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Serratus plane block versus standard of care for pain control after totally endoscopic aortic valve replacement: a double-blind, randomized controlled, superiority trial

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ABSTRACT

Introduction Serratus anterior plane block has been proposed to reduce opioid requirements after minimally invasive cardiac surgery, but high-quality evidence is lacking.

Methods This prospective, double-blinded, randomized controlled trial recruited patients undergoing totally endoscopic aortic valve replacement. Patients in the intervention arm received a single-injection serratus anterior plane block on arrival to the intensive care unit added to standard of care. Patients in the control group received routine standard of care, including patient-controlled intravenous analgesia. Primary outcome was piritramide consumption within the first 24 hours after serratus anterior plane block placement. We hypothesized that compared with no block, patients in the intervention arm would consume 25% less opioids.

Results Seventy-five patients were analyzed (n=38 in intervention arm, n=37 in control arm). When comparing the serratus anterior plane group with the control group, median 24-hour cumulative opioid use was 9 (IQR 6–19.5) vs 15 (IQR 11.3–23.3) morphine milligram equivalents, respectively (p<0.01). Also, pain scores at 4, 8 and 24 hours were lower in the intervention arm at 4, 8 and 24 hours, respectively.

Conclusion Combined deep and superficial single-injection serratus anterior plane block is superior to standard of care in reducing opioid requirements and postoperative pain intensity up to 24 hours after totally endoscopic aortic valve replacement.

Trial registration number NCT04699422.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Opioids remain analgesic standard of care after minimally invasive cardiac surgery (MICS). Evidence on the opioid-sparing effect of serratus anterior plane block (SAPB) after MICS is limited to non-randomized studies.

WHAT THIS STUDY ADDS

⇒ We performed the first double-blinded, randomized controlled trial of SAPB after MICS and found a >25% reduction in opioid requirements.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Future studies should focus on optimization of timing, drugs and dosage of SAPB after MICS.

INTRODUCTION

Aortic valve disease is a relevant healthcare problem.[1] Approximately 3–4% of the Western population suffer from moderate to severe aortic valve disease, and its prevalence rises to 6% in patients over the age of 75 years.[1] Considering the increase in life expectancy, aortic valve disease will even become more prevalent in the future.[1] The only curative treatment for moderate to severe disease is aortic valve replacement (AVR) or aortic valvuloplasty. Aortic valve surgery has undergone a tremendous evolution, going from open-heart surgery requiring sternotomy to minimally invasive cardiac surgery (MICS) to transcatheter techniques.[2] Totally endoscopic aortic valve replacement (TEAVR) is an innovative technique in which access to the surgical field is acquired by making four access points in the right anterolateral hemithorax.[3–5] Consequently, sternal fractures or costal spreading is averted, and surgical trauma is reduced. This technique fits the concept of enhanced recovery after cardiac surgery (ERACS) to promote early resumption of daily activities.[6]

In contrast to the surgical advancements, analgesic regimens after cardiac surgery did not change significantly.[7] Opioids remain the cornerstone of analgesia in the postoperative cardiac surgical recovery units, despite known side effects such as respiratory depression, postoperative nausea and vomiting (PONV) and the risk of long-term dependence.[8] Intrathecal opioid anesthetic techniques after cardiac surgery have been proven to reduce opioid consumption.[9] Their implementation in clinical practice however remains controversial for two reasons.[9] First, heparinization is required for cardiac surgery. This anticoagulated state increases the risk of neuraxial hematoma, leading to deleterious complications such as paraplegia. Second, neuraxial anesthesia induces orthosympathicolysis, which contributes to prolonged need for vasopressors, impeding early intensive care discharge. A

