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Comparison of Postoperative Analgesia in Thoracotomy Patients by Thoracic Epidural versus Paravertebral Block with Ropivacaine and Clonidine

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Abstract

Background: Postoperative pain after thoracotomy is not only responsible for patient's suffering but also brings about postoperative respiratory complications. The authors compared two techniques as a component of multimodal analgesia in thoracotomy patients: firstly, thoracic epidural which is the gold standard and secondly paravertebral block with the same drug ropivacaine and clonidine.

Methods: 34 adult patients 20 to 60 years of age, ASA status of I & II undergoing elective lateral and posterolateral thoracotomy were included in this study. Exclusion criteria were, patients with any systemic comorbidity and any contraindication to regional anesthesia. Patients were allocated into two groups by computer generated randomisation chart: Group 1 received thoracic epidural analgesia and group 2 received paravertebral analgesia. Parameters recorded were postoperative analgesia by visual analogue scale (VAS) at rest, during deep breathing and during coughing, total rescue analgesic requirement, pH and PaCO2, capillary blood glucose, intraoperative heart rate and blood pressure, extubation time, ICU stay, total hospital stay phenylephrine requirement and incidence of complications.

Result: Analgesia was better in thoracic epidural group for some duration but no persistent effect. Intraoperative heart rate and blood pressure was lower in thoracic epidural group. Total rescue analgesic requirement, pH and PaCO2, capillary blood glucose, extubation time, ICU stay and total hospital stay showed no significant difference. Incidence of bradycardia and phenylephrine requirement was higher in thoracic epidural group.

Conclusion: Although thoracic epidural technique provides better analgesia at some point of time, paravertebral block is preferred because of lower incidence of hypotension, bradycardia and lesser requirement of vasopressor.

Keywords: Thoracic epidural; Paravertebral block; Post thoracotomy analgesia; Multimodal analgesia

Introduction

Pain after thoracotomy is very severe, probably the most severe pain experienced after surgery [1,2]. The thoracotomy procedure involves incision through skin, multiple muscles, rib resection which is continuously stretched during respiration and

movement in postoperative period resulting in severe dynamic pain [1]. Inadequately treated pain sometimes become so intense that it causes splinting effect and interferes with cough and deep breathing, and ultimately culminate in increased incidence of postoperative atelectasis, pneumonia and other respiratory complications, even progression to chronic pain syndrome [3-8]. As the origin of the pain is multifactorial and involving multiple nerves, control of both the static and dynamic pain requires multimodal analgesia incorporating a regional analgesia technique [3,9]. The purpose of the study is to compare the analgesic efficacy of thoracic epidural technique to that of paravertebral block as a part of multimodal analgesia technique using ropivacaine and clonidine.

Method

After obtaining institutional ethics committee permission and written informed consent 34 adult patients, 20 to 60 years of age, ASA status of I & II undergoing elective lateral and posterolateral thoracotomy were included in this study. Patients with any systemic comorbidity like diabetes mellitus, ischemic heart disease, raised intracranial pressure, sepsis and any contraindication to regional anesthesia like, infection at the site of injection, coagulopathy or other bleeding diathesis, severe stenotic valvular heart lesion, severe spinal deformity and uncooperative patients were screened in preanesthesia check-up and excluded [10-14].

