Comparison of analgesic interventions for traumatic rib fractures: a systematic review and meta-analysis

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Abstract
Purpose Many studies report on outcomes of analgesic therapy for (suspected) traumatic rib fractures. However, the literature is inconclusive and diverse regarding the management of pain and its effect on pain relief and associated complications. This systematic review and meta-analysis summarizes and compares reduction of pain for the different treatment modalities and as secondary outcome mortality during hospitalization, length of mechanical ventilation, length of hospital stay, length of intensive care unit stay (ICU) and complications such as respiratory, cardiovascular, and/or analgesia-related complications, for four different types of analgesic therapy: epidural analgesia, intravenous analgesia, paravertebral blocks and intercostal blocks.

Methods PubMed, EMBASE and CENTRAL databases were searched to identify comparative studies investigating epidural, intravenous, paravertebral and intercostal interventions for traumatic rib fractures, without restriction for study type. The search strategy included keywords and MeSH or Emtree terms relating blunt chest trauma (including rib fractures), analgesic interventions, pain management and complications.

Results A total of 19 papers met our inclusion criteria and were finally included in this systematic review. Significant differences were found in favor of epidural analgesia for the reduction of pain. No significant differences were observed between epidural analgesia, intravenous analgesia, paravertebral blocks and intercostal blocks, for the secondary outcomes.

Conclusions Results of this study show that epidural analgesia provides better pain relief than the other modalities. No differences were observed for secondary endpoints like length of ICU stay, length of mechanical ventilation or pulmonary complications. However, the quality of the available evidence is low, and therefore, preclude strong recommendations.

Keywords Analgesia · Anesthesia · Hospitalization · Mortality · Pain Management · Rib Fractures

Introduction
Traumatic rib fractures are a common injury among the trauma population and can cause severe pain in both isolated rib fractures and fractures which are a part of more extensive chest injuries [1, 2]. Rib fractures are clinically important. Even isolated fractures are associated with significant consequences, such as prolonged pain and disabilities [3]. Rib fractures sustained following blunt chest trauma are a surrogate for significant trauma, particularly in more vulnerable patients [1, 4, 5]. The number of rib fractures is indicative of the trauma severity. More than 90% of the patients with multiple rib fractures have associated injuries, most commonly involving head, abdomen and/or extremities [1]. An increased number of fractures, older age, and polytrauma patients with rib fractures are associated with increased rates of morbidity and mortality [1, 4, 5].

The thoracic pain caused by rib fractures or chest contusion limits patients to cough and breathe deeply, which can result in atelectasis and pneumonia. Besides most of these, patients also suffer from a pulmonary contusion, due to their injury. This can lead to an acute respiratory
distress syndrome and/or respiratory failure and the need for mechanical ventilation has been reported [6, 7].

A combination of adequate pain control, respiratory assistance, and physiotherapy are considered to be the key in the management of patients with fractured ribs [4, 8]. In the current practice, different analgesic modalities including epidural catheters, intravenous (patient controlled) narcotics, intercostal, paravertebral or interpleural blocks, oral opioids, or a combination of the aforementioned interventions, are used as therapy [9, 10].

The literature on the use of the different analgesic interventions is inconclusive. A clinical guideline supported by the Eastern Association for the Surgery of Trauma recommends epidural analgesia or a multimodal approach over opioids alone in patients with blunt chest trauma [9]. On the other hand, two recently performed systematic reviews and meta-analyses of Duch et al. [10] and Carrier et al. [11] stated that the evidence for the use of epidural analgesia as preferred modality is insufficient, and that there is no firm evidence for benefit or harm of the epidural modality compared to the other interventions.

However, to date, no comprehensive study compared the single modalities independently with each other, including both observational studies and randomized controlled trials. Therefore, the aim of this systematic review and meta-analysis is to compare epidural, intravenous, paravertebral and intercostal analgesia for the primary outcome of pain reduction and the secondary outcomes of mortality during hospitalization, length of mechanical ventilation, length of hospital stay, length of intensive care unit stay (ICU) and complications, in patients with traumatic rib fractures.

Methods

A published protocol for this review does not exist. No ethical committee approval was necessary for this literature review.

Literature search and eligibility criteria

This systematic review and meta-analysis was written in accordance to the PRISMA guidelines for reporting systematic reviews and meta-analyses [12]. Two reviewers (JP, DS) independently performed a structured literature search, on September 16th 2017, to identify comparative studies investigating epidural, intravenous, paravertebral and intercostal analgesia for the primary outcome of pain reduction and the secondary outcomes of mortality during hospitalization, length of mechanical ventilation, length of hospital stay, length of intensive care unit stay (ICU) and complications, in patients with traumatic rib fractures.

Quality assessment

The methodological quality of the articles was independently assessed by two reviewers (JP, DS) using the validated methodological index for non-randomized studies (MINORS) score [13]. Additional criteria, described in Appendix Table 3, were defined to make further distinction in quality between the included studies. The quality was determined by means of the total MINORS score. Studies were not excluded based on the quality assessment. Disagreement was resolved by discussion with a third independent reviewer (MJ), followed by consensus.

Data extraction

Data were retrieved by two independent reviewers (JP, DS). Data extracted included first author, year of publication, country, study design, setting and treatment groups. For each treatment group, age, sex, type of analgesia and injury severity score (ISS) were extracted. The extracted data were shown as mentioned in the original studies. If exact pain scores were not given, an estimation of the scores was made on the basis of the figures. Outcomes were retrieved including confidence intervals (CI’s) and/or p values.

Outcome measures

The predefined primary outcome was the reduction of pain, preferably expressed in a Numeric Rating Scale (NRS). Secondary outcomes were mortality during hospitalization,
length of mechanical ventilation, length of hospital stay, length of intensive care unit stay (ICU) and complications.

**Data analysis**

Data were pooled according to the analgesic modalities that were compared. Meta-analyses were performed if the endpoints were reported by two or more studies. If the extracted data were initially noted as median with an interquartile range, the mean and standard deviation (SD) were estimated as follows: the reported median value was used as mean value, and the standard deviation was estimated by dividing the interquartile range with 1.35. Statistical heterogeneity was assessed by visual inspection of the forest plots and estimated by means of the $I^2$, Tau² and Cochran’s Q (Chi-square test). A random-effects model was used if high heterogeneity was present (where $I^2 > 75\%$ reflects a high heterogeneity). Odds ratios and 95% confidence intervals (95% CI) were calculated for dichotomous variables. Studies that reported zero events in one or both arms were included by adding a continuity correction of 1.0 to all cells in the 2 × 2 table of that study [14]. $p$ values < 0.05 were considered statistically significant.

After the primary statistical analyses, sensitivity and subgroup analyses were conducted. In the sensitivity analyses on study design, only RCTs were included. In the sensitivity analyses on time, only studies published after the year 2000 were included. In the sensitivity analyses on quality, arbitrarily all studies with more than 16 points were included [15]. A sensitivity analyses on outlier studies was conducted. For the subgroup analyses on etiology, only studies describing cohorts with solely traumatic rib fractures were included. Studies describing mixed cohorts of patients with blunt chest trauma were excluded.

All statistical analyses were performed using Review Manager (RevMan, Version 5.3.5 Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014).

**Results**

**Search**

The literature search yielded 1129 studies and after removal of duplicates and screening titles and abstracts for relevance, 44 articles were assessed for eligibility. After application of the inclusion and exclusion criteria, 19 articles were finally included in this systematic review [6, 8, 16–32]. Twenty-four studies were excluded, mainly because analgesic modalities, other than epidural, intravenous, paravertebral or intercostal were described [33–46]. Five studies were excluded because data of the interventions used in the control group could
not be extracted [4, 47–50]. There were no eligible studies excluded by the language restriction. No additional articles were identified during the reference and citation check. A flow chart of the complete selection procedure is shown in Fig. 1.

**Quality assessment**

The total MINORS score of the included articles are listed in Appendix Table 3. On average the included articles scored 15.7 ± 2.9 points, with a range of 11–23 points.

**Baseline characteristics**

Of the 19 included studies, 8 were RCTs, 10 were retrospective cohort studies, and 1 study was a prospective cohort study using a historical control group. The included studies describe a total of 2801 patients. Eleven studies [8, 16–21, 27–29] compared epidural analgesia with intravenous analgesia. Eight of these studies [4, 16–18, 20, 21, 27, 28] compared epidurals with local anesthetics with or without opioids as drugs, with intravenous analgesia. Three studies [19, 24, 29] compared epidurals, with only opioids as drugs, with intravenous analgesia. Three studies [22, 25, 26] compared epidural analgesia with intercostal blocks, three studies compared epidural analgesia with paravertebral blocks [6, 30, 31], one study compared paravertebral blocks with intravenous analgesia [32] and one study [23] compared intercostal blocks with intravenous analgesia. The characteristics of the included studies are shown in Appendix Table 4.

**Epidural analgesia versus intravenous analgesia**

The results of the studies comparing epidural with intravenous analgesia are summarized in Appendix Table 5. Meta-analyses are shown in Fig. 2. Of the 11 included studies,
4 studies [16, 20, 21, 28] examined pain scores on different intervals after treatment with epidural or intravenous analgesia. One study [16] described lower pain scores at all intervals of the study period in the group that received epidural analgesia \((p < 0.05)\). Significant lower pain scores on coughing were found in the first 24 h in the epidural group \((p < 0.05)\). One study [20] found significantly lower pain scores at all intervals \((p < 0.05)\), except on the baseline interval \((p = 0.82)\), in the group that received epidural analgesia. One [28] study found significant differences \((p < 0.05)\) in pain relief on day 1 and on day 3 in favor of the patients that received epidural analgesia, no differences were found on day two. One study [21] reported that the improvement in pain was more pronounced in the group that received epidural analgesia, but no significant difference was found between the two groups \((p = 0.08)\). The results on pain relief are shown in Table 1.

Eight studies reported on the length of hospital stay [8, 16, 18–21, 24, 28]. The average number of days of hospitalization was lower in the epidural group \((12.4 ± 4.5)\) compared with the group that received intravenous analgesia \((15.5 ± 14.1)\), pooled analysis failed to show statistical significance \([95\% CI, \text{ mean difference (MD)} − 1.84 (− 5.34, 1.66), I^2 = 92\%, p = 0.30]\). Eight studies reported on the length of ICU stay [8, 17–19, 21, 25, 28, 29;17–19;21;25;28;29]. The average number of days on the ICU was lower in the epidural group \((6.4 ± 2.3)\) compared with the intravenous group \((9.7 ± 6.5)\), again pooled analysis showed no significant differences \([95\% CI, \text{ MD}− 2.20 (− 4.92, 0.53), I^2 = 93\%, p = 0.11]\). Five [8, 16, 17, 24, 27] studies reported on the duration of mechanical ventilation. Four [8, 17, 24, 27] studies were eligible for pooled analysis because the data of one study were not available. The average of days on mechanical ventilation was lower \((5.2 ± 2.3)\) in the epidural group compared with the intravenous group \((9.9 ± 6.2)\). Pooled analysis

| C | Study or Subgroup | Epidural Events | Total | Intravenous Events | Total | Mean Difference (IV, Random, 95% CI) | Mean Difference (IV, Random, 95% CI) |
|---|------------------|----------------|-------|-------------------|-------|-------------------------------------|-------------------------------------|
| **Total** | **Study or Subgroup** | **Epidural Mean SD** | **Total** | **Intravenous Mean SD** | **Total** | **Heterogeneity: Tau^2 = 60.95; Chi^2 = 23.38, df = 2 (p < 0.00001); I^2 = 91%** | **Test for overall effect: Z = 1.42 (p = 0.16)** |
| **1.3.2 Observational** | **Baker et al. 2017** | 3.5 4.4 6 | 3.3 4.6 159 & 159 | 28.2% 0.20 | -3.39 3.79 | **Test for overall effect: Z = 0.11 (p = 0.91)** |
| **Subtotal (95% CI)** | **1.3.2 Observational** | **6 159** & 159 | 28.2% 0.20 | -3.39 3.79 | **Test for overall effect: Z = 0.11 (p = 0.91)** |
| **Total (95% CI)** | **53 206 100.0%** | -5.09 | -11.76 1.58 | **Favours epidural Favours intravenous** | **Fig. 2 (continued)**

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| First author | Pain assessment tool | Outcome (mean ± SD) |
|--------------|----------------------|---------------------|
| **Epidural analgesia vs intravenous analgesia** |
| Waqar et al. | Verbal Rating Scale (0–5) | Significant lower pain scores at all intervals in epidural group ($p < 0.05$) 
Significant lower pain scores on coughing in the first 24 h in epidural group ($p < 0.05$) |
| Wu et al. | Standardized form (0–5)* | Baseline [4 (3, 4) vs 4 (3.3, 4), $p < 0.82$] 
After 8 h [2 (2, 1) vs 3 (2, 4), $p < 0.001$] 
After 24 h [1 (1, 2) vs 3 (3, 4), $p < 0.001$] 
After 48 h [2 (1, 2) vs 3 (2, 3), $p < 0.001$] 
After 72 h [1 (1, 2) vs 3 (2, 3), $p < 0.001$] |
| *Moon et al. | Verbal Rating Scale (0–10)* | First 24 h (5.8 vs 7.5, $p < 0.05$) 
After 48 h (6.0 vs 6.3) 
After 72 h (3.8 vs 6.2, $p < 0.05$) |
| *Mackersie et al. | Visual Analogue Scale (0–100)* | Percentage change in VAS score 
At rest $(-32 ± 24 vs -27 ± 27, p < 0.05)$ 
Coughing and deep breathing $(-42 ± 25 vs -25 ± 26, p < 0.05)$ |
| **Epidural analgesia vs intercostal block** |
| *Hashemzadeh et al | Verbal rating scale (0–10) | Mean pain score during hospital admission 
At rest $(2.2 ± 0.74 vs 3.3 ± 1.005)$ 
Coughing $(3.05 ± 0.88 vs 4.95 ± 0.99)$ |
| Truitt et al | Numeric pain score (0–10) | Significant improvement of pain score after CINB catheter placement ($p < 0.05$) 
At rest (7.5) 
Coughing (3.6) |
| **Epidural analgesia vs paravertebral block** |
| Shapiro et al | Visual Analogue Scale (0–10) | Mean change in pain from admission to discharge: 3.0 vs 4.0 ($p = 0.28$) |
| *Mohta et al | Visual Analogue Scale (0–100)* | No significant differences in mean VAS scores at rest ($p = 0.426$) and on coughing ($p = 0.721$) |
| **Intercostal block vs intravenous analgesia** |
| Hwang et al | Visual Analogue Scale (0–10) | Baseline (66 vs 66) 
Post-analgesia (97 vs 97) 
After 0.5 h (13 vs 13) 
After 24 h (42 vs 34) 
After 72 h (32 vs 32) |
showed no significant differences between the groups [95% CI, MD $-5.09 (-11.76, 1.58)$, $I^2 = 90\%$, $p = 0.14$].

Ten studies [8, 16–21, 24, 28, 29] reported on the occurrence of pulmonary complications. The number of pulmonary complications ranged from 10 to 90% and pooled analysis showed no significant differences [95% CI, OR $0.79 (0.37, 1.66)$, $I^2 = 70\%$, $p = 0.53$].

**Epidural analgesia versus intercostal block**

The results of the studies comparing epidural analgesia with intercostal blocks are summarized in Appendix Table 6. Meta-analyses are shown in Appendix Fig. 3. As a consequence of insufficient data and variability of outcome measurement, meta-analyses were only possible for the length of hospital and ICU stay.

Two studies [22, 26] reported on pain scores. One study [26] described solely pain scores of the group that received intercostal blocks. Placement of the intercostal catheter resulted in significant improvement in pain severity ($p < 0.05$). No comparison was made with the historical control group that received epidural analgesia. According to one study [22], epidural analgesia provides better control of pain than the intercostal modality. The mean VAS scores that were observed during hospitalization were $2.2 \pm 0.74$ at rest and $3.05 \pm 0.88$ with cough in the epidural group, respectively $3.3 \pm 1.01$ and $4.95 \pm 0.99$ in the intercostal group.

Three studies [22, 25, 26] reported on the length of hospital stay. The average number of days of hospitalization was $7.1 \pm 2.3$ with epidural analgesia and $6.0 \pm 2.7$ with intercostal blocks. One study [26] was not included for pooled analysis because the standard deviations were not reported. Pooled analysis of the two remaining studies showed no significant differences [95% CI, MD $-0.13 (-4.18, -3.91)$, $I^2 = 81\%$, $p = 0.95$].

Two studies [22, 25] reported on the length of ICU stay, pooled analysis showed no significant differences [95% CI, MD $0.09 (-0.45, 0.63)$, $I^2 = 0\%$, $p = 0.74$], respectively, for the length of ICU stay [MD $-0.08 (-1.68, 1.52)$, $I^2 = 87\%$, $p = 0.92$].

**Epidural analgesia versus paravertebral block**

The results of the studies comparing epidural analgesia with paravertebral blocks are summarized in Appendix Table 7. Meta-analyses are shown in Appendix Fig. 4. Two studies reported on pain scores. One study [6] found no significant intergroup difference in mean pain scores either at rest ($p = 0.426$) or on coughing ($p = 0.721$) on different intervals, and one study [30] described that there was no difference between both groups in the mean change of pain during hospital admission (Table 1).

Three studies [6, 30, 31] reported on the length of hospital and ICU stay. The average number of days of hospitalization was $8.3 \pm 1.7$ with epidural analgesia and $8.6 \pm 2.6$ with paravertebral blocks, respectively, $4.5 \pm 2.1$ and $4.6 \pm 1.9$ for the length of ICU stay. Pooled analysis showed no significant differences for the length of hospital stay [95% CI, MD $0.09 (-0.45, 0.63)$, $I^2 = 1\%$, $p = 0.74$], respectively, for the length of ICU stay [MD $-0.08 (-1.68, 1.52)$, $I^2 = 87\%$, $p = 0.92$].

| First author | Pain assessment tool | Outcome (mean ± SD) |
|--------------|----------------------|---------------------|
| *Yeying et al* | Visual Analogue Scale (0–10) | At rest | Coughing |
| **Epidural block vs intravenous analgesia** | | Baseline | (7.6 ± 2.2 vs 7.8 ± 2.1) | (7.9 ± 2.0 vs 8.0 ± 2.2) |
| | | After 1 h | (3.9 ± 1.3 vs 4.9 ± 1.5, $p < 0.05$) | (4.5 ± 1.6 vs 5.6 ± 1.7, $p < 0.05$) |
| | | After 24 h | (3.4 ± 1.0 vs 4.1 ± 1.2, $p < 0.05$) | (3.9 ± 1.1 vs 4.5 ± 1.3, $p < 0.05$) |
| | | After 48 h | (2.8 ± 0.9 vs 3.0 ± 1.0) | (3.3 ± 0.8 vs 3.5 ± 0.9, $p < 0.05$) |
| | | After 72 h | (2.1 ± 0.5 vs 2.2 ± 0.6) | (2.7 ± 0.6 vs 2.8 ± 0.7, $p < 0.05$) |

* CINB: continuous intercostal nerve block, h: hour, SD: standard deviation, VAS: visual Analogue scale, vs: versus
* a: Pain scores expressed as median (with 25th and 75th percentiles)
* b: Pain scores shown as estimated scores by reading of the figures
Intercostal block versus intravenous analgesia

One study [23] compared intravenous analgesia with intercostal blocks. The average number of hospital days and the VAS pain scores were reported, and are summarized in Appendix Table 8, respectively, Table 1. Significant differences in pain relief were described on different intervals, in favor of the intercostal blocks.

Paravertebral block versus intravenous analgesia

One study [32] compared paravertebral blocks with intravenous analgesia. The mortality and the VAS pain scores were reported, and are summarized in Appendix Table 9, respectively Table 1. Significant differences in pain relief were described on different intervals, in favor of the paravertebral blocks.

Sensitivity and subgroup analyses

The sensitivity and subgroup analyses are shown in Appendix Table 10. The results remained non-significant for all secondary outcomes in the group comparing epidural analgesia with intravenous analgesia and in the group comparing epidural analgesia with paravertebral blocks.

Discussion

This systematic review and meta-analysis of both RCTs and cohort series focused on the analgesic therapy for patients with traumatic rib fractures. Results of this study show that overall epidural analgesia provides better pain relief than the other modalities. In three studies [16, 20, 28] significant differences ($p < 0.05$) were found in the improvement of pain in favor of epidural analgesia when compared with intravenous analgesia. In one study [21], the reduction of pain appeared to be more definite in the group that received epidural analgesia.

With respect to the secondary outcomes, our systematic review and meta-analysis failed to show significant differences between the analgesic modalities. Most of these outcome parameters are multifactorial and heterogeneously determined. Therefore, the relationship between the intervention and the secondary outcome parameters is influenced by multiple underlying factors, other than the type of analgesia. To alleviate the influence of these factors, heterogeneity corrections and sensitivity analyses were conducted. As a result, the trends that were initially observed in the group comparing epidural analgesia with intravenous analgesia for length of ICU stay ($p = 0.11$) and length of mechanical ventilation ($p = 0.14$), were not consistent after excluding outlier studies [24].

A recent systematic review and meta-analysis on this subject by Duch et al. [10], found a significant increased intervention effect for the reduction of pain, in favor of epidural analgesia, when compared with the paravertebral or intercostal modality. Because these results were based on only two studies and no significant differences were found on the other outcomes, they concluded that there was no firm evidence to assume that epidural analgesia has advantages over the other modalities. Likewise, a systematic review of 2008 from Carrier et al. [11], reported that there was no improvement in mortality, length of hospital and ICU stay, or duration of mechanical ventilation, if epidural analgesia was compared with other analgesic interventions. Our results differ from theirs in several aspects. Most importantly, our study showed that there is evidence that epidural analgesia results in better pain relief than the other modalities. The results of our secondary outcomes are in accordance with the aforementioned reviews, and seem to rely on a multifactorial basis. In contrast to the studies of Duch et al. [10] and Carrier et al. [11], we included observational studies. Therefore, we were able to include several (new) studies [16–20, 23, 25–27, 29–32] resulting in a larger patient database.

The current guideline of the Eastern Association for the Surgery of Trauma (EAST) recommend epidural analgesia or a multimodal approach over opioids alone, for pain relief in patients with blunt chest trauma [9]. In comparison with this guideline of the EAST, our study differs in certain respects. First, a major distinction is that in our study, the results of the single modalities were separately compared with each other. In the guideline of the EAST, the single modalities were compared with the merged results of larger groups. The epidural, paravertebral and intercostal modalities were in particular compared with the results of patients receiving “non regional” analgesia, and the interpleural modality was compared with “other regional modalities”. Analysis to demonstrate the differences between the single modalities were not implemented. Second, four studies [4, 47, 49, 50] using mixed cohorts of patients, in which the analgesic interventions used in the control group were not extractable, were also excluded in our study. Third, we were able to include six new studies [16, 17, 27, 30–32].

A potential advantage of our method is that by comparing the single analgesic interventions, subtle differences might be more accurately ascertainable. Besides, because the studies were compared separately, our method and results might approach closer to reality.

Another strength of this systematic review is that a considerable amount of extra studies was included due to inclusion of observational studies. In addition, as stated in recently published systematic reviews [15, 51, 52], the inclusion of both RCTs and observational studies might lead to more study power. If observational studies are of sufficient quality, the results will correspond with those of an RCT.
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Furthermore, it appears to give a better reflection of common clinical practice, which might improve the generalizability and applicability of the outcomes of a systematic review [51, 52].

On the other hand, the included studies were of low methodological quality, as assessed using the MINORS score. Therefore, the overall quality and applicability of the available evidence is low, and there is potentially a high risk of bias. Besides, merely a small amount of studies investigated the management of pain. Of the studies reporting on pain, patient samples were overall small, outcome measurements varied and exact pain scores were often not or poorly reported. Pooled analyses for pain in patients with traumatic rib fractures were not feasible due to inadequate reported data. Conversion of pain scores to one comprehensive score was not performed due to increase of bias. Furthermore, the studies were overall difficult to compare because of the heterogeneity in the study method and investigated endpoints. Analgesia-related complications such as nausea, vomiting, catheter inflammation, hypotension, respiratory depression, itching and rash, were also not frequently reported. However, pulmonary complications, which are considered to be important complications in patients with traumatic rib fractures, were in general adequately reported and could be properly investigated. As described in the results, there were no significant differences in the occurrence of pulmonary complications between the three analgesic therapies.

Pooled analyses between epidural and paravertebral was for a greater part determined by the large sample size of Malekpour et al. [31]. As we could only include three studies in these analyses, this might have influenced the outcome.

The value of the different analgesic modalities in critical care patients is insufficiently described. Only one of our included studies compared epidural analgesia with parenteral analgesia in mechanically ventilated ICU patients with flail chest [17]. This RCT described a significant difference in the length of ICU stay, the duration of mechanical ventilation and the change in tidal volume in the first 24 h of ICU admission, in favor of epidural analgesia.

The type of medication is not reflected in our analysis. The different modalities were compared, as described in the baseline characteristics (Appendix Table 4). However, it could be relevant if only opioids were administered, or if local anesthetics were also applied. Furthermore, there was insufficient information about any additional pain medication and whether escape medication was prescribed.

Although there seemed to be significant differences between the different analgesic therapies, further research on the analgesic therapy for traumatic rib fractures is desirable to extend our knowledge of the reduction of pain. Many different pain assessment tools are used in the current practice. The NRS pain score at breathing/coughing seems to be the most reliable outcome parameter, since it reflects the influence of pain on function of the rib cage. To compare the results of pain reduction more homogeneously, future studies should use a universal pain assessment tool. Second, besides pain measurement, there should also be data available on the use of other multimodal treatments started, the daily total opioid consumption and efficacy of the interventional analgesic therapy. On account of the increasing contraindications and the high probability of failure of the epidurals, research into safe and effective
pain management by other analgesic methods must be continued.

Another future perspective is to determine the contribution of surgical rib fixation for the primary and secondary outcomes as described in this systematic review.

**Conclusion**

Results of this study show that epidural analgesia provides better pain relief than the other modalities. No differences were observed for secondary endpoints like length of ICU stay, length of mechanical ventilation or pulmonary complications. However, the quality of the available evidence is low, and therefore, preclude strong recommendations.

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**Compliance with ethical standards**

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**Appendix**

See Tables (2, 3, 4, 5, 6, 7, 8, 9, 10) and Figs. (3, 4).

| **Table 2** Search syntax representing the used search strings in the different databases |
| Database   | Search string                                                                 | Hits   |
|------------|-------------------------------------------------------------------------------|--------|
| PubMed      | (((((fracture[Title/Abstract] OR fractured[Title/Abstract]) OR fractures[Title/Abstract]) AND (“Ribs”[Mesh] OR rib[Title/Abstract] OR ribs[Title/Abstract]) OR “Rib Fractures”[Mesh]) AND (((epidural[Title/Abstract] OR intercostal[Title/Abstract] OR interpleural[Title/Abstract] OR paravertebral[Title/Abstract] OR intrathecal[Title/Abstract] OR oral[Title/Abstract] OR parenteral[Title/Abstract]) OR analgesia[Title/Abstract] OR analgesics[Title/Abstract]) OR blocks[Title/Abstract]) OR (“Pain”[Mesh] OR ((pain[Title/Abstract] OR pains[Title/Abstract]) AND (manage*[Title/Abstract] OR alleviat*[Title/Abstract] OR control*[Title/Abstract] OR reduc*[Title/Abstract] OR therap*[Title/Abstract] OR scor*[Title/Abstract]))) OR (epidural[Title/Abstract] OR ‘epidural anesthesia’ OR ‘intravenous regional anesthesia’ OR ‘intercostal nerve block’) | 708    |
| EMBASE      | fracture:ab,ti OR fractures:ab,ti OR fractured:ab,ti AND (rib:ab,ti OR ‘rib’/exp OR ‘rib fracture’/exp OR ‘rib fracture’:ab,ti OR ribs:ab,ti) AND (epidural:ab,ti OR intercostal:ab,ti OR interpleural:ab,ti OR paravertebral:ab,ti OR intrathecal:ab,ti OR oral:ab,ti OR parenteral:ab,ti) AND (anesthesia:ab,ti OR analgesia:ab,ti OR analgesics:ab,ti OR blocks:ab,ti OR ‘anaesthesia’/exp OR ‘epidural anaesthesia’ OR ‘intravenous regional anaesthesia’/exp OR ‘intercostal nerve block’) | 238    |
| CENTRAL     | Rib fracture                                                                 | 183    |
### Table 3 Quality assessment of the included studies using the methodological index for non-randomized studies

| MINORS          | Baker et al. | Ahmed et al. | Waqar et al. | Yeh et al. | Kieninger et al. | Bulger et al. | Wu et al. | Moon et al. | Mackersie et al. | Wisner et al. | Ullman et al. | Britt et al. | Hashemzadeh et al. | Truitt et al. | Shapiro et al. | Malekpour | Mohta et al. | Yeying et al. | Hwang et al. |
|-----------------|--------------|--------------|--------------|------------|------------------|---------------|-----------|-------------|------------------|----------------|----------------|--------------|------------------|----------------|----------------|-----------|-------------|--------------|-------------|
| A clearly stated aim* | 2            | 2            | 1            | 2          | 2                | 2             | 2         | 2           | 2                | 2              | 2              | 2            | 2                | 2              | 2              | 2         | 2           | 2            | 2           |
| Inclusion of consecutive patients | 1            | 0            | 0            | 2          | 1                | 1             | 2         | 1           | 0                | 0              | 2              | 2            | 0                | 0              | 0              | 0         | 2           | 0            | 2           |
| Prospective collection of data | 0            | 2            | 0            | 0          | 0                | 0             | 2         | 2           | 0                | 0              | 0              | 0            | 2                | 0              | 2              | 0         | 2           | 2            | 0           |
| Endpoints appropriate to the aim of study | 2            | 2            | 1            | 2          | 2                | 2             | 2         | 2           | 2                | 2              | 2              | 2            | 2                | 2              | 2              | 2         | 2           | 2            | 2           |
| Unbiased assessment of the study endpoint | 0            | 0            | 1            | 0          | 0                | 0             | 1         | 1           | 0                | 0              | 0              | 0            | 0                | 0              | 0              | 0         | 1           | 1            | 0           |
| Follow-up period appropriate to the aim of the study** | 1            | 1            | 1            | 1          | 1                | 1             | 1         | 1           | 1                | 1              | 1              | 1            | 1                | 1              | 1              | 1         | 2           | 2            | 2           |
| Loss to follow-up less than 5% | 2            | 2            | 0            | 2          | 2                | 2             | 1         | 2           | 0                | 2              | 2              | 2            | 0                | 0              | 2              | 0         | 2           | 2            | 2           |
| Prospective calculation of the study size | 0            | 0            | 0            | 0          | 0                | 1             | 0         | 0           | 0                | 0              | 0              | 2            | 0                | 0              | 0              | 1         | 0           | 2            | 0           |
The items are scored 0 (not reported), 1 (reported but inadequate), or 2 (reported and adequate). Additional criteria are established for the following points:

* A clearly stated aim: 2 points if described according to the PICO model for clinical questions [48], 1 point if one of the PICO criteria has not been satisfied, 0 points if not reported according to the PICO model.

** Follow-up period: 2 points if follow-up > 6 weeks after hospitalization, 1 point if patients only were reviewed during hospitalization period, 0 points if not reported.

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Here is a table showing the MINORS score for each study:

| MINORS | Baker et al. | Ahmed et al. | Waqar et al. | Yeh et al. | Kieninger et al. | Bulger et al. | Wu et al. | Moon et al. | Mackersie et al. | Wisner et al. | Ullman et al. | Britt et al. | Hashemzadeh et al. | Truitt et al. | Shapiro et al. | Malekpour et al. | Mohta et al. | Yeying et al. | Hwang et al. |
|--------|-------------|--------------|-------------|----------|------------------|-------------|---------|------------|------------------|------------|-----------|-------------|------------------|-----------|--------------|------------------|-------------|------------|-------------|
| Adequate control group | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| Contemporary groups | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 1 | 0 | 2 | 2 | 2 | 2 |
| Baseline equivalence of groups | 1 | 2 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 0 |
| Adequate statistical analyses | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| Total MINORS score | 15 | 17 | 11 | 16 | 15 | 17 | 16 | 17 | 16 | 16 | 17 | 18 | 18 | 11 | 14 | 18 | 23 | 13 |
## Table 4 Baseline characteristics

| First author, year of publication | Country    | Design, setting | Patient characteristics | Intervention | Comparator | Number of patients | Male, n (%) | Age (mean ± SD) | ISS (mean ± SD) |
|-----------------------------------|------------|-----------------|-------------------------|--------------|------------|-------------------|-------------|----------------|-----------------|
| Baker et al. 2016                 | UK         | R, Level I trauma center | > 16 years ≥ 1 thoracic fractures (ribs, sternum, scapular and clavicular fractures) | Continuous epidural analgesia, containing bupivacaine and fentanyl | Intravenous analgesia, morphine delivered by PCA | 6 159 | 4 (66.7%) 122 (76.7%) | 65.9 ± 18.4 | 46.5 ± 17.8 | 25.3 ± 10.5 24.1 ± 10.5 |
| Ahmed et al. 2015                 | India      | RCT, ICU | 18–55 years ≥ 3 rib fractures with flail segment required mechanical ventilation | Thoracic epidural analgesia, fentanyl 12 µg/kg | Intravenous analgesia, fentanyl 2 µg/kg | 10 10 | 7 (70%) 8 (80%) | 39.8 ± 8.8 | 36.7 ± 10.6 | 25 ± 7 28 ± 7 |
| Waqar et al. 2013                 | Pakistan   | R, Surgical ICU | > 18 years ≥ 3 rib fractures | Thoracic epidural analgesia, bupivacaine | Intravenous opioid analgesia | 47 38 | 35 (75%) 29 (76%) | 54 ± 17 | 45 ± 22 | 23.6 ± 10.3 21.0 ± 6.7 |
| First author, year of publication | Country, setting | Patient characteristics | Intervention | Comparator | Number of patients | Male, n (%) | Age (mean ± SD) | ISS (mean ± SD) |
|---------------------------------|-----------------|------------------------|--------------|------------|--------------------|-------------|----------------|----------------|
| Yeh et al. 2012 | USA, R, Trauma service | > 18 years ≥ 3 rib fractures | Contraindications to epidural catheter, acute spine fractures or pre-existing spine deformity, traumatic brain injury or altered mental status or spinal cord injury, unstable pelvic fracture or open abdomen, hemodynamic instability and coagulopathies | Epidural analgesia, containing bupivacaine and fentanyl | Oral or intravenous narcotics, delivered by PCA | 34 | 153 | 26(76.5%) | 113(73.9%) | 51.4 ± 15.0 | 48.8 ± 18.4 | 22.5 ± 8.2 | 22.6 ± 9.6 |
| Kieninger et al. 2005 | USA, R, Level I trauma center | > 55 years ≥ 1 rib fracture ISS score < 16 | Sternal fracture, required intubation before admission to the trauma service or associated injuries that included intracranial hemorrhage | Epidural analgesia | Intravenous opioids | 53 | 134 | 18(33.9%) | 52(38.8%) | 77.7 ± 10.2 | 77.3 ± 10.5 | 10.3 ± 3.6 | 8.3 ± 3.9 |
Table 4 (continued)

| First author, year of publication | Country | Design, setting | Patient characteristics | Intervention | Comparator | Number of patients | Male, n (%) | Age (mean ± SD) | ISS (mean ± SD) |
|----------------------------------|---------|----------------|-------------------------|--------------|------------|-------------------|-------------|-----------------|----------------|
| Bulger et al. 2004               | USA     | RCT, Level I trauma center | > 18 years ≥ 3 rib fractures | Thoracic epidural analgesia, bupivacaine, morphine and fentanyl | Intravenous opioid analgesia, morphine and fentanyl by PCA for alert patients and with nurse assistance for patients who could not participate in self-administration | 22 | 24 | 17(77%) | 16(67%) | 49±18 | 46±16 | 26±8 | 25±8 |
| Wu et al. 1999                   | USA     | R, NR          | > 18 years ≥ 3 rib fractures Following motor vehicle crash | Thoracic epidural analgesia, 0.125 to 0.25% bupivacaine and 2.5 µg/kg fentanyl | Intravenous morphine, delivered by PCA | 25 | 39 | 13(52%) | 20(51%) | 56±17 | 45±22 | 21.6±10.3 | 21.9±6.7 |
| First author, year of publication | Country Design, setting | Patient characteristics | Intervention | Comparator | Number of patients | Male, n (%) | Age (mean ± SD) | ISS (mean ± SD) |
|----------------------------------|-------------------------|------------------------|--------------|------------|-------------------|-------------|----------------|----------------|
| Moon et al. 1999                | USA RCT, NR 18–60 years > 3 consecutive rib fractures or a flail chest segment or pulmonary contusion or sternal fracture | Contraindications to epidural catheter placement (coagulopathy, infection at insertion site, sepsis, or hypovolemic shock), morbid obesity, evidence of spinal cord injury, GCS < 15, adrenal insufficiency, use of steroids, need for vasoactive agents to support blood pressure, immunodeficiency disease, pregnancy, inability to communicate effectively, or history of allergy to local anesthetics or opioids | Thoracic epidural analgesia, initial bolus of fentanyl 50 µg and morphine 3 mg followed by continuous infusion of bupivacaine 0.25% and morphine 0.005%, at a rate of 4 to 6 ml/hr | Intravenous analgesia, intravenous morphine 0.1 mg/kg loading doses followed by morphine 1 mg/ml delivered by PCA in bolus doses of 2 mg | 13 11 | 8(61.5%) 6(54.5%) | 37 ± NR 40 ± NR | 26.6 ± NR 23.4 ± NR |
| Mackersie et al. 1991 | USA RCT, Level I trauma center | ≥ 18 years ≥ 3 rib fractures and flail chest or flail sternum or ≥ 2 rib fractures and exploratory laparotomy or pulmonary contusion | Continuous epidural analgesia, fentanyl bolus 10 µg/kg followed by continuous administration at an initial rate of 0.5 µg/kg/hour | Continuous intravenous fentanyl bolus 5 µg/cc followed by continuous administration at an initial rate of 0.5 mg/kg/hour | 15 17 | NR | 49.3 ± 19 47.8 ± 14 | 20 ± 7.6 16.0 ± 7.2 |
Table 4 (continued)

| First author, year of publication | Country | Design, setting | Patient characteristics | Intervention | Comparator | Number of patients | Male, n (%) | Age (mean ± SD) | ISS (mean ± SD) |
|----------------------------------|---------|----------------|-------------------------|--------------|------------|--------------------|-------------|----------------|----------------|
| Wisner et al. 1990               | USA     | R, NR, NR      | ≥ 60 Admission diagnosis of either rib fracture or sternal fracture | Epidural analgesia, morphine sulfate bolus or continuous infusions of fentanyl | Intravenous or intramuscular | 52 167 | 22(42.3%) 74(44.3%) | 71.0 ± 1.1 69.4 ± 0.6 | 15.7 ± 1.0 14.6 ± 0.8 |
| Ullman et al. 1989               | USA     | RCT, Surgical ICU | ≥ 3 unilateral fractured ribs or flail segment with significant contusion of the chest wall with impaired ventilation | Thoracic epidural analgesia, loading dose fentanyl 100 µg with morphine 5 mg, and continuous morphine 70 µg/ml | Continuous intravenous morphine | 15 13 | 11(73.3%) 11(84.6%) | 46.1 ± 4.6 53.0 ± 6.0 | 19.5 ± 2.03 25.3 ± 2.9 |

**Epidural analgesia vs intercostal block**

| Britt et al. 2015 | USA | R, Level II trauma center | > 18 years ≥ 2 rib fractures | Epidural analgesia, bupivacaine 0.1% with 5 µg/ml fentanyl | Continuous intercostal nerve block, bupivacaine 0.5% continuous 4 mL/hour | 45 64 | 31(68.9%) 38(58.5%) | 60.9 ± 17.3 70.5 ± 6.9 | 13.6 ± 5.2 12.5 ± 6.2 |

| Hashemzadeh et al. 2011 | Iran | RCT, ICU | > 18 years > 1 rib fracture, GCS > 14 | Liver or blunt splenic trauma, decreased consciousness, cerebral injury, mechanical ventilation, coagulopathy, liver and systemic or epidural infection | Intercostal nerve block, bupivacaine 0.25% every 8 h, and pethidine 0.5 ml PRN | 30 30 | 28(93%) 27(90%) | 45.5 ± 15.4 64.5 ± 7.2 | NR NR |
Table 4 (continued)

| First author, year of publication | Country Design, setting | Patient characteristics | Intervention | Comparator | Number of patients | Male, n (%) | Age (mean ± SD) | ISS (mean ± SD) |
|----------------------------------|------------------------|-------------------------|--------------|------------|--------------------|-------------|----------------|----------------|
|                                   |                        |                         |              |            | INT COM            | INT COM     | INT COM        | INT COM        |
| Truitt et al. 2011                | USA P, NR              | > 18 years ≥ 3 unilateral rib fractures | Intubated before CINB placement, confounding injuries (traumatic brain injury, pelvic fracture, and long bone fracture), and allergy to anesthetics | Continuous intercostal nerve block | Epidural analgesia | 102          | 75 NR NR       | 69 68 14 15    |
| Shapiro et al. 2017               | USA R, Level II trauma center | ≥ 2 unilateral rib fractures | Bilateral rib fractures | Epidural analgesia | Paravertebral analgesia, bupivacaine 0.5% | 31 79       | NR NR          | 61.4 ± 18.1 68.7 ± 18.1 | 61.4 ± 18.1 68.7 ± 18.1 |
| Malekpour et al. 2017             | USA R, NR              | > 18 years > 1 rib fracture | Patients with sternum, larynx, and trachea fractures | Epidural analgesia | Paravertebral block | 1073 1110 | 740 (69%) 706 (63.9%) | 58 ± 16.3 54.5 ± 17.8 | 17 (11–22) 14 (10–22) |
| Mohta et al. 2009                  | India RCT NR           | > 18 years ≥ 3 unilateral rib fractures | Unconscious patients, unstable cardiac status or severely altered mental status, liver or kidney disease, contraindications to TEA or TPVB, preexisting spinal deformity, use of anticoagulants or coagulopathy | Continuous thoracic epidural | Thoracic paravertebral | 15 15 | 12 (80%) 12(80%) | 38.9 ± 14.9 40.4 ± 14.8 | 15.9 ± 7.1 13.6 ± 5.6 |
### Table 4 (continued)

| First author, year of publication | Country | Design, setting | Patient characteristics | Intervention | Comparator | Number of patients | Male, n (%) | Age (mean ± SD) | ISS (mean ± SD) |
|-----------------------------------|---------|----------------|------------------------|--------------|------------|-------------------|-------------|----------------|----------------|
| Yeying et al. 2017               | China   | RCT, Level I trauma center | ≥ 18 years, ≥ 3 unilateral rib fractures | Paravertebral block, 250 ml 0.2% ropivacaine 5 mL/h, with a 5 mL bolus dose, and lockout interval of 15 min | Intravenous analgesia, 100 ml 2 µg/kg sufentanil (diluted with saline) 2 ml/h, with a 2 ml bolus dose, and lockout interval of 15 min | 45 | 45 | 29 (64.4%) | 68.9% | 39.1 ± 8.9 | 41.2 ± 9.7 | 14.2 ± 5.1 | 13.7 ± 5.5 |

**Paravertebral block vs intravenous analgesia**

Yeying et al. 2017: China RCT, Level I trauma center. Comparison of analgesic interventions for traumatic rib fractures: a systematic review and meta-analysis.

**Inclusion criteria:** Age < 18 or > 70, severe head injury or unconsciousness, pathological obesity (BMI ≥ 35), thoracic and abdominal visceral injuries, unstable cardiac status, severe liver or kidney disease, coagulopathy, spinal or pelvic fracture, infection at the puncture site and allergy to local anesthetics.

**Exclusion criteria:** Paravertebral block vs intravenous analgesia.

**Hwang et al. 2014:** Korea R, NR ≥ 1 rib fracture

| Design, setting | Patient characteristics | Intervention | Comparator | Number of patients | Male, n (%) | Age (mean ± SD) | ISS (mean ± SD) |
|-----------------|------------------------|--------------|------------|-------------------|-------------|-----------------|-----------------|
|                |                        |              |            |                   |             |                 |                 |
|                |                        |              |            |                   |             |                 |                 |

**Intercostal block vs intravenous analgesia**

Hwang et al. 2014: Korea R, NR ≥ 1 rib fracture

| Design, setting | Patient characteristics | Intervention | Comparator | Number of patients | Male, n (%) | Age (mean ± SD) | ISS (mean ± SD) |
|-----------------|------------------------|--------------|------------|-------------------|-------------|-----------------|-----------------|
|                |                        |              |            |                   |             |                 |                 |
|                |                        |              |            |                   |             |                 |                 |

**Continuous intercostal nerve block (CINB)**

**Comparator group**: Conventional pain control (IV PCA and/or fentanyl patch).

| Design, setting | Patient characteristics | Intervention | Comparator | Number of patients | Male, n (%) | Age (mean ± SD) | ISS (mean ± SD) |
|-----------------|------------------------|--------------|------------|-------------------|-------------|-----------------|-----------------|
|                |                        |              |            |                   |             |                 |                 |
|                |                        |              |            |                   |             |                 |                 |

**CINB** continuous intercostal nerve block, **COM** comparator group, **GCS** Glasgow coma score, **ICU** intensive care unit, **INT** intervention group, **ISS** injury severity score, **NR** not reported, **PCA** patient-controlled analgesia, **PRN** pro re nata, **RCT** prospective cohort study, **TEA** thoracic epidural analgesia, **TPVB** thoracic paravertebral block; **UK** United Kingdom; **USA** United States of America.

*Patient characteristics before propensity matching.*
| First author     | Number of patients | Mortality (during hospital admission) | Mechanical ventilation (days) | Length of ICU stay (days) | Pulmonary complications | Other complications |
|------------------|--------------------|---------------------------------------|------------------------------|---------------------------|-------------------------|----------------------|
|                  | EPI IV             | EPI IV                                | EPI IV                       | EPI IV                    | EPI IV                  | EPI IV               |
| Baker et al.     | 6 159             | 0 (0%)                                | 3.5 ± 4.4                    | 4.6 ± 4.4                 | Pneumonia n=3 (50%)     | Respiratory tract infection n=1 (16.7%) |
|                  |                    |                                      |                              |                           |                         | Pneumonia n=5 (34.6%)  | Respiratory tract infection n=12 (7.5%) |
| Ahmed et al.     | 10 10             | 0 (0%)                                | 6 ± 2                        | 9 ± 3                     | NR                      | Pneumonia n=2 (20%)   | Respiratory tract infection n=5 (50%)  |
|                  |                    |                                      |                              |                           |                         | ARDS n=10 (26%)        | Cardiac n=2 (4%)      |
| Waqar et al.     | 47 38             | 2 (4%)                                | Reduction of days in epidural group | 19 ± 3.1                  | Pneumonia n=6 (13%)    | Overall n=4 (11.8%)   | Overall n=7 (20.6%)   |
|                  |                    |                                      |                              | 21 ± 4.1                  | ARDS n=6 (13%)         | Overall n=17 (11%)    | Overall n=25 (16.3%)  |
| Yeh et al.       | 34 153            | NR                                    | NR                           | 7 (5–12)                  | Overall n=38 (72%)     | Overall n=58 (43%)    | Overall n=25 (16.3%)  |
|                  |                    |                                      |                              | 5 (4–10)                  |                         |                      |                      |
|                  |                    |                                      |                               | 0 (0–1)                   |                         |                      |                      |
| Kieninger et al. | 53 134            | 5 (2.6%)                              | NR                           | 8.6 ± 4.6                 | Pneumonia n=4 (20%)    | Overall n=4 (11.8%)   | Overall n=7 (20.6%)   |
|                  |                    |                                      |                              | 5.6 ± 5.1                 | ARDS n=10 (45%)        | Overall n=58 (43%)    | Overall n=25 (16.3%)  |
| Bulger et al.    | 22 24             | 2 (9%)                                | 8 ± 16                       | 18 ± 16                   | Pneumonia n=4 (18%)    | Overall n=4 (11.8%)   | Overall n=7 (20.6%)   |
|                  |                    |                                      |                              | 16 ± 13                   | ARDS n=10 (45%)        | Overall n=58 (43%)    | Overall n=25 (16.3%)  |
|                  |                    |                                      |                              | 10 ± 15                   |                         |                      |                      |
| Wu et al.        | 25 39             | 0 (0%)                                | NR                           | 12.0 ± 6.1                | Pneumonia n=3 (12%)    | Cardiac n=1 (4%)      | Cardiac n=1 (4%)     |
|                  |                    |                                      |                              | 12.3 ± 7.1                | ARDS n=10 (45%)        | Neurologic n=1 (4%)   | Neurologic n=1 (4%)  |
| Moon et al.      | 13 11             | 0 (0%)                                | NR                           | 11 ± 6.1                  | NR                      | Cardiac n=1 (4%)      | Cardiac n=1 (4%)     |
|                  |                    |                                      |                              | 9.6 ± 6.2                 | Nausea/vomiting n=6 (25%) | Neurologic n=1 (4%)   | Neurologic n=1 (4%)  |
| Mackersie et al. | 15 17             | 0 (0%)                                | NR                           | 8.7 ± 4.2                 | NR                      | Nausea/vomiting n=5 (29%) | Nausea/vomiting n=4 (23%) |
|                  |                    |                                      |                              | 7.1 ± 6.2                 |                         |                        |                      |
|                  |                    |                                      |                              | NR                       |                         |                        |                      |

Table 5 Results of studies comparing epidural analgesia with intravenous analgesia.
| First author  | Number of patients | Mortality (during hospital admission) | Mechanical ventilation (days) | Hospital LOS (days) | Length of ICU stay (days) | Pulmonary complications | Other complications |
|---------------|--------------------|--------------------------------------|------------------------------|--------------------|--------------------------|-------------------------|-----------------------|
|               | EPI IV EPI IV      | EPI IV                               | EPI IV                       | EPI IV             | EPI IV                   | EPI IV                  | EPI IV                |
| Wisner et al. | 52 167             | 2 (4%) 26 (16%)                       | 4.4 ± 0.7                    | NR NR NR NR NR NR | NR NR NR NR NR NR NR | Pneumonia n=4 (8%)      | Pneumonia ARDS n=32 (19%) Major complications n=0 (0%) |
|               |                    |                                     |                              |                    |                          |                         | Effusion Effusion       | Delayed respiratory depression n=0 (0%) |
|               |                    |                                     |                              |                    |                          |                         | Effusion Effusion       | Erythema at catheter site n=2 (4%) |
|               |                    |                                     |                              |                    |                          |                         | Pneumothorax Pneumothorax Lung collapse Lung collapse Lung collapse | Urinary retention n=2 (13.3%) |
|               |                    |                                     |                              |                    |                          |                         | 0 (0%) 0 (0%) 0 (0%) 0 (0%) | None None None |
| Ullman et al. | 15 13              | NR NR                               | 3.1 ± 1.3                    | 18.2 ± 8.1         | 14.9 ± 2.2 47.7 ± 14.7 5.9 ± 1.4 18.7 ± 5.2 | None                    | None                  | Urinary retention  |

ARDS acute respiratory distress syndrome, EPI epidural group, IV intravenous group, LOS length of stay, NR not reported

*Average of all studied groups, including patients receiving epidural analgesia, PCA, combination of epidural and PCA, and interval administered analgesia (including oral, intramuscular, subcutaneous and narcotic agents given intermittently or Pro Re Nata)

*Data presented as median (interquartile range)
Table 6  Results of studies comparing epidural analgesia with intercostal block

| First author | Number of patients | Mortality | Mechanical ventilation (days) | Hospital LOS (days) | Length of ICU stay (days) | Pulmonary complications | Other complications |
|--------------|--------------------|-----------|-------------------------------|--------------------|--------------------------|------------------------|---------------------|
|              | EPI IB             | EPI IB    | EPI IB                        | EPI IB             | EPI IB                   | EPI IB                 | EPI IB              |
| Britt et al. | 45 64              | NR NR     | No significant intergroup difference in ventilator days ($p = 0.61$) | 9.7 ± 9.9          | 7.5 ± 6.2$^a$           | 3.7 ± 4.4              | 4.5 ± 4.9           |
| Hashemzadeh et al. | 30 30              | NR NR     | NR                            | NR                 | 5.7 ± 2.0                | 7.7 ± 3.7              | NR NR |
| Truitt et al. | 75 102             | NR NR     | NR                            | NR                 | 5.9                      | 2.9                    | NR NR |

*EPI* epidural group, *IB* intercostal block group, *ICU* intensive care unit, *LOS* length of hospital stay

$^a$Includes outlier

$^b$No comparison with historical epidural control group

Table 7  Results of studies comparing epidural analgesia with paravertebral block

| First author | Number of patients | Mortality | Mechanical ventilation (days) | Hospital LOS (days) | Length of ICU stay (days) | Pulmonary complications | Other complications |
|--------------|--------------------|-----------|-------------------------------|--------------------|--------------------------|------------------------|---------------------|
|              | EPI PVB            | EPI PVB   | EPI PVB                       | EPI PVB            | EPI PVB                  | EPI PVB                | EPI PVB             |
| Shapiro et al. | 31 79              | 0 (0%)    | 0 (0%)                        | NR NR              | 6.77 ± 2.6               | 6.08 ± 3.69            | NR NR |
| Malekpour et al. | 557 557            | 8 (14%)   | 12 (2.2%)                     | 4 ± 4.4            | 8 ± 4.4                  | 5 ± 3.7                | 4 ± 4.4 |
| Mohta et al. | 15 15              | 0 (0%)    | 0 (0%)                        | NR NR              | 10.1 ± 3.5               | 11.7 ± 5.5             | NR NR |

*EPI* epidural group, *PVB* paravertebral group, *ICU* intensive care unit, *LOS* length of hospital stay, *NR* not reported
Table 8 Results of studies comparing intercostal block with intravenous analgesia

| First author  | Number of patients | Mortality | Mechanical ventilation (days) | Hospital LOS (days) | Length of ICU stay (days) | Pulmonary complications | Other complications |
|---------------|--------------------|-----------|-------------------------------|--------------------|--------------------------|------------------------|--------------------|
|               | IB | IV | IB | IV | IB | IV | IB | IV | IB | IV | IB | IV | IB | IV |
| Hwang et al.  | 23 | 31 | NR | NR | NR | NR | 9.35 (2–49) | 10.61 (4–22) | NR | NR | 0 (0%) | 0 (0%) | NR | NR |

*IB* intercostal block group, *IV* intravenous group, *ICU* intensive care unit, *LOS* length of hospital stay, *NR* not reported

Table 9 Results of studies comparing paravertebral block with intravenous analgesia

| First author  | Number of patients | Mortality | Mechanical ventilation (days) | Hospital LOS (days) | Length of ICU stay (days) | Pulmonary complications | Other complications |
|---------------|--------------------|-----------|-------------------------------|--------------------|--------------------------|------------------------|--------------------|
|               | PVB | IV | PVB | IV | PVB | IV | PVB | IV | PVB | IV | PVB | IV | PVB | IV |
| Yeying et al. | 45 | 45 | 0 (0%) | 0 (0%) | NR | NR | NR | NR | NR | NR | 3 (6.7%) | 9 (20%) | Nausea/vomiting $n = 3$ (6.7%) | Nausea/vomiting $n = 13$ (28.9%) |

*EPI* epidural group, *ICU* intensive care unit, *LOS* length of hospital stay, *NR* not reported, *PVB* paravertebral group
Table 10 Results of sensitivity and subgroup analysis

| Comparison | Outcome | Results | Sensitivity analyses on study design | Sensitivity analyses on study quality | Sensitivity analyses on time | Sensitivity analyses on outlier studies | Subgroup analyses on etiology |
|------------|---------|---------|--------------------------------------|--------------------------------------|-----------------------------|----------------------------------------|-------------------------------|
| Epidural analgesia vs intravenous analgesia | Hospital LOS* | −1.84 (−5.34; 1.66) | −6.69 (−19.81; 6.42) | −6.99 (−16.66; 2.67) | 1.08 (−1.82; 3.98) | 0.97 (−0.98; 2.91) | −2.33 (−6.16; 1.49) |
| | Length of ICU stay* | −2.20 (−4.92; 0.53) | −4.85 (−11.18; 1.47) | *** | −1.28 (−3.50; 0.95) | −0.55 (−2.27; 1.18) | −2.79 (−6.09; 0.52) |
| | Mechanical ventilation* | −5.18 (−11.77; 2.67) | −6.99 (−16.66; 2.67) | −2.15 (−4.60; 0.30) | −1.96 (−4.09; 0.18) | −1.96 (−4.09; 0.18) | −5.18 (−11.77; 1.42) |
| | Pulmonary complications** | 0.79 (0.37; 1.66) | 0.58 (0.21; 1.61) | 0.35 (0.03; 4.56) | 0.97 (0.39; 2.44) | **** | 0.89 (0.41; 1.92) |
| Epidural analgesia vs paravertebral blocks | Hospital LOS* | 0.09 (−0.45; 0.63) | *** | −0.05 (−0.65; 0.55) | 0.14 (−0.41; 0.68) | **** | *** |
| | Length of ICU stay* | −0.08 (−1.68; 1.52) | *** | 0.68 (−0.53; 1.88) | 0.03 (−1.93; 2.00) | **** | *** |

*Results are presented as mean difference (95%CI)
**Results are presented as odds ratio (95%CI)
***Analysis not performed because < one study can be included
****Analysis not performed because no outlier studies present

Fig. 3 Forest plot of the length of a hospital stay b intensive care unit stay (epidural vs intercostal)
Comparison of analgesic interventions for traumatic rib fractures: a systematic review and...

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