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ORIGINAL ARTICLE

Comparison between lumbar and thoracic epidural morphine for severe isolated blunt chest wall trauma: a randomized open-label trial

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Abstract
Purpose The aim of this randomized, parallel-arm, open-label trial was to compare lumbar versus thoracic epidural morphine for severe isolated blunt chest wall injury as regards the incidence of pulmonary complications and pain control.
Methods Fifty-five patients who sustained severe isolated blunt chest wall trauma were randomized using a computer-generated list to receive epidural morphine injection every 24 h through an epidural catheter inserted into the lumbar ($n = 28$) or thoracic ($n = 27$) region. Need for mechanical ventilation, incidence of pneumonia, arterial blood gas values, and pulmonary function tests were compared in both groups. Pain scores, supplemental analgesic consumption, length of intensive care unit (ICU) stay, and occurrence of epidural morphine-related side effects were compared as well. Primary outcome measures were need for mechanical ventilation and incidence of pneumonia.
Results Five (17.9 %) patients in the lumbar group were mechanically ventilated, compared with six (22.2 %) in the thoracic group (hazard ratio 1.35; 95 % CI 0.41–4.4; $P = 0.611$). Seven (25 %) patients in the lumbar group developed pneumonia versus six (22.2 %) in the thoracic group (hazard ratio 0.97; 95 % CI 0.33–2.9; $P = 0.96$). Both groups were comparable as regards the duration of mechanical ventilation ($P = 0.141$) and length of ICU stay ($P = 0.227$). Pain scores, supplemental analgesic consumption, pulmonary function, and occurrence of epidural morphine-related side effects were, likewise, comparable ($P > 0.05$).
Conclusion Lumbar and thoracic epidural morphine administered as once-daily injection to patients with severe isolated blunt chest wall trauma were comparable in terms of pain control, incidence of pulmonary complications, and occurrence of epidural morphine-related side effects.

Keywords Blunt trauma · Chest wall · Morphine · Epidural

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Introduction

Blunt trauma accounts for around 73 % of thoracic injuries [1]. The chest wall is commonly involved in blunt thoracic trauma, and the extent of this involvement may range from minor bruising to severe injury resulting in multiple fractured ribs (MFR), flail injury, or pulmonary contusion with considerable respiratory compromise [2]. Isolated injuries confined to the chest wall occur in a significant number of patients who sustain blunt thoracic trauma [1]. Although the lungs may not be directly involved in such injuries, the associated pain could be quite severe, resulting in splinting of the chest wall with inadequate ventilation, ineffective cough, and atelectasis, which may eventually culminate into respiratory decompensation [3].

An evident transformation in the management of chest wall fractures has been the move from injured bony cage stabilization to the utilization of effective analgesic techniques to combat the associated pain and its untoward consequences [4]. In this respect, several analgesic modalities, including non-steroidal anti-inflammatory drugs, opioids, and various regional analgesic techniques, have been utilized [5]. Among these modalities, epidural

opioids have been extensively studied, either alone [6–11] or in combination with local anesthetic agents [12–14], and utilizing the thoracic [6, 7, 12–14] or the lumbar [8–11] approach to the epidural space.

Notably, previous studies have consistently compared epidurally administered opioids with systemically dispensed analgesics [6–8, 10–14] or epidurally administered local anesthetics [9]. Nonetheless, to the authors' knowledge, no previous study has compared the thoracic and lumbar approaches for epidural opioid administration in the setting of blunt chest trauma.

Conventionally, epidural morphine is administered at or close to the desired level of analgesia. However, the drug is believed to penetrate the meningeal coverings to gain access to the cerebrospinal fluid, where it spreads to more rostral levels by virtue of its hydrophilic properties. Although the level of administration of epidural morphine may influence the speed of onset of analgesic actions, the duration of this analgesia does not seem to be influenced by the site of administration [15]. In this regard, there is evidence from studies conducted in the setting of thoracic surgery that lumbar and thoracic epidural morphine may be comparable in terms of analgesic as well as unwanted effects [16–18]. In fact, the administration of epidural morphine utilizing the lumbar approach has been advocated as a technically less demanding and potentially less hazardous alternative to thoracic epidural morphine for post-thoracotomy pain control [19].

The primary aim of this trial was to compare lumbar with thoracic epidural morphine in patients with severe isolated blunt chest wall injury as regards the incidence of pulmonary complications (i.e., respiratory decompensation necessitating mechanical ventilation or pneumonia). A secondary aim was to compare the two approaches as regards the efficacy of pain control and length of intensive care unit (ICU) stay. For this purpose, we have used the term "isolated blunt chest wall trauma" to identify non-penetrating injuries localized to the bony thorax and related soft tissue that exert their morbid effects through pain and underlying pulmonary contusion [20].