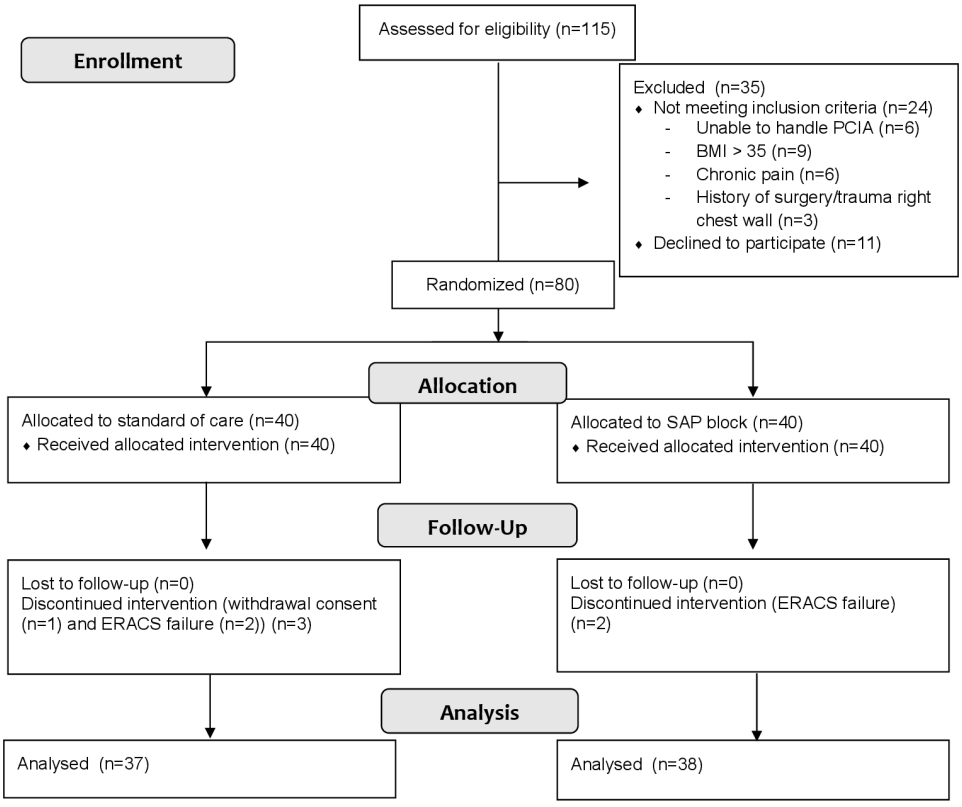

Figure 1 CONSORT participant flow diagram. BMI, body mass index; CONSORT, Consolidated Standards of Reporting Trials; ERACS, enhanced recovery after cardiac surgery; PCIA, patient-controlled intravenous analgesia; SAP, serratus anterior plane.

recent systematic review by Yu *et al* called for prospective studies investigating the role of ultrasound (US)-guided fascial plane blocks to reduce opioid consumption after cardiac surgery.[10] These blocks fit well in future ERACS programs since they lack sympathicolysis and the associated risks and consequences of superficial hematoma are limited.[11] Recently, a multitude of fascial chest wall blocks has been described.[12] US-guided serratus anterior plane block (SAPB) is a chest wall block targeting the lateral cutaneous branches of the thoracic intercostal nerves (T2–T9).[13] Its analgesic efficacy has been studied in thoracic surgery and rib fractures but data from the cardiac surgical population are limited.[14] Therefore, we propose the first double-blinded, randomized controlled, superiority trial comparing US-guided SAPB with standard of care after TEAVR. We hypothesize that compared with no block, patients with SAPB would consume 25% less opioids over the first 24 postoperative hours.

METHODS

Trial design and eligibility criteria

This double-blinded, single-centre, prospective, randomized controlled, superiority trial is registered on ClinicalTrials.gov on November 30, 2020 (NCT04699422). The first patient was included on December 3, 2020. This study is conducted in accordance with the Declaration of Helsinki and structured in the format as suggested by the Consolidated Standards of Reporting Trials (CONSORT) statement.[15]

All patients scheduled for TEAVR were counseled on the risks of general anesthesia and SAPB and were approached for participation in the preoperative assessment clinic. After obtaining written informed consent, 80 consecutive adult patients with a European System for Cardiac Operative Risk Evaluation (EuroSCORE II), the current ≤30% undergoing TEAVR, were included. EuroSCORE II is an objective scoring system taking into account patients' comorbidities as well as surgical circumstances. The patient's EuroSCORE reflects the probability (expressed as a percentage) for in-hospital mortality. Exclusion criteria included (1) refusal to participate, (2) chronic use of opioids and/or analgesic antidepressants and/or analgesic antiepileptics, (3) history of chronic pain, major trauma or prior surgery to right chest wall, (4) allergy to opioids, acetaminophen and/or local anesthetics, (5) morbid obesity (body mass index (BMI) >35), (6) low body weight (<50 kg), (7) pregnancy, (8) perioperative events compromising early postoperative recovery, and (9) the inability to understand and adhere to the study design.

