## Intraoperative haemodynamic stability and stress response to surgery in patients undergoing thoracotomy: comparison between ultrasound-assisted thoracic paravertebral and epidural block

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#### **Objectives and aim**

Thoracotomy is a procedure usually associated with severe postoperative pain. This study aimed to evaluate intraoperative haemodynamics and stress response to thoracotomy in patients receiving thoracic epidural or thoracic paravertebral block.

#### Patients and methods

Sixty patients undergoing elective thoracotomy were randomly allocated into two equal groups: the thoracic paravertebral analgesia (TPVA) group, which received ultrasound-assisted thoracic paravertebral catheter, and the thoracic epidural analgesia (TEA) group, which received ultrasound-assisted thoracic epidural catheter. The primary outcome was the measuring of stress response to surgery using plasma cortisol level. The secondary outcomes included intraoperative haemodynamic parameters, visual analogue pain score and postoperative complications.

#### Results

Heart rate showed significantly lower values in the TEA group compared with the TPVA group. The mean arterial blood pressure showed significantly lower values in the TEA group compared with the TPVA group. In both groups, there was a significant increase in plasma cortisol level after surgical stress compared with basal values. Moreover, there were significantly lower values in the TPVA group compared with the TEA group at 2 h after surgical incision, 2 h postoperatively and 24 h postoperatively. Visual analogue pain score was noncomparable in both groups at all measurement timepoints. As regards complications, group TPVA had less complications compared with group TEA.

## Conclusion

Thoracic paravertebral block is an effective analgesic technique showing greater haemodynamic stability and less stress response to surgery compared with epidural analgesia in patients undergoing thoracotomy.

#### Keywords:

epidural block, haemodynamic stability, stress response, thoracic paravertebral, thoracotomy

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## Introduction

Thoracotomy is a procedure usually associated with severe postoperative pain [1], which increases perioperative morbidity, activates neuroendocrine reflexes and may lead to chronic pain [2,3]. Thoracic epidural analgesia (TEA) with local anaesthetic, opioid, or both has become commonplace and has been regarded as the 'gold standard' [4]. The epidural blockade has been shown to lessen the intraoperative surgical stress response and has potential advantages for cardiovascular, respiratory, coagulation, gastrointestinal and metabolic systems [5]. However, thoracic epidurals can cause hypotension and neurological injury, and are contraindicated in the presence of coagulopathy or local sepsis [6]. Thoracic paravertebral block (TPVB), both single-injection and continuous infusion, has been reported to be comparable to thoracic epidural in terms of analgesia while avoiding the possibility of hypotension and urinary retention in the postoperative period [7]. Recent advances in ultrasound technology have made it possible to image thoracic paravertebral and thoracic epidural spaces and accurately determine their distance, which may be translated into improved technical outcomes, higher success rates, and reduced needlerelated complications [8]. Our aim was to evaluate intraoperative haemodynamics and stress response to thoracotomy in patients receiving TEA or thoracic paravertebral analgesia (TPVA).

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## Patients and methods

This study was conducted in Benha University Hospitals between February 2014 and October 2015. After obtaining local ethical committee approval and informed written consent from patients, this prospective randomized double-blind clinical trial was conducted on 60 patients above 18 years of age of ASA I, II and III undergoing elective thoracotomy. Patients were randomized into two equal groups. An online randomization program was used to generate random number list. Patient randomization numbers were concealed in opaque envelops, which were opened by the study investigator. These patients were randomly allocated into two equal groups:

*Group TPVA* received ultrasound-assisted thoracic paravertebral catheter.

*Group TEA* received ultrasound-assisted thoracic epidural catheter.

Patients with empyema, neoplastic mass occupying paravertebral space, kyphoscoliosis, BMI less than 18.5 or greater than  $30 \text{ kg/m}^2$ , history of cerebrovascular disease, seizure disorders, central nervous system diseases, coagulation disorders, or local skin infection, and patients with known hypersensitivity to one of the used drugs were excluded from the study.

In the preoperative room, wide bore intravenous line was inserted, and midazolam (0.01–0.02 mg/kg) was administered to all patients, and then an arterial line was inserted. Patients were transferred to the operation room, and routine monitoring was applied.

Thoracic paravertebral space and thoracic epidural space were identified with the patient in sitting position using ultrasound. A 9MHz linear array probe was placed over a spinous process in the midline in a longitudinal manner. The probe was then moved laterally to visualize the transverse process, the point at which the transverse process and the rib intersects, and the superior costotransverse ligament and the pleura with lung tissue were visualized anteriorly. The probe was then turned in a lateral transverse manner and the transverse process, the shimmering pleura, which dip medially, and the lung tissue anterior to the pleura were visualized. The thoracic epidural space was identified using a low-frequency 5 MHz curved array probe by adjusting the depth (10 cm), gain and focus of ultrasound machine. Ultrasound probe was placed in parasagittal (PS) orientation 3-4 cm lateral to midline.