Materials and methods

This randomized, parallel-arm, open-label study was conducted at Ain Shams University Hospitals, Cairo, Egypt, during the period from December 2008 to August 2011. The study was approved by the Institutional Review Board (Research Ethics Committee, Faculty of Medicine, Ain Shams University, Cairo, Egypt), and informed consent was obtained from all participants. The study was independently overseen by the local institutional Data and Safety Monitoring Board. Details of the trial protocol can be obtained from the Department of Anesthesiology, Faculty of Medicine, Ain Shams University, Cairo, Egypt.

Patient selection

Patients 18 years of age or older who sustained severe isolated blunt chest wall injuries were eligible for the study. Severe chest wall trauma was defined as presence of three or more consecutive fractured ribs, flail chest injury, sternal fracture, or pulmonary contusion [12]. Flail chest injury was identified by the fracture of a series of adjacent ribs at two or more fracture points such that the involved segment moved independently and paradoxically from the remaining chest wall [21]. Lung contusion was identified radiologically as opacification of the lung parenchyma on postero-anterior plain chest radiographs. To quantify the extent of pulmonary contusion, the pulmonary contusion score (PCS) described by Tyburski et al. [22] was used. According to this score, each lung field on the chest radiograph is divided into three zones: upper, middle, and lower one-third, respectively. A score of 1–3 is assigned to each of these zones based on the extent of opacification, with a completely opacified zone receiving a score of 3. So, each chest radiograph was assigned a PCS ranging from 0 to 18.

Patients with penetrating chest injury, associated pneumothorax or hemothorax, cardiac contusion, esophageal or diaphragmatic rupture, bronchial or tracheal injury, or associated nonthoracic injuries were excluded. Other exclusion criteria were immediate need for mechanical ventilation, circulatory instability, altered mental status (Glasgow Coma Score [23] of 14 or less), morbid obesity, pregnancy, or contraindications to epidural blockade (e.g., coagulation defects, infection at puncture site, spine deformity, or previous back surgery).

Initial management in the ICU

As per institutional policy, patients with severe chest wall trauma were managed in the ICU. Initial management protocols included standard monitoring, stabilization of cardiorespiratory functions, and control of pain. Pain control was provided with intravenous morphine 0.1 mg/kg given at a rate of 1 mg/min. If needed, increments of 0.025 mg/kg could be given every 5 min at the same injection rate up to a total dose of 0.3 mg/kg.

Patient randomization and interventions

After initial stabilization and the completion of the standard trauma work-up, recruited subjects were randomly assigned to one of two groups in the ratio of 1:1 using a computer-generated random number list created with

GraphPad StatMate™ v.1.01i software (GraphPad Software Inc., San Diego, CA, USA) in permuted blocks of size 4.

In group L, an epidural catheter was inserted at the L2–L3 or L3–L4 interspace using a median approach. In group T, a paramedian approach was utilized to insert an epidural catheter at the T5–T6 or T6–T7 interspace. In both groups, loss of resistance to saline was employed to identify the epidural space utilizing an 18-G Tuohy needle, and a 20-G epidural catheter was advanced 4 cm in a cephalad direction up the epidural space. During epidural placement, patients assumed the sitting or lateral position according to their preference. After testing catheter placement using 3 ml of 2 % lidocaine with 5 μg/ml of epinephrine, a bolus of 6 mg of morphine (Duramorph®, Baxter Healthcare Corporation, Deerfield, IL, USA) diluted in 10 ml of 0.9 % saline was injected through the epidural catheter in either group. This dose was repeated every 24 h thereafter until the epidural catheter was removed.

Supplemental analgesia was available to all patients as intravenous morphine via a patient-controlled analgesia (PCA) device, with which the patients were made acquainted. The PCA regimen comprised bolus doses of 0.01–0.02 mg/kg with lock-out intervals of 7–15 min, 4 h limit of 0.2–0.4 mg/kg, and no background infusion. The PCA device was initially programmed to deliver morphine at the lower limit of the dosage range and the upper limit of the lock-out interval. If patients were not satisfied with the analgesia, the PCA device was reprogrammed to deliver higher doses at shorter lock-out intervals.

