Original Article

Efficacy of ultrasound-guided second serratus anterior plane block on postoperative quality of recovery and analgesia after video-assisted thoracic surgery: a randomized, triple-blind, placebo-controlled study

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Background: Despite widespread application of minimally invasive video-assisted thoracic surgery (VATS), postoperative pain following this procedure is still a constant clinical challenge. Serratus anterior plane (SAP) block is one of the regional analgesic techniques with promising outcomes. However, due to the limited duration of action, optimal analgesia is often not achieved with a single injection. We tested whether in patients who have been subjected to routine SAP block under preoperative anesthesia, the addition of a second SAP block 24 hours after surgery, improves quality of recovery, lowers postoperative opioid consumption, and reduces the prevalence of chronic pain.

Methods: The present study is a single institutional, prospective, randomized, triple-blinded, placebo-controlled study. Ninety patients undergoing VATS from January 2022 to April 2022 were randomized at 1:1 ratio to receive ultrasound-guided second SAP block with 15 mL 0.375% ropivacaine (SAP block group) or 15 mL normal saline (control group) 24 hours after both groups received routine SAP block with 15 mL 0.375% ropivacaine. The primary outcome was quality of patient recovery, measured using 40-item quality of recovery questionnaire (QoR-40) at postoperative day 2 (POD 2). Secondary outcomes included: postoperative pain scores at rest, postoperative opioid consumptions, number of times that patient controlled analgesia (PCA) pump button was pressed, perioperative complications and adverse effects, prevalence of chronic pain at 2nd and 3rd month postoperatively, and length of hospital stay (LOS).

Results: A total of 83 patients completed the study: 43 patients in SAP block group and 40 patients in the control group. The global QoR-40 scores on POD 2 and POD 3 were significantly higher among SAP block group patients (180.07±11.34, 182.09±8.20) compared with the control group (172.18±6.15, 177.50±6.94) (P=0.01, P=0.008) respectively. Postoperative pain scores, opioid consumptions and incidence of postoperative nausea and vomiting were significantly lower among patients in SAP block group versus control group. There were no statistically significant differences in perioperative complications and LOS between the two groups. The prevalence of chronic pain at the 2nd and 3rd month postoperatively for patients in SAP block group and control group was 16.3%, 14%, and 32.5%, 27.5% respectively.

Conclusions: In patients undergoing VATS, application of ultrasound-guided second SAP block 24 hours after surgery improved postoperative quality of life, reduced opioid consumption and related side effects, and lowered the prevalence of chronic pain.

Keywords: Video-assisted thoracic surgery (VATS); serratus anterior plane block (SAP block); thoracic nerve block

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Introduction

Video-assisted thoracic surgery (VATS) is gradually replacing open thoracotomy for lung surgery with benefits such as minimal tissue damage, reduced surgical stress response, and quicker recovery (1,2). However, postoperative pain following this procedure remains a persistent clinical problem (3,4). If it is not addressed, acute postoperative pain can limit the patients' ability to cough, which is required to excrete secretions from airway and operation site, thereby causing complications such as pneumonia and atelectasis (5). Acute postoperative pain can also limit patients' mobility, restricting them to their beds, thus increasing the risk of deep vein thrombosis among other complications (6); these complications are likely to lower patients' satisfaction rates and in general negatively impact their enhanced recovery after surgery (ERAS).

Highlight box

Key findings

- This study found that in patients who have been subjected to routine serratus anterior plane (SAP) block under preoperative anesthesia, the addition of a second SAP block 24 hours after surgery, improves the quality of recovery, prolongs analgesia, lowers postoperative opioid consumption, and reduces the prevalence of chronic pain.

What is known and what is new?

- SAP block provides promising analgesic outcomes after video-assisted thoracic surgery (VATS). However, due to the limited duration of action, optimal analgesia is often not achieved with a single injection. This study implies that the addition of a second SAP block 24 hours after surgery, not only prolongs analgesia, but also lowers the dependency on postoperative opioids medications. Moreover, through application of a second SAP block, prolonged analgesia can be achieved without relying on more invasive techniques such as thoracic epidural analgesia.

What is the implication, and what should change now?

- The conclusions of this study address postoperative opioids dependence, postoperative pain control and prevalence of chronic pain in patients undergoing VATS.

Moreover, acute postoperative pain is one of the risk factors for developing chronic pain, which is estimated to be around 33% after VATS (7,8). Chronic post-thoracoscopic pain (CPTP) prolongs patient recovery and exposes patients to long-term use of pain medication, such as opioids, thus negatively impacting their quality of life (9). Therefore, adequate post-thoracoscopic pain control is vital because it enhances recovery after thoracic surgery (ERATS) (10).

