni correction for multiple testing. An adjusted p-value < 0.05 defined statistical significance. Statistical analysis was performed using the R statistical software package, version 4.2.2. (2022 The R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/)

Results

We assessed 141 patients for eligibility; 7 were withdrawn due to a change of surgical plan (conversion to sternotomy), 18 declined to participate and 6 met the exclusion criteria. The analysed population included 91 patients, of whom 46 were randomized to SAPB and 45 to the institutional standard of care. One patient withdrew from the study after having received group allocation and subsequent treatment. Ten patients were excluded from the analysis due to protocol violation. Finally, 80 patients were included for statistical analysis. The CONSORT flow diagram with patient inclusion and exclusion details is presented in Figure 2.

Patient characteristics and demographics are summarized in Table I and Supplementary Table 3 and 4. None of the variables indicate a significant difference, hereby implying adequate balance between both groups. No additional adjustments for the following analyses were made. Intraoperative protocol adherence is implied by the non-significant difference in piritramide loading dose at the end of surgery.

For the primary analysis, there was no treatment effect on static pain intensity, measured by NRS, at 12 hours after extubation compared to the control group (mean difference 0.238 [95% CI: -0.70 – 1.19; p = 0.78]). For the secondary analysis, there was no treatment effect at 2h, 6h and 24h post extubation as indicated in Table II. Furthermore, absent evidence of a treatment effect on the cumulative opioid consumption up until 48 hours after extubation was

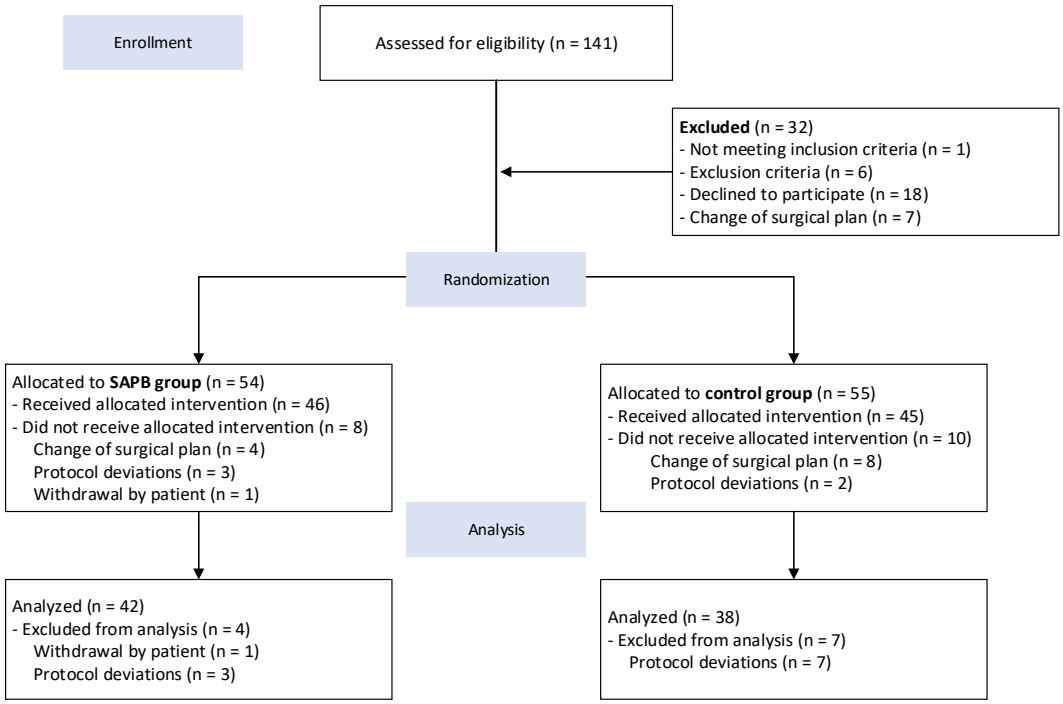

Fig. 2 — Consort flow diagram.

demonstrated with a mean difference of 0.10 mg morphine equivalent dose (95% CI: -2.65 – 2.83; p = 0.911) between the two groups. Similarly, no significant differences were noted for the remaining secondary outcome parameters (Table II): postoperative nausea and vomiting, time to extubation with a mean difference of -0.04 min (95% CI: -0.63 – 0.52; p = 0.954), length of ICU stay with a mean difference of 0.532 hours (95% CI: -7.65 – 9.28; p = 0.923) and length of hospital stay with a mean difference of -1.17 days (95% CI: -3.16 – 0.36; p = 0.216). No significant differences in PaCO2 at predefined timepoints were observed between the two groups.

