

Comparison between patient-controlled tramadol infusion and additional thoracic paravertebral block in the management of post-thoracotomy pain; a retrospective study

 Mustafa Cenk Çetin¹,  Mehtap Tunç¹,  Hilal Sazak¹,  Onur Küçük¹,  Musa Zengin²,  Ramazan Baldemir¹
 Ali Alagöz¹

¹Department of Anesthesiology and Reanimation, Ankara Atatürk Sanatorium Training and Research Hospital, University of Health Sciences, Ankara, Türkiye

²Department of Anesthesiology and Reanimation, Ankara Etlik City Hospital, Ankara, Türkiye

Received: 15/05/2024

Accepted: 11/06/2024

Published: 06/08/2024

Cite this article: Çetin MC, Tunç M, Sazak H, et al. Comparison between patient-controlled tramadol infusion and additional thoracic paravertebral block in the management of post-thoracotomy pain; a retrospective study. *Eurasian J Anesthesiol Intens Care*. 2024;1(3):47-52.

Corresponding Author: Ali Alagöz, mdalagoz@gmail.com

ABSTRACT

Aims: Thoracic paravertebral block (TPVB) provides effective analgesia in patients undergoing thoracotomy. In this study, we aimed to compare the level of analgesia, hemodynamic parameters, and analgesic consumption in post-thoracotomy patients who received iv patient-controlled analgesia (PCA) with the patients who received TPVB plus iv PCA.

Methods: We retrospectively evaluated the pain and anesthesia forms of 100 patients. Patients were divided into two groups according to analgesia methods. All patients were given 100 mg iv tramadol 30 minutes before the end of the operation. Intravenous tramadol infusion by using PCA was applied in both groups for postoperative 24 hours. In Group II, 5 levels of TPVB was performed just before the end of the operation. Additional analgesic (paracetamol 1 g infusion) was given when visual analog scale (VAS) was ≥ 4 . Demographic data of patients and analgesia methods of patients were recorded. Hemodynamic parameters, peripheral oxygen saturation, respiratory rate, sedation scores, resting and coughing VAS score, additional analgesic requirement, side effects and complications, amounts of consumed analgesics, and analgesia-related satisfaction scores were recorded preoperatively, before PCA, and 1, 6, 12, and 24. hours postoperatively to use patients' pain forms.

Results: Hemodynamic parameters were comparable between groups ($p > 0.05$). Resting and coughing VAS scores were significantly lower in the TPVB group ($p < 0.05$). The additional analgesic requirement was also lower in Group II ($p < 0.05$). Cumulative tramadol consumption was significantly lower in Group II ($p < 0.05$).

Conclusion: TPVB combined with iv tramadol PCA provided effective analgesia, and it decreased cumulative tramadol use in thoracotomy patients.

Keywords: Thoracotomy, thoracic paravertebral block, tramadol, visual analog scale.

INTRODUCTION

Post-thoracotomy pain is one of the most severe postoperative pains, is constantly stimulated by respiratory movements, and the first 4-6 hours postoperatively is the period with the highest analgesic requirement. Complications resulting from this pain include an inability to cough due to decreased respiratory movements, an inability to expel bronchial secretions, atelectasis, pneumonia, bronchitis, hypoxemia, respiratory failure, and prolonged mechanical ventilation.¹⁻³

The administration of analgesics following a thoracotomy can effectively reduce the incidence of postoperative complications. The pharmacological and non-pharmacological methods employed to relieve pain following thoracotomy encompass a range of agents and

techniques. These include systemic opioids, non-steroidal anti-inflammatory drugs (NSAIDs), systemic analgesia therapy, including ketamine, and regional techniques such as intercostal, paravertebral, intrapleural and epidural blocks.^{1,4} To minimize the potential for complications and provide adequate analgesia, a combination of both drugs and techniques, rather than a single method, is more effective in patients undergoing thoracotomy.⁴

In recent years, post-thoracotomy pain has been successfully prevented with the use of a thoracic paravertebral block (TPVB). A review of the literature reveals that TPVB applications result in effective analgesia with a lower complication rate than that observed with thoracic epidural

applications.⁴ The paravertebral nerves in the surgical area are the sole nerves blocked in a TPVB application, which results in a lower incidence of hypotension and bradycardia than in a thoracic epidural block.⁴⁻⁷

The hypothesis in this study is adding TPVB for postoperative analgesia in patients undergoing thoracotomy may positively affect postoperative analgesia and perioperative parameters. This retrospective study aimed to assess the analgesic efficacy, hemodynamic parameters, analgesic consumption, adverse effects and complications in patients who received a thoracic paravertebral injection in addition to intravenous patient-controlled analgesia (PCA) following a thoracotomy.