Traditionally used systematic analgesia drugs such as opioids are effective in managing moderate to severe postoperative pain; however, adverse effects such as postoperative nausea and vomiting (PoNV) limit their clinical use. Moreover, prolonged opioid use is thought to be independently associated with reduced long-term disease-specific survival after lung cancer surgery (11). Similarly, widely popular regional analgesia techniques such as thoracic epidural analgesia (TEA) and paravertebral block (PVB) carry risks of urinary retention, respiratory depression, hypotension and pneumothorax (12,13), which can be fatal if not timely and adequately managed.

Facing this dilemma, there has been a growing interest in interfacial plane blocks over the last decade. Compared with traditional and regional pain control methods, these plane blocks are limited to the area of applications, hence, they are associated with fewer side effects. Serratus anterior plane (SAP) block was first described by Blanco *et al.* (14) in 2013 as a novel analgesic method that can provide long-lasting paresthesia (750–840 min) in the chest region with fewer side effects. Since then, various studies have reported its efficacy in providing analgesia following VATS. However, owing to its limited duration of efficacy, optimal analgesic efficacy is often not achieved by a single-injection. In a recent Korean study (15), the efficacy of single-injection SAP block was investigated among patients undergoing VATS, the authors found that the difference in opioid consumption between the intervention group (SAP block group) and control group (normal saline group) was only significant up to 24 hours postoperatively. Similarly, a good chunk of previous studies (16-18) have demonstrated that single-injection SAP block lowers postoperative

opioid consumption only in the first 24 hours post-surgery. Since opioid medications are the mainstay management of moderate to severe postoperative pain (19), this shows that the analgesic efficacy of a single-injection SAP block beyond 24 hours is weak, and unless supplementary pain medication is provided, patients can quickly be exposed to pain stimulus, which not only negatively impacts ERATS but also increases the risk of developing CPTP (8).

In this prospective, randomized, triple-blind, placebo-controlled, single-center study, we tested the hypothesis that in patients who have been subjected to routine SAP block under preoperative general anesthesia, the addition of a second SAP block 24 hours after VATS, improves quality of recovery, prolongs analgesia, reduces opioid consumption in postoperative day 2 (POD 2) and POD 3, and lowers prevalence of CPTP. We present this article in accordance with the CONSORT reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-982/rc).

Methods

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by ethics review board of Tongji Hospital affiliated to Tongji Medical College of Huazhong University of Science and Technology (reference number TJ-IRB20220141) and informed consent was obtained from all individual participants. We enrolled patients scheduled for elective thoracic procedures in our department from January 31, 2022, to April 30, 2022. The individual indications for surgery were bullectomy, mediastinal tumor resection, wedge resection, segmentectomy, and lobectomy.

Inclusion criteria were American Society of Anesthesiologists (ASA) physical status I–III patients, aged between 18 to 70 years old, patients who volunteered to join this study, who were willing to cooperate with follow-up and who agreed to use patient-controlled analgesia (PCA) pump after surgery. Exclusion criteria were patients scheduled for thoracotomy or converted to thoracotomy, with history of drug abuse or long-term use of analgesic drugs, with previous history of chest surgery, with history of chronic pain diseases, infection or scar tissue at the puncture site, and with allergic history of local anesthetic drugs.

This study employed a parallel randomized trial design. All participants signed an informed consent form before commencement of the study and were randomly allocated to either the experimental group (SAP block) or the control group (normal saline) in a 1:1 ratio using SPSS 26.0 (IBM Corp, Armonk, NY, USA) software by an independent study investigator who was not involved in the study process. Group allocation and study code were folded, sealed in an opaque envelope and handed over to the anesthesia nurse. The anesthesia nurse prepared 15 mL 0.375% ropivacaine and 15 mL 0.9% normal saline according to group allocation, stored them in identical syringes and labelled them drug A or drug B accordingly. The nurse only prepared the intervention drugs and was not involved in the study process, hence maintaining her blind status. Similarly, the attending surgeons, attending anesthesiologists who administered the SAP block, patients, study investigators, the data collection and analysis team, and the postoperative care nurse team were all blinded to the group allocation.