Additionally, we performed a subgroup analysis to investigate whether the treatment effect differed as per surgical approach (between groups comparison). In the first subgroup analysis, we demonstrate a significant mean reduction in static pain intensity at 6 hours after extubation of -1.71 (95% CI: -2.94 – -0.40; p = 0.021) in patients undergoing MIDCAB surgery (see figure 3). Also, patients in this group had a lower cumulative opioid consumption during their ICU stay with a non-significant mean difference of -1.71 mg (95% CI: -5.50 – 2.90; p = 0.14). Finally, the subgroup analysis showed a significant reduction in length of ICU stay with MIDCAB patients in comparison

Table I. — Patient demographics.

	SAPB group (n = 42)	Control group (n = 38)	
Age (median (IQR))	69.5 (13.75)	67 (10.75)	p = 0.765
Sex – male (n (%)) Sex – female (n (%))	27 (49.1%) 15 (60%)	28 (50.9%) 10 (40%)	χ^2 – p = 0.51
BMI (mean (95% CI))	26.3 (18.71 – 33.87)	26.4 (19.43 – 33.39)	p = 0.888
Weight (mean (95% CI))	77.84 (49.5 – 106.2)	80.31 (51.4 – 109.2)	p = 0.454
Height (mean (95% CI))	171.7 (151.2 – 191.2)	173.9 (156.1 – 191.8)	p = 0.293
Smoking (n (%))	6 (14.3%)	4 (10.5%)	χ^2 – p = 0.866
EuroSCORE II (%, median (IQR))	1.23 (0.78 – 1.57)	0.93 (0.7 – 1.49)	p = 0.461
Piritramide loading dose at end of surgery (mg) (mean (95% CI))	7.51 (4.68 – 10.34)	7.90 (5.22 – 10.57)	p = 0.227
Subgroup – MVS (n) Subgroup – AVR-RAT (n) Subgroup – MIDCAB (n)	14 13 15	7 14 17	

BMI, Body Mass Index; EuroSCORE, European System for Cardiac Operative Risk Evaluation; MVS, Mitral Valve Surgery; AVR-RAT, Aortic Valve Replacement via Right Anterior Thoracotomy; MIDCAB, Minimal Invasive Direct Coronary Artery Bypass; IQR, Interquartile Range; CI, Confidence Interval.

Table II. — Primary and secondary outcome measures.

	SAPB (n = 42)	Control (n = 38)	Difference between groups, p-value
Primary outcome			
NRS at 12h	3 (3)	3 (2.25)	0.238 (95%CI -0.70 – 1.19), p = 0.78
Secondary outcomes			
NRS at 2h	6 (3)	5 (5)	-0.393 (95%CI -1.56 – 0.76), p = 0.63
NRS at 6h	3 (3)	3 (4)	0.57 (95%CI -0.37 – 1.51), p = 0.29
NRS at 24h	3 (3)	2 (2)	-0.31 (95%CI -1.19 – 0.59), p = 0.40
Cumulative opioid consumption (MME; mg)	7.5 (6)	7.5 (9.75)	0.10 (95%CI -2.65 – 2.83), p = 0.91
Nausea (%)	12 (28.6)	10 (26.3%)	χ^2 – p = 1.00
Vomiting (%)	8 (19%)	7 (18.4%)	χ^2 – p = 1.00
Median time to extubation (min)	182 (142.02)	180 (123.48)	-0.04 (95%CI -0.63 – 0.52), p = 0.95
Median ICU stay (hours)	37.5 (22.75)	35 (24)	0.523 (95%CI -7.65 – 9.28), p = 0.92
Median length of hospital stay (days)	6 (2)	6 (1)	-1.17 (95% CI -3.16 – 0.36); p = 0.22
$PaCO_2$ at 4h (mmHg)	39.09 (5.57)	39.7 (3.3)	0.61 (95% CI -1.29 – 2.52); p = 0.52
$PaCO_2$ at 12h (mmHg)	39.56 (3.49)	39.38 (3.15)	0.44 (95% CI -1.45 – 1.07); p = 0.53
$PaCO_2$ at 24h (mmHg)	37.28 (3.01)	36.98 (3)	-0.30 (95% CI -1.07 – 0.48); p = 0.49