Baseline assessment measurements included the patients' age, gender, BMI, medical history, EuroSCORE II, fear of the surgical procedure (using an eight-item Surgical Fear Questionnaire),[16 17] and preoperative pain (the baseline Numeric Rating Scale (NRS) score on an 11-point scale (where 0=no pain and 10=worst pain imaginable).

Randomization

Participants were randomly assigned in a 1:1 ratio to US-guided SAPB in addition to standard of care (patient-controlled intravenous analgesia (PCIA) with piritramide) (n=40) or standard of care (n=40). A block randomization of 6 was performed using a computer-generated random allocation sequence created by the study statistician. Allocation numbers were sealed in opaque envelopes, which were opened in sequence by a member from the block team before entering the intensive care unit (ICU) room. Members from the block team were never involved in the perioperative care or in the assessment of outcomes. The

Table 1 Perioperative variables

	PCIA only	PCIA+SAPB	Standardized difference*†
Sample size, n	37	38	
Sociodemographic characteristics			
Mean age (SD) in years	67.0 (10)	71.7 (8.7)	−0.50
Sex, n (%)			
Male	22 (59.5)	25 (65.8)	0.06
Female	15 (40.5)	13 (34.2)	
Surgical characteristics			
Mean surgical time (SD) in min	142.0 (42.5)	137.7 (30)	0.12
Type of surgery, n (%)			
Aortic valve replacement	37 (100)	37 (97.4)	
Aortic valvuloplasty	0 (0)	1 (2.6)	
Mean surgical fear (SD) in points	3.1 (2.4)	3.2 (2.0)	
Mean intraoperative dose (SD)			
Sufentanil in µg	45.6 (23.4)	39.0 (21.8)	0.29
Ketamine in mg	38.8 (21.8)	40.0 (41.8)	−0.27
Intensive care characteristics			
Mean total dexmedetomidine dose (SD) in µg	261.4 (99.1)	280.7 (100.7)	−0.19
Postoperative use of NSAIDs, n (%)			
Yes	23 (62.2)	30 (79.0)	−0.17
No	14 (37.8)	89 (21.1)	
Mean time (SD) between ICU arrival and SAPB placement in min	46 (15.0)	40 (20.0)	0.12
Median chest tube indwelling time (IQR) in hours	20.8 (16.3–26.3)	20.6 (17.7–23.1)	0.28
Median (IQR) baseline pain in rest	0 (0–0.5)	0 (0–0.3)	0.05
Mean BMI (SD) in kg/m^2	28.1 (3.8)	27.4 (3.3)	0.2
Mean ASA classification (SD)	3.7 (0.5)	3.7 (0.5)	0.04
Mean EuroSCORE II (SD) in %	1.4 (0.5)	1.7 (0.8)	−0.5
Diabetes mellitus, n (%)	8 (21.6)	7 (18.4)	0.03
Baseline LVEF (SD) in %	58.7 (10.9)	59.2 (7.2)	−0.04
Baseline pain at rest (IQR) in points	0 (0–0.5)	0 (0–0.25)	0.05
Baseline quality of life			
EQ5D			
Index	0.8 (0.8–0.9)	0.8 (0.8–0.9)	0.32
VAS score	73.0 (60.0–80.0)	70.0 (63.8–81.3)	0.05
SF-36			
Physical functioning	80.0 (65.0–95.5)	67.5 (42.5–85.0)	0.64
Role-physical health	100.0 (0.0–100.0)	100.0 (0.0–100.0)	0.02
Pain	100.0 (78.8–100.0)	100.0 (77.5–100.0)	0.22
General health	80.0 (65.0–85.0)	70.0 (60.0–85.0)	0.27
Role-emotional health	100.0 (100.0–100.0)	100.0 (100.0–100.0)	−0.29
Energy	70.0 (55.0–90.0)	65.0 (50.0–85.0)	0.27
Emotional well-being	88.0 (76.0–100.0)	88.0 (79.0–96.0)	−0.75
Social functioning	100.0 (100.0–100.0)	100.0 (85.0–100.0)	0.28