On arrival at the theatre, standard preoperative routine was followed. Vascular access was established using a 20 G cannula. All patients were pre-oxygenated with 100% oxygen for 3 min to achieve 100 arterial saturations. With the help of ultrasound, 20 G radial arterial cannula was inserted to monitor arterial blood pressure throughout the operation period. 20 G Central venous catheter was inserted only for patients deemed high risk for anesthesia or according to the preference of the attending anesthesiologist. Fifteen minutes prior to the induction of general anesthesia, dexmedetomidine 1 μg/kg (Lot No. 11162023, Jiangsu Hengrui Pharmaceutical Co., Ltd., China) was administered via an intravenous pump. After adequate preoxygenation, general anesthesia was induced by intravenous propofol 1.5 to 2.5 mg/kg (titrated to loss of verbal response), sufentanil 3 μg/kg, cis-atracurium sulfonate 0.2 mg/kg followed by intubation of the Mallinckrodt double-lumen endotracheal tube, a successful intubation was confirmed using a fiberoptic bronchoscope. During this period, mechanical ventilation was maintained, respiratory ginseng was regulated, and $PetCO_2$ was maintained at 35–45 mmHg. Anesthesia was maintained using sevoflurane inhalation, remifentanil (0.05–1 μg/kg/min) and intermittent intravenous injection of cis-atracurium to maintain muscle relaxation. During the course of the operation, the concentrations of remifentanil and inhaled sevoflurane were regulated to maintain bispectral index (BIS) between 40–60. Arterial blood pressure during surgery was maintained within 20% of baseline while the maintenance of anesthesia and other vital signs throughout the operation was determined by the attending anesthesiologist. At the end of the operation, when the patient was awake and met extubation indications, the double-lumen tube was

extubated and the patient was transferred to the post-anesthesia care unit (PACU).

VATS was performed by the same surgical team. All operations involved uniportal technique, in which a single incision of about 4 cm was made on the fifth intercostal rib between the anterior axillary line and posterior axillary line.

SAP block procedure

The patient was positioned in the lateral decubitus position with the arm abducted at an angle of 90° for the SAP block. The block was performed by an anesthesiologist with more than 5 years of experience in SAP block administration. All patients received the first SAP block as follows: After correct positioning, the anterior lateral and posterior chest walls were exposed. A standard aseptic procedure was performed. A linear ultrasound transducer (SonoSite HFL 50×; SonoSite, Inc., Bothell, WA, USA) covered in a sterile sleeve was placed over the second rib in the mid-axillary line, and then moved downward laterally to the sixth rib towards the posterior axillary line to make the latissimus dorsi and serratus anterior muscles visible. Once the serratus anterior muscle was visible, 80 mm block needle (Stimuplex; B. Braun AG, Melsungen, Germany) was inserted into the superficial plane using in-plane technique from the inferior posterior to the superior anterior region under ultrasound guidance (SonoSite Edge). With the needle in the targeted plane, 3 mL normal saline solution was injected to confirm correct needle positioning by hydro dissecting the intended plane. Once intended needle position was confirmed, 15 mL 0.375% ropivacaine was injected into the plane while observing real-time spread using ultrasound. The patient remained in this position for the rest of surgery duration.

Twenty-four hours from the end of surgery, the same anesthesiologist visited the patient in the ward to administer the second block. First, the envelope was opened to reveal group allocation. All Patients received their second block using the same procedure described above, the only difference was in the local anesthetic agent used to administer SAP block: for patients randomized to the SAP block group (group A), 15 mL 0.375% ropivacaine (labelled drug A) was used while for patients in the control group (group B) 15 mL 0.9% normal saline (labelled drug B) was administered.

Postoperative procedure

After extubation, all patients were transferred to PACU for observation. PCA device (CPE-101, Royal Fornia Medical Equipment Ltd., Zhuhai, China) for post operative pain control was attached to all patients for the next 48 h. The PCA regimen consisted of butorphanol 15 mg, oxycodone 20 mg, and tropisetron 10 mg mixed with 123 mL of normal saline. PCA device was set to deliver a 1.5 mL/hour background infusion and 0.5 mL on demand with a lockout time of 10 min. Pain assessment was performed at rest using 11-point numeric rating scale (NRS), with zero representing no pain at all and 10 representing worst imaginable pain; any score of ≥4 prompted immediate administration of rescue analgesics [IV oxycodone hydrochloride (2 mL; 20 mg)] or on demand. Continuous monitoring of vital signs and post-anesthesia side effects such as hypotension, nausea and vomiting, and respiratory depression was performed and treated accordingly. Patients deemed stable following the assessment by the attending anesthesiologist were transferred back to the ward for further routine postoperative care.

At the ward, all patients were monitored for further side effects such as hypoxemia, arrhythmias, hypotension, nausea and vomiting, and respiratory depression. Any identified incidences were treated accordingly. Routine postoperative pain control medication that included oral codeine phosphate tablet (25 mg), and oral oxycodone (4.48 mg) were activated on demand or based on the assessment of the attending postoperative care surgeon. Patients who still had an NRS score of ≥4 despite the intervention were prescribed rescue drug [intravenous oxycodone hydrochloride (2 mL; 20 mg)]. Antiemetics (intramuscular injection of 10 mg metoclopramide) were administered to patients with nausea and vomiting symptoms.