Two views obtained PS transverse view where's transverse processes appeared as curvilinear hyperechoic structures with finger-like acoustic shadowing beneath.

Once the examination in the PS plane was completed, the probe was rotated 90° into a transverse orientation and centred on the neuraxial midline. Sliding the probe in a cephalad or caudate direction from the transverse spinous process view aligns the beam with the interspinous and the interlaminar space and provides a transverse interlaminar view of the contents of the vertebral canal. Thereafter, the probe was moved medially to obtain PS articular process view. The probe was then tilted from lateral-to-medial direction towards the median sagittal plane.

In both groups, once the best image of structures was captured, the transducer was stabilized, the skin was marked and the transducer removed. The insertion point was infiltrated with lidocaine 1%.

Under sterile conditions, an 18-G epidural needle (Perifix; B. Braun Melsungen AG, Germany) was used to locate the thoracic paravertebral space and the thoracic epidural space using the loss of resistance to saline technique. When the loss of resistance was established, the depth of the needle was identified using the markings on the needle and then a 20-G epidural catheter (B. Braun) was inserted 5 cm beyond the loss of resistance depth. After negative aspiration, a test dose of 3 ml of lidocaine 1% mixed with epinephrine 1 : 200 000 was given.

In the supine position and after the test dose proven negative, 15–20 and 5–8 ml of bupivacaine 0.5% in the TPVA group and the TEA group, respectively, was given. In both groups, continuous infusion of bupivacaine 0.25% was given at a rate of 0.1 ml/kg/h and maintained throughout the whole operation.

General anaesthesia (GA) was induced after 20 min from bolus dose with propofol 1–3 mg/kg followed by rocuronium 0.6 mg/kg to facilitate endotracheal intubation. Anaesthesia was maintained with isoflurane 1.5% and rocuronium 0.15 mg/kg as a maintenance dose every 30 min until the end of the procedure. Ventilation parameters were adjusted to maintain end-tidal  $CO_2$  at 35–45 mmHg.

After emerging from anaesthesia, the patients were transferred to the cardiothoracic ICU for 24 h under postoperative observation. Postoperative analgesia was provided immediately after surgery with an infusion of 0.125% bupivacaine at a rate of 0.1 ml/kg/h plus

 $2 \mu g/ml$  fentanyl. If visual analogue pain score (VAS) was higher than 4, the infusion was increased up to 10 ml/h. If pain score exceeded 4 despite the maximum infusion rate of bupivacaine, rescue analgesia 5 mg bolus of morphine was administered intravenously to achieve satisfactory pain control, and can be repeated every 4–6 h.

The primary outcome was the evaluation of stress response to surgery using plasma cortisol level as a marker at the following intervals: before surgery, 2 h after surgical incision, 2 h postoperatively and 24 h postoperatively.

The secondary outcomes included the following: intraoperative haemodynamic parameters [heart rate (HR) and mean arterial blood pressure (MAP)], which were recorded before block, 10 min and 20 min after block, 10 min after induction of GA, after lateral positioning of probe, after skin incision and after rib retraction; VAS every 6 h postoperatively; and postoperative complications in the form of significant hypotension (SPB <30% from baseline), nausea, vomiting, urine retention and itching.

## Data management and statistical analysis

Data were analysed using SPSS (version 16; SPSS Inc., Chicago, Illinois, USA). Quantitative data were presented

as mean±SD and were analysed using unpaired Student's *t*-test. Qualitative data were presented as numbers and percentages and were analysed using the  $\chi^2$ -test and the Z-test. A *P* -value less than 0.05 was considered statistically significant and a *P* -value less than 0.01 was considered statistically highly significant.

Sample size was calculated according to a pilot study of the first eight patients using a power of 80% and twosided  $\alpha$ -error of 5% to detect the difference in cortisol level (primary outcome). The calculated effect size was 0.762. We calculated that 30 patients were required for each group.

## Results

Of the 75 patients screened during the study period, 12 patients did not match the inclusion criteria and two patients refused to participate. Sixty-one patients were included in the study but one more uncooperative patient was excluded before analysis. Thus, 60 patients completed the study protocol (Fig. 1).

Demographic characteristics were nonsignificant between the two groups (Table 1).