*Standardized difference compares PCIA only versus PCIA plus SAPB.
†Cohen's d estimator used to calculate standardized mean differences between both groups.
ASA, American Society of Anesthesiologists; BMI, body mass index; EQ5D, 5-Dimensional European Quality of Life; EuroSCORE, European System for Cardiac Operative Risk Evaluation; ICU, intensive care unit; LVEF, left ventricular ejection fraction; NSAIDs, non-steroidal anti-inflammatory drugs; PCIA, patient-controlled intravenous analgesia; SAPB, serratus anterior plane block; SF-36, 36-Item Short Form Health Survey; VAS, Visual Analog Scale.

randomization list remained with the study statistician for the whole duration of the study.

Interventions, study procedures and blinding

In TEAVR, access is gained by four points on the right anterior hemithorax: next to three 5 mm trocar ports, one utility port of 3 cm is inserted in the second intercostal space and spread with a soft tissue retractor (online supplemental figure 1A).

The anesthesia and critical care treatment was standardized according to our ERACS protocol. Anesthesia was induced with 0.2 µg/kg sufentanil, 1–2 mg/kg propofol and 1 mg/kg rocuronium. Anesthesia was maintained by sevoflurane with Patient State Index (Sedline, Masimo) targeted between 25 and 50. On incision, 1 mg/kg ketamine was administered. Intraoperatively, sufentanil top-ups were allowed as judged by the attending blinded anesthesiologist. Dexmedetomidine was initiated at 0.8 µg/kg/hour on cardiopulmonary bypass. PONV prophylaxis was provided with dexamethasone (5 mg), ondansetron and alizapride unless contraindications. Fluid regimen, and use of vasopressors and/or inotropes were based on judgment by

Table 2 Primary and key secondary outcomes

	PCIA only	PCIA+SAPB	Difference (95% CI)	P value*†
Sample size, n	37	38		
Primary outcome				
24-hour piritramide use (MME)	15.0 (11.3–23.3)	9.0 (6.0–19.5)	5.8 (1.5, 10.1)	<0.01
Secondary outcome				
Pain scores (NRS)				
4 hours	3.0 (1.0–5.0)	2.0 (0.0–3.0)	1.0 (0.0, 2.0)	0.05
8 hours	3.0 (1.0–4.3)	1.0 (0.0–4.0)	1.0 (0.0, 2.0)	0.03
12 hours	2.5 (0.0–5.0)	2.0 (0.0–3.8)	0.0 (–1.0, 2.0)	0.47
24 hours	4.0 (2.0–5.0)	2.0 (1.0–4.0)	1.0 (0.0, 2.0)	0.04

*P value compares PCIA only versus PCIA+SAPB.
†Student's t-test was used to compare means and Mann-Whitney U test was used to compare medians.
MME, morphine milligram equivalent; NRS, Numeric Rating Scale; PCIA, patient-controlled intravenous analgesia; SAPB, serratus anterior plane block.

the attending anesthesiologist. Postoperatively, the patient was transferred intubated to the ICU with dexmedetomidine as sole sedative agent. Transfer was performed by the blinded anesthetic team who handed over to the blinded ICU staff. At this point, a member from the block team opened the sealed envelope.

US-guided SAPB group

The block team approached the patient immediately after ICU admission while all ICU personnel left the room. All equipment to perform the SAPB was brought in a closed box by the block team. SAPB was performed according to the method described by Blanco *et al*.[13] Patients were maintained in the supine position and the right arm was abducted. The fifth rib was identified in the midaxillary line with A Sono Site Xporte US (Fujifilm, Japan) machine using a 15 MHz linear transducer placed in a coronal orientation. Next, the latissimus dorsi, teres major and serratus muscles were identified overlying the fifth rib. Additionally, the thoracodorsal artery was identified in the plane superior to the serratus muscle. After disinfection of the skin, a 22 G Stimuplex Ultra 100 mm (B Braun Medical, Melsungen, Germany) needle was introduced in-plane from anterosuperior to posteroinferior until the needle tip was positioned in the plane underneath the serratus muscles. Under continuous US guidance, bupivacaine 0.25% 30 mL was injected. Afterwards, the needle was withdrawn to the plane superficial to the serratus muscles where

