Adding sufentanil to ropivacaine in continuous thoracic paravertebral block fails to improve analgesia after video-assisted thoracic surgery

A randomised controlled trial

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BACKGROUND The benefit of adding opioid to a local anaesthetic for continuous thoracic paravertebral analgesia after video-assisted thoracic surgery (VATS) is unclear.

OBJECTIVES To analyse the analgesic efficacy of ropivacaine and sufentanil in combination compared with ropivacaine alone after VATS.

DESIGN A randomised, double-blinded, single-centre clinical trial.

SETTING A tertiary university hospital between March 2010 and April 2014.

PATIENTS Ninety patients were recruited, two were not included leaving 88 randomised into two groups. Eighteen patients were excluded from analysis and 70 completed the study.

INTERVENTION To receive thoracic paravertebral analgesia with either 2 mg ml$^{-1}$ ropivacaine and 0.25 $\mu$g ml$^{-1}$ sufentanil (ropivacaine+sufentanil group) or 2 mg ml$^{-1}$ ropivacaine alone (ropivacaine group) for 48 h postoperatively. Infusion rate was set at 0.15 ml kg$^{-1}$ h$^{-1}$ in both groups.

MAIN OUTCOME MEASURES The primary endpoint was the mean total amount of self-administered morphine by the patients in each group at 48 h postoperatively.

RESULTS The mean ± SD total amount of self-administered morphine was not significantly different between groups (53.1 ± 27.2 mg in the ropivacaine + sufentanil group vs. 58.8 ± 34.3 mg in the ropivacaine group; $P = 0.72$). No significant differences were found between the two groups in either pain scores at rest or during movement, in opioid-related adverse reactions, in patient satisfaction or length of hospital stay.

CONCLUSION Adding 0.25 $\mu$g ml$^{-1}$ sufentanil to 2 mg ml$^{-1}$ ropivacaine in continuous thoracic paravertebral analgesia for VATS did not reduce morphine consumption or pain scores when compared with ropivacaine alone. We cannot recommend its use for routine clinical practice. Further studies analysing different concentrations and infusion rates of sufentanil are needed before a lack of efficacy can be confirmed.


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Introduction

The use of video-assisted thoracic surgery (VATS) is growing, because it has several advantages over open thoracotomy, such as better preservation of respiratory function, few respiratory complications and shorter hospital stay. However, patients who benefit from VATS complain of moderate-to-severe postoperative pain due to intercostal nerve damage caused by the ports and chest drains, and the extent of surgery. For these
reasons, analgesia after VATS remains an important consideration.

There is currently no clear gold standard for analgesia after VATS procedures. 4 Thoracic paravertebral block (TPVB) has been shown to be as effective as thoracic epidural analgesia for pain relief after thoracotomy, with less frequent adverse reactions such as hypotension, urinary retention and nausea and vomiting. 5,6 TPVB therefore represents an attractive technique for VATS procedures. Whereas there is evidence supporting the efficacy of combining local anaesthetics and opioid for thoracic epidural analgesia after thoracotomy, 7 little research to determine the optimal regimen for TPVB exists. Previous publications report the use of opioid in combination with local anaesthetics for TPVB after thoracic surgery. 8,9 However, comparative studies are rare and no formal recommendations can be made. A single randomised controlled study found that, after breast surgery, continuous thoracic paravertebral infusion of fentanyl with levobupivacaine provided superior analgesia than levobupivacaine alone. 10

The objectives of this study were to evaluate the efficacy and safety of continuous thoracic paravertebral infusion of 0.25 μg ml⁻¹ sufentanil with 2 mg ml⁻¹ ropivacaine compared with 2 mg ml⁻¹ ropivacaine alone for postoperative analgesia following VATS. The hypothesis tested was that the combination of sufentanil and ropivacaine would provide superior analgesia to ropivacaine alone.

**Methods**

Ethical approval for this double-blinded randomised trial (Ethical Committee No. 2009-019-B) was provided by the Ethical Committee Sud-Est III of Groupement Hospitalier Est, Bron, France on 7 September 2010. The study protocol and the informed consent form were approved by the French national medicines agency (Agence Nationale de Sécurité du Médicament et des Produits de Santé) on 18 January 2010 (No. A 91428-48). The trial was registered with EudraCT (No. 2009-014832-38) on 18 January 2010 and with ClinicalTrials.gov (No. NCT 01082744) on 8 March 2010. The study took place at the Hôpital Cardiologique et Pneumologique Louis Pradel (Hospices Civils de Lyon, France) and was monitored by the clinical research department of the hospital (Direction de la Recherche Clinique et de l’Innovation).