Intraoperative data and hospital stay were noncomparable between groups (Table 2).

## Figure 1



Consort flow diagram. TEA, thoracic epidural analgesia; TPVA, thoracic paravertebral analgesia.

#### Table 1 Demographic characteristics

	Group TPVA ( <i>n</i> =30)	Group TEA ( <i>n</i> =30)	P-value		
Age (years)	49.36±11.73	48.53±9.43	0.76		
Weight (kg)	78.36±9.47	78.06±7.52	0.89		
Height (cm)	168.03±7.26	168.56±7.30	0.77		
Sex [n (%)]					
Male	21 (70)	24 (80)	0.37		
Female	9 (30)	6 (20)			
ASA status [n (%)]					
I	7 (23.3)	3 (10)	0.3		
II	20 (66.7)	25 (83.3)			
111	3 (10)	2 (6.7)			

Data were presented as mean $\pm$ SD. Sex and ASA status data were presented as *n* (%). TEA, thoracic epidural analgesia; TPVA, thoracic paravertebral analgesia.

Table 2	0	perative	data	and	hospital	stay	of	both	group	bs
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	Group TPVA ( <i>n</i> =30)	Group TEA ( <i>n</i> =30)	P-value
Type of surgery [n (%	)]		
Bilobectomy	4 (13.3)	2 (6.7)	0.38
Lobectomy	20 (66.7)	23 (76.7)	0.39
Segmentectomy	0 (0)	1 (3.3)	0.31
Bronchtomy	6 (20)	4 (13.3)	0.48
Site of surgery [n (%)	]		
Right	17 (56.7)	20 (66.7)	0.42
Left	13 (43.3)	10 (33.3)	
Blood loss (ml)	591.66±124.62	651.66±171.9	0.12
Duration of	166.83±32.25	165.33±28.03	0.84
surgery (min)			
Hospital stay (days)	10.63±2.87	10.53±2.75	0.89
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Data were presented as mean $\pm$ SD. Type and site of surgery data were presented as *n* (%). TEA, thoracic epidural analgesia; TPVA, thoracic paravertebral analgesia.

HR showed significantly lower values in the TEA group compared with the TPVA group at 20 min from bolus dose injection, 10 min after induction of GA, after lateral positioning of the probe, after skin incision and after rib retraction (Fig. 2).

MAP showed significantly lower values in the TEA group compared with the TPVA group at 10 min from bolus dose injection, 20 min from bolus dose injection, 10 min after induction of GA, after lateral positioning of the probe, after skin incision and after rib retraction (Fig. 3).

In both groups, there was a significant increase in plasma cortisol level after surgical stress compared with basal values. Moreover, there were significantly lower values in the TPVA group compared with the TEA group at 2h after surgical incision, 2h postoperatively and 24h postoperatively (Table 3).

VAS was nonsignificant between the two groups at all measurement timepoints (Fig. 4).

Figure 2



Heart rate. \*Significant change between the two groups.  $^{\diamond}$ Highly significant change between the two groups. GA, general anaesthesia; TEA, thoracic epidural analgesia; TPVA, thoracic paravertebral analgesia.

#### Figure 3



Mean arterial pressure (MAP). \*Significant change between the two groups.  $^{\diamond}$ Highly significant change between the two groups. GA, general anaesthesia; TEA, thoracic epidural analgesia; TPVA, thoracic paravertebral analgesia.

#### Figure 4



Visual analogue pain score (VAS). TEA, thoracic epidural analgesia; TPVA, thoracic paravertebral analgesia.

#### Table 3 Plasma cortisol level (µg/ml)

	Group TPVA (n=30)	Group TEA (n=30)	P-value
Basal	17.7±0.6	17.9±0.5	0.1
2 h after surgical incision	25.2±2.6	27.3±2.9	< 0.01**
2 h postoperative	34.1±4.3	40.1±4.6	< 0.01**
24 h postoperative	29.9±3.1	27.9±2.6	< 0.01**

Data were presented as mean±SD. TEA, thoracic epidural analgesia; TPVA, thoracic paravertebral analgesia. <sup>\*\*</sup>Significant change in both groups.

As regards complications, six patients (20%) in group TEA developed significant hypotension in comparison with one patient (3.3%) in group TPVA. Urine retention showed a significantly higher incidence in group TEA (five patients) in comparison with group TPVA (no patients) (Table 4).

## Discussion

Thoracotomy is associated with major changes in the circulation as operations in the pleural cavity are connected with circulatory changes in pulmonary circulation and general changes in haemodynamics. These changes are influenced by the position of patient's body on the operation table and by the introduction of artificial pneumothorax [9].