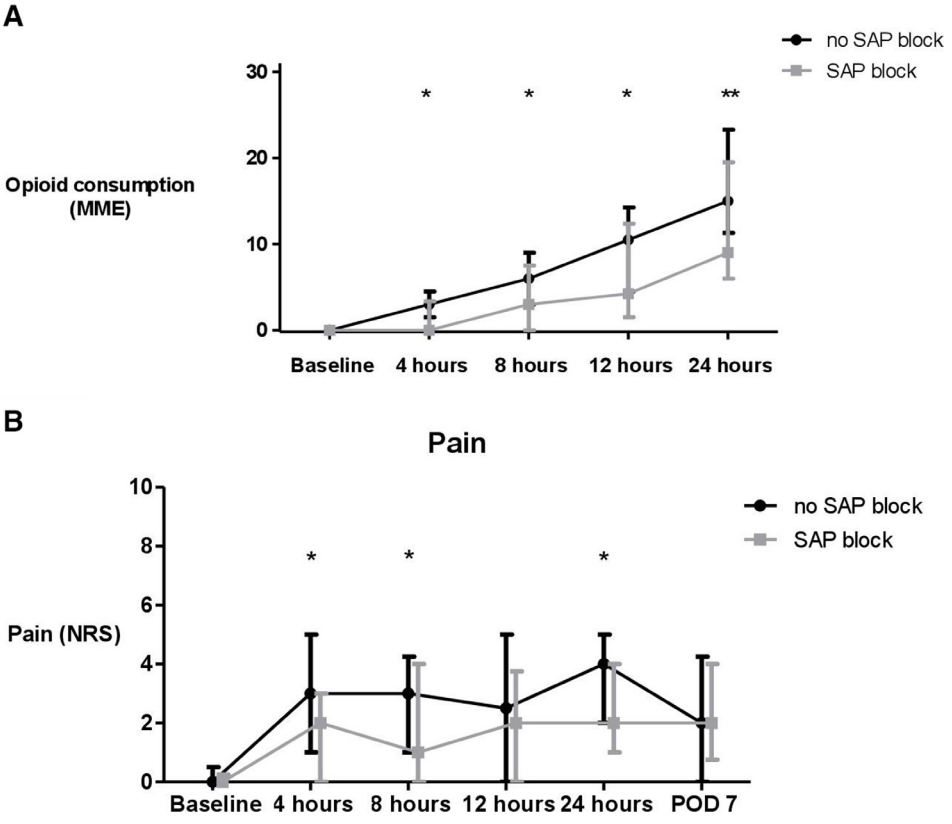

Figure 2 (A) Cumulative opioid consumption (MME) up to 24 hours after block placement. Significant differences (p<0.05) are marked with an asterisk (*). Strongly significant p<0.01 is marked with **. (B) Pain scores (NRS) at predefined time intervals. Statistically significant differences (p<0.05) are marked with an asterisk (*). MME, morphine milligram equivalent; NRS, Numeric Rating Scale; POD, postoperative day; SAP, serratus anterior plane.

Table 3 Secondary outcomes

	PCIA only	PCIA+SAPB	Difference (95% CI)	P value*†
Opioid-free postoperative	0 (0)	2 (5.3)	−0.1 (−0.2, 0.1)	0.49
Severe PONV	1 (2.7)	1 (2.6)	0.0 (−0.6, 0.1)	0.98
Need for PONV treatment				
Ondansetron	6 (16.2)	7 (18.4)	0.0 (−0.2, 0.2)	0.80
Alizapride	5 (13.5)	6 (15.8)	0.1 (−0.2, 0.1)	0.78
Time to first defecation (SD), days	2 (1.0–3.0)	2 (1.0–4.0)	0.0 (−1.0, 1.0)	0.61
Use of laxatives	7 (19.4)	14 (36.8)		0.09
Time to extubation (SD), in min	145.0 (86.5–246.5)	173 (124.5–274.3)	−28.0 (−76.0, 19.0)	0.26
LOS ICU (SD), in hours	20.5 (17.7–27.2)	21.3 (17.4–26.1)	−17 (−3.8, 3.8)	0.92
LOS hospital (SD), in hours	4.0 (3.0–5.0)	4.0 (3.0–5.0)	0.0 (−1.0, 0.0)	0.53