Between March 2010 and April 2014 all patients scheduled for unilateral VATS were recruited for possible enrolment in the study. Written informed consent was obtained from the study participants. To be included, patients had to be at least 18 years old and scheduled for planned VATS under general anaesthesia with TPVB. Exclusion criteria were bilateral surgical procedures, refusal of paravertebral block, allergy to local anaesthetics, evidence of general inflammation, infection around the site of catheter insertion, coagulation disorder, treatment with thienopyridines within 8 days preoperatively, pregnancy, patients under guardianship or unable to give consent, iodinated contrast medium allergy, previous thoracic spine surgery, intolerance of opioids, chronic pain treated with opioids, and opioid addiction. Patients who were initially included were excluded from review if the catheter was misplaced or subsequently became displaced, disconnected or occluded, or there was catheter disconnection or occlusion, intra-operative conversion to thoracotomy or revision surgery within the study period, or if there were any technical issues concerning the patient-controlled analgesia (PCA) pump or the syringe infusion pump administering the study treatment. Actual body weight was used for dose calculations. The trial is reported in accordance with the CONSORT guidance. 11

**Pre-operative procedure**

Randomisation was performed at the pharmacy using a computer-generated list established by the biostatistics unit of the hospital (Service de Biostatistique, Hospices Civils de Lyon) before study initiation, and group assignment was not revealed until the end of study. The investigators, study centre nursing staff and patients were blinded to treatment group assignment. Patients were randomised to one of the following two groups: ropivacaine group (R group) with continuous paravertebral infusion of 2 mg ml⁻¹ ropivacaine; ropivacaine + sufentanil group (RS group) with continuous paravertebral infusion of 2 mg ml⁻¹ ropivacaine with 0.25 μg ml⁻¹ sufentanil. The study medication was prepared by the pharmacy the day before surgery and distributed to the postanaesthesia care unit (PACU) on the day of surgery. Medication bags were identical in both groups and volume was enough to cover the study period. The use of a 10-cm continuous line going from ‘no pain’ (scored 0) to ‘worst imaginable pain’ (scored 10) was used for self-evaluation of pain, and the instructions for the PCA pump were explained to the patients before surgery. All patients were premedicated orally 1 h before surgery with 50 mg hydroxyzine and 0.5 mg alprazolam.

**Intra-operative paravertebral block technique**

Upon arrival in the operating theatre, the paravertebral catheter was placed, with the patient in the sitting position, by one of the two investigators experienced in the technique. The paravertebral space ipsilateral to the surgical site was located at the 4th intercostal space with a 15 to 6-MHz ultrasound linear array probe (SonoSite S-Nerve; SonoSite, Inc., Bothwell, Washington, USA) in the transverse position and an out of plane technique was used, as described by Marhofer et al. 12 An 18-gauge Tuohy needle (PlexoLong NanoLine Tuohy, Pajunk Gmbh, Geisingen, Germany) was advanced with hydrodissection until an anterior movement of the parietal...
pleura was observed (see Video, Supplemental Digital Content 1, http://links.lww.com/EJA/A138) which demonstrates the anterior movement of the parietal pleura TP: transverse process. IIM: internal intercostal membrane. The 20-gauge catheter with a central opening was then introduced through the needle and advanced by 2 cm. Negative aspiration through the catheter was confirmed and all patients received 0.2 ml kg⁻¹ ropivacaine at 5 mg ml⁻¹ through the catheter.

**Intra-operative procedure**

Subsequently, the patient was placed in the supine position, and general anaesthesia was induced with 0.5 µg kg⁻¹ intravenous sufentanil and a target-controlled infusion of propofol to achieve a plasma concentration of 4 µg ml⁻¹. A bolus of 0.2 mg kg⁻¹ intravenous cisatracurium was given to facilitate tracheal intubation with a double-lumen endobronchial tube. After induction the patient was placed in the lateral decubitus position and one-lung ventilation was initiated. The surgery was carried out using a three-port VATS technique. All cases of recurrent spontaneous pneumothorax underwent apical wedge lung resection, and pleurodesis was performed either mechanically with abrasion or chemically with povidone-iodine, depending on surgeon preference. If a paravertebral catheter was visualised in the interpleural space, it was withdrawn after surgery and the patient was excluded from the study. At the end of the operation, two chest tubes were inserted through the port incisions. All patients were extubated in the operating theatre.