The primary outcome of this study was quality of recovery measured using 40-item quality of recovery score (QoR-40) questionnaire on POD 2. QoR-40 questionnaire is an important validated measurement tool for early postoperative health status of patients that contains 40 questions assessing five recovery domains: emotional status, physical comfort, psychological support, physical independence, and pain (20,21). Each question was graded on a 5-point Likert scale:1 = none of the time, 2 = some of the time, 3 = usually, 4 = most of the time, and 5 = always. The highest score was 200 and the minimum score was 40. This questionnaire was completed by the patient 24 hours before surgery, at postoperative 48 hours (POD 2), and at postoperative 72 hours (POD 3). The contents of the QoR-40 questionnaire were explained to all participants preoperatively, and we verified that each patient understood fully.

Secondary outcomes included pain score at rest, assessed using NRS chart at 24th, 30th, 48th and 72nd hour post-surgery. NRS chart was also explained in detail to all participants before surgery and we made sure they were conversant with it; Amount of opioids consumed on POD 2 and POD 3, we converted POD 2 and POD 3 opioids consumed to IV morphine equivalents using GlobalRPh calculator (https://globalrph.com/medcalcs/opioid-pain-management-converter-advanced/); the number of times the PCA pump button was pressed, an investigator masked to group allocation retrieved the PCA pump at POD 2 and recorded the number of times PCA button was pressed; Incidence of perioperative pulmonary complications, Patients were assessed daily for any perioperative pulmonary complications sign and symptoms, this was supplemented by hospital routine postoperative chest imaging practice, comprising of a chest X-ray (taken 24 hours before removal of chest tube) and computed tomography (taken 24 hours after chest tube removal). The patient was said to have perioperative complications if either they showed signs and symptoms and a radiological diagnosis or radiological diagnosis alone; length of hospital stay (LOS), counted from the time the patient was admitted for elective VATS to the time they were discharged after surgery; Incidence of postoperative adverse effects, incidence of adverse effects such as nausea and vomiting, hypoxemia, respiratory depression were recorded for 48 hours post operation; prevalence of chronic pain, at the 2nd and 3rd month post-operation, patients were contacted via a phone call by an independent investigator blinded to group allocation to access the prevalence of chronic pain. First, patients were asked whether they experienced any form of pain emanating from or around the surgical incision. Those who answered yes were asked to rate their pain using NRS chart.

Statistical analysis

The validated standard deviation of QoR-40 after major surgery is 16.2 (20). With a 10-point difference in global QoR-40 scores between the two groups considered clinically significant (22), assuming a type I error (α) = 0.05 and type II error (β) = 0.20 (power=80%), the sample size was 41 patients per group. We enrolled four more patients in each group to cater for 10% dropout rate.

Data were recorded in Excel™ (Microsoft Corp., Redmond, WA, USA) and exported to GraphPad Prism (version 9.5.0 for Windows, GraphPad Software, San Diego, CA, USA) for analysis. Kolmogorov-Smirnov test and QQ plot were used to test for normality of data between the two groups. Independent sample *t*-test was used to analyze all data that were normally distributed, while data that did not fit normal distribution were analyzed using Mann-Whiney *U* test. Chi-squared test or Fisher exact test was used to analyze categorical data. Statistical significance was set at $P<0.05$.

Results

The CONSORT flow diagram for this study is shown in *Figure 1*. A total of 106 patients were initially screened and assessed for eligibility, of which eight patients failed to meet the inclusion criteria, five patients declined to participate in the study, and three were excluded based on the exclusion criteria. Thus 90 patients were randomly assigned to the SAP block group and control group of 45 patients each. After randomization, two patients in the SAP group withdrew their consent. During VATS procedure, one patient in the control group was converted to open thoracotomy while four patients withdrew consent. The remaining 83 patients were successfully followed up, with no loss of follow-up or missing data.

Baseline characteristics of the participants in both groups are detailed in *Table 1*. There were more females enrolled in the SAP group (n=29) than in the control group (n=19). Segmentectomy was the most common indication for VATS in both groups, whereas lobectomy was performed more in the SAP block group than in the control group. The other remaining variables were comparable in both groups.

Table 2 details the analysis of the preoperative QoR-40 questionnaire score. Although SAP block group registered slightly higher scores in terms of the global QoR-40 questionnaire score, physical comfort, and emotional status domain, none of the differences were statistically significant (P=0.30, P=0.16, P=0.69, respectively).

Postoperative QoR-40 questionnaire scores on POD 2 and POD 3 are detailed in *Table 3*. The global QoR-40 questionnaire scores on both POD 2 and POD 3 were significantly higher in the SAP block group (180.07±11.34, 182.09±8.20) than in the control group (172.18±6.15, 177.50±6.94) (P=0.001, P=0.008) respectively. Additionally, patients in the SAP block group also registered significantly higher scores in the emotional status and pain domain of the QoR-40 questionnaire on both POD 2 and POD 3, while for physical comfort domain the significant difference between the two groups did not persist on POD 3 (P=0.32).