METHODS

The study was carried out with the permission of the Keçiören Training and Clinical Researches Ethics Committee (Date: 28.11.2012, Decision No: B.10.4.İSM.4.06.68.49). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. Following the granting of, a retrospective analysis was conducted on the standard pain monitoring forms used in the postoperative analgesia practices of 100 patients who underwent thoracotomy between 2009 and 2012. Patients with incomplete or incorrectly recorded data were excluded from the study.

Interventions

Before undergoing surgery, patients were informed about TPVB, which is a method used to treat postoperative pain. They were also informed about the use of the PCA device and their consent was obtained. The Visual Analogue Scale (VAS) method was employed to assess pain intensity, with patients being provided with a detailed explanation of the method. Upon examination of the pain follow-up forms, the patients were divided into two groups, designated Group I and Group II, according to the postoperative analgesia methods applied. Patients were selected from those who underwent the same anesthesia method. The amounts of fentanyl used for induction and maintenance of anesthesia were recorded from the intraoperative anesthesia forms.

For postoperative analgesia, 100 mg of tramadol (Contramal ampul® 100 mg/2 ml, Abdi İbrahim, Türkiye) was administered via intravenous slow infusion 30 minutes prior to the patient's awakening after surgery. Once the patients had been discharged from the operating room and admitted to the surgical intensive care unit, intravenous PCA (Abbott Laboratories, North Chicago, IL, USA) was administered for 24 hours following the operation. A solution containing 5 mg of tramadol in 1 ml was prepared for intravenous PCA. The device was programmed as a 10 mg/hour infusion, a 20 mg bolus, a half-hour locked time, and a 4-hour limit of 120 mg. The same intravenous PCA analgesia protocol was applied to both groups. Patients in Group II underwent TPVB after the surgical procedure, immediately preceding the termination of anesthesia, with the patient positioned in the lateral decubitus position.

The TPVB application was initiated at the caudal and cephalad incision lines of the thoracotomy incision, with two

levels each including the thoracic vertebral segment, resulting in a total of five levels. The spinous processes of the vertebrae were identified and a point 2.5 cm lateral to the spinous process on the thoracotomy side was marked as the injection point. A 22-gauge spinal needle (Exelint®, California, USA) was inserted at the designated point and the transverse process was palpated. The needle was then withdrawn and advanced just above the transverse process in a cephalic direction for a maximum of 2 cm. 4 ml of bupivacaine hydrochloride (Marcaïne vial® 0.5% 20ml, Astra Zeneca, Turkey) was administered for each level.

During the follow-up of patients in the intensive care unit, 1 gram of paracetamol (Perfalgan 100ml vial® 10mg/ml Bristol-Myers Squibb Inc.) was administered via intravenous infusion as an additional analgesic when the VAS score was 4 or higher. Any adverse effects or complications that arose during this period were duly recorded.

The postoperative pain follow-up forms were examined, and the following variables were recorded: gender, age, diagnosis, body mass index (BMI), surgical method, ASA score, and postoperative analgesia methods. The follow-up data included systolic arterial pressure (SBP), diastolic arterial pressure (DAP), mean arterial pressure (MAP), heart rate (HR), peripheral oxygen saturation (SpO₂), respiratory rate (RR), resting and cough VAS scores, the need for additional analgesics, side effects and complications related to analgesia, the number of analgesics consumed and Ramsay sedation scores. The data above were recorded at a total of six time points: preoperatively, before the commencement of PCA, and at 1, 6, 12 and 24 hours postoperatively. Furthermore, analgesic method satisfaction scores were recorded after 24-hour (0=poor, 1=moderate, 2=good, 3=very good, 4=excellent).