**Postoperative procedure**

Immediately upon arrival in the PACU, a chest radiograph was performed after injection of 8 ml iodixanol (Visipaque; GE Healthcare SAS, Velizy-Villacoublay, Paris, France) through the paravertebral catheter. As previously described, we sought longitudinal paravertebral and intercostal spreading pattern (Fig. 1).¹⁻¹ Such spreading patterns were required before injection of the allocated treatment. If radiographic contrast medium was observed in the pleural cavity or in the chest drains, the patient was excluded from the study. The infusion of the study medication was started at 0.15 ml kg⁻¹ h⁻¹ for both groups by the PACU staff.

Acute pain in the PACU was treated with intravenous morphine titration. After pain relief was obtained, defined by a VAS score at rest lower than 3, the PCA pump which contained 50 ml morphine (1 mg ml⁻¹) and droperidol 2.5 mg was given to the patient. The size of the bolus dose was set to 1 mg, the lock-out interval to 7 min and the limit to 25 mg every 4 h. Additional analgesia (intravenous paracetamol 1 g every 6 h) was also administered. Once PACU discharge criteria were met, the patients were transferred to the ward where the nursing staff measured noninvasive blood pressure (BP), heart rate (HR), respiratory rate, and oxygen saturation obtained by plethysmography every 4 h during the 48-h study period. Sedation intensity was assessed and recorded every 12 h using a four-point scale (1, awake and alert; 2, infrequently drowsy and easily aroused; 3, frequently drowsy but arousable; 4, somnolent). Any adverse event occurring during the study period was recorded and reported. Satisfaction with the treatment was assessed using a five-point scale (1, very satisfied; 2, satisfied; 3, no opinion; 4, dissatisfied; 5, very dissatisfied) and recorded by the nursing staff at 48 h after surgery. The paravertebral catheter was withdrawn at the end of the study period.

**Endpoints**

The primary endpoint was the mean total amount of self-administered morphine in each group at 48 h postoperatively. The secondary endpoints included the cumulative dose of morphine over time during the 48-h postoperative period, the patient reported pain intensity (VAS) at rest and during movement (cough) at 2, 12, 24, 36 and 48 h postoperatively, the occurrence of adverse reactions during the first 48 h postoperatively (oxygen desaturation, hypotension, bradycardia, sedation, drowsiness, nausea, vomiting, itching, respiratory depression and urinary retention) and length of hospital stay (LOHS). Duration of chest drainage was also recorded by the nursing staff.

**Statistical analysis**

A decrease in the cumulative morphine dose by 40% in the RS group vs. the R group was defined as a clinically relevant benefit (e.g. from 20 to 12 mg per 48 h). For this
difference to be statistically significant with 5% \( \alpha \) risk (two-tailed) and assuming a standard deviation of 10 mg in the two groups, 34 patients in each group were needed to test the primary study hypothesis with 90% power. The inclusion of 80 patients in total was planned to anticipate patient dropouts due to failures in inserting the paravertebral catheter. The subjects were randomised in a double-blind fashion and in a 1:1 ratio.

The efficacy analyses followed an intention-to-treat (ITT) approach regardless of treatment status at the time of analysis. The primary analysis compared the primary endpoint between the two groups using a two-sided Wilcoxon–Mann–Whitney test (WMW). The significance threshold was 0.05. Missing data at 48 h were replaced by the cumulative dose of morphine at 36 h and the mean difference between the cumulative dose at 36 and 48 h. A secondary analysis was performed to compare the groups at 2, 12, 24, 36 and 48 h using a mixed regression model of the cumulative dose of morphine (mg) as a function of the time of the measurement (hours). The baseline model included fixed effects, the intercept, the linear and quadratic coefficients of time and random effects to allow for individual variations of intercept and curves. The test model included three supplementary coefficients for the group effect on the intercept and linear and quadratic coefficients of time. Random and fixed coefficients were estimated using the restricted Log-likelihood method. Variance heterogeneity over time was taken into account using a power variance function structure. Missing measurements were considered as missing at random and having the same mean as nonmissing measurements. The test model was compared with the baseline model (maximum likelihood estimations) using a Log-likelihood ratio. The treatment effect on the cumulative dose of morphine was considered significant if the \( P \) value was lower than 0.05. The same method was used to test the significance of the covariates.