The median pain scores at rest at 30th, 48th and 72nd hour

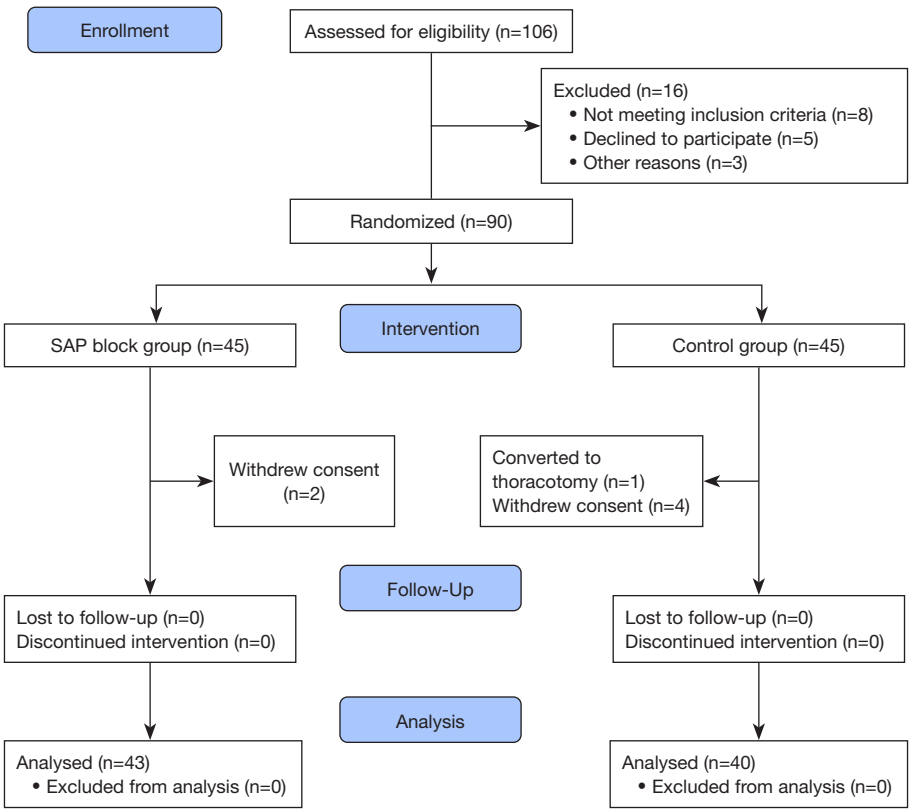

Figure 1 CONSORT flowchart. SAP, serratus anterior plane.

post-surgery were significantly lower in the SAP block group than in the control group (Table S1). Additionally, patients in the SAP block group had less "pain burden" as demonstrated by the smaller area under the curve (AUC) of the median NRS score against time (*Figure 2*).

Details of secondary outcome data are presented in *Table 4*. The median number of times that the PCA pump button was pressed was significantly lower in the SAP block group (5 [2–8]) than in the control group (7 [4–13]) (P=0.02). Likewise, SAP block group had shorter LOS compared to the control group, however, this difference in LOS failed to reach statistical significance (P=0.17). In terms of perioperative complications, there was only one incidence of postoperative pneumonia in SAP block group, accounting for 2.3% with no incidence of atelectasis, while the control group registered four (10%) incidences of pneumonia and one (2.5%) incidence of atelectasis; none of the differences in perioperative complications were statistically significant. The incidence of PoNV was significantly lower among patients in SAP block group compared with those in the control group (P=0.02). No block-related complications were reported in either group of patients. The incidence of chronic pain at 2nd and 3rd months after surgery was 16.3%, 14% in the SAP block group versus 32.5%, 27.5% in the control group, respectively.

The median opioid consumption on POD 2 and POD 3 is illustrated in *Figure 3*. SAP block group registered significantly lower opioid consumption on both POD 2 and POD 3 compared to the control group (P=0.001, P=0.003) respectively.

Discussion

This randomized, placebo-controlled, tripled-blind study showed that the addition of a second SAP block 24 hours after VATS resulted in clinically meaningful improvement in postoperative quality of recovery measured using the global QoR-40 questionnaire on POD 2 and POD 3. Other findings of this study were: opioids consumption at POD 2 and POD 3 were significantly lower in SAP block group compared to control group, second SAP block resulted in better analgesia among patients in the SAP block group