Outcomes

The primary outcome of the study was the intensive care unit discharge VAS scores in patients who underwent thoracotomy with and without thoracic paravertebral injection in addition to intravenous PCA for postoperative pain control. The other outcomes of our study were hemodynamic parameter measurements, total tramadol consumption, need for additional analgesia and incidence of side effects in the first 24 hours postoperatively in patients with and without thoracic paravertebral injection.

Statistical Analysis

The data was analyzed using the Statistical Package for Social Science (SPSS) for Windows 11.5 package program. Descriptive statistics were expressed as mean±standard deviation or median (minimum-maximum) for continuous variables and as number of cases (n) and (%) for nominal variables. The significance of the difference between the groups in terms of means was investigated using a Student's t-test, while the significance of the difference in terms of median values was investigated through a Mann-Whitney U test. Nominal variables were analyzed using Pearson's chi-square, Fisher's chi-square with Fisher's exact test or likelihood ratio test. A repeated-measures analysis of variance was employed to assess the hemodynamic measurements. The percentage changes between follow-up times, which were considered clinically important, were calculated and comparisons were made between the groups.

The friedman test was employed to ascertain whether there was a statistically significant change in VAS and sedation scores according to time within the groups. If the result of the friedman test statistic was found to be significant, the Wilcoxon signed-rank test with Bonferroni correction was employed to ascertain the follow-up times that were responsible for the observed difference. The results were considered statistically significant if the p-value was less than 0.05.

RESULTS

There was no statistically significant difference between the groups in terms of age, gender, body weight, height, body mass index, and ASA assessment ($p > 0.05$), as shown in Table 1.

Parameters	Group I (n:50) (mean ± SD)	Group II (n:50) (mean ± SD)	p	
Age (year)	50.6 ± 14.8	50.9 ± 15.7	0.922	
Gender	Male (%)	30 (60.0)	38 (76.0)	0.086
	Female (%)	20 (40.0)	12 (24.0)	
BMI (kg/m ²)	24.9 ± 4.6	26.5 ± 5.1	0.092	
ASA I/II/III	1 / 21 / 28	0 / 31 / 19	0.080	

Demographic data are given as mean ± SD or %.
ASA: American Society of Anesthesiologists, BMI: Body mass index, SD: Standard deviation

The change in SAB over time was statistically similar between the groups ($F=0.379$ and $p=0.812$). In Group I, the only statistically significant change in SAB was the decrease observed between pre-PCA and 24 hours ($p=0.023$). In group II, there was no statistically significant difference in mean SAB between the follow-up times ($p=0.198$). The change in DAB over time was statistically similar between the groups ($F=0.623$ and $p=0.664$). In group I, there was no statistically significant difference in DAB between the follow-up times ($p=0.115$). In group II, the only statistically significant change in DAB was the decrease observed between the preoperative and first-hour time points ($p=0.004$).

There was no statistically significant difference in MAP between the groups ($F=0.254$ and $p=0.900$). There was no statistically significant difference in MAP between the follow-up times in both Group I and Group II ($p=0.433$ and $p=0.713$), as shown in Table 2.

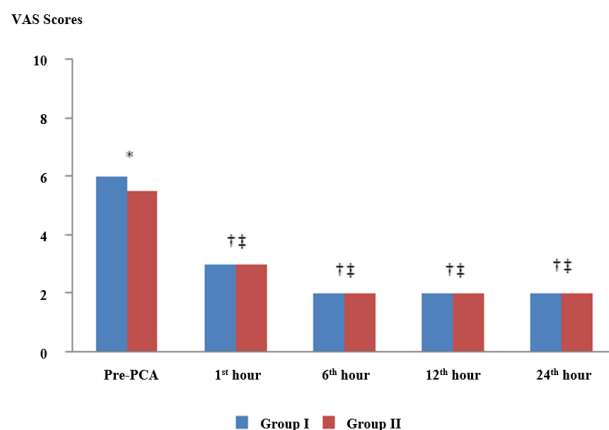
Times	Group I (n:50) (mean ± SD)	Group II (n:50) (mean ± SD)	p ^a
Preoperative	91.5 ± 9.7	91.6 ± 8.2	0.938
Pre-PCA	92.5 ± 16.6	90.4 ± 15.1	0.506
1st hour	89.7 ± 11.2	88.8 ± 11.2	0.669
6th hour	91.2 ± 11.5	90.0 ± 13.2	0.623
12th hour	91.0 ± 11.0	89.4 ± 13.5	0.527
24th hour	89.3 ± 8.5	89.7 ± 10.8	0.814