Supplemental oxygen was provided with nasal prongs or a face mask as required to keep the arterial oxygen saturation (SaO_2) >90 % and/or the arterial oxygen tension (PaO_2) >60 mmHg. Tracheal intubation and mechanical ventilation were instituted in any patient fulfilling two of the following four criteria: (1) respiratory rate >25 breaths per minute; (2) PaO_2 <60 mmHg with a fractional concentration of inspired oxygen (FiO_2) of 0.6 or arterial carbon dioxide tension ($PaCO_2$) >55 mmHg; (3) systolic arterial pressure <100 mmHg despite fluid resuscitation; and (4) heart rate >100 beats per minute [24, 25]. Management of and weaning from mechanical ventilation were standardized in all patients as per the institutional protocol.

Measurements

Since interventions could not be concealed, both patients and their assessors were not blinded as to the allocation groups.

Arterial blood pressure, heart rate, respiratory rate, and oxymetry-measured arterial oxygen saturation (SpO_2) were recorded as per the institutional protocol. Arterial blood gases (ABG) were assessed as frequently as deemed necessary until satisfactory parameters had been maintained for 6 h. Frequency of assessment was then gradually reduced to every 8 h.

Pulmonary function tests were assessed immediately before randomization, and then on a daily basis. This comprised the measurement of maximal inspiratory force (MIF) using an aneroid manometer, and the measurement of tidal volume (V_T) and forced expiratory volume in 1 s (FEV_1) using a Boehringer respirometer.

Severity of pain was scored by a trained nurse immediately before randomization and then every 8 h using a visual analogue scale (VAS) for pain, which consisted of a 100 mm unmarked line with no pain representing one end of the line and worst pain possible representing the other end [26]. Supplemental morphine consumption using PCA and the duration of epidural analgesia, defined as the time from catheter insertion to catheter removal were noted as well. The end-point for the removal of epidural catheters was consistently recording pain scores of 20 or less on the VAS for 24 h.

Need to institute mechanical ventilation and incidence of pneumonia were recorded. The Centers for Disease Control and Prevention/National Healthcare Safety Network (CDC/NHSN) criteria for the diagnosis of pneumonia were employed [27].

Measurements recorded from time of admission to the ICU until patients were discharged or mechanically ventilated, whichever was earlier, were collected for statistical analysis. For this purpose, records were prepared for the following follow-up periods: (1) from admission to the ICU until randomization; (2) the first 24 h after randomization; and (3) the second 24 h after randomization until the end of the follow-up.

Outcome measures

The primary outcome measures were the need to institute mechanical ventilation and incidence of pneumonia. Secondary outcome measures were duration of mechanical ventilation, length of stay in ICU, pain scores, supplemental analgesic consumption, and occurrence of epidural morphine-related side effects.

Statistical analysis

The required sample size was calculated using the G*Power© software package, version 3.1.0 (Institut für Experimentelle Psychologie, Heinrich Heine Universität, Düsseldorf, Germany). It was estimated that a sample size of 27 patients in each study group would achieve a detection power of 84 % for an effect size (w) of 0.4 for either of the primary outcome measures using a parallel-arm design. The test statistic used was the two-sided Pearson χ^2 test with one degree of freedom, and significance was targeted at the 95 % confidence level.

Statistical analysis was done on a personal computer using the MedCalc® for Windows® software package, version 11.4.2.0 (MedCalc Software, Mariakerke, Belgium). All statistical analyses were based on the intention to treat. This approach requires that patients be analyzed according to the group to which they are randomly assigned, regardless of any subsequent withdrawal or deviation from the protocol [28].

The Kolmogorov–Smirnov goodness-of-fit test was initially performed to test the hypothesis that data were normally distributed. Normally distributed quantitative data were presented as the mean (standard deviation), and between-group differences were compared using the independent-samples Student *t* test. Non-normally distributed quantitative data were presented as the median (interquartile range), and intergroup differences were compared nonparametrically using the Wilcoxon rank sum test. Qualitative data were presented as a ratio or as a number (percentage), and differences between the two groups were compared using the Pearson χ^2 test, applying Fisher's exact test if >20 % of the cells in a cross-tabulation had an expected count of <5. For within-group comparisons of normally distributed quantitative data, the paired-samples Student *t* test was applied. Kaplan–Meier analysis was performed to compare the failure function of the need for mechanical ventilation and the occurrence of pneumonia in the two groups using the log rank test.

All reported *P* values are two-tailed. $P < 0.05$ was regarded as statistically significant.