Table 1 Baseline characteristics, surgical and pathological diagnosis details

Variable	SAP block group (n=43)	Control group (n=40)	P value
Age (years)	50.74±11.14	52.3±13.3	0.55
Sex (male/female)	14/29	21/19	0.08
BMI (kg/m^2)	24.0±3.3	23.0±2.7	0.55
ASA status (1/2/3)	2/40/1	3/36/1	0.86
Smoking history (yes/no)	5/38	11/29	0.10
Hypertension	7	12	0.19
Diabetes	4	4	>0.99
Lung function test			
FEV_1 (% predicted)	96.5±11.9	99.8±13.1	0.12
FVC (% predicted)	95.8±12.3	98.4±12.6	0.17
FEV_1/FVC × 100 (%)	78.6±4.9	77.3±8.5	0.30
Anesthesia time (min)	203.0±52.1	197.1±42.2	0.57
Intraoperative remifentanil (μg)	680.1±173.5	667.9±173.3	0.75
Operation time (min)	168.7±50.7	164.6±42.6	0.69
Type of surgery			
Lobectomy	13 (30.23)	8 (20.0)	0.32
Segmentectomy	19 (44.2)	21 (52.5)	0.51
Wedge resection	4 (9.3)	5 (12.5)	0.73
Mediasectomy	5 (11.6)	3 (7.5)	0.71
Bullectomy	1 (2.3)	1 (2.5)	>0.99
Others	1 (2.3)	2 (5.0)	0.61
Operation side (right)	23	19	0.08
Pathological diagnosis			
Adenocarcinoma	29 (67.4)	28 (70.0)	0.82
Squamous cell carcinoma	2 (4.7)	3 (7.5)	0.67
Benign	7 (16.3)	5 (12.5)	0.76
Others	5 (11.6)	4 (10.0)	>0.99

Data are presented as mean ± standard deviation, number of patients, or n (%). SAP, serratus anterior plane; BMI, body mass index; ASA, American Society of Anesthesiologists; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity.

versus the control group, and there was lower prevalence of CPTP at 2nd and 3rd month among patients in SAP block group versus the control group.

SAP block is known to be a simple, effective and easy to perform technique that can provide pain relief with fewer side effects (14). This block can be applied in two different ways: superficial SAP block that involves injection of a local anesthetic agent between the latissimus dorsi and serratus anterior muscles, and the deep technique that entails injection of local anesthetics between serratus anterior muscle and external intercostal muscle (23). In our study, we applied superficial technique because it has been demonstrated to block not only the lateral cutaneous branches of intercostal nerves but also the long thoracic nerve, resulting in more effective pain relief (14). The role of SAP block in postoperative analgesia after thoracic

Table 2 Preoperative QoR-40 questionnaire scores

Variable	SAP block group (n=43)	Control group (n=40)	P value
Global QoR-40 score	197 [192–199]	196 [188–198]	0.30
Physical comfort	59 [58–60]	58 [55–60]	0.16
Emotional status	44 [41–45]	43 [41–45]	0.69
Psychological support	35 [35–35]	35 [35–35]	0.68
Physical independence	25 [25–25]	25 [25–25]	0.43
Pain	34 [33–35]	35 [32–35]	0.87

Data are presented as median [interquartile range]. QoR-40, 40-items quality of recovery questionnaire; SAP, serratus anterior plane.

Table 3 Postoperative QoR-40 scores

Variable	SAP block group (n=43)	Control group (n=40)	P value
Global QoR-40 score			
POD 2	180.07±11.34	172.18±6.15	0.001
POD 3	182.09±8.20	177.50±6.94	0.008
Physical comfort			
POD 2	52.70±4.75	50.23±3.84	0.01
POD 3	53.74±4.10	52.90±3.60	0.32
Emotional status			
POD 2	40.56±3.33	38.48±2.90	0.003
POD 3	41.26±2.81	39.00±2.80	0.001
Physical independence			
POD 2	21.00±3.21	21.10±2.60	0.88
POD 3	21.35±2.56	21.63±2.20	0.60
Psychological support			
POD 2	34.12±2.03	33.38±1.90	0.09
POD 3	33.35±2.46	33.83±1.81	0.33
Pain			
POD 2	31.70±2.03	29.50±2.90	0.001
POD 3	32.19±1.94	30.68±2.31	0.002

Data are presented as mean ± standard deviation. QoR-40, 40-items quality of recovery questionnaire; SAP, serratus anterior plane; POD, postoperative day.

surgery has been investigated in different studies, and shown to provide favorable outcomes in terms of low pain scores (24-26). However, although low pain scores are vital, they may not be perceived by patients as better quality of recovery if they are accompanied by other adverse effects. Therefore, the adoption of more patient-centered anesthesia efficacy evaluation is recommended to maximize patient satisfaction and experience (27). Hence, the primary outcome of this study was quality of recovery measured using global QoR-40 questionnaire. This is a reliable and valid tool for accessing quality of recovery after surgery, which is internationally recognized and has been validated for use in Chinese patient population (20,28). The maximum score a patient can attain is 200 while the minimum score is

40. In our study cohort, the mean score for patients in the SAP block group at POD 2 was 180.07±11.34, which was significantly higher than that of the control group (P=0.001). This finding is similar to the mean of 182.3±12.1 at POD 2 reported by Kim *et al.* (15). Although one study reported a higher global QoR-40 mean score than our study after application of single injection and continuous injection of SAP block in patients undergoing VATS (29), that study apart from SAP block also administered PVB block which is known to provide similar analgesia to SAP block, hence, the co-analgesia action brought by the two blocks yielded better quality of recovery than our study. Nonetheless, we relate the improved quality of recovery observed in the present study to prolonged analgesia, decreased cumulative opioid consumption and reduced postoperative side effects such as nausea and vomiting.