a: Results were considered statistically significant for $p < 0.0083$ according to Bonferroni Correction. PCA: patient-controlled analgesia

In Group I, there was a statistically significant increase in HR at 12 hours compared to all follow-up times ($p < 0.025$).

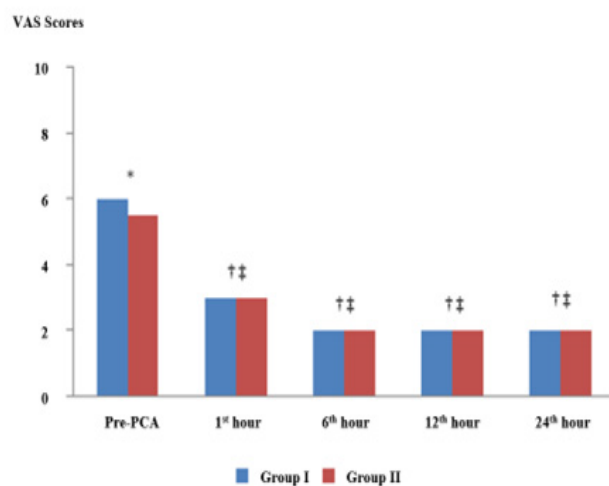
In Group II, the HR values at pre-operative and before PCA were statistically lower ($p < 0.001$). In the context of intergroup comparison, it was observed that the HR in the pre-operative period was significantly higher in Group I ($p=0.008$).

There was no statistically significant difference in SpO₂ between the groups ($p > 0.05$). The SpO₂ values were found to be statistically lower than the preoperative values at all times ($p < 0.01$). A statistically significant decrease was observed in the resting VAS values in Group I and Group II when the data from the pre-PCA and all follow-up times were compared ($p < 0.001$). In the intergroup comparison, resting VAS values in Group II were found to be statistically significantly lower before PCA ($p = 0.001$) (Figure 1).



*: The difference between groups is statistically significant ($p = 0.001$).
†: In Group I, the difference between pre-PCA and other follow-up times was statistically significant ($p < 0.001$).
‡: In Group II, the difference between pre-PCA and other follow-up times was statistically significant ($p < 0.001$).
Figure 1. Resting visual analog scale (VAS) levels according to monitoring times.

A statistically significant decrease in cough VAS values was observed in both Group I and Group II at all other follow-up times in comparison to the pre-PCA values ($p < 0.001$). In the intergroup comparison, cough VAS values before PCA were found to be statistically significantly lower in Group II ($p < 0.002$), as illustrated in Figure 2.



*: The difference between groups is statistically significant ($p = 0.002$).
†: In Group I, the difference between pre-PCA and other follow-up times was statistically significant ($p < 0.001$).
‡: In Group II, the difference between pre-PCA and other follow-up times was statistically significant ($p < 0.001$).
Figure 2. Coughing visual analog scale (VAS) levels according to monitoring times.

A comparison of sedation levels within Group I revealed a statistically significant reduction at all subsequent follow-up times in comparison to the baseline measurement prior to PCA ($p < 0.001$). There was no statistically significant difference between the other follow-up times in terms of sedation levels ($p > 0.025$). In Group II, the lower sedation levels observed at other follow-up times in comparison to the pre-PCA period were found to be statistically significant ($p < 0.001$). There was no statistically significant difference between the other follow-up times in terms of sedation levels ($p > 0.025$). A comparison of the groups in terms of the need for additional analgesics revealed a statistically significant reduction in this need in Group II ($p < 0.05$) (Table 3).