NRS, cumulative opioid consumption, time to extubation, ICU and hospital length of stay are reported as median (IQR). PaCO2 at each reported timepoint is reported as mean (SD).
NRS, Numeric Rating Scale; MME, Morphine Milligram Equivalents; PaCO2, Arterial partial pressure of carbon dioxide; IQR, Interquartile Range; CI, Confidence Interval.

to the other surgical procedures (within groups comparison). In none of the other predefined analyses, we were not able to demonstrate a treatment effect between the two groups (see supplementary figures).

Discussion

In this monocentric, outcome-assessor blinded, prospective randomized clinical trial, we demonstrated that a single-shot superficial SAPB did not reduce the static pain intensity at 12 hours after extubation. Subsequently, the superficial SAPB fails to influence static pain intensity on the other predefined timepoints, cumulative opioid consumption in the ICU or any of the other secondary outcomes following MICS.

To our knowledge, this is the first RCT investigating the effects of a single-shot superficial SAPB in MICS. Available literature on the subject mainly focuses on deep SAPBs[10-12,16-18] with one trial combining a deep and superficial SAPB[19]. Based on the pilot study by Blanco et al.[9], we opted to administer a superficial SAPB as they showed a longer duration and better spread of the local anaesthetic in the superficial block compared to a deeper block. Although for exploratory reasons initiated, our subgroup analysis demonstrated a minimal clinical important reduction in static pain intensity by 39% in MIDCAB patients, 6 hours

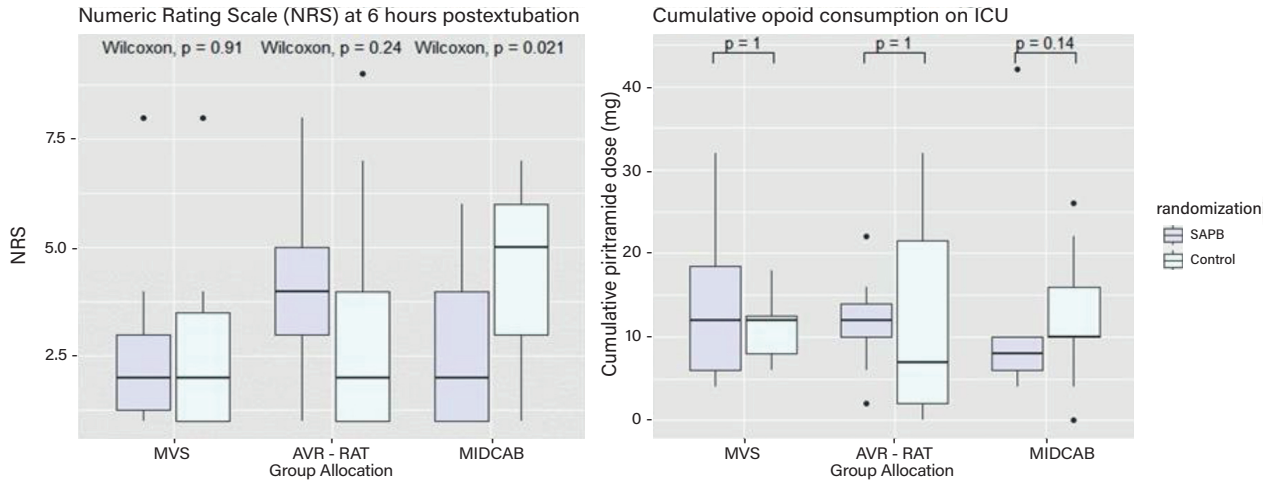

Fig. 3 — Subgroup analysis: NRS scores 6h after extubation and cumulative opioid consumption on ICU.
MVS, Mitral Valve Surgery; AVR-RAT, Aortic Valve Replacement via Right Anterior Thoracotomy; MIDCAB, Minimal Invasive Direct Coronary Artery Bypass; SAPB, Serratus Anterior Plane Block; NRS, Numeric Rating Scale.