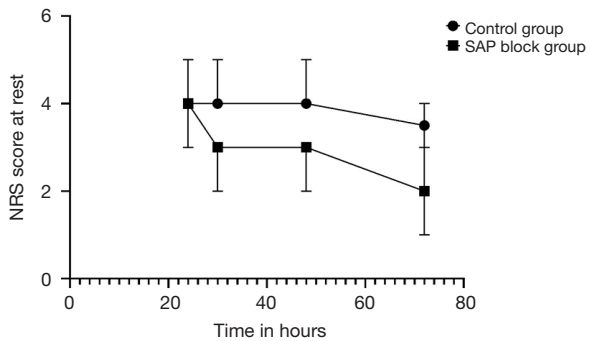

Figure 2 Median pain scores at rest at 24th, 30th, 48th and 72nd hour post-surgery. SAP, serratus anterior plane; NRS, numeric rating scale.

Previous studies on pain management after thoracic surgery have investigated the use of opioid medications and revealed that thoracic surgical patient cohort has the highest rate of persistent opioid use after surgery compared to other surgical cohorts despite it being the least likely surgical cohort to receive preoperative opioid prescription use (30,31). For instance, in a study by Brescia *et al.*, 14% of patients who underwent lung resection reported opioid use 3–6 months after surgery (32). This points to opioid dependence after thoracic surgery. In light of this, a large number of studies have investigated the role of single-injection SAP block analgesia technique in terms of reduction of postoperative opioid consumption and have presented conflicting results. In a randomized trial by Park *et al.* (18), patients who received a single-injection SAP block significantly consumed less opioids than those who received no block for up to 24 hours post VATS. Similarly, Ökmen *et al.* (16) compared opioid consumption in patients who received a single-injection SAP block to those who received PCA and found that a single-injection SAP block significantly lowered opioid consumption for 24 hours after

Table 4 Secondary outcome measures

Variable	SAP block group (n=43)	Control group (n=40)	P value
LOS (days)	11±3	12±5	0.17
PCA pump pressing times	5 [2–8]	7 [4–13]	0.02
Pulmonary complications			
Atelectasis	0	1 (2.5)	0.48
Pneumonia	1 (2.3)	4 (10.0)	0.19
48 hours adverse effects incidence			
PoNV	6 (14.0)	15 (37.5)	0.02
Respiratory depression	0	0	>0.99
Hypoxemia	2 (4.7)	3 (7.5)	0.67
Prevalence of CPTP			
At 2nd month	7 (16.3)	13 (32.5)	0.12
At 3rd month	6 (14.0)	11 (27.5)	0.18

Data are presented as mean ± standard deviation, median [interquartile range], number of patients, or n (%). SAP, serratus anterior plane; LOS, length of hospital stay; PCA, patient-controlled analgesia; PoNV, postoperative nausea and vomiting; CPTP, chronic post-thoracoscopy pain.

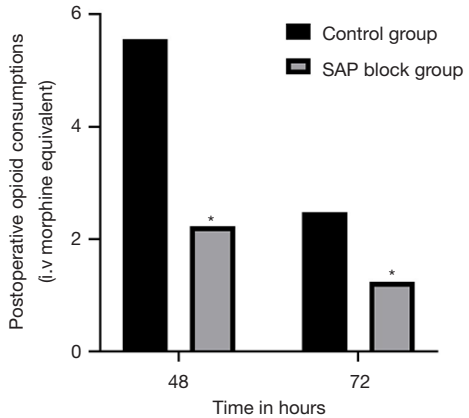

Figure 3 Amount of i.v morphine equivalent consumed (mg) at postoperative 48 hours (postoperative day 2) and postoperative 72 hours (postoperative day 3). *, statistical significance. i.v, intravenous; SAP, serratus anterior plane.