Results

The study was open-ended, with the intention to stop patient recruitment once the required number of patients had been studied. During the study period, 368 patients were admitted to the ICU with severe blunt chest wall injury, 239 (64.9 %) of whom did not meet eligibility criteria, while 74 (20.1 %) declined to participate. Reasons for ineligibility were associated extrathoracic injuries ($n = 12$, 3.3 %), cardiac contusion ($n = 19$, 5.2 %), pneumothorax ($n = 29$, 7.9 %), hemothorax ($n = 21$, 5.7 %), hemopneumothorax ($n = 16$, 4.3 %), immediate need for mechanical ventilation ($n = 31$, 8.4 %), morbid obesity ($n = 4$, 1.1 %), previous back surgery ($n = 2$, 0.5 %), spinal deformity ($n = 3$, 0.8 %), and pregnancy ($n = 2$, 0.5 %). Fifty-five (14.9 %) patients were enrolled and randomized to group L ($n = 28$) or group T ($n = 27$). Two (7.1 %) patients in group L and one (3.7 %) in group T requested to withdraw from the study because of intolerable pruritus. One (3.6 %) patient in group L and another (3.7 %) in group T developed an acute confusional state and exited the study. Fifty patients (25 in each group) completed the study protocol (Fig. 1).

Table 1 shows demographic and injury-related data, time to epidural placement, and duration of epidural analgesia. Table 2 shows cardiopulmonary variables, pain scores, and morphine consumption during the study period. There were no statistically significant differences between the two groups as regards any of these variables ($P > 0.05$). In either group, heart rate, mean arterial pressure, respiratory rate, and pain score were significantly lower, while the SaO_2, PaO_2, PaO_2/FiO_2, $PaCO_2$, MIF, V_T, and FEV_1 % were significantly higher during the first 24 h after randomization as compared with their corresponding values before randomization ($P < 0.05$).

Seven (25 %) patients in group L were complicated with pneumonia versus six (22.2 %) patients in group T ($P = 0.808$). The Kaplan–Meier curves for incidence of pneumonia had a hazard ratio of 0.97 (95 % CI 0.33–2.9; $P = 0.96$). On the other hand, five (17.9 %) patients in group L required mechanical ventilation, compared with six (22.2 %) patients in group T ($P = 0.686$). The Kaplan–Meier curves for need for mechanical ventilation had a hazard ratio of 1.35 (95 % CI 0.41–4.4; $P = 0.611$) (Table 3, Figs. 2, 3).

There were no statistically significant differences between the two groups as regards the duration of mechanical ventilation ($P = 0.141$) or length of ICU stay ($P = 0.227$). Incidence of epidural morphine-related side effects was, likewise, comparable in both groups ($P > 0.05$) (Table 3).

Discussion

The present study showed that in patients who sustained severe isolated blunt chest wall injuries, both the lumbar and the thoracic approaches to the epidural space for the administration of morphine in a once-daily injection through an indwelling catheter were comparable as regards the incidence of pneumonia, need for mechanical ventilation, and incidence of epidural morphine-related side effects. Both approaches were also equivalent as regards pain scores, rescue analgesic consumption, pulmonary function tests, and arterial blood gas indices.

There is evidence that opioid-based epidural analgesia may be associated with a more favorable outcome after blunt chest trauma compared with parenteral analgesia, at least in the elderly. In this regard, one study identified the use of epidural opioids as an independent predictor of decreased mortality and lower incidence of pulmonary complications in elderly patients with blunt chest trauma [8]. Although opioids have been an integral element in epidural analgesic techniques employed for blunt chest trauma, relatively few randomized trials have investigated the role of epidural morphine as a primary analgesic