The VAS scores, at rest and on movement, were analysed separately and with the same methods used for the cumulative dose of morphine. None of the covariates were selected for the VAS score at rest. For the VAS score on movement, age, sex, BMI and surgery type were selected either for their effect on the intercept (age) or for their effect on the slope (sex, BMI and surgery type). The individual scores for patient satisfaction, LOHS and duration of chest drainage (in days) were compared between treatment groups using the Cochran–Armitage trend test.

The occurrence of adverse reactions was compared in the ITT population using Fisher’s exact test. Reported \( P \) values were not adjusted for multiple testing, as the efficacy inference was based on a single primary endpoint and a global test was performed for secondary endpoints with repeated measurements. Analyses were performed with SAS/STAT software, version 9.4 of the SAS System for Windows (SAS Institute Inc., Cary, North Carolina, USA) and the packages nlme and lme4 of R software, version 3.2.1 (http://www.r-project.org).

Results

The study flow chart is presented in Fig. 2. We planned to include 80 patients, anticipating a drop-out rate of 15% (12 patients) but 18 were excluded (13 after randomisation and five during follow-up) so a total of 90 patients were finally enrolled to achieve an adequate sample size. Two of these were not included, leaving 88 randomised to receive either ropivacaine (R group, \( n = 43 \)) or ropivacaine with sufentanil (RS group, \( n = 45 \)). In total, 70 patients received the study treatment and were analysed (R group, \( n = 37 \); RS group, \( n = 33 \)); these represented the ITT population. Those for whom the primary endpoint was available (\( n = 67 \)) represented the per-protocol population (96% of the ITT population). Missing primary endpoint data was due to loss of recordings for two patients at 48 h postoperatively and one hallucinatory episode at postoperative day 2 led to discontinuation of study treatment for another.

There were no statistically significant differences between the two groups in terms of personal characteristics, ASA physical status class, type, duration, side of surgery and total amount of intra-operative sufentanil (Table 1). The mean ± SD titration dose of morphine was similar in both groups (7.05 ± 4.9 mg in the R group vs. 6.5 ± 5.8 mg in the RS group, \( P = 0.57 \)).

The primary endpoint, mean ± SD total amount of self-administered morphine by the patients at 48 h, was not significantly different between the groups (ITT population: 58.8 ± 34.3 mg in the R group vs. 53.1 ± 27.2 mg in the RS group; WMW: \( Z = -0.36, P = 0.72 \); per-protocol population: 57.4 ± 33.7 mg in the R group vs. 53.1 ± 28.1 mg in the RS group; WMW: \( Z = -0.22, P = 0.83 \)).

The change of morphine dose over time during the 48-h postoperative period was not significantly different between groups (\( P = 0.49 \); Fig. 3). There was no significant difference between the groups with regards to change in pain score over time during the 48-h postoperative period, either at rest (\( P = 0.15 \)) or on movement (\( P = 0.50 \) (Fig. 4).

Twenty-four patients from the R group (65%) and 22 from the RS group (69%) had at least one adverse reaction, including nausea and vomiting [11 patients from R group (30%) and nine patients from RS group (27%)], urinary retention [10 patients from R group (27%) and four patients from RS group (12%)], drowsiness [five patients from R group (14%) and nine patients from RS group (27%)] and itching [four patients from R group (11%) and five patients from RS group (15%)]. Most were assessed as mild or moderate in severity by the patients themselves. There was no statistically significant
difference in the incidence of overall adverse reactions between groups ($P = 0.80$).

Although of little clinical significance, SBP and DBP were significantly higher in the R group at 48 h postoperatively ($P = 0.01$ and 0.03, respectively). A significant difference between the groups was already present for SBP on arrival in the PACU, whereas DBP was not statistically different ($P = 0.12$). There were no statistically significant differences between the groups with regard to mean HR ($P = 0.93$), mean respiratory rate ($P = 0.78$), mean oxygen saturation ($P = 0.60$) and mean sedation score ($P = 1.00$) at 48 h postoperatively (see Table 2, Supplemental Digital Content 2, http://links.lww.com/EJA/A139, which shows the BP, HR, respiratory rate and oxygen saturation values and the sedation scores). Patient satisfaction at 48 h did not differ statistically between the groups ($P = 0.60$); (see Table 3, Supplemental Digital Content 3, http://links.lww.com/EJA/A139, which shows the satisfaction scores at 48 h postoperatively). The mean ± SD duration of chest drainage was significantly shorter in the R group (4.5 ± 1.4 days vs. 5.3 ± 1.7 days; $P = 0.04$). Mean (± SD) LOHS was not statistically different between the groups (7.1 ± 5.5 days in the R group vs. 7.4 ± 5.2 days in the RS group; $P = 0.21$).