*P value compares PCIA only versus PCIA+SAPB.
†Student's t-test was used to compare means and Mann-Whitney U test was used to compare medians.
ICU, intensive care unit; LOS, length of stay; PCIA, patient-controlled intravenous analgesia; PONV, postoperative nausea and vomiting; SAPB, serratus anterior plane block.

10 mL bupivacaine 0.25% 10 mL was injected (online supplemental figure 1B).

A Band-Aid was placed over the entry hole of the needle. The block team remained in the room for 15 min in total. No block equipment was left to keep ICU physicians, ICU nurses and surgical staff blinded.

Control group

To ensure blinding, these patients were similarly approached by the block team after ICU admission while all ICU personnel left the room. Likewise, all equipment to perform the SAPB was brought into the closed ICU box. The block team disinfected the skin at the right hemithorax region. For infection prophylaxis reasons, no sham SAPB was performed. A Band-Aid was placed over the hypothetical needle entry point. The block team stayed for 15 min in the patient's room.

Postoperatively, all patients received a multimodal pain regimen including acetaminophen 15 mg/kg every 6 hours, ketorolac 10 mg (<60 kg body weight) or 20 mg (>60 kg body weight) every 8 hours unless contraindications and a PCIA system (IVAC PCAM, Cardinal Health) with piritramide programmed at 2 mg bolus on request with lockout interval of 15 min. Decision-making concerning extubation and discharge to the ward was left to the discretion of the blinded ICU staff.

Outcome measures

The primary superiority outcome measure was the cumulative opioid consumption (piritramide delivered by the PCIA system) during the first 24 hours after block placement. Information on total amount of piritramide consumption was extracted from the PCIA system and converted to morphine milligram equivalents (MMEs) according to the opioid conversion table.

Key secondary superiority outcome measures were opioid consumption at 4-hour intervals (0–4 hours, 4–8 hours, 8–12 hours) and 12-hour interval (12–24 hours), number of opioid-free patients 24 hours after surgery and postoperative pain intensity at rest measured by an 11-point NRS at 4 hours, 8 hours, 12 hours and 24 hours after ICU arrival and on postoperative day (POD) 7.

Quality of recovery (QoR) was assessed on POD 2 and POD 7 with the 5-Dimensional European Quality of Life[18] and 36-Item Short Form Health Survey (SF-36) questionnaires.[19] PONV was assessed on POD 1 by the simplified Postoperative Nausea and Vomiting Impact Scale.[20] Severe PONV was defined as a score of 5 or more. Overall patient satisfaction with analgesic therapy was assessed on POD 1 with an 11-point NRS (where 0=not satisfied at all and 10=extremely satisfied). Finally, time to extubation; duration of vasopressor infusion; incidences of subcutaneous emphysema, new-onset postoperative atrial fibrillation, constipation, and pneumonia (defined as need for empiric antibiotic therapy during hospital stay); ICU and hospital length of stay were assessed. All data were collected by a blinded research team member.

Sample size calculation

The sample size was determined for the primary outcome aiming to demonstrate superiority of SAPB compared with standard of care analgesia. A 25% reduction in opioid consumption between groups was considered clinically relevant. Based on a retrospective analysis of unpublished data from our hospital, we assumed a mean cumulative piritramide consumption over 24 hours of 12±4.6 mg (in patient who underwent TEAVR). Assuming $\alpha=0.05$ and power=0.80 for a 25% difference in cumulative piritramide consumption at 24 hours using a two-sided X^2 test, the calculated sample size was 74. To account for a possible 10% drop-out rate, the sample size was increased to 40 patients per group.