after extubation and a reduced non-significant opioid consumption during their ICU stay. The within-group comparison also demonstrated a significant reduction in ICU length of stay for MIDCAB patients. However, this is the case in both SAPB and control group. As such, we believe this reduction in ICU length of stay is independent of the intervention and probably attributable to the nature of surgery (e.g. avoidance of cardiopulmonary bypass) and the lesser occurrence of atrioventricular blockade and atrial fibrillation without the need for additional temporary pacing and rhythm monitoring. Two RCTs demonstrated equally positive results in patients undergoing MIDCAB surgery with SAPB. Gautam et al.[16] demonstrated in 50 patients following MIDCAB surgery a reduction in static and dynamic pain intensity in patients receiving a deep SAPB followed by ropivacaine 0.2% continuous infusion. In an observational trial, Saikat et al.[17] demonstrated that a deep SAPB in patients following MICS could reduce VAS scores by nearly 2 points compared to patients receiving fentanyl. Additionally, a 30 hours shorter ICU length of stay was noted in the treatment group. A retrospective study by Moll et al.[18] failed to show a reduction in opioid consumption in robotic assisted-MIDCAB patients receiving SAPB. Moreover, the SAPB significantly underperformed with lesser opioid consumption in patients receiving a paravertebral block (PVB).

Our results acknowledge the diversity in results on the effect of a SAPB technique on pain intensity and opioid consumption relative to different surgical approaches. Our results fail to demonstrate that a superficial SAPB affects the outcomes in patients undergoing MVS via right anterior minithoracotomy. This result contrasts the findings of Toscano and colleagues[11] who reported significantly lower NRS scores and opioid consumption when administering a continuous deep SAPB in comparison to a continuous morphine IV infusion in patients undergoing minimally invasive MVS. Remarkably, their study was designed as an observational, non-blinded trial and they did report a high intraoperative sufentanil administration that could impair post-anaesthesia recovery significantly. In another surgical approach, AVR via right anterior thoracotomy, our results do not show an apparent benefit on pain intensity and opioid consumption. However, in a recent double-blinded RCT by Vandenbrande et al.[19], SAPB proved to be superior in terms of pain scores and cumulative opioid consumption compared to intravenous opioids alone in patients undergoing totally endoscopic aortic valve replacement (TEAVR) for up to 24 hours after surgery. Although these results are promising, we need to stress the difference in surgical approach and the SAPB administered which was a combination of a superficial and a deep SAPB.

In their 2021 consensus paper[20], both the American and European society of regional anaesthesia stressed the need for harmonization and standardisation of nomenclature in order to ultimately improve patient care. In order to investigate whether chest wall fascial plane blocks may improve patient care, one must understand the appropriate anatomic planes, the innervation of the specific regions of the chest wall and correlate these to the different surgical approaches[21]. Our study demonstrates this by failing to indicate a treatment effect in patients following AVR-RAT procedures. This more cranial and anteromedial incision could possibly explain why these patients in our study did not benefit from this block as opposed to the patients following MIDCAB surgery. Secondly, visceral pain, which is transmitted by different structures than skin-related pain, will not be addressed completely by a SAPB which could still trigger postoperative pain caused by chest tubes[21]. Moreover, the mechanism of action of FPBs still remains unclear, involving a lot of different factors (e.g. anatomical, technical, pharmacokinetical, physiological) contributing to the variability in block performance[22]. For this reason, all patients in both groups received local wound infiltration at the end of surgery along the incision site and ports for trocars/chest tubes to potentially diminish pain at these sites. Local wound infiltration is already known for its ability to reduce postoperative pain in cardiothoracic surgery[23,24]. The combination of a locoregional technique and local wound infiltration makes it less apparent to find additional analgesic results as our pain scores and cumulative opioid doses were relatively low in both groups. More specifically, our cumulative piritramide dose was 10 mg in both the SAPB group and control group, which is the equivalent of 7.5 mg morphine (MMEs), as per the opioid conversion table[15]. Lastly, one could argue the time-limited analgesic efficacy of a single-shot FPB as opposed to a catheter technique allowing continuous infusion of the same local anaesthetic agent. However, trials with continuous FPBs continue to produce inconclusive results as well. Recent published studies by Vanden Bussche et al.[25] and Hoogma et al.[26, 27] failed to demonstrate any treatment effect of a continuous SAPB and ESPB, respectively. Relative to the local anaesthetic administered, a single-shot SAPB may be beneficial ranging from 12h[10] up to 24h[19] postoperatively which coincides with the peak pain intensity after cardiac surgery[28]. Worth mentioning is recent work by Alfirevic et al.[29] in 194 patients under robotic assisted MVS. They