VATS. In another study conducted by Chen *et al.* (33), a single-injection SAP block significantly lowered opioid consumption for only up to 8 hours postoperatively, while Jack *et al.* reported that a combination of SAP block and systematic analgesia significantly reduced postoperative opioid consumption for up to 12 hours compared to systematic analgesia alone (34). A point to note is that none of these studies demonstrated that single-injection SAP block is effective in lowering postoperative opioid consumption beyond 24 hours. In other words, if opioid medications are the mainstay of moderate to severe pain control after surgery (19), and maximum post-VATS pain relief is important up to at least POD 3 in order to prevent the development of chronic pain (8), then, an analgesia technique that can result in lower pain scores for at least POD 3 is likely to reduce opioids consumption and lower incidence of occurrence of chronic pain. Our study is the first prospective randomized trial to demonstrate that application of a second SAP block 24 hours after VATS significantly lowered opioid consumptions on both POD 2 and POD 3. This also significantly reduced PoNV side effects, as manifested by higher scores in the physical comfort domain of QoR-40 questionnaire obtained by patients in the SAP block group compared to the control group, the domain examined patients on the instances of PoNV among others; side effects which are associated with opioid medication use (35-37). It is worth noting, however, that the significantly higher scores on the physical domain of QoR-40 questionnaire did not persist until POD 3 (P=0.32). We believe that this phenomenon is best explained by the fact that as part of routine hospital standards, PCA pump was only used up to POD 2 in all patients regardless of the group allocation. Since patients in the control group consumed significantly more PCA drugs (pressed PCA pump button more times) that also contained opioid medications, the withdrawal of PCA pump on POD 2 raised their scores on POD 3, narrowing the difference in scores between the two groups and resulting in no statistically significant difference observed on POD 3.

As many as one-third of patients who undergo VATS experience chronic pain (8), defined as pain that persists for 2 to 3 months post-surgery. While the exact mechanism behind its development remains unclear, pain intensity during the first 3 days after surgery was revealed as the only predictor of chronic pain in Bayman's study (8). Our study was powered to test the hypothesis that in patients undergoing VATS, the addition of a second SAP block at 24 hours after surgery leads to maximum pain relief during the early postoperative period, thereby lowering the incidence of progression to CPTP. Out of the 43 patients that completed the study in the SAP block group, six patients (14%) reported mild pain at the third month. To the best of our knowledge, the present study is the first to show that the addition of a second SAP block on POD 1 lowers the prevalence of chronic pain 3 months after VATS. In comparison, one study (38) reported 14.8% prevalence of CPTP at the third month when single-injection SAP block was used for postoperative analgesia, the difference between that study and our study apart from being retrospective is that SAP block was administered in combination with continuous infusion of nonsteroidal anti-inflammatory drugs and therefore, there is a possibility that this supplemented analgesia action of SAP block continues upon "expiry", lengthening duration of action and thus achieving longer postoperative analgesia as in the SAP block group of our study.

Despite better outcomes due to application of the second SAP block, there was no significant difference in LOS between the two groups in our study (P=0.17). By comparison, Kim *et al.* (15) found that a single injection SAP block improved patient quality of recovery; however, similar to our study, the improvement in quality of recovery in their study did not lead to a significant difference in LOS between the two study groups. Similarly, a study by Viti *et al.* (39) reported no significant difference in LOS between the SAP block group and the control group despite SAP block group registering better pain control and performance

during postoperative rehabilitation exercises. When we further reviewed some more similar studies, we found that lack of statistically significant difference in LOS between study groups is a common phenomenon (33,40-42), which can partly be explained by the fact that LOS is a complex variable that is easily affected by many external factors such as patient economic status, psychological status, and age. Some of these factors are difficult to regulate in a clinical trial.

This study had some limitations: First, block success was not performed to test the range of sensory blockade hence the possibility that some blocks were not effective could not be overruled. However, considering that real-time ultrasound guidance was used to guide the process and that all blocks were performed by a single anesthesiologist with more than five years of experience in performing SAP block, we are certain that the majority of blocks were effective.

Second, we did not examine patients QoR-40 questionnaire scores on POD 1, therefore, comparison between baseline POD 1 QoR-40 questionnaire scores before administration of the second block and POD 2 QoR-40 questionnaire scores after second block was not done. Nonetheless, the global QoR-40 questionnaire scores obtained on POD 2 in the present study was similar to a previous study that recorded both POD 1 and POD 2 global QoR-40 questionnaire scores (15); therefore, this did not affect the interpretation of the results.

Third, this study is a single-center study. Although we ensured standardization and accuracy by making sure the operation was performed by the same surgical team and blocks were administered by the same anesthesiologist, our results need further confirmation by other centers.

Conclusions

In conclusion, this single-center, randomized, triple-blind trial has shown that in patients undergoing VATS, the addition of a second SAP block at POD 1 enhances patients postoperative quality of recovery, prolongs analgesia, reduces opioid consumption, and lowers the prevalence of CPTP.

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Footnote

Reporting Checklist: The authors have completed the CONSORT reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-982/rc

Trial Protocol: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-982/tp

Data Sharing Statement: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-982/dss

Peer Review File: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-982/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-982/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by ethics review board of Tongji Hospital affiliated to Tongji Medical College of Huazhong University of Science and Technology (reference number TJ-IRB20220141) and informed consent was obtained from all individual participants.

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