Before the surgery the use of VAS were explained to the patients. The patients were recruited sequentially to thoracic epiodural or paravertebral group according to a computer generated randomisation chart. Before surgery, epidural or paravertebral catheter was placed as per individual group after proper aseptic precaution and local anesthesia at a level between T4 and T7, according to the site of incision. The test dose of lignocaine 2% (3 ml) with adrenaline was used to check any intravascular or intraspinal placement of catheter. Intravenous premedication with glycopyrrolate 0.2 mg, ondansetron 4 mg and fentanyl 2 µg/kg was administered. After preoxygenation for 5 minutes with 100% oxygen, induction of anaesthesia was done with intravenous thiopentone (4-6 mg/kg body weight) followed by inj. rocuronium 1 mg/kg. After proper relaxation direct laryngoscopy was done and a double lumen tube (DLT) of appropriate size was introduced and the position was confirmed. Patient positioning was done as required and loading dose of Inj Ropivacaine (20 ml of 0.2%) and Inj Clonidine 20 µg for epidural or para-vertebral block was administered. Maintenance of anesthesia was done with isoflurane, vecuronium and nitrous oxide with oxygen (2:1) during both lung ventilation and 100% oxygen during one lung ventilation. Intraoperative analgesia was provided with fentanyl 25 µg every 30 minutes and intravenous paracetamol 20 mg/kg. After the end of surgery, patients were shifted to postoperative recovery unit. Postoperative analgesia was maintained with continuous infusion of Inj ropivacaine (0.2% at the rate of 6ml/hour) and clonidine (20 µg/hour) for 24 hours via the epidural or paravertebral catheter and intravenous paracetamol 20 mg/kg 8 hourly. Parameters recorded were postoperative analgesia by visual analogue scale (VAS) administered at rest, during deep breathing and during coughing, time of first rescue analgesic, total rescue analgesic requirement, adequacy of ventilation by pH and $PaCO_2$, postoperative stress response by capillary blood glucose, intraoperative hemodynamic parameters in terms of heart rate and blood pressure, extubation time, ICU stay, total hospital stay phenylephrine requirement and incidence of complications like hypotension, bradycardia, tachycardia, nausea and vomiting. Data collection was done by a post-doctoral surgery trainee not aware of the nature of the study.

The Study Definitions Used by the Authors

Significant hypotension

Fall of systolic BP below 25% of baseline or mean arterial pressure below 65mm hg. Treated with phenylephrine 50µg bolus.

Significant bradycardia

Heart rate less than 60 per minute with significant hypotension (as stated above) or less than 45 per minute with any blood pressure. Treated with atropine 0.5 mg.

Significant pain

Patient complaining of discomforting pain or VAS score more than 4. Treated with morphine 0.1 mg/kg.

Any incidence of nausea and vomiting was treated with adequate hydration and ondansetron 4 mg.

For sample size calculation postoperative VAS score with cough was considered as the primary outcome measure. It was estimated that 17 subjects would be required per group in order to detect a difference of VAS score with cough of 1 with 80% power and 5% probability of type I error. This calculation assumes a standard deviation of 1 in this parameter. Data was summarized as mean and standard deviation for parametric numerical variables and median and interquartile range for nonparametric numerical variables. Counts and percentages were used for categorical variables. The independent samples t test was employed for intergroup comparison of parametric numerical variables or the Mann-Whitney U for non-parametrics. Categorical variables were compared between groups by Fisher's exact test. All analyses were two-tailed and $p < 0.05$ was considered statistically significant.

Results

34 patients were enrolled for this study and were randomised into two groups by computer generated randomisation chart: Group 1 received postoperative analgesia by continuous infusion of local anaesthetic via thoracic epidural route and group 2 received same infusion via paravertebral route. There was no incidence of dropout or perioperative death among the study population.

Patient characteristics, baseline patient parameters, anesthesia details and operative data were comparable in the groups **(Table 1).**

Comparison of intraoperative hemodynamic data revealed significantly lower mean arterial pressure in thoracic epidural

Table 1 Comparison of baseline patient characteristics and clinical parameter.
N.B. - HR: Heart Rate, MAP: Mean Arterial Pressure.

	Group 1 (Mean ± Standard deviation)	Group 2 (Mean ± Standard deviation)	P value
Age (yrs)	48.5 ± 11.06	43.9 ± 12.04	0.256
Gender (Male/Female)	8/9	7/10	1.000
Weight (kg)	59.6 ± 8.98	59.5 ± 9.46	0.971
Height (cm)	156.1 ± 9.78	155.1 ± 11.98	0.792
Baseline HR/min	82.0 ± 13.23	81.6 ± 14.1	0.931
Baseline MAP mm Hg	85.8 ± 11.35	85.6 ± 11.2	0.952
Duration of surgery (min)	187.4 ± 35.18	193.5 ± 31.61	0.594
Fentanyl requirement	150 (100-175)	135 (125-150)	0.783

Table 2 Comparison of mean arterial pressure and heart rate.
[**N.B.: MAP1:** Mean arterial pressure at 30 minutes after incision, MAP2: Mean arterial pressure at 60 minutes after incision, AP3: Mean arterial pressure at 90 minutes after incision, MAP4: Mean arterial pressure at 120 minutes after incision. HR1: Heart rate at 30 minutes after incision, HR2: Heart rate at 60 minutes after incision, HR3: Heart rate at 90 minutes after incision, HR4: Heart rate at 120 minutes after incision]