Statistical analysis

All primary and secondary endpoints were analyzed on an intention-to-treat basis according to a superiority design. Missing baseline values were imputed using multiple imputation. The number of imputations was set to 10. Categorical variables are presented as frequencies and percentages. Numerical variables are presented as mean±SD for normally distributed data and median (25%, 75%) in case of non-normal distribution. Standardized mean differences were calculated to evaluate differences between groups at baseline and perioperatively (Cohen's d estimator). Normal distributed data were compared using a Student's t-test. Non-normal distributed data were compared using the Mann-Whitney U test. The Hodges-Lehmann estimator was used to compute the median difference and the 95% CI. Additionally, a X^2 test (or Fisher's exact test if necessary) was used to compare proportions. For repeated measures, a Bonferroni correction was applied. A p value of <0.05 was considered statistically significant for the primary outcome. All analyses were performed with SPSS V.28.

RESULTS

A CONSORT flow chart depicting patient inclusion and exclusion is presented in figure 1. From January 2021 until June

2022, 115 patients were screened for eligibility, of which 35 patients were excluded due to refusal to participate (n=11) or not meeting the inclusion criteria (n=24). Finally, 80 patients were recruited and received the allocated treatment. Five patients were excluded from the statistical analysis: two patients in both the intervention group and control group required revision surgery within 24 hours and one patient in the control arm withdrew informed consent shortly after awakening. Follow-up until POD 7 was complete in the remaining 75 cases.

Baseline and perioperative characteristics are presented in table 1. Groups were comparable at baseline except for age and EuroSCORE II where a small difference was noted (table 1).[21] A medium-sized baseline difference was observed for the physical functioning part of the SF-36 questionnaire, in favor of the control group.

For the primary outcome, median piritramide opioid consumption over the first 24 postoperative hours was 9.0 MME (6.0–19.5) in the SAPB group vs 15.00 MME (11.3–23.3) in the control group. Hence, superiority of SAPB, defined as a 25% reduction in opioid consumption, was confirmed (mean difference (95% CI): 5.8 MME (1.5 to 10.1 MME); p<0.01) (table 2).

Also, within the first 4 hours after block placement, patients in the SAPB group (median 0 MME; quartiles, 0–3.3 MME) consumed significantly less piritramide than patients without block (median 3 MME; quartiles, 1.5–4.5) (p=0.02) (figure 2A).

Postoperative pain intensity at rest was lower in the SAPB group at 4 hours (median NRS 2; quartiles, 0–3 vs 3; quartiles, 1–5 in the control group; p=0.05), at 8 hours (median NRS 1; quartiles, 0–2 vs 3; quartiles, 1–4 in the control group; p=0.03) and at 24 hours (median NRS 2; quartiles, 1–4 vs 4; quartiles, 2–5 in the control group; p=0.04) after block placement (table 2 and figure 2B).

Nil opioid-free patients were observed in the no block group vs 2 in the SAPB group (p=0.16) (table 3).

QoR outcome results at PODs 2 and 7, patient satisfaction and side effects are presented in online supplemental table 1.

Other secondary outcome results are presented in table 3.

DISCUSSION

In the present study, a US-guided SAPB was found to be superior in reducing the cumulative opioid consumption as compared with standard of care up to 24 hours after TEAVR. The cumulative opioid consumption was significantly lower in the SAPB group in all 4-hour intervals (0–4 hours, 4–8 hours, 8–12 hours) and also between 12 and 24 hours after surgery. Also, pain scores at rest were also lower in the SAPB group at 4, 8 and 24 hours after surgery.