In our study, we compared pre-emptive thoracic parav ertebral versus thoracic epidural with intraoperative continuous infusion of local anaesthetic on intraop erative haemodynamics. Current study findings are similar to the findings of Mukherjee et al. [10], Casati et al. [11], and Baidya et al. [12], who found that there were statistically significant MAP differences between TPVB and thoracic epidural block, which were lower in the TEA group. However, it is contradictory to the findings of Santhosh Kumar and Rajendran [13], who found that there was no fall in blood pressure after the first hour and the MAP between the two groups was not statistically significant. This can be attributed to the fact that in both groups only 8 ml of 0.25% bupivacaine was used after the completion of the surgical procedure and the patient did not receive intraoperative opioid analg esia, and intraoperative analgesia was maintained with N<sub>2</sub>O only. Our findings are contradictory to the findings of Pintaric et al. [14] as well, who found that both groups did not differ significantly in HR, MAP, or systemic vascular resistance indices. This can be attributed to the fact that a greater volume of colloid infusion and phenylephrine is required in the epidural than in the paravertebral group to maintain the targeted oxygen delivery index. Our study findings are contradictory to the findings of Dhole et al. [15], who found that no signif icant differences were found as regards haemodynamic parameters, HR and MAP, whereas cardiac index at 4 and 6 h was significantly higher in the TEA group than in the TPVA group. Systemic vascular resistance was

## **Table 4 Complications**

	Group TPVA ( <i>n</i> =30)	Group TEA ( <i>n</i> =30)	P-value
Hypotension	1 (3.3)	6 (20)	0.04*
Nausea	5 (16)	9 (30)	0.2
Vomiting	0 (0)	3 (10)	0.07
Urine retention	0 (0)	5 (16.6)	0.01*
Itching	2 (6.6)	5 (16.6)	0.22

Data were presented as n (%). TEA, thoracic epidural analgesia; TPVA, thoracic paravertebral analgesia. Significant.

lower in the TEA group throughout the study period, although there was no statistical difference.

The current study showed a significant increase in plasma cortisol level from preoperative values in both groups, with lower significant values in the TPVA group, which may indicate less neuroendocrine axis stimulation. These results may be explained by blocking of sympathetic chain in paravertebral block, which is anatomically distant in epidural block.

Our study findings are similar to the findings of Wedad *et al.* [16] and Richardson *et al.* [3], who demonstrated a lower plasma cortisol level in the paravertebral block.

In the current study, the VAS was lower in the TEA group. However, the difference was not statistically significant (P>0.05). The findings of current study are similar to the findings of Pintaric et al. [14], Gulbahar et al. [17], Aly et al. [8], and Messina et al. [18], who found no significant differences between TEA and TPVA as regards VAS. However, it is not in agreement with the findings of Richardson et al. [3], who found significantly lower VAS pain scores both at rest and on coughing in the paravertebral block group compared with the TEA group (P=0.02 and 0.0001, respectively). The statistically significant difference in the VAS scores between the two groups can be attributed to the fact that their studied population was heterogeneous in comparison with our study. They included patients undergoing oesophagectomy and antireflux measures besides lung resection surgery, and this might be responsible for the greater difference between the two groups. Moreover, current study findings are contradictory to the findings of Debreceni et al. [19], who found that thoracotomy pain management with continuous epidural analgesia was superior to that with continuous TPVA, in the early postoperative period. The statistically significant difference in the VAS scores between the two groups can be attributed to the large volume injected into the epidural space (0.2 ml/kg). The extent of the sensory blockade in each group was not recorded for further statistical analysis in their study. The current study is contradictory to the findings of Raveglia et al. [7] as well, who found a statistically significant VAS in favour of the PA group (P=0.002), which can be attributed to the higher concentration of local anaesthetic in the PA group.

As regards comparison of complication between the two groups, the current study showed a nonsignificant difference in both groups as regards nausea, vomiting and itching, whereas there was a highly significant difference in urine retention and hypotension in the TEA group. Current study findings are similar to the findings of Ding *et al.* [20], who found that TPVB resulted in significantly lower incidence rates of urinary retention, nausea and vomiting, and hypotension.

### **Study limitation**

The possible shortcomings of our study are as follows: the study did not include a placebo control group, and haemodynamic parameters were compared between the two groups for only intraoperative period.

## Conclusion

The TPVB is effective analgesic technique showing greater haemodynamic stability and less stress response to surgery compared with epidural analgesia in patients having thoracotomy.

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## **Conflicts of interest**

There are no conflicts of interest.

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