	Group 1 [Mean ± Standard deviation]	Group 2 [Mean ± Standard deviation]	P value
MAP1	69.5 ± 10.18	76.6 ± 9.17	0.040
MAP2	69.6 ± 7.25	75.4 ± 7.47	0.029
MAP3	71.2 ± 6.17	74.2 ± 6.19	0.175
MAP4	70.6 ± 6.79	71.5 ± 5.46	0.679
HR1	75.8 ± 15.71	78.1 ± 14.06	0.665
HR2	68.5 ± 17.64	85.7 ± 12.82	0.003
HR3	69.1 ± 11.59	81.5 ± 11.55	0.004
HR4	75.0 ± 10.51	82.3 ± 14.67	0.105

Table 3 Comparison of VAS score with cough, deep braeathing and at rest.
[**N.B. - VASC1:** VAS score with cough 4 hours after surgery, VASC2: VAS score with cough 8 hours after surgery, VASC3: VAS score with cough 12 hours after surgery, VASC4: VAS score with cough 16 hours after surgery, VASC5: VAS score with cough 20 hours after surgery, VASC6: VAS score with cough 24 hours after surgery; VASD1: VAS score with deep breathing 4 hours after surgery, VASD2: VAS score with deep breathing 8 hours after surgery, VASD3: VAS score with deep breathing 12 hours after surgery, VASD4: VAS score with deep breathing 16 hours after surgery, VASD5: VAS score with deep breathing 20 hours after surgery, VASD6: VAS score with deep breathing 24 hours after surgery; VASR1: VAS score at rest 4 hours after surgery, VASR2: VAS score at rest 8 hours after surgery, VASR3: VAS score at rest 12 hours after surgery, VASR4: VAS score at rest 16 hours after surgery, VASR5: VAS score at rest 20 hours after surgery, VASR6: VAS score at rest 24 hours after surgery;]

	Group1 [Median (interquartile range)]	Group 2 [Median (interquartile range)]	P value
VasC1	3.0 (3-4)	3.0 (3-4)	0.361
VasC2	3.0 (2-3)	4.0 (3-4)	0.073
VasC3	2.0 (2-3)	3.0 (3-4)	0.073
VasC4	2.0 (2-2)	2.0 (2-3)	0.125
VasC5	2.0 (2-2)	2.0 (2-2)	0.241
VasC6	2.0 (2-2)	2.0 (2-2)	0.399
VasD1	3.0 (3-4)	3.0 (3-4)	0.918
VasD2	3.0 (2-3)	4.0 (3-4)	0.091
VasD3	2.0 (2-2)	2.0 (2-4)	0.293
VasD4	2.0 (2-2)	2.0 (1-2)	0.263
VasD5	2.0 (2-2)	2.0 (1-2)	0.796
VasD6	2.0 (1-2)	1.0 (1-2)	0.191
VasR1	3.0 (3-4)	3.0 (3-4)	0.823
VasR2	2.0 (2-3)	3.0 (3-4)	0.102
VasR3	2.0 (2-2)	2.0 (2-2)	0.836
VasR4	2.0 (1-2)	2.0 (1-2)	0.502
VasR5	1.0 (1-2)	2.0 (1-2)	0.558
VasR6	2.0 (1-2)	1.0 (1-2)	0.770

Table 4 Comparison of pH and PCO_2.
[**N.B. - pH1:** pH value 4 hours after surgery, pH2: pH value 8 hours after surgery, pH3: pH value 12 hours after surgery, pH4: pH value 16 hours after surgery, pH5: pH value 20 hours after surgery, pH6: pH value 24 hours after surgery; PCO21: PCO2 4 hours after surgery, PCO22: PCO2 8 hours after surgery, PCO23: PCO2 12 hours after surgery, PCO24: PCO2 16 hours after surgery, PCO25: PCO2 20 hours after surgery, PCO26: PCO2 24 hours after surgery]