**Discussion**

In this randomised study, we have shown that adding 0.25 $\mu$g$\cdot$ml$^{-1}$ sufentanil to 2 mg$\cdot$ml$^{-1}$ ropivacaine for continuous paravertebral analgesia for VATS did not reduce morphine consumption by 40% at 48 h postoperatively. The difference was only about 5 mg. Our study was not powered to measure such a small decrease as it is probably clinically irrelevant. Also, although this was only a secondary endpoint, our study suggests that adding 0.25...
Intention-to-treat population

epidural analgesia,7,14 transferring this evidence to para-
centrations of sufentanil.

At 48 h after surgery when compared with ropivacaine
ropivacaine group and in the ropivacaine

Table 1 Personal, baseline pre-operative characteristics, disorder,
type of surgery and intra-operative characteristics in the
ropivacaine group and in the ropivacaine + sufentanil group for the
intention-to-treat population

<table>
<thead>
<tr>
<th></th>
<th>Total population, n = 70</th>
<th>R group, n = 37</th>
<th>RS group, n = 33</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>Mean ± SD (Range)</td>
<td>42.3 ± 17.3 (19 to 79)</td>
<td>44.8 ± 17.6 (19 to 79)</td>
</tr>
<tr>
<td>Sex, n (%)</td>
<td>Male 50 (71) Female 20 (29)</td>
<td>28 (76) 9 (24)</td>
<td>22 (67)</td>
</tr>
<tr>
<td>BMI (kg m⁻²)</td>
<td>Mean ± SD (Range)</td>
<td>22.5 ± 4.0 (16 to 32)</td>
<td>23.5 ± 4.1 (17 to 32)</td>
</tr>
<tr>
<td>ASA PS class</td>
<td>Male 43 (61) Female 37 (53)</td>
<td>22 (59) 11 (33)</td>
<td>21 (64)</td>
</tr>
<tr>
<td>Disorder, n (%)</td>
<td>Pneumothorax 43 (61) Intestinal lung disease 13 (19) Pleural effusion 5 (7) Sarcoidosis 2 (3) Lymphangioleiomyomatosis 2 (3) Broncholitis obliterans 2 (3) Lung nodule 2 (3) Pleuro-pneumonia 1 (1)</td>
<td>22 (59) 11 (33)</td>
<td>21 (64)</td>
</tr>
<tr>
<td>Type of surgery, n (%)</td>
<td>Mechanical pleuradesis 11 (16) Chemical pleuradesis 33 (48) Lung biopsies 23 (33) Pleura biopsies 2 (3) Lung ± pleura biopsies 1 (1)</td>
<td>6 (16) 18 (49) 12 (32) 2 (3) 1 (1)</td>
<td>5 (15) 15 (45) 11 (33) 1 (3)</td>
</tr>
<tr>
<td>Side of surgery, n (%)</td>
<td>Right 41 (59) Left 29 (41)</td>
<td>22 (60) 15 (40)</td>
<td>19 (55) 14 (42)</td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>Mean ± SD (Range)</td>
<td>53.7 ± 20.3 (22 to 112)</td>
<td>55.5 ± 18.7 (22 to 110)</td>
</tr>
<tr>
<td>Sufentanil intra-operative (µg)</td>
<td>Mean ± SD (Range)</td>
<td>35.2 ± 8.5 (18 to 60)</td>
<td>36.3 ± 9.7 (25 to 55)</td>
</tr>
</tbody>
</table>

ASA PS, American Society of Anesthesiology physical status classification; R group, ropivacaine group; RS group, ropivacaine + sufentanil group.

µg ml⁻¹ sufentanil did not have an impact on VAS scores at 48 h after surgery when compared with ropivacaine alone. This finding cannot be extrapolated to other concentrations of sufentanil.

Although there is evidence to support a benefit from combining opioids and local anaesthetics for thoracic epidural analgesia,7,14 transferring this evidence to paravertebral analgesia is questionable. In thoracic surgery, no randomised controlled study has investigated the addition of opioids to local anaesthetics for continuous paravertebral analgesia. The current study is, to our knowledge, the first to determine whether adding sufentanil to ropivacaine is beneficial in the postoperative period.