Table 3. Rates of additional analgesic requirement

Times	Group I (n:50) n (%)	Group II (n:50) n (%)	p
Pre-PCA	50 (100.0)	37 (74.0)	<0.001
1st hour	1 (2.0)	4 (8.0)	0.362
6th hour	1 (2.0)	-	1.000
12th hour	-	-	-
24th hour	-	-	-

p < 0.05 statistically significant. PCA: patient-controlled analgesia

In terms of analgesic method satisfaction, three patients in Group I indicated moderate satisfaction, 37 patients indicated high satisfaction, and 10 patients indicated very high satisfaction. In Group II, three patients were moderately satisfied, 30 were well satisfied, and 17 were very well satisfied with the analgesia method. Although the overall satisfaction rate was higher in Group II, there was no statistically significant difference between the groups ($p = 0.277$).

Although there was no statistically significant difference between the groups in terms of total tramadol consumption at 1 and 6 hours, total tramadol consumption at 12 and 24 hours was found to be statistically significantly lower in Group II compared to Group I ($p = 0.040$ and $p = 0.006$) (Table 4).

Table 4. Total amounts of tramadol (mg) consumed

Times	Group I (n:50) (mean ± SD)	Group II (n:50) (mean ± SD)	p
1st hour	51.7 ± 10.3	48.7 ± 10.9	0.162
6th hour	183.5 ± 70.9	158.9 ± 59.3	0.063
12th hour	308.6 ± 80.1	271.2 ± 98.7	0.040
24th hour	502.9 ± 70.4	443.8 ± 128.1	0.006

p < 0.05 statistically significant, SD: Standard Deviation, n: Number

DISCUSSION

In this retrospective study, hemodynamic parameters were found to be similar in both groups. VAS scores at admission to intensive care were found to be statistically significantly lower in the TPVB group. Additionally, the need for additional analgesics was found to be less in this group. It was observed that the TPVB application also reduced 24-hour cumulative tramadol use.

TPVB is a regional blockade method that is becoming increasingly popular due to its ease of application and similar results to thoracic epidural analgesia. The sympathetic

blockade is less observed in TPVB application compared to thoracic epidural analgesia. TPVB can also be applied with multiple injection or catheter techniques.⁸⁻¹¹ Although there are studies on paravertebral catheter application in thoracotomies, studies combining multiple paravertebral injections with iv PCA are limited.^{4,12}

LA and opioid administration via thoracic epidural catheter negatively affects hemodynamic parameters due to the blocking of sympathetic cardiac fibers. This situation may also occur during iv PCA administration due to the systemic effects of iv opioids. Studies indicate that sympathetic blockade is less after TPVB and that complications that may develop due to this can be limited.⁴ In a study comparing TPVB with thoracic epidural analgesia, Richardson et al.⁵ found lower pain scores and less morphine consumption in the thoracic paravertebral group. They also reported that pulmonary functions were better preserved in the TPVB group and nausea-vomiting and hypotension were more common in the epidural group. In our study, no difference was detected in hemodynamic parameters in the iv PCA group (Group I) and the TPVB+iv PCA group (Group II), and no hemodynamic complications occurred due to analgesic treatment. We think that the lower 24-hour iv analgesic consumption in the TPVB group will also reduce the complications that may develop due to iv opioid use.

After thoracic surgery, respiratory functions may deteriorate due to inadequate pain treatment. Additionally, the risk of respiratory depression with excessive opioid use makes pain treatment difficult. Therefore, a situation that requires multimodal analgesia arises.¹³ In multimodal analgesia, different analgesia combinations can be used in combination with central and peripheral blocks.¹⁴ Tramadol is an agent with weak opioid effects and limited respiratory depressant effects. It is widely used in postoperative analgesia.¹⁵⁻¹⁷ Considering the negative effects that may occur on respiratory functions after thoracotomy, iv PCA application with tramadol is also used as a component of multimodal analgesia in our clinic. Although SpO₂ values in the postoperative period were found to be statistically lower than in the preoperative period, no situation requiring treatment was encountered.