	Group 1 (Mean ± Standard deviation)	Group 2 (Mean ± Standard deviation)	P value
pH1	7.441 ± 0.07	7.443 ± 0.06	0.950
pH2	7.429 ± 0.08	7.416 ± 0.08	0.653
pH3	7.444 ± 0.07	7.463 ± 0.07	0.437
pH4	7.474 ± 0.06	7.434 ± 0.08	0.109
pH5	7.471 ± 0.06	7.472 ± 0.06	0.965
pH6	7.468 ± 0.06	7.471 ± 0.07	0.919
PCO21	38.3 ± 6.44	38.4 ± 3.98	0.954
PCO22	38.5 ± 6.45	40.9 ± 6.40	0.294
PCO23	37.9 ± 7.17	36.4 ± 6.82	0.548
PCO24	35.4 ± 5.19	34.8 ± 5.58	0.762
PCO25	35.5 ± 5.28	34.0 ± 5.44	0.419
PCO26	35.7 ± 3.47	34.2 ± 4.95	0.296

Table 5 Comparison of vasopressor and rescue analgesic requirement and stays.

	Group 1 [Median (interquartile range)]	Group 2 [Median (interquartile range)]	P value
Phenylephrine requirement	150.0 (0.0-200.0)	0.0 (0.0-100.0)	0.042
Time of extubation	0.0 (0.0-0.0)	0.0(0.0-5.0)	0.757
Recovery stay	24.0 (24.0-24.0)	24 (24-24)	0.558
Total Hospital stay	19.0 (16-22)	19.0 (14-23)	0.757
Total morphine requirement	0.0 (0.0-4.0)	0.0 (0.0-5.0)	0.863
Time of administration of first rescue analgesic	0.0 (0.0-5.0)	0.0 (0.0-7.0)	0.796

group during the first hour of surgery. Heart rate was significantly lower in the thoracic epidural group after 30 minutes of surgery and was significantly lower for one hour **(Table 2).**

VAS scores, phenylephrine requirement, extubation time, rescue analgesic time and stays followed nonparametric distribution by Kolmogorov-Smirnoff goodness-of-fit test, and compared by Mann-whitney U test revealed significantly lower pain in thoracic epidural group at different times but significance was not persistent. From this the authors conclude that pain control was adequate and comparable between two groups with the thoracic epidural technique having a better analgesic profile **(Table 3).**

Comparison of arterial blood gas analysis values, (pH and PaCO2) normally distributed by Kolmogorov-Smirnoff goodness-of-fit test, was done by student's unpaired t test and no significant difference was found **(Table 4).**

Post operative stress response was reflected by capillary blood glucose measured every 4 houry and compared by student's unpaired t test and no significant difference found **(Figure 1).**

Comparison of vasopressor and rescue analgesic requirement and stays **(Table 5)** revealed phenylephrine requirement was significantly higher in thoracic epidural group. Time of extubation, recovery stay, total Hospital stay, total morphine requirement and time of administration of first rescue analgesic showed no

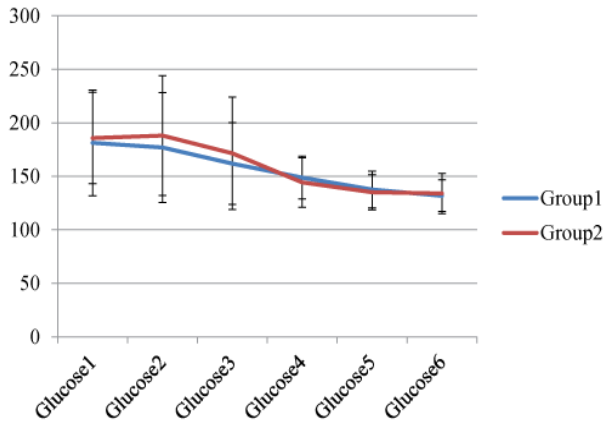

Figure 1 Comparison of postoperative capillary blood ww

[N.B.: Glucose1- Capillary blood glucose value after 4 hours of surgery, Glucose2- Capillary blood glucose value after 8 hours of surgery, Glucose3- Capillary blood glucose value after 12 hours of surgery, Glucose4- Capillary blood glucose value after 16 hours of surgery, Glucose5- Capillary blood glucose value after 20 hours of surgery, Glucose6- Capillary blood glucose value after 24 hours of surgery**]**

significant difference between the groups.

Incidence of postoperative complications, like hypotension, tachycardia, bradycardia, postoperative nausea and vomiting were expressed in count and percentage and Fisher's exact test was applied. Comparison revealed significantly more incidence of Bradycardia in thoracic epidural group and incidence of hypotension showed a trend towards significance in the same group.