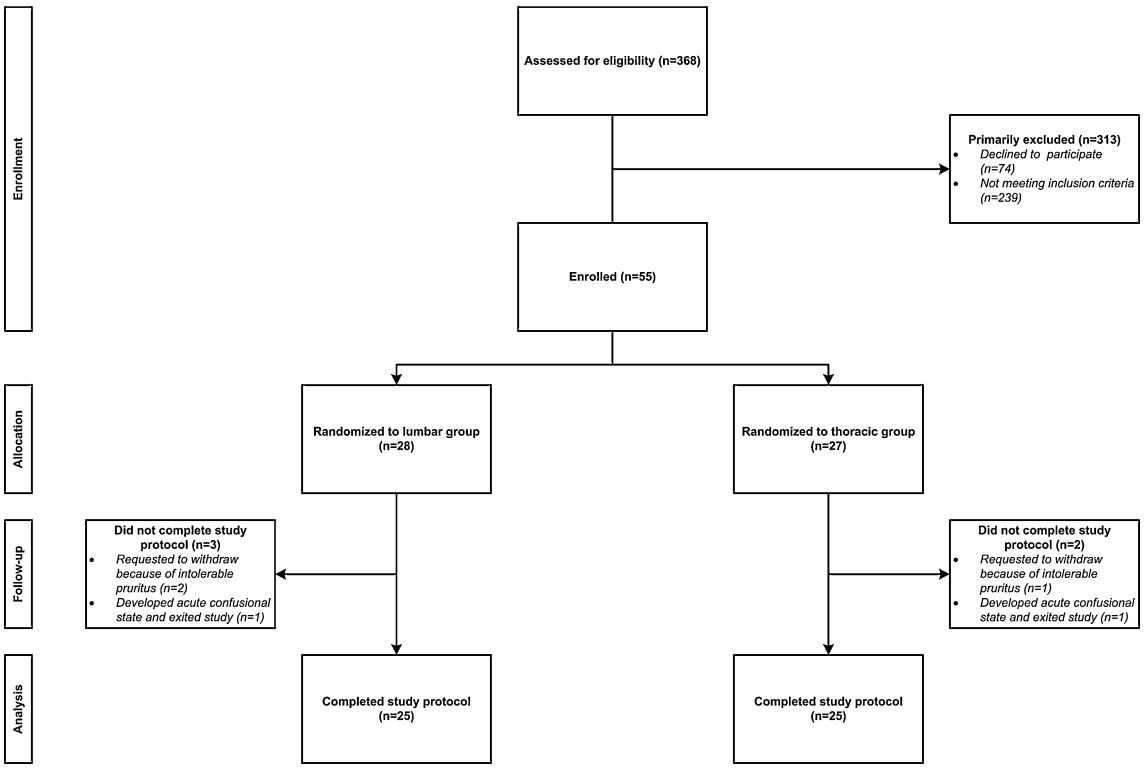

Fig. 1 Flowchart showing patient enrollment, randomization, follow-up, and analysis

Table 1 Demographic and injury-related data, time to epidural placement, and duration of epidural analgesia

Variable	Group L ($n = 28$)	Group T ($n = 27$)	P value
Age (years)	41.3 (9.3)	39.1 (13.5)	0.555
Gender, male/female	15/13	17/10	0.480
Weight (kg)	70.3 (9.5)	72.7 (7.9)	0.421
Height (cm)	168.3 (5.1)	171.0 (7.0)	0.107
History of chronic lung disease, *n* (%)			
Nil	24 (85.7 %)	25 (92.6 %)	1.0
COPD	2 (7.1 %)	1 (3.7 %)	
Bronchial asthma	2 (7.1 %)	1 (3.7 %)	
Type of injury, *n* (%)			0.836
MFR	8 (28.6 %)	7 (25.9 %)	
MFR with pulmonary contusion	14 (50 %)	12 (44.4 %)	
Chest wall bruise with pulmonary contusion	5 (17.9 %)	7 (25.9 %)	
Flail injury	1 (3.6 %)	0	
Flail injury with pulmonary contusion	0	1 (3.7 %)	
Side of injury, *n* (%)			0.745
Right	12 (42.9 %)	11 (40.7 %)	
Left	14 (50 %)	12 (44.4 %)	
Bilateral	2 (7.1 %)	4 (14.8 %)	
PCS	4 (2–6)	5 (0–6)	0.701
Time to epidural placement (h)	6 (5–6)	5 (4–6)	0.828
Duration of epidural analgesia (days)	3 (3–4)	3 (2–4)	0.057

Data are presented as mean (standard deviation), ratio, number (percentage), or median (interquartile range)

COPD chronic obstructive pulmonary disease, *MFR* multiple fractured ribs, *PCS* pulmonary contusion score

strategy in this setting [29]. One such study randomized patients with MFR to receive an intravenous or thoracic epidural morphine infusion and reported significantly shorter lengths of stay in the ICU and hospital as well as duration of mechanical ventilation in the epidural group [7]. Another study randomized patients with MFR to

Table 2 Cardiorespiratory variables, pain scores, and rescue morphine consumption in the two study groups