administered a combined SAPB and interpectoral-pectoserratus plane block with a mixture of plain and liposomal bupivacaine (Exparel®). Their results failed to show any (prolonged) treatment effect in terms of postoperative analgesia, cumulative opioid consumption or respiratory mechanics during the initial three days.

We emphasize that our study suffers from several limitations. Firstly, our study indicates the need to relate surgical approach to the regional chest wall technique applied. Subject to the different surgical approaches, this evident heterogeneity impacts the efficacy of the study and may weigh on potential results. Secondly, we could only show a significant result in our subgroup analyses which were set up as exploratory outcomes. However interesting and potentially hypothesis generating, these findings are difficult to interpret as we failed to demonstrate a significant effect on our predefined primary outcome. This could be attributable to the additive effects of a weight-based loading dose of piritramide, NRS-driven opioid administration, local wound infiltration and static NRS assessment 12 hours after extubation, which all may raise the detection limit of the provided analgesia due to the superficial SAPB. Additionally, the static NRS assessment after 12 hours needs to be read as performed 15 hours after block execution due to a median extubation time of 180 minutes. Moreover, we need to be careful to extrapolate these possible beneficial results from the MIDCAB subgroup as our study was not designed in this manner. The small sample sizes in our subgroup analyses complicate the generalisability of our findings. Thirdly, block administration was performed at the end of surgery. Due to the study design, we were not able to confirm dermatomal spread by postoperative assessment or to investigate the intraoperative effects of a preoperatively administered superficial SAPB. Fourthly, we opted not to use a sham block in the control group because the patient was asleep during block performance and avoiding getting the patient potentially exposed to serious harm (haemothorax, infection, pneumothorax, nerve injury)[30]. However, we would like to emphasise that all outcomes were assessed by blinded research personnel. We acknowledge that this choice of restricted blinding may induce bias to the study results. Fifthly, during the study design, the decision to investigate static pain intensity as the only pain intensity parameter was based on available literature[10]. The quality of the pain intensity assessment would have been more informative if dynamic pain intensity was assessed accordingly. Moreover, we acknowledge that we did not differentiate for the exact localisation causing pain (incision, chest tube or groin). The assessment of static and dynamic pain scores in combination with the precise location of pain would give us more information on block performance. Also, evidence on regional fascial plane techniques remains inconclusive. Future work that investigates block volume, type and concentration of local anaesthetic and the usefulness of repeat single shot blocks compared to catheter techniques is necessary before we standardise these blocks in our day-to-day patient care. Lastly, before data analysis we excluded 10 patients due to protocol violation. These violations were all minor violations in terms of study protocol execution. However, the potential bias inflicted upon the primary and secondary outcomes could weigh on the conclusions drawn.

To conclude, in our study setup, we could not demonstrate a reduction in static pain intensity at 12 hours after extubation in patients receiving a single-shot superficial serratus anterior plane block compared to intravenous opioid analgesia following MICS. Subsequently, we could not demonstrate a treatment effect on the static pain intensity scores at the other predefined timepoints and the cumulative opioid consumption in the first 48 postoperative hours. Results from the subgroup analyses suggest that patients undergoing MIDCAB surgery could potentially benefit from this block. Given the inconclusive available evidence, future research should aim to reduce heterogeneity in study design with a focus on patient-centred outcomes before we implement this technique in our standard clinical practice.

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Conflicts of Interest: Nothing to declare.

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