Summary of Results

The two groups were comparable in terms of age, sex, height and preoperative hemodynamic parameters. Duration of surgery and fentanyl requirement was also comparable in two groups. The differences found in both groups were significantly lower blood pressure and heart rate and higher requirement of phenylephrine to combat hypotension in thoracic epidural group probably due to more sympathetic blockade. Post operative VAS score was comparable between two groups. Time to adminster first rescue analgesic and amount of rescue analgesic required in both groups were comparable. Post operative stress response was comparable between two groups as reflected by capillary blood glucose level. Adverse effects like bradycardia, hypotension was much more common in the thoracic epidural group than the paravertebral group. Incidence of nausea and vomiting was higher in thoracic epidural group but whether it is due to the technique or due to more requirement of morphine is unclear **(Figure 2).**

Discussion

Ropivacaine and clonidine was selected as anesthetic solution in both the groups for certain reasons. Although bupivacaine is the most common anesthetic used for this purpose, ropivacaine has

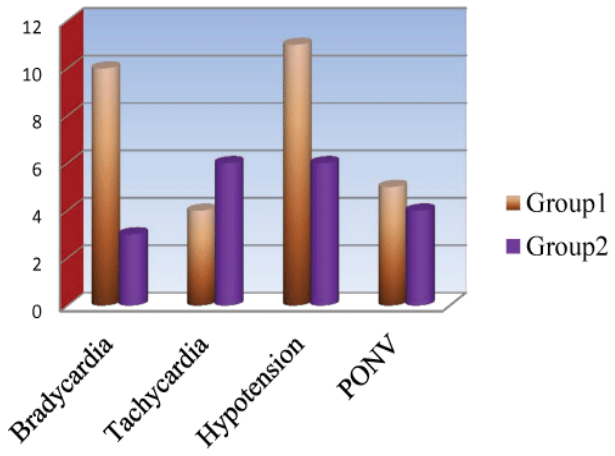

Figure 2 Comparison of postoperative complications

almost similar pharmacokinetics but less risk of cardiovascular toxicity. Animal studies indicated that ropivacaine is less toxic than both levobupivacaine and bupivacaine when administered at the same rate and ropivacaine-induced cardiac arrest appeared to be more susceptible to treatment than that induced by bupivacaine or levobupivacaine [15]. Fentanyl was not used as adjuvant because some authors [16,17] questioned applicability of fentanyl in epidural route. The authors used fentanyl intravenously during intraoperative period but avoided postoperatively for the risk of respiratory depression.

No study was found till date in literature review comparing ropivacaine and clonidine via TEA and PVB in thoracotomy patients. The authors considered different studies for dose adjustment of ropivacaine and clonidine.

The paravertebral space is a potential space behind parietal pleura and loading dose in paravertebral block is essential for expanding the space and for proper distribution of local anesthetic in the space. Different studies have indicated 15-20 ml drug [18] should be used as a loading dose if a paravertebral catheter is used. The loading dose used by the authors, 20 ml 0.2% Ropivacaine with clonidine, was inspired by a study done by Fibla et al. [2]. Maintenance dose of ropivacaine, i.e., 12 mg/hour or 6ml 0.2% solution/hour was inspired by Sakai et al. [19]. The loading dose of clonidine advocated by different studies ranges from 1 to 3 µg/kg but most of the study used clonidine as sole anesthetic agent and as a single bolus dose [20]. At the same time, most study indicated occurrence of severe haemodynamic instability in the form of bradycardia and hypotension. Therefore the authors considered much lower dose, i.e., 1 µg/ml or 20µg in loading dose as used in studies by Liu et al. [21] and Huang et al. [22]. The maintenance dose of clonidine advocated is 5-20µg/hour14. The authors considered 20 µg/hour from a randomized, double-blind, dose-finding trial of clonidine in combination with bupivacaine and fentanyl by Paech et al. [23].