This finding might not be surprising since SAPB provides analgesia to the anterolateral chest wall and its analgesic potency has been demonstrated in studies after thoracic surgery and chest wall trauma. Data in the cardiac surgical population however originate from non-blinded and non-randomized controlled trials. Berthoud *et al* found significantly lower opioid consumption and pain scores with single-injection SAPB compared with continuous wound infiltration after MICS.[22] Both ICU and hospital length of stay were reduced in the SAPB group. Their retrospective study was limited to 46 patients undergoing various types of MICS. Another retrospective analysis in 197 robotic coronary artery bypass graft patients did not show any significant decrease in opioid recruitment after SAPB.[23] In contrast, a prospective study by Toscano *et al* observed a significant decrease in opioid consumption and pain scores when continuous deep SAPB was added to standard of care after minimally invasive mitral valve repair.[24] In the latter study, no differences in duration of mechanical ventilation, ICU nor hospital length of stay were noted.[24] Although prospective in design, patients were not randomized in Toscano *et al*'s study.[24] Also, opioid regimen was based on a pro re nata regimen as judged by a non-blinded caregiver. Nonetheless our double-blind, randomized controlled trial confirms this earlier weak evidence for reduced opioid consumption and pain scores at rest when SAPB is added to standard of care after minimally invasive cardiac valve surgery. Only Moll *et al* did not find the same favorable outcome but their study population underwent robotic coronary artery bypass grafting, which involves a more extensive surgical field.[23] After cardiac surgery, a mean morphine consumption of 27 mg during the first 24 postoperative hours is generally accepted.[25] In our study, a median morphine equivalent of 9 mg was required in the SAPB group vs 13.3 mg in the standard of care group. This 40% reduction in MME is classified as a minimal clinically important difference according to orthopedic pain management literature.[26] Also, regarding the ongoing opioid pandemic, this reduction is important since higher initial opioid doses are a risk factor for persistent opioid (mis)use after cardiac surgery.[27]

In this study, we opted for a combined deep plus superficial SAPB. As TEAVR is performed anteriorly, we opted for a higher volume in the deep SAPB since MRIs suggest that the deep injectate appeared to spread more anteriorly compared with the superficial SAPB.[13] On the other hand, blockade of the long thoracic and thoracodorsal nerves superficial to the serratus muscle is important to reduce chest tube pain and has a longer time of action. Various previous studies on the effect of SAPB after cardiac or thoracic surgery used various planes for their injection: single injections in the superficial or deep plane or a combination of both.[14] To the best of our knowledge, no clinical study directly compared single-injection deep with single-injection superficial SAPB so outcome data are lacking. As a comparator, in studies on SAPB after MICS, all authors performed uniquely deep SAPB[22–24] with variable results as described earlier.

Our study has some limitations. First, we performed a single-center study in patients undergoing an innovative surgical technique. Generalizability of our findings to other centers and similar techniques such as AVR via right anterolateral thoracotomy needs to be established. Second, patients in the no-block group appeared to be slightly younger. This gap however seems clinically irrelevant for two reasons: the found difference in opioid consumption between both groups doubled the predicted difference as expected by age.[28] Furthermore, in the population above 65 years, high frailty rather than younger age is the primary predictor for increased postoperative opioid consumption.[29] Patients randomized to the SAPB group in our study appeared to be more frail as indicated by their lower SF-36 physical component summary scores.[30] However, they consumed significantly less opioids in the postoperative phase. Finally, our study did not find differences in secondary outcome parameters such as postoperative mechanical ventilation time or length of stay. This might question the clinical relevance of observed lower opioid consumption and pain scores or might be attributed to the limited sample size and residual use of high intraoperative opioid doses.

In conclusion, our data demonstrate that up to 24 hours after TEAVR, combined deep and superficial single-injection SAPB is superior to standard of care in reducing need of opioids and postoperative pain intensity at rest. Future studies are needed to investigate the clinical relevance of SAPB in this population.

Contributors JV, BS and HJ conceived of the study. JV, BS, BJ and HJ initiated the study design. IC, EvH, LP and AY helped with the implementation. IC was responsible for the statistical analysis. EvH and LP were responsible for the data collection. JV, BS, HJ, LS and RB were responsible for the data interpretation. All authors were responsible for the writing of the manuscript and approved the final manuscript. JV is the guarantor.

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Competing interests None declared.

Patient consent for publication Obtained.

Ethics approval This study involves human participants. This double-blinded, single-center, prospective, randomized controlled, superiority trial is approved by the ethical committee of the Jessa Hospital, Hasselt, Belgium (Chairperson Dr K Magerman, registration number B2432020000026) on November 23, 2020. Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article or uploaded as supplemental information. Due to the applicable privacy regulation (GDPR) and Good Clinical Practices (GCP) legislation, the full underlying dataset supporting the study cannot be provided. This dataset contains potentially identifying information, for example, age, BMI and comorbidities such as diabetes mellitus leading to a unique subject in the dataset. Therefore, descriptive statistics have been used for a general overview of our study population, and all other relevant information is provided in table 1.

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