Although thoracic epidural analgesia is considered the gold standard in the treatment of post-thoracotomy pain, in recent years it has been advocated that TPVB application may be an alternative to thoracic epidural block.^{18,19} It has been shown that opioid+LA or LA-only administration with a paravertebral catheter in the treatment of pain after thoracotomy provides effective and safe analgesia, reducing the need for iv opioids and the incidence of side effects.⁹ In a study conducted by Hill et al.²⁰ in which they performed multiple paravertebral injections for the treatment of pain after video-assisted thoracoscopic surgery, they observed a significant decrease in VAS scores and a significant decrease in morphine consumption in the first 6 hours. Kaya et al.²¹ found a significant decrease in VAS scores and cumulative morphine consumption in patients who underwent video-assisted thoracoscopic surgery, in their 24-hour postoperative follow-up after multiple TPVB. In the present study, it was observed that in the TPVB+iv PCA group, both resting and cough VAS scores were lower and there was a significant

decrease in 24-hour tramadol consumption in the pre-PCA period. The need for additional analgesics in the group in which TPVB was not performed in the pre-PCA period (Group I) was found to be statistically higher than in the group in which TPVB was performed (Group II). In our study, we observed that since severe pain occurred after thoracotomy, a decrease in VAS scores could not be achieved in the early period, and accordingly, the need for additional analgesics was higher in this period. In the group that received only iv PCA, VAS levels were high before PCA despite 100 mg tramadol administered at the end of surgery. More additional analgesics were required to achieve acceptable VAS scores in this group. While VAS levels were 5 and above in all patients in this group before PCA, VAS resting scores were between 0 and 4 in 12 patients in the TPVB+iv PCA group (Group II).

Kotze et al.,²² in a study they conducted on TPVB, stated that studies on complications developing after TPVB application are limited. They concluded that most studies focused on complications specifically on LA toxicity. In most of these studies, bupivacaine was used as LA. In our study, no LA toxicity or method-related complications were encountered in any of the patients after TPVB.

Limitations

There are some limitations in this study. First of all, the study is single-center and retrospective. Secondly, we could only access 24-hour follow-up in patient records. There was a lack of data for the 48th and 72nd hours after surgery in terms of long-term analgesic effectiveness. Finally, the chronic pain conditions of the patients could not be accessed from the records.