Analgesics can be administered by bolus or continuous infusion. In the absence of evidence to support one technique over the other for pain control,15 we decided to use a continuous infusion for paravertebral analgesia. To determine the infusion rate, in the absence of consensus, we considered previous reports that used rates ranging from 0.1 to 0.2 ml kg⁻¹ h⁻¹ and chose 0.15 ml kg⁻¹ h⁻¹.9,10,16–18 Without any published data concerning the optimal dose of sufentanil for TPVB, we used the existing pharmacokinetic data for the epidural route that show that sufentanil infused at a rate of 3.75 µg h⁻¹ for 96 h had a positive effect on analgesia with plasma concentrations within the range of minimal effective concentration.14 Therefore, with the chosen concentration of 0.25 µg ml⁻¹, our patients received 1.69 to 3.86 µg of sufentanil per hour.

Our results agree with a recent metaregression that demonstrated no difference in analgesia between those patients treated with local anaesthetics only and those treated with both local anaesthetics and fentanyl in TPVBs for thoracotomy.19 However, in a prospective randomised trial conducted in breast surgery, the combination of fentanyl 4 µg ml⁻¹ with levobupivacaine 0.5 mg ml⁻¹ provided better analgesia and more morphine sparing than levobupivacaine 1 mg ml⁻¹ alone.10 In contrast, we did not observe any analgesic effect from adding sufentanil, an opioid that is comparable with fentanyl regarding its lipophilic nature and systemic uptake.20 For epidural analgesia, the sufentanil/fentanyl analgesic potency ratio has been reported to be 5:9.21 The sufentanil concentration should have been set at...
0.68 \mu g/ml to be equipotent to the fentanyl concentration used by Burlacu et al., a concentration well above that used in our study. We cannot, therefore, rule out the possibility that a greater concentration of sufentanil could have produced an analgesic effect.

Although epidural spread from a TPVB has been demonstrated in 25% of cases, the lack of analgesic effect of sufentanil found in the current study makes such a spread of little clinical significance. The failure of sufentanil to contribute in the current study could be explained by administration close to the spinal and intercostal nerves. Sufentanil and fentanyl may partially suppress conduction in peripheral nerves but only at concentrations well above those commonly used in clinical practice, suggesting that their local anaesthetic-like action has little clinical effect. Furthermore, evidence supporting an analgesic benefit of lipophilic opioids as adjuncts in peripheral nerve blocks is weak.

Thoracic paravertebral block is associated with less nausea and vomiting than thoracic epidural block, but the overall incidence reported in the study is fairly significant. Paravertebral sufentanil cannot be blamed for the occurrence of nausea and vomiting, nor for urinary retention, drowsiness and itching in the current study. It is probable that these opioid-related adverse reactions were mainly due to systemic morphine.

The current study presents several limitations. First, it has been shown that the sensory block of TPVB is unpredictable. Despite correct needle-tip placement, the tip of the catheter is found outside the paravertebral space in as many as 25% of the cases. We did not assess the level of sensory block to confirm block quality before randomising patients. We preferred to rely on the observation of the anterior movement of the parietal pleura and on radiography with contrast to confirm the correct placement of the catheter. We sought to identify specific spreading patterns that are indicative of correct catheter placement, and we believe that this would assure us that all randomised patients had a successful paravertebral block. Second, the study concerned only minor VATS procedures and among them the surgical treatment of recurrent and primary spontaneous pneumothorax represented nearly two-thirds of cases. Chemical pleurodesis was used three times more often than pleurectomy, with a similar distribution across groups. After pleurectomy and because of the disruption of the parietal pleura, there is a possibility of leakage of local anaesthetic from the subpleural space into the pleural cavity with a risk of analgesic failure and ropivacaine toxicity. The similar incidence of pleurectomy in both groups served to minimise potential bias. Furthermore, the systematic search for presence of contrast in the pleural cavity or the drains prevented the inclusion of patients with a significant leak.
Finally, it would have been of interest to administer a bolus dose of the allocated treatment prior to continuous administration. That would have allowed us to evaluate the effect of paravertebral sufentanil in the immediate postoperative period more precisely.

In conclusion, after minor VATS procedures the addition of 0.25 \( \mu \text{g.m}^{-1} \text{l}^{-1} \) sufentanil to 2 \( \text{m.g.m}^{-1} \) ropivacaine during continuous thoracic paravertebral administration over 48h did not confer any analgesic benefit when compared with ropivacaine alone. Further studies analysing different concentrations and infusion rates of sufentanil are needed before the lack of efficacy can be confirmed. At the current time, we cannot recommend the use of 0.25 \( \mu \text{g.m}^{-1} \text{l}^{-1} \) sufentanil as an additive to ropivacaine for routine clinical practice.

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Conflicts of interest: none.

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