Davies, Myles and Graham [24] conducted a meta-analysis of 10 randomized trials between 1989 and 2005 to compare the analgesic efficacy and side-effects of paravertebral vs. epidural blockade for thoracotomy that had enrolled 520 patients. None of the trial was blinded and none of the studies used our study drug ropivacaine and clonidine. There was no significant difference in paravertebral and epidural groups for pain scores [95% confidence interval (CI): –0.5, 121], P<0.05 at 8, 24, 48 h. PVB was associated with fewer pulmonary complications [odds ratio (OR) 0.36 [0.14, 0.92]], urinary retention (OR 0.23 [0.10, 0.51]), nausea and vomiting OR 0.47 ([0.24, 0.53]) and hypotension, (OR 0.28 [0.2, 0.6]). In we' study pain control was similar, hospital stay and ICU stay were similar and there was fewer incidences of side effects in the paravertebral block group. The postoperative pulmonary function assessment was not included in our study.

Joshi et al. [25] conducted a systematic review of data between 1966 and May 2004 and found continuous PVB was as effective as thoracic epidural analgesia with local anaesthetic (both with and without opioid) at day 1. PVB was associated with a reduced incidence of hypotension and pulmonary complications. The authors study yielded similar results.

Richardson et al. [26] conducted a prospective randomized study between thoracic epidural and paravertebral bupivacaine in 100 adult patients. The visual analogue pain score (VAS) at rest and on cough and pulmonary function, as assessed by peak expiratory flow rate (PEFR), oxymetric recordings were significantly better preserved in the paravertebral group. Plasma concentrations of cortisol increased markedly in both groups, but the increment was statistically different in favour of the paravertebral group (P=0.003). PVB was considered by them as effective as epidural and better in terms of pulmonary function, neuroendocrine stress response and side effects. In the authors' study VAS scores were lower in thoracic epidural group than the PVB group but there was no persistent difference. (Least p value of VAS with cough, deep breathing and at rest was 0.073, 0.091 and 0.102 respectively). Pulmonary complications were not included and cortisol measurement could not be done in our study. But stress response as reflected by capillary blood glucose and pulmonary function by pH and PaCO2 were similar in both group.

Kaiser et al. [27] observed pain control, recovery of ventilatory function and pulmonary complications in 30 thoracic surgery patients undergoing lung resection. PVB was superior to epidural in the first 24 h postoperatively. Statistically significant differences (FVC 46.8% for PVB and 39.3% for epidural group P-0.05; FEV 48.4% in PVB group 1 and 35.9% in epidural group, P-0.05) were reached in day 2 and continued until day 3. Epidurals were related to a higher complication rate (atelectasis, pneumonia) compared to the PVB.

Casati et al. [28] conducted a prospective, randomized, blinded study comparing the efficacy of the PVB vs. epidural analgesia in 42 patients undergoing lung resection. The outcome variable was expressed as the area under the curve of the VAS during coughing (AUCVAS), PaO2:FiO2 ratio, systolic arterial pressure, rescue analgesic morphine requirement and they found that PVB was as effective as epidural blockade in controlling post-thoracotomy pain, but was associated with less haemodynamic effects in their study.Gulbahar et

al. [13] studied 44 consecutive patients who underwent elective posterolateral thoracotomy to compare epidural and paravertebral catheterisation techniques in post-thoracotomy pain management and found no significant difference between the two groups with regard to age, gender, VAS, FEV1, PEFR, serum cortisol and glucose levels, necessity for additional analgesia and hospital staying days. In contrast, adverse effects and duration of catheterisation were found to be statistically significantly lower in group PVB ($p = 0.001$ and $p < 0.001$, respectively). Except respiratory parameters and cortisol measurement other results corroborated with the authors' study.

The authors also found no significant difference between the groups in terms of post operative VAS score, requirement of first rescue analgesic and amount of total rescue analgesic required, stress response and recovery unit stay; but requirement of phenylephrine was higher in the thoracic epidural group to treat hypotension, adverse effects like bradycardia, hypotension, incidence of nausea and vomiting was much more common in the thoracic epidural group than the paravertebral group. So, PVB was equally effective as TEA in the authors' study with lower incidence of side effects.

Conclusion

From the aforementioned study, the authors conclude continuous thoracic epidural analgesia and continuous paravertebral block, both, provide excellent and similar postoperative analgesia in thoracotomy patients. Although TEA provides better analgesia at some point of time, PVB is preferred to TEA because of lower incidence of hypotension, bradycardia and lesser requirement of vasopressor. The authors recommend multimodal analgesia with intravenous paracetamol and paravertebral infusion of ropivacaine and clonidine as a safe and effective multimodal analgesia in thoracotomy patients.

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