CONCLUSION

As a result, we think that multiple TPVB applications in the acute postoperative period in thoracotomy, when combined with iv PCA applied with tramadol, provide effective analgesia without causing any complications in hemodynamic and respiratory parameters.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of the Keçiören Training and Research Hospital Clinical Researches Ethics Committee (Date: 28.11.2012, Decision No: B.10.4.İSM.4.06.68.49).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Senturk M. Acute and chronic pain after thoracotomies. *Curr Opin Anaesthesiol.* 2005;18(1):1-4.
2. Zengin M, Ülger G, Baldemir R, Sazak H, Alagoz A. Is there a relationship between body mass index and postoperative pain scores in thoracotomy patients with thoracic epidural analgesia? *Medicine.* 2021;100(50):28010.
3. Zengin M, Alagoz A. Comparison of thoracic epidural analgesia and thoracic paravertebral block applications in the treatment of acute pain after thoracotomy in geriatric patients. *Cureus.* 2021;13(10):18982. doi: 10.7759/cureus.18982
4. Dhole S, Mehta Y, Saxena H, Juneja R, Trehan N. Comparison of continuous thoracic epidural and paravertebral blocks for postoperative analgesia after minimally invasive direct coronary artery bypass surgery. *J Cardiothorac Vasc Anesth.* 2001;15(3):288-292.
5. Richardson J, Sabanathan S, Jones J, et al. A prospective, randomized comparison of preoperative and continuous balanced epidural or paravertebral bupivacaine on post-thoracotomy pain, pulmonary function and stress responses. *Br J Anaesth.* 1999;83(3):387-392. doi: 10.1093/bja/83.3.387
6. Zengin EN, Alagöz A, Yiğit H, et al. The effect of body mass index on thoracic paravertebral block analgesia after video-assisted thoracoscopic surgery; a prospective interventional study. *BMC Anesthesiol.* 2023;23(1):297. doi: 10.1186/s12871-023-02264-0
7. Zengin M, Alagöz A, Sazak H, et al. Comparison of efficacy of erector spinae plane block, thoracic paravertebral block, and erector spinae plane block and thoracic paravertebral block combination for acute pain after video-assisted thoracoscopic surgery: a randomized controlled study. *Minerva Anesthesiol.* 2023;89(3):138-148. doi: 10.23736/S0375-9393.22.16639-3
8. Lönnqvist PA, MacKenzie J, Soni AK, Conacher ID. Paravertebral blockade. Failure rate and complications. *Anaesthesia.* 1995;50(9):813-815. doi: 10.1111/j.1365-2044.1995.tb06148.x
9. Karmakar MK. Thoracic paravertebral block. *Anesthesiology.* 2001;95(3):771-780. doi: 10.1097/0000542-200109000-00033
10. Richardson J, Sabanathan S. Thoracic paravertebral analgesia. *Acta Anaesthesiol Scand.* 1995;39(8):1005-1015. doi: 10.1111/j.1399-6576.1995.tb04219.x
11. Davies RG, Myles PS, Graham JM. A comparison of the analgesic efficacy and side-effects of paravertebral vs epidural blockade for thoracotomy--a systematic review and meta-analysis of randomized trials. *Br J Anaesth.* 2006;96(4):418-426. doi: 10.1093/bja/ael020. *Br J Anaesth.* 2007;99(5):768.
12. Das S, Bhattacharya P, Mandal MC, et al. Multiple-injection thoracic paravertebral block as an alternative to general anaesthesia for elective breast surgeries: a randomised controlled trial. *Indian J Anaesth.* 2012; 56(1):27-33. doi: 10.4103/0019-5049.93340
13. Cuschieri RJ, Morran CG, Howie JC, McArdle CS. Postoperative pain and pulmonary complications: comparison of three analgesic regimens. *Br J Surg.* 1985;72(6):495-498. doi: 10.1002/bjs.1800720631
14. Kehlet H, Dahl JB. The value of "multimodal" or "balanced analgesia" in postoperative pain treatment. *Anesth Analg.* 1993;77(5):1048-1056. doi: 10.1213/00000539-199311000-00030
15. James MF, Heijke SA, Gordon PC. Intravenous tramadol versus epidural morphine for postthoracotomy pain relief: a placebo-controlled double-blind trial. *Anesth Analg.* 1996;83(1):87-91. doi: 10.1097/00000539-199607000-00015
16. Bloch MB, Dyer RA, Heijke SA, James MF. Tramadol infusion for postthoracotomy pain relief: a placebo controlled comparison with epidural morphine. *Anesth Analg.* 2002;94(3):523-528.
17. Soto RG, Fu ES. Acute pain management for patients undergoing thoracotomy. *Ann Thorac Surg.* 200;75(4):1349-1357. doi: 10.1016/s0003-4975(02)04647-7
18. Savage C, McQuitty C, Wang D, Zwischenberger JB. Postthoracotomy pain management. *Chest Surg Clin N Am.* 2002;12(2):251-263. doi: 10.1016/s1052-3359(02)00011-x
19. Elsayed H, McKeivith J, McShane J, Scawn N. Thoracic epidural or paravertebral catheter for analgesia after lung resection: is the outcome different? *J Cardiothorac Vasc Anesth.* 2012;26(1):78-82.
20. Hill SE, Keller RA, Smith SM, et al. Efficacy of single-dose, multilevel paravertebral nerve blockade for analgesia after thoracoscopic procedures. *Anesthesiology.* 2006;104(5):1047-1053.

21. Kaya FN, Turker G, Mogol EB, Bayraktar S. Thoracic paravertebral block for video-assisted thoracoscopic surgery: single injection versus multiple injections. *J Cardiothorac Vasc Anesth.* 2012;26(1):90-94.
22. Kotzé A, Scally A, Howell S. Efficacy and safety of different techniques of paravertebral block for analgesia after thoracotomy: a systematic review and meta-regression. *Br J Anaesth.* 2009;103(5):626-636. doi: 10.1093/bja/aep272. PMID: 19837806