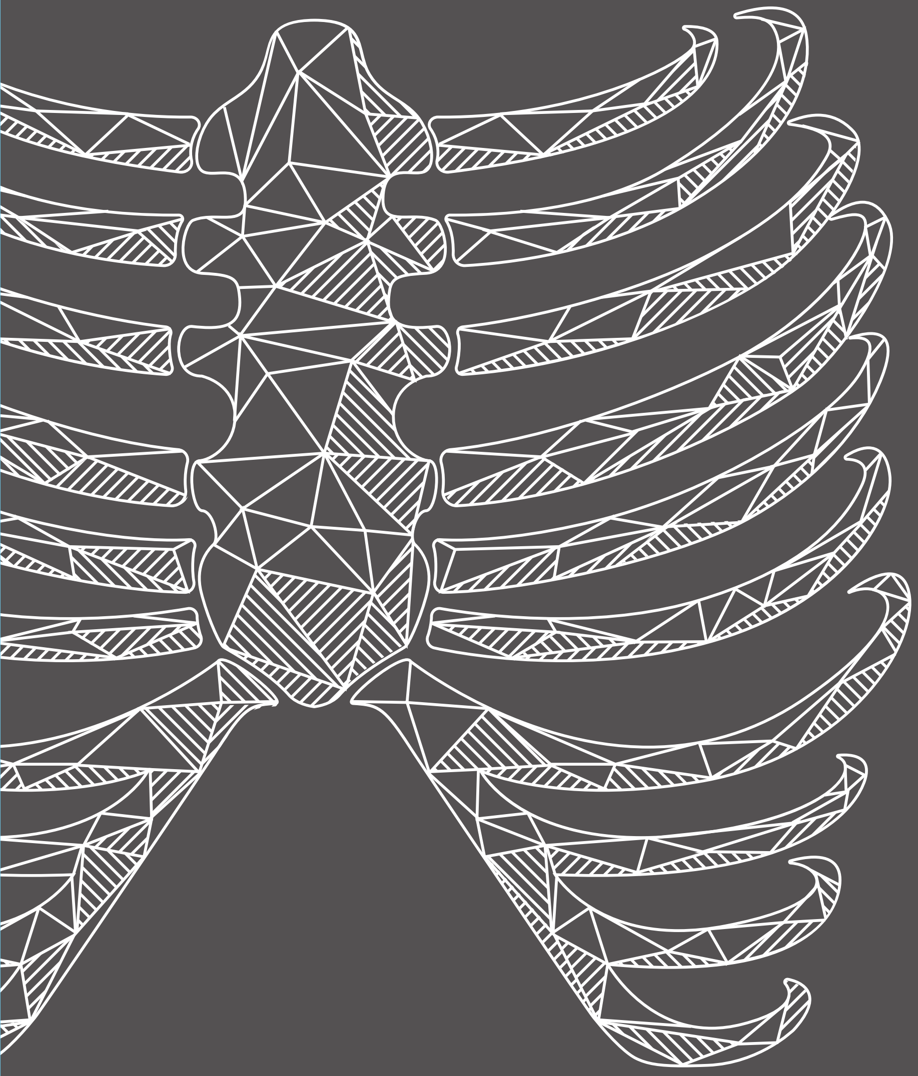

Traumatic Rib Fractures

Epidemiology, Treatment and Outcome

JESSE PEEK

Traumatic Rib Fractures: Epidemiology, Treatment and Outcome

Jesse Peek

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Traumatic Rib Fractures: Epidemiology, Treatment and Outcome

Traumatische Ribfracturen: Epidemiologie, Behandeling en Uitkomsten

(*met een samenvatting in het Nederlands*)

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1 | General introduction and thesis outline

GENERAL INTRODUCTION

Trauma-related injury remains a major global health problem.[1,2] According to the World Health Organization, trauma as a result of physical injury accounts for 10% of the worldwide mortality and is the primary cause of death in the population under the age of 45.[3] Besides, trauma poses a high burden of disease in non-fatal injury, as most musculoskeletal injuries are associated with long-lasting adverse effects on patient's health-related quality of life, daily function, and return to work.[4,5]

Thoracic injuries are considered the third most commonly encountered injury among the trauma population, responsible for 10 to 15 percent of all trauma-related hospitalizations.[6,7] Thoracic trauma encompasses a wide variety of injuries, including chest wall fractures, pulmonary injury, or injury to the cardiovascular system. Depending on the nature of trauma, thoracic injuries can be classified into blunt or penetrating trauma. Blunt chest trauma is the most common cause of thoracic injury with an incidence of 90%, predominantly as a result of motor-vehicle accidents. Penetrating injury, such as gunshot or knife wounds, are inflicted at a much lower rate, representing only 10% of all cases worldwide.[7]

Rib fractures are the most frequently sustained injuries following blunt chest trauma.[6,8] They are identified in approximately 10% of all polytrauma patients and can manifest in a broad spectrum of severity, ranging from relatively harmless isolated fractures to a life-threatening flail chest.[9,10] A flail chest can occur when three or more consecutive ribs are fractured in two or more places, causing paradoxical movement of the flail segment during respiration. The patterns and overall severity of the thoracic injuries depend to a large extent on the intensity and mechanism of trauma. In polytrauma patients, rib fractures are considered to be a surrogate marker of severe injury, with the vast majority of patients sustaining serious concomitant intra-thoracic and extra-thoracic injuries.[6,11,12] Therefore, rib fractures are clinically relevant injuries, they occur in a considerable heterogeneous patient population and are associated with a significant (pulmonary) morbidity and mortality. Besides, even single isolated rib fractures can have profound consequences with long-term disability, chronic pain, and dyspnea.[13–15]

Rib fractures can lead to serious complications. Pain associated with rib fractures or the accompanied chest contusions can compromise the normal mechanics of breathing as it limits patients to cough or breathe deeply. In addition, the common underlying pulmonary injuries, such as pulmonary contusion or pneumothorax, can be negatively affecting the pulmonary function.[16] Consequently, due to inadequate ventilation and impaired clearance of pulmonary secretions, there is an increased risk of developing atelectasis, pneumonia, and respiratory failure requiring mechanical ventilation.[17] Therefore, prompt evaluation and adequate therapy are key to reduce the likelihood of severe (pulmonary) complications and to enhance patients' overall well-being.