Variable	Group L ($n = 28$)	Group T ($n = 27$)	P value*
Heart rate, beats/min			
BR	109.1 (9.8)	112.2 (8.4)	0.223
AR1	91.4 (9.0)	87.7 (6.6)	0.087
AR2	81.6 (5.5)	84.2 (6.5)	0.108
P value†	<0.001	<0.001	
MAP, mmHg			
BR	113.0 (10.2)	109.5 (7.6)	0.153
AR1	95.1 (10.8)	92.0 (9.0)	0.252
AR2	89.5 (6.8)	86.4 (6.9)	0.098
P value†	<0.001	<0.001	
Respiratory rate, breaths/min			
BR	29.5 (3.6)	28.2 (3.6)	0.196
AR1	16.2 (4.5)	14.9 (2.2)	0.183
AR2	14.8 (2.7)	13.7 (1.6)	0.088
P value†	<0.001	<0.001	
SaO2, %			
BR	91.0 (1.6)	90.3 (1.6)	0.091
AR1	94.2 (2.0)	93.3 (1.6)	0.073
AR2	95.4 (2.5)	94.4 (2.4)	0.110
P value†	<0.001	<0.001	
PaO_2, mmHg			
BR	63.3 (5.2)	60.9 (3.8)	0.057
AR1	81.8 (11.8)	76.4 (9.5)	0.069
AR2	85.9 (11.2)	79.5 (12.8)	0.055
P value†	<0.001	<0.001	
PaO_2/FiO_2, mmHg			
BR	186.4 (40.7)	167.8 (36.0)	0.079
AR1	252.8 (65.5)	225.6 (57.6)	0.110
AR2	278.5 (82.8)	256.8 (79.4)	0.326
P value†	<0.001	<0.001	
$PaCO_2$, mmHg			
BR	33.8 (2.5)	34.4 (3.0)	0.386
AR1	37.5 (6.1)	36.5 (4.3)	0.495
AR2	39.6 (5.3)	37.4 (2.6)	0.058
P value†	0.014	0.038	
MIF, cmH_2O			
BR	51.6 (10.9)	49.6 (9.0)	0.465
AR1	71.2 (19.9)	65.6 (15.9)	0.253
AR2	71.9 (20.2)	74.4 (21.7)	0.649
P value†	<0.001	<0.001	
V_T, ml			
BR	379.4 (18.8)	372.3 (16.5)	0.142
AR1	427.5 (50.4)	409.7 (49.3)	0.192
AR2	426.2 (49.1)	420.9 (55.0)	0.708
P value†	<0.001	<0.001	
FEV_1, % of predicted			
BR	54.4 (8.1)	56.6 (6.0)	0.256
AR1	68.8 (13.1)	65.7 (15.3)	0.426
AR2	71.4 (14.8)	69.1 (16.9)	0.602
P value†	<0.001	0.001	
VAS			
BR	62.9 (9.7)	67.3 (7.4)	0.064
AR1	36.1 (6.3)	39.6 (6.7)	0.053
AR2	30.7 (4.4)	32.6 (4.7)	0.129
P value†	<0.001	<0.001	
Morphine consumption, mg (mg/day for second 24 h until the end of the study)			
BR	12 (10–13)	10 (9–14)	0.159
AR1	6 (4–8)	7 (5–9)	0.231
AR2	4 (3–5)	3 (2–4)	0.074
P value†	<0.001	<0.001	

Data are presented as mean (standard deviation) or median (interquartile range). For repeated measures, averaged values are displayed

AR1 first 24 h after randomization, *AR2* second 24 h after randomization until the end of the study, *BR* before randomization, FEV_1 forced expiratory volume in 1 s, FiO_2 fractional concentration of inspired oxygen, *MAP* mean arterial pressure, *MIF* maximum inspiratory force, $PaCO_2$ arterial carbon dioxide tension, PaO_2 arterial oxygen tension, SaO_2 arterial oxygen saturation, *VAS* visual analogue score, V_T tidal volume

* P values are for between-group comparisons

† P value is for within-group comparison of data before randomization and in the first 24 h after randomization

receive intravenous morphine-based PCA or lumbar epidural morphine and demonstrated that patients receiving epidural morphine spent significantly fewer days both in the ICU and in the hospital, and experienced significantly less pain compared with the other group [11].

To the authors' knowledge, no previous study has compared lumbar and thoracic epidural morphine in chest wall trauma. However, evidence from trials comparing the two approaches in the setting of thoracic surgery indicated that both could be comparable in terms of postoperative pain and analgesic consumption. In one study, patients who received lumbar or thoracic epidural morphine injections after thoracotomy were reviewed retrospectively. In that study, epidural morphine was administered as intermittent injections (3–4 mg for the thoracic group or 5–6 mg for the lumbar group) on an as-needed basis every 24 h. Supplemental analgesia was also provided with parenteral narcotics if required. The doses of epidural morphine and durations of analgesia were comparable in both groups. Moreover, there was no statistically significant difference between the two groups as regards the number of patients who requested supplemental parenteral analgesia. The authors of that study concluded that after thoracotomies,

Table 3 Incidence of pulmonary complications, length of stay in the intensive care unit, and occurrence of epidural morphine-related side effects

Variable	Group L ($n = 28$)	Group T ($n = 27$)	P value
Incidence of pneumonia, *n* (%)	7 (25 %)	6 (22.2 %)	0.808
Need for MV, *n* (%)	5 (17.9 %)	6 (22.2 %)	0.686
Duration of MV, days	5 (4–5.25)	6 (5–7)	0.141
Length of ICU stay, days	5 (5–7)	5 (4–9)	0.227
Epidural morphine-related side effects			
Urinary retention, *n* (%)	12 (42.9 %)	11 (40.7 %)	0.874
Pruritus, *n* (%)	17 (60 %)	15 (55.6 %)	0.698
Nausea and/or vomiting, *n* (%)	7 (25 %)	8 (29.6 %)	0.700
Excessive sedation, *n* (%)	2 (7.4 %)	4 (14.8 %)	0.669
Respiratory depression, *n* (%)	1 (3.6 %)	2 (7.4 %)	0.611

Data are presented as number (percentage) or median (interquartile range)

ICU intensive care unit, *MV* mechanical ventilation

lumbar epidural morphine provided analgesia that was virtually equivalent to that of thoracic epidural morphine [17].

Although thoracic epidural morphine may be associated with a faster onset of action compared with the lumbar approach, both approaches could be comparable as regards the quality of analgesia. In this respect, Yang et al. [16] randomized patients who underwent thoracic surgery to receive thoracic or lumbar epidural morphine after operation and assessed pain scores for up to 2 h after the injection of morphine. The authors reported that analgesia was better after thoracic epidural morphine injection for up to 40 min. However, this difference disappeared after 50 min. In contrast to these findings, another study reported that the thoracic approach was associated with a lower consumption of epidural morphine after thoracotomy compared with the lumbar approach, although pain scores and pulmonary functions were comparable in both groups [18]. However, in view of the small number of patients who completed that study (ten patients in each group), those results should be interpreted with caution.

Among opioid analgesics, morphine is perhaps the most suitable for epidural administration in view of its physicochemical properties. As it is highly hydrophilic, morphine lingers for a long time in the cerebrospinal fluid [19], and shows a propensity for rostral spread [15], possibly by mass movement of the cerebrospinal fluid in a cephalad direction. In fact, there is convincing evidence that epidural morphine administered at the lumbar region could reach the brainstem and fourth ventricle within 6 h after injection [15]. The implication of this is that epidural morphine need not be administered at or close to the spinal cord segments where analgesia is desired. In fact, it has been recommended that for thoracic pain, the lumbar approach to the epidural space may be a safer alternative to the thoracic approach for the administration of morphine [19]. In this regard, compared with the lumbar vertebrae, the spinous processes in the thoracic region are more angulated, and the intervertebral spaces are narrower. Besides, the ligamentum flavum is close to the dural covering, and the spinal cord itself lies in close proximity to the dura, such that inadvertent dural puncture would carry a significant risk of direct trauma to the spinal cord [30]. Epidural placement at the lumbar region to effect analgesia at the thoracic level may therefore present an attractive option in view of the technical difficulty and complications associated with the latter approach.

Little data is available regarding the optimal dosage or volume of injectate for the administration of epidural morphine to patients with blunt chest trauma. However, in view of the dosage regimens reported by other researchers in this clinical setting [7, 11, 17], we opted for a dose of 6 mg of morphine diluted to a volume of 10 ml and administered at 24 h intervals.

One limitation to the current study is that we did not include a control group against which our interventions were contrasted. However, our hypothesis was that there would be no difference in our outcome measures if a hydrophilic opioid such as morphine was administered at the lumbar epidural space or at a more rostral thoracic level. Therefore, no attempt was made to contrast lumbar or thoracic epidural morphine against other analgesic modalities or interventions. Nonetheless, we did conduct paired comparisons within each group for relevant outcome measures before randomization and in the first 24 h thereafter, a period during which respiratory compromise and pain associated with the injury were expected to be greatest. In this context, pre-randomization values could be regarded as the baseline against which post-randomization values were contrasted.

Another limitation to our study is that we assessed pain only at rest. Although coughing was expected to be associated with intensification of the pain, we did not assess this exacerbation for the following reasons. First, we believed that asking the patients to cough in order to induce this sort of pain would have been distressing, especially early after sustaining the chest trauma. On the other hand, simply inquiring about cough-related pain without actually

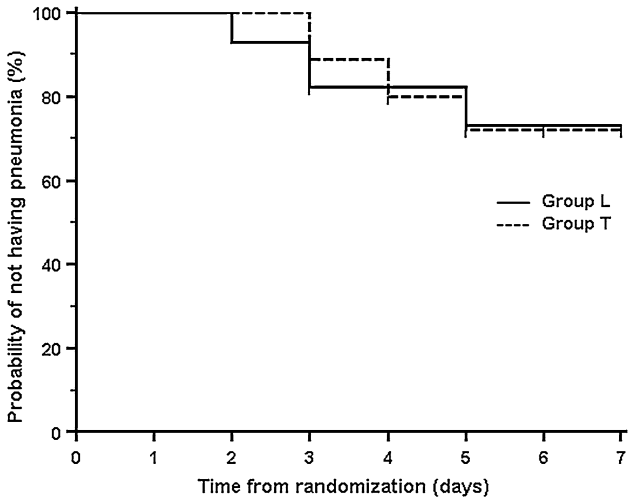

Fig. 2 Kaplan–Meier failure function curves for the incidence of pneumonia. *Vertical dashes along curves* indicate censored data. Hazard ratio 0.97 (95 % CI 0.33–2.9; $P = 0.96$)

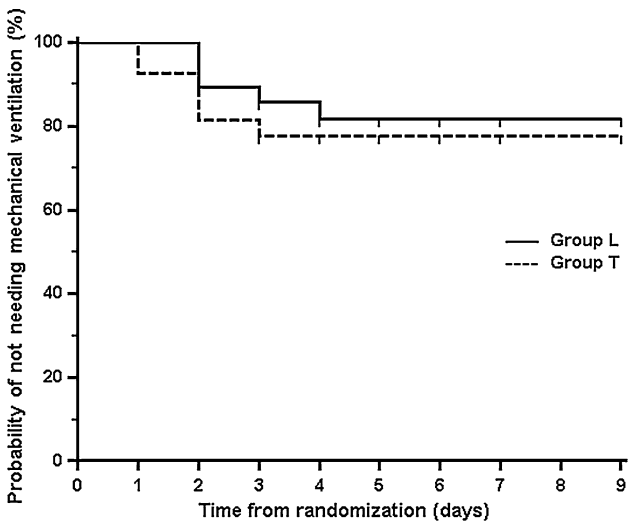

Fig. 3 Kaplan–Meier failure function curves for the need to institute mechanical ventilation. *Vertical dashes along curves* indicate censored data. Hazard ratio 1.35 (95 % CI 0.41–4.4; $P = 0.611$)

inducing it at the time of assessment could have been subject to a recall bias that might confound our assessment. Second, in the context of chest trauma, pain experienced at rest could still be representative of the overall pain experience, as it may be viewed as the product of two distinct ingredients: background pain and pain associated with respiratory movements. In this regard, resting pain could be assessed reliably with no recall bias, and would be regarded as a valid estimate of the level of pain experienced most of the time by our patients.

In the current study, we provided rescue analgesia with intravenous morphine PCA. Although it could have been more convenient when testing our hypothesis to utilize the epidural route to administer supplemental analgesia, the main limitation to this approach was the possibility of an unduly high incidence of unpleasant side effects. In this regard, the incidence of undesired nonrespiratory side effects associated with a 10 mg dose of epidural morphine was demonstrated by a previous study to be strikingly high. In that study, the incidence rates of generalized itching, nausea, vomiting, and urinary retention were reported to be as high as 90, 60, 50, and 90 %, respectively [31]. Moreover, another dosage-directed study demonstrated that the incidence rates of pruritus and urinary retention increased linearly with the dose of epidural morphine. In that study, the incidence of urinary catheterization was approximately 50 % in patients receiving a dose of 5 mg, while pruritus occurred in over half of those receiving a dose of 4 mg [32]. Based on our institutional data and published reports [31, 32], we expected to see an unacceptably high incidence of these unpleasant side effects when supplemental doses of epidural morphine were allowed. In fact, the overall incidence rates of urinary retention and pruritus observed in the current study using a daily dose of 6 mg were on the order of 42 and 58 %, respectively. Besides, the use of parenteral opioids to supplement epidural morphine has been described by other investigators in a related setting [17].

Another limitation to the current study is that, owing to the evident location of the epidural catheter, the interventions could not be concealed either from the patients or from their assessors. Thus, although the study was randomized, it was not blinded (i.e., open label), a fact that should be viewed as a shortcoming to our study.

Conclusion

In patients with severe isolated blunt chest wall trauma, epidural morphine administered as once-daily injection through the lumbar approach was comparable to the thoracic approach in terms of associated pain, supplemental analgesic consumption, incidence of pulmonary complications, and occurrence of epidural morphine-related side effects. Larger trials are recommended to validate the results of the current study and to identify the ideal dosage of lumbar epidural morphine that would be most effective and least likely to be associated with untoward effects in this setting.

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Conflict of interest Nothing to disclose.

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