Historically, non-operative treatment has been the gold standard for patients with fractured ribs, consisting of a triad of adequate pain control, pulmonary hygiene, and (non) invasive ventilation.[8] With respect to pain management, different analgesic modalities have been described over the years, including oral analgesics, intravenous (patient-controlled) opioids, epidural catheters, and interpleural, intercostal or paravertebral blocks.[18,19] However, according to the management guidelines of the Eastern Association for the Surgery of Trauma (EAST), epidural analgesia has remained the recommended analgesic method in the treatment of rib fractures. Although several studies reported on favorable outcomes of epidural analgesia, its use is an important subject of the clinical and scientific debate.[19] The use of epidural analgesia has been fraught with different challenges such as a high risk of failure, the need for additional analgesic interventions, and the large number of contraindications, which particularly limits its applicability in polytraumatized patients. Therefore, there is growing evidence questioning its advantages over other analgesic modalities.[6,15,20]

Over the years, the focus has shifted from non-operative treatment to operative treatment, especially in patients with multiple rib fractures and flail chest.[21] There has been increased interest in surgical fixation of rib fractures, as it is assumed that rib fixation might improve the in-hospital outcomes as well as the long-term outcomes. Previous studies have shown favorable outcomes after rib fixation in flail chest patients, including a lower rate of pulmonary complications, a shorter hospital and intensive care unit stay, and a reduction in the total number of ventilation days.[22] However, only very few studies are available evaluating the treatment effect in patients with multiple rib fractures and no consensus has yet been reached regarding the indication and patient selection for rib fixation. Besides, less is known about the long-term outcomes of rib fixation, the risk of complications, and whether it might be beneficial to restore the pulmonary function. Therefore, despite that surgical fixation could have a great potential with respect to the treatment of rib fractures, there are still many challenges to be overcome.

Finally, although it is well-known that rib fractures are common injuries, little is known about the exact epidemiology and outcome of these patients. Studies reporting on epidemiological characteristics are mainly from the beginning of this millennium and are mostly flawed by the fact that they do not report on the absolute incidence rates of rib fractures among both the trauma and general population.[10] In order to establish up-to-date normative data on the epidemiology and outcome of specific injuries, trauma registries can play a pivotal role as they systematically collect data on trauma patients. However, as it has become apparent that trauma registries have its own set of challenges with respect to the quality and representativeness of its data, knowledge of these limitations is essential if registry data are used for such scientific purposes.[23,24]

AIMS AND OUTLINE OF THIS THESIS

The general aims of this thesis are 1) to define the epidemiology, injury-characteristics and outcome of patients with rib fractures following trauma, 2) to assess the different analgesic modalities in the context of pain management, and 3) to evaluate the value of surgical fixation in the management of traumatic rib fractures. This thesis consists of three parts:

Part I – Epidemiology and outcome of traumatic rib fractures

The central theme of the first part of this thesis is the epidemiology of rib fractures. **Chapter 2** and **Chapter 3** focus on the establishment of normative benchmark data on the epidemiology, injury-characteristics and outcome of patients with rib fractures, based on the Dutch Trauma Registry and The National Trauma Databank, respectively.

Part II – Pain management of traumatic rib fractures

The second part of this thesis portrays the different analgesic modalities that can be used in the pain management of rib fractures. In **Chapter 4** the outcomes of the different treatment modalities are reviewed and independently compared with each other. **Chapter 5** analyses the efficacy and safety of epidural analgesia for severe chest trauma.

Part III – Operative management of traumatic rib fractures

The third part of this thesis includes studies on the operative treatment of rib fractures. **Chapter 6** presents the current evidence on outcome after rib fixation compared to nonoperative treatment for both flail chest and multiple rib fractures. **Chapter 7** provides an overview of the complications associated with rib fixation and their incidence. The effect of surgical fixation on the pulmonary function is presented in **Chapter 8**. **Chapter 9** assesses the long-term quality of life and functional outcome after rib fixation.

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Part I
Epidemiology and outcome of traumatic rib fractures

2 | Epidemiology and outcome of rib fractures: a nationwide study in the Netherlands.

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Eur J Trauma Emerg Surg 2020

ABSTRACT

Purpose Rib fractures following thoracic trauma are frequently encountered injuries and associated with a significant morbidity and mortality. The aim of this study was to provide current data on the epidemiology, in-hospital outcomes and 30-day mortality of rib fractures, and to evaluate these results for different subgroups.

Methods A nationwide retrospective cohort study was performed with the use of the Dutch Trauma Registry which covers 99% of the acutely admitted Dutch trauma population. All patients aged 18 years and older admitted to the hospital between January 2015 and December 2017 with one or more rib fractures were included. Incidence rates were calculated using demographic data from the Dutch Population Register. Subgroup analyses were performed for flail chest, polytrauma, primary thoracic trauma, and elderly patients.

Results A total of 14,850 patients were admitted between 2015 and 2017 with one or more rib fractures, which was 6.0% of all trauma patients. Of these, 573 (3.9%) patients had a flail chest, 4438 (29.9%) were polytrauma patients, 9273 (63.4%) were patients with primary thoracic trauma, and 6663 (44.9%) were elderly patients. The incidence rate of patients with rib fractures for the entire cohort was 29 per 100.000 person-years. The overall 30-day mortality was 6.9% (n = 1208) with higher rates observed in flail chest (11.9%), polytrauma (14.8%), and elderly patients (11.7%). The median hospital length of stay was 6 days (IQR, 3–11) and 37.3% were admitted to the intensive care unit (ICU).

Conclusions Rib fractures are a relevant and frequently occurring problem among the trauma population. Subgroup analyses showed that there is a substantial heterogeneity among patients with rib fractures with considerable differences regarding the epidemiology, in-hospital outcomes, and 30-day mortality.

INTRODUCTION

Thoracic injuries are the third most common injuries in trauma patients after head and extremity injuries.[1] Rib fractures are considered the most prevalent injury following thoracic trauma and can occur in a broad spectrum of severity, ranging from a single isolated fracture to flail chest. Fractured ribs are associated with a significant morbidity and even isolated fractures can result in severe pain and long-term disability.[2,3] The mortality rates among hospitalized patients with rib fractures range from 10 to 22%, with higher mortality rates among the elderly and in patients with flail chest.[4-8]

Over the past decades, there has been increasing interest concerning different treatment strategies for rib fractures with a large number of studies reporting on the surgical treatment of these injuries.[9,10] However, little is known about the current incidence of rib fractures and how extensive the problem is among the trauma population. Existing studies on the epidemiology of rib fractures do not report on absolute incidence rates and are mainly from the beginning of this millennium.

Previous studies have shown worse outcomes in the elderly with rib fractures and patients with a flail chest.[5,11] Furthermore, differences in outcome are to be expected in polytrauma patients with rib fractures as compared to monotrauma patients. Consequently, there is a large heterogeneity present among patients with rib fractures, which requires reporting on specific subgroups. However, in the current literature there is insufficient data available regarding incidence rates and differences in outcome between subgroups of patients with rib fractures.

Therefore, the aim of this nationwide study was to provide current data on the incidence rates and outcomes of rib fractures and to compare these results for the different subgroups: flail chest, polytrauma, primary thoracic trauma, and elderly patients.

METHODS

The Medical Ethical Review Board of the University Medical Center Utrecht approved this study and granted a waiver of consent (METC number WAG/dgv/18/019105). This article was written in adherence to the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement.[12]

A nationwide retrospective cohort study was performed with the use of the Dutch Trauma Registry (DTR). The DTR was founded in 2007 and is maintained by the Dutch Trauma Network of Acute Care with the general purpose of monitoring trauma care with a standardized registry and to ensure high quality care for severely injured patients. The DTR covers approximately 99% of all hospitals in the Netherlands and prospectively collects data on all trauma patients who are admitted to the hospital after presenting to the emergency department, within 48h after trauma. Patients presented to the emergency department by pre-hospital Emergency Medical Services, as well as by self-admission, are included in the DTR. Excluded are patients declared dead on arrival, who are discharged home, and those admitted to the hospital for reasons other than their traumatic injury.[13] To determine the incidence rate of rib fractures requiring hospital admission, national demographic data were obtained using the Dutch Population Register from the Central Bureau of Statistics .[14]

All patients aged 18 years and older admitted to the hospital between January 2015 and December 2017 with one or more rib fractures were identified using Abbreviated Injury Scale (AIS) codes for rib fractures. Eligible patients were divided into four groups: flail chest, polytrauma, primary thoracic trauma, and elderly. Flail chest was defined as three or more sequential rib fractures in at least two places. Polytrauma was defined as an Injury Severity Score (ISS) of 16 or higher. Primary thoracic trauma was defined as an AIS thorax score higher than the AIS score of all other domains. Elderly patients were defined as patients aged 65 years and older.

The following baseline variables were obtained from the DTR: age at trauma, sex, American Society of Anesthesiologists (ASA) score, mechanism of injury, mode of transport (i.e., ambulance, own transport, or trauma helicopter) and involvement of the Mobile Medical Team (MMT), Glasgow Coma Scale (GCS), vital parameters upon time of admission (i.e., systolic blood pressure and respiratory rate), need for emergency intervention, fracture- and injury-related characteristics including number of fractured ribs and presence of a flail chest, ISS, AIS scores for all body regions, and Revised Trauma Score (RTS). In the Netherlands, the MMT consists of a trauma surgeon or anesthesiologist and a trained nurse to provide acute care on the site of the accident. The Revised Trauma Score is a widely used 13-point scoring tool to determine the initial trauma severity based on the GCS, systolic blood pressure, and respiratory rate. A lower score reflects a higher severity of injury.

The in-hospital outcome variables obtained were hospital length of stay (HLOS), admission to intensive care unit (ICU), ICU length of stay (ILOS), mortality, and Glasgow Outcome Scale (GOS) score at the time of hospital discharge.

Data were analyzed using descriptive statistics and presented as frequencies with percentages for categorical data, means with standard deviations (SD) for normally distributed continuous data, and medians with interquartile ranges (IQR) for non-normally distributed continuous data. The Shapiro–Wilk test and quantile–quantile plots were applied to detect deviations from the normal distribution. The incidence rate was calculated by dividing the total number of patients with rib fractures by the total Dutch population during the study period. Incidence rates were expressed per 100,000 person-years. Statistical analyses were performed using SPSS statistical software (SPSS 23.0; IBM Inc., Armonk, NY, USA).

RESULTS

Between January 2015 and December 2017, a total of 245,548 patients were acutely admitted to the hospital through the emergency department after suffering from trauma. Of these, 14,850 patients had rib fractures (6.0%). There were 573 (3.9%) patients with a flail chest, 4438 (29.9%) with polytrauma, 9273 (62.4%) with primary thoracic trauma, and 6663 (44.9%) were elderly patients.

The incidence rate of rib fractures requiring hospital admission for the entire cohort was 29 per 100,000 person- years. The median age at the time of trauma was 62 (IQR 49–75) years and 67.8% (n = 10,073) were male. The overall 30-day mortality was 6.9% (n = 1028). The baseline characteristics and outcomes are presented in Table 1 and Table 4, respectively.

Flail chest

The incidence rate of patients with flail chest was 1 per 100,000 person-years. Among the 573 patients with a flail chest, the median age was 62 (IQR 51–73) years and 70.2% (n = 402) were male. The median ISS was 17 (IQR 10–27) with a median AIS thorax of 3 (IQR 3–3) (Table 2). The most common mechanisms of injury were low energy falls (22.5%, n = 129), followed by bicycle accidents (14.3%, n = 82), high energy falls (13.6%, n = 78), and motor vehicle accidents (10.8%, n = 62) (Table 3). Among flail chest patients, the median HLOS was 9 (IQR 5–16) days and 63.5% required admission to the ICU with a median ILOS of 3 (IQR 2–6) days. The 30-day mortality was 11.9% (n = 68).

Polytrauma

The incidence rate of polytrauma patients with rib fractures was 9 per 100,000 person-years. Among the 4438 polytrauma patients, the median age was 59 (IQR 46–73) years and 70.5% (n = 3131) were male. The median ISS was 22 (IQR 17–29) with a median AIS thorax of 3 (IQR 3–4) (Table 2). The most common mechanisms of injury were high energy falls (19.2%, n = 850), followed by low energy falls (16.3%, n = 725), bicycle accidents (16.1%, n = 713), and motor vehicle accidents (15.7%, n = 696) (Table 3). Among polytrauma patients, the median HLOS was 10 (IQR 5–18) days and 65.8% (n = 2918) required admission to the ICU with a median ILOS of 3 (IQR 2–9) days. The 30-day mortality was 14.8% (n = 655).

Primary thoracic trauma

The incidence rate of primary thoracic trauma patients with rib fractures was 18 per 100,00 person-years. Among the 9273 patients with primary thoracic trauma, the median age was 62 (IQR 51–75) years and 68.8% (n = 6378) were male. The median ISS was 10 (IQR 9–14) with a median AIS thorax of 3 (IQR 2–3) (Table 2). The most common mechanisms of injury were low energy falls (34.0%, n = 3155), followed by bicycle accidents (14.8%, n = 1373), high energy falls (11.0%, n = 1017), and motor vehicle accidents (8.1%, n = 752) (Table 3). Among patients with primary thoracic trauma, the median HLOS was 6 (IQR 3–10) days and 28.7% required admission to the ICU with a median ILOS of 2 (IQR 2–4) days. The overall 30-day mortality was 4.2% (n = 393).

Table 1. Demographic- and pre-hospital data of patients with rib fractures stratified by subgroups.

		Flail chest		Polytrauma (ISS ≥ 16)		Primary thoracic trauma		Elderly (≥ 65 years)	
	Total patients	Yes	No	Yes	No	Yes	No	Yes	No
Variable	n = 14,850	n = 573	n = 14,277	n = 4,438	n = 10,412	n = 9,273	n = 5,577	n = 6,663	n = 8,187
Demographic data									
Age at trauma, median (IQR)	62 (49-75)	62 (51-73)	62 (49-75)	59 (46-73)	63 (51-76)	62 (51-75)	61 (47-75)	77 (70-84)	51 (42-57)
Sex, n (%)									
Male	10,073 (67.8)	403 (70.2)	9.670 (67.7)	3,131 (70.5)	6,942 (66.6)	6,379 (68.8)	3,694 (66.2)	3,819 (57.3)	6,254 (76.4)
Female	4,777 (32.2)	171 (29.8)	4.606 (32.3)	1,307 (29.5)	3,470 (33.3)	2,894 (31.2)	1,883 (33.8)	2,844 (42.7)	1,933 (23.6)
Comorbidity ASA, n (%) *									
Normal healthy patient	5,027 (33.9)	190 (33.2)	4,837 (33.9)	1,649 (37.2)	3,378 (32.4)	3,069 (33.1)	1,958 (35.1)	882 (13.2)	4,145 (50.6)
Mild systemic disease	5,518 (37.2)	189 (33.0)	5,329 (37.3)	1,527 (34.4)	3,991 (38.3)	3,464 (37.4)	2,054 (36.8)	3,329 (50.0)	2,189 (26.7)
Moderate systemic disease	1,569 (10.6)	49 (8.6)	1,520 (10.6)	429 (9.7)	1,140 (10.9)	981 (10.6)	588 (10.5)	1,193 (17.9)	376 (4.6)
Severe systemic disease	131 (0.9)	6 (1.0)	125 (0.9)	36 (0.8)	95 (0.9)	76 (0.8)	55 (1.0)	115 (1.7)	16 (0.2)
Moribund patients	5 (0)	0 (0)	5 (0)	1 (0)	4 (0)	4 (0)	1 (0)	4 (0.1)	1 (0)
Pre-hospital data									
Glasgow Coma Scale, median (IQR)	15 (15-15)	15 (14-15)	15 (15-15)	15 (12-15)	15 (15-15)	15 (15-15)	15 (14-15)	15 (15-15)	15 (15-15)
Mode of transport, n (%) *									
Ambulance	10,471 (70.5)	414 (72.3)	10,057 (70.4)	3,244 (73.1)	7,227 (69.4)	6,351 (68.5)	4,120 (73.9)	4,848 (72.8)	5,623 (68.7)
Own transport	2,228 (15.0)	58 (10.1)	2,170 (15.2)	185 (4.2)	2,043 (4.2)	1,759 (19.0)	469 (8.4)	947 (14.2)	1,281 (15.6)
Trauma helicopter	166 (1.1)	13 (2.3)	153 (1.1)	137 (3.1)	29 (0.3)	52 (0.6)	114 (2.0)	51 (0.8)	115 (1.4)
Ambulance with helicopter MMT	862 (5.8)	60 (10.5)	802 (5.6)	690 (15.5)	172 (1.7)	305 (3.3)	557 (10.0)	259 (3.9)	603 (7.4)
Other	48 (0.3)	3 (0.5)	45 (0.3)	10 (0.2)	38 (0.4)	35 (0.4)	13 (0.2)	21 (0.3)	27 (0.3)
Involvement of MMT, n (%)	1,431 (9.6)	477 (83.2)	13,058 (91.5)	1,129 (25.4)	302 (2.9)	505 (5.4)	926 (16.6)	408 (6.1)	1,023 (12.5)
Intubation on-scene, n (%)	712 (4.8)	70 (12.2)	642 (4.5)	655 (14.8)	57 (0.5)	171 (1.8)	541 (9.7)	223 (3.3)	489 (6.0)
Emergency intervention, n (%)									
Thoracotomy/Laparotomy	144 (1.0)	11 (1.9)	133 (0.9)	136 (3.1)	8 (0.1)	47 (0.5)	97 (1.7)	21 (0.3)	123 (1.5)
Craniotomy	99 (0.7)	8 (1.4)	91 (0.6)	99 (2.2)	0 (0)	0 (0)	99 (1.8)	35 (0.5)	64 (0.8)
Other	548 (3.7)	46 (8.0)	502 (3.5)	448 (10.1)	100 (1.0)	226 (2.4)	322 (5.8)	163 (2.4)	385 (4.7)

Abbreviations: ASA, American Society of Anesthesiologists; IQR, Interquartile Range; ISS, Injury Severity Score; MMT, Mobile Medical Team

* *Percentages may not add up to 100 due to missing data.*

Table 2. Fracture- and injury-related characteristics of patients with rib fractures stratified by subgroups.

		Flail chest		Polytrauma (ISS ≥ 16)		Primary thoracic trauma		Elderly (≥ 65 years)	
	Total patients	Yes	No	Yes	No	Yes	No	Yes	No
Variable	n = 14,850	n = 573	n = 14,277	n = 4,438	n = 10,412	n = 9,273	n = 5,577	n = 6,663	n = 8,187
Number of fractured ribs, n (%)									
1	2,662 (17.9)	N/A	2,654 (18.6)	371 (8.4)	2,291 (22.0)	888 (9.6)	1,774 (31.8)	1,153 (17.3)	1,509 (18.4)
2	2,627 (17.7)	N/A	2,514 (18.3)	430 (9.7)	2,197 (21.1)	1,374 (14.8)	1,253 (22.5)	1,209 (18.1)	1,418 (17.3)
≥ 3	9,561 (64.4)	573 (100)	9,009 (63.1)	4,438 (81.9)	5,924 (56.8)	7,011 (75.6)	2,550 (45.7)	4,301 (64.6)	5,260 (64.3)
Flail chest, n (%)									
Yes	573 (3.9)	573 (100)	0 (0)	312 (7.0)	261 (2.5)	416 (4.5)	157 (2.8)	259 (3.9)	314 (3.8)
No	14,277 (96.1)	0 (0)	14,277 (100)	4,261 (93.0)	10,151 (97.5)	8,857 (95.5)	5,420 (97.2)	6,404 (96.1)	7,873 (96.2)
ISS, median (IQR)	12 (9-17)	17 (10-27)	11 (9-17)	22 (17-29)	9 (8-13)	10 (9-14)	18 (9-27)	10 (9-17)	13 (9-18)
Polytrauma (ISS ≥ 16), n (%)									
Yes	4,438 (29.9)	312 (54.5)	4,216 (28.9)	4,438 (100)	0 (0)	1,642 (17.7)	2,796 (50.1)	1,787 (26.8)	2,651 (32.4)
No	10,412 (70.1)	261 (45.5)	10,151 (71.1)	0 (0)	10,412 (100)	7,631 (82.3)	2,781 (49.9)	4,876 (73.2)	5,536 (67.6)
AIS, median (IQR)									
Head	0 (0-1)	0 (0-2)	0 (0-1)	1 (0-3)	0 (0-0)	0 (0-0)	1 (1-3)	0 (0-1)	0 (0-1)
Face	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-1)	0 (0-0)	0 (0-0)	0 (0-1)	0 (0-0)	0 (0-0)
Thorax	3 (2-3)	3 (3-3)	3 (2-3)	3 (3-4)	3 (2-3)	3 (2-3)	2 (2-3)	3 (2-3)	3 (2-3)
Abdomen	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)
Spine	0 (0-0)	0 (0-2)	0 (0-0)	0 (0-2)	0 (0-0)	0 (0-0)	0 (0-2)	0 (0-0)	0 (0-0)
Extremities	0 (0-0)	0 (0-1)	0 (0-0)	0 (0-2)	0 (0-0)	0 (0-0)	0 (0-2)	0 (0-0)	0 (0-0)

Abbreviations: AIS, Abbreviated Injury Scale; IQR, Interquartile Range; ISS, Injury Severity Score; No, Number;N/A, Not Applicable.

Table 3. Mechanism of injury in patients with rib fractures stratified by subgroups.

		Flail chest		Polytrauma (ISS ≥ 16)		Primary thoracic trauma		Elderly (≥ 65 years)	
	Total patients	Yes	No	Yes	No	Yes	No	Yes	No
Variable	n = 14,850	n = 573	n = 14,277	n = 4,438	n = 10,412	n = 9,273	n = 5,577	n = 6,663	n = 8,187
Mechanism of injury, n (%)									
Motor vehicle accident	1,456 (9.8)	62 (10.8)	1,394 (9.8)	696 (15.7)	760 (7.3)	752 (8.1)	704 (12.6)	457 (6.9)	999 (12.2)
Motorcycle accident	589 (4.0)	34 (5.9)	555 (3.9)	225 (5.1)	364 (3.5)	354 (3.8)	235 (4.2)	54 (0.8)	535 (6.5)
Bicycle accident	2,327 (15.7)	82 (14.3)	2,245 (15.7)	713 (16.1)	1614 (15.5)	1,373 (14.8)	954 (17.1)	1,042 (15.6)	1,285 (15.7)
Low energy fall	4,474 (30.1)	129 (22.5)	4,345 (30.4)	725 (16.3)	3,749 (36.0)	3,155 (34.0)	1,319 (23.7)	2,850 (42.8)	1,624 (19.8)
High energy fall	1,938 (13.1)	78 (13.6)	1,860 (13.0)	850 (19.2)	1,088 (10.4)	1,017 (11.0)	921 (16.5)	759 (11.4)	1,179 (14.4)
Other	1,517 (10.2)	58 (10.1)	1,459 (10.2)	539 (12.1)	978 (9.4)	898 (9.7)	619 (11.1)	438 (6.6)	1,079 (13.2)

Abbreviations: ISS, Injury Severity Score; n, Number. Percentages may not add up to 100 due to missing data.

Table 4. In-hospital outcomes and 30-day mortality of patients with rib fractures stratified by subgroups.

		Flail chest		Polytrauma (ISS ≥ 16)		Primary thoracic trauma		Elderly (≥ 65 years)	
	Total patients	Yes	No	Yes	No	Yes	No	Yes	No
Variable	n = 14,850	n = 573	n = 14,277	n = 4,438	n = 10,412	n = 9,273	n = 5,577	n = 6,663	n = 8,187
Admission to trauma center, n (%)	5,533 (37.3)	304 (53.1)	5,229 (36.6)	3,022 (68.1)	2,511 (24.1)	2,638 (28.4)	2,895 (51.9)	2,044 (30.7)	3,489 (42.6)
Admission to ICU, n (%)	4,854 (32.7)	363 (63.4)	4,491 (31.5)	2,918 (65.8)	1,936 (18.6)	2,658 (28.7)	2,196 (39.4)	2,001 (30.0)	2,853 (34.8)
HLOS, median (IQR)	6 (3-11)	9 (5-16)	6 (3-11)	10 (5-18)	5 (3-9)	6 (3-10)	7 (3-13)	7 (4-12)	5 (3-10)
ILOS, median (IQR)	3 (2-6)	3 (2-6)	3 (2-6)	3 (2-9)	2 (2-3)	2 (2-4)	3 (2-9)	3 (2-6)	3 (2-6)
Mortality (30-day), n (%)	1,028 (6.9)	68 (11.9)	960 (6.7)	655 (14.8)	373 (3.6)	393 (4.2)	635 (11.4)	782 (11.7)	246 (3.0)
Destination after discharge, n (%)									
Home	9,781 (65.9)	276 (48.2)	9,505 (66.6)	1,902 (42.9)	7,879 (75.7)	6,820 (73.5)	2,961 (53.1)	3,544 (53.2)	6,237 (76.2)
Nursing home	1,210 (8.2)	45 (7.9)	1,165 (8.2)	407 (9.2)	803 (7.7)	654 (7.1)	454 (9.9)	1,044 (15.87)	166 (2.1)
Rehabilitation clinic	976 (6.6)	44 (7.7)	841 (5.9)	527 (11.9)	358 (3.4)	338 (3.6)	547 (9.8)	491 (7.4)	394 (4.8)
Other hospital	134 (0.9)	12 (2.1)	122 (0.9)	93 (2.1)	41 (0.4)	93 (1.0)	77 (1.4)	60 (0.9)	74 (0.9)
GOS Score, n (%)									
Good recovery	4,198 (28.3)	113 (19.7)	4,085 (28.6)	727 (16.4)	3,471 (33.3)	2,984 (32.2)	1,214 (21.8)	1,648 (24.7)	2,550 (31.1)
Moderate disability	5,942 (40.0)	220 (38.4)	5,722 (40.1)	1,733 (39.0)	4,209 (40.4)	3,703 (39.9)	2,239 (40.1)	2,667 (40.0)	3,275 (40.0)
Severe disability	832 (5.6)	57 (9.9)	775 (5.4)	623 (14.0)	209 (2.0)	284 (3.1)	548 (9.8)	338 (5.1)	494 (6.0)
Persistent vegetative state	21 (0.1)	0 (0)	21 (0.1)	18 (0.4)	3 (0.0)	3 (0.0)	18 (0.3)	8 (0.1)	13 (0.2)
Death	749 (5.0)	48 (8.4)	701 (4.9)	550 (12.4)	199 (1.9)	245 (2.6)	504 (9.0)	533 (8.0)	216 (2.6)

Abbreviations: GOS, Glasgow Outcome Scale; HLOS, Hospital Length of Stay; ICU, Intensive Care Unit; IQR, Interquartile Range; ILOS, Intensive Care Unit Length of Stay. Percentages may not add up to 100 due to missing data.

Elderly

The incidence rate of elderly patients with rib fractures was 72 per 100,000 person-years. Among the 6,663 elderly patients, the median age was 77 (IQR 70–84) years and 57.3% (n = 3819) were male. The median ISS was 10 (9–17) with a median AIS thorax of 3 (IQR 2–3) (Table 2). The most common mechanisms of injury were low energy falls (42.8%, n = 2850), followed by bicycle accidents (15.6%, n = 1042), high energy falls (11.4%, n = 759), and motor vehicle accidents (6.9%, n = 457) (Table 3). Among elderly patients, the median HLOS was 7 (IQR 4–12) days and 30.0% required admission to the ICU (n = 2001) with a median ILOS of 3 (IQR 2–6) days. The 30-day mortality was 11.7% (n = 782) (Table 4).

DISCUSSION

This nationwide study shows that rib fractures occur in a very heterogeneous patient population. Rib fractures should be regarded as a marker of severe injury as 30% of the patients sustained multiple injuries. Furthermore, this study shows that rib fractures impose a severe burden on society, as 45% were elderly patients with an incidence rate of 72 per 100,00 person-years and a mean hospital length of stay of 7 days. Although flail chest was present in only 3.9% of the patients, it should be considered as a different entity due to the high mortality rate and prolonged hospital length of stay.

Previous studies on the epidemiology of rib fractures are mainly from the beginning of this millennium. Although absolute population-based incidence rates are lacking, these studies described that rib fractures are identified in approximately 10%–40% of all trauma patients.[7,15,16] With the present study, we demonstrate that 6.0% of all admitted trauma patients sustained fractured ribs following thoracic trauma. Although non-admitted patients with rib fractures were not included, it is likely that the current incidence (29 per 100,000 person-years) is lower than that previously described. In addition, this is the first study reporting on the exact incidence rate of flail chest in patients with rib fractures.

In the current literature, the reported mortality of patients with rib fractures requiring hospital admission ranges between 10 and 22%, with higher rates observed in the elderly patients and patients with a flail chest.[5,7,16] This nationwide study demonstrates an overall 30-day mortality of 6.9%, which is lower than previously reported mortality rates.[16] The decrease in mortality is thought to be a consequence of implementation of trauma systems and the extensively improved trauma and critical care resulting in survival of previously lethal injuries.[17-20] Furthermore, since patients not admitted to hospital were not included in this analysis, the overall mortality risk of rib fractures among the general trauma population is expected to be even lower.

The findings of our subgroup analyses illustrate the considerable clinical heterogeneity among patients with rib fractures and emphasizes the importance of subgroup identification. Flail chest patients had a higher mortality rate compared to patients without a flail chest (11.9% vs. 6.7%). However, half of the patients with a flail chest were considered polytrauma which could in part account for the higher mortality. Greater differences might be demonstrated when distinguishing between a radiological and clinical flail chest. However, this distinction is not made in the DTR. Still, the results showed substantial differences between patients with and without a flail chest regarding total HLOS (median, 9 vs. 6 days) and need for intensive care admission (53.1% vs. 36.6%). Polytrauma patients tend to be younger compared to non-polytrauma patients and have an almost threefold risk of suffering a flail chest, indicating both more severe extra-thoracic and thoracic injury. Patients with primary thoracic trauma appear to be younger and have a lower mortality rate than those with extra-thoracic injuries (4.2% vs. 11.4%), which emphasizes the impact of the extra-thoracic injury on the outcome.

Elderly patients had a lower median ISS compared to their younger counterparts (10 vs. 13) and only a third were polytrauma patients. Nevertheless, the elderly showed to have a considerably higher mortality rate (11.7% vs. 3.0%) as well as a longer HLOS than patients under 65 years of age (7 vs. 5 days). This illustrates the high clinical impact of rib fractures on the elderly population, and once again emphasizes the importance of subgroup identification. Furthermore, with the increase in aging population, rib fractures might impose the largest burden of disease after hip fractures in the elderly trauma population.

This study has several limitations. First, data from registries are subject to miscoding and incomplete data. However, a recent study of Olthof et al. reported that the reliability of the registered AIS codes in the DTR was 'substantial' (intraclass correlation coefficient (ICC) = 0.70), and 'almost perfect' for the registered ISS (ICC = 0.84) and survival status (Cohen's κ = 0.82).[21] Second, the total incidence of rib fractures might be underestimated, as the DTR only registers patients who have been admitted to a hospital, leaving out patients with rib fractures without the need for admission. Nevertheless, with the present study, we provide data on the absolute incidence rate of trauma patients admitted with rib fractures, as 99% of all Dutch hospitals are affiliated with the DTR. Third, since this study represented hospitalized patients only, caution should be exercised when comparing the results with other studies, as the incidence rates depends on the design of healthcare systems, selection of patients, and inclusion criteria of the different trauma registries. Fourth, data on complications and information about the cause of death cannot be extracted from the DTR. Fifth, as the DTR does not record the interventions performed during hospital admission, we were not able to determine the incidence and outcomes of patients who received rib fixation.

This epidemiological study reports on the population-based incidence rates of rib fractures and demonstrates that rib fractures remain a frequently occurring injury associated with a significant morbidity. By the stratification of our subgroups, we have shown that there is still substantial mortality among flail chest, polytrauma, and elderly patients, while patients with primary thoracic trauma have lower mortality rates. Furthermore, as the general population continues to increase in age, it is to be expected that more elderly patients with fractured ribs require clinical care. The average hospital stay is still 6 days, and more than one-third of all patients require intensive care treatment. These findings indicate that rib fractures are a relevant and frequently occurring problem among the trauma population.

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3 | Traumatic rib fractures: a marker of severe injury. A nationwide study using the National Trauma Data Bank.

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ABSTRACT

Background In recent years, there has been increasing interest in the treatment of patients with rib fractures. However, the current literature on the epidemiology and outcomes of rib fractures is outdated and inconsistent. Furthermore, although it has been suggested that there is a large heterogeneity among patients with traumatic rib fractures, there is insufficient literature reporting on the outcomes of different subgroups.

Methods A retrospective cohort study using the National Trauma Data Bank was performed. All adult patients with one or more traumatic rib fractures or flail chest who were admitted to a hospital between January 2010 and December 2016 were identified by the International Classification of Diseases Ninth Revision diagnostic codes.

Results Of the 564,798 included patients with one or more rib fractures, 44.9% (n=253,564) were polytrauma patients. Two percent had open rib fractures (n=11,433, 2.0%) and flail chest was found in 4% (n=23,388, 4.1%) of all cases. Motor vehicle accidents (n=237,995, 51.6%) were the most common cause of rib fractures in patients with polytrauma and flail chest. Blunt chest injury accounted for 95.5% (n=539,422) of rib fractures. Rib fractures in elderly patients were predominantly caused by high- and low-energy falls (n=67,675, 51.9%). Ultimately, 49.5% (n=279,615) of all patients were admitted to an intensive care unit, of whom a quarter (n=146,191, 25.9%) required invasive mechanical ventilatory support. The overall mortality rate was 5.6% (n=31,524).

Discussion Traumatic rib fractures are a marker of severe injury as approximately half of patients were patients with polytrauma. Furthermore, patients with rib fractures are a very heterogeneous group with a considerable difference in epidemiology, injury characteristics and in- hospital outcomes. Worse outcomes were predominantly observed among patients with polytrauma and flail chest. Future studies should recognize these differences and treatment should be evaluated accordingly.

INTRODUCTION

Thoracic trauma is a frequently encountered injury, comprising 10%–15% of all trauma- related hospital admissions.[1] Currently, it is responsible for approximately 35% of all trauma-related deaths in the USA, making it one of the leading causes of death among the trauma population after cardiovascular injury and traumatic brain injury.[2,3]

Traumatic rib fractures represent the most common injury sustained following thoracic trauma and are often caused by a high impact force to the chest wall. Rib fractures are clinically relevant injuries as they are associated with significant pulmonary morbidity, mortality and decreased long-term quality of life.[4,5] Prompt evaluation with pre-emptive pain control, pulmonary hygiene and timely respiratory support is essential in the management of rib fractures.[6,7]

Fractured ribs can occur as simple isolated injury or as part of more extensive thoracic and extra-thoracic injuries. Previous studies implied that rib fractures should be considered as a marker of severe injury, as >90% of patients have severe concomitant injuries mostly involving head, abdomen and extremities.[1,8]

The clinical significance of the number of fractured ribs has been debated in the literature. Several studies have suggested that there is a direct correlation between an increased number of rib fractures and pulmonary morbidity and mortality.[5,9-13] Furthermore, other studies have reported that age, associated injuries and polytrauma might be better predictors for morbidity and mortality.[14,15]

A systematic review and meta-analyses reported an age of 65 years or more, three or more rib fractures and the presence of pre-existing disease, especially cardiopulmonary disease, to be risk factors for mortality following blunt chest wall trauma. In addition, the development of pneumonia post-injury was a significant risk factor for mortality. However, the results of the review were limited by the small number and variable quality of studies included.[14] Different subgroups of patients with traumatic rib fractures are at risk of developing complications, however, currently no guidelines exist to assist in the recognition of these high-risk patient populations.

The primary aim of this nationwide database study was to determine the epidemiology, injury characteristics and in-hospital outcomes of patients with traumatic rib fractures. Secondarily, all data were presented for patients with polytrauma, elderly, isolated thoracic trauma, flail chest and type of injury to describe the differences among these subgroups. Finally, we sought to determine factors associated with mortality.

METHODS

Study design and participants

A study using the National Trauma Data Bank (NTDB) was performed. The NTDB, maintained by the American College of Surgeons, is the largest trauma registry of the USA and contains prospectively gathered data regarding trauma admissions at level I–V trauma centers from over

900 registered US trauma centers.[16] Patients were identified using the International Classification of Diseases Ninth Revision (ICD-9) diagnosis codes 807.00–807.09 for closed rib fractures, 807.10–807.19 for open rib fractures and 807.4 for flail chest. In addition, patients were screened for the presence of concomitant sternum fractures using ICD-9 diagnosis codes 807.3 and 807.4. To identify key interventions, the following ICD-9 procedure codes were used: 03.91 and 03.92 for epidural analgesia, 34.02 for exploratory thoracotomy and 34.79 and 79.39 for rib fixation. All patients aged 18 years or older, with one or more traumatic rib fractures or flail chest who were admitted to hospital between January 2010 and December 2016 were eligible for inclusion.

Patient characteristics and outcome measures

Patient demographics and injury-related characteristics that were obtained from the database included age, sex, mechanism of injury (motor vehicle accident, fall from heights/stairs, pedestrian, assault, struck-by and other), type of injury (blunt or penetrating), Abbreviated Injury Scale (AIS), Injury Severity Score (ISS), Glasgow Coma Scale (GCS), pre-existent comorbidities (congestive heart failure, hypertension, diabetes mellitus and respiratory disease), current smoking status, obesity, number of rib fractures, presence of a flail segment and presence of sternum fracture. The key interventions included epidural analgesia, thoracotomy and rib fixation.

The in-hospital outcomes included mortality, length of stay (LOS), admission to the intensive care unit (ICU), ICU length of stay (ILOS), need and duration of invasive mechanical ventilation (IMV) and complications. Complications that were retrieved included pneumonia, pneumothorax, acute respiratory distress syndrome, venous embolism and thrombosis of deep vessels of lower extremity, pulmonary embolism, and acute myocardial infarction. All pre-existent comorbidities and complications were also identified with the corresponding ICD-9 codes.

Statistical analysis

The in-hospital outcomes including LOS, admission to ICU, ILOS, need and duration of IMV and the incidence of complications were presented as descriptive data. Stratification into patient groups was performed to describe the difference in demographics, injury-related characteristics and in-hospital outcomes for: (1) patients with polytrauma, (2) elderly patients, (3) patients with isolated thoracic trauma and (4) patients with a flail chest. In addition, subgroup analysis was performed according to the type of injury (blunt vs penetrating chest injury). Elderly patients were defined as all patients aged 65 years or older. Patients with polytrauma were defined as all patients with an ISS score of 16 or higher. Patients with isolated thoracic trauma were defined as those patients in which the AIS was the highest for the thoracic domain. In addition, patients were excluded if they had an AIS higher than two in one or more of the other AIS domains. Categorical and dichotomous variables were presented as numbers with percentages (%). Continuous variables were expressed as means with SD for normally distributed data, or as median with IQR for non- normally distributed data. The Shapiro-Wilk test and Q- Q plots were performed to determine the distribution of the continuous variables.

Categorical variables were compared using the χ^2 test, as appropriate. For the comparison of dichotomous and continuous variables, the Mann-Whitney U was used. Multivariable binary logistic regression analyses were performed to identify factors that were associated with the in-hospital mortality and presented as OR with 95% CI. The covariates to adjust for in the multivariable binary logistic regression analyses were selected a priori based on clinical relevance and directed acyclic graphs.

All statistical analyses were performed using Stata Version 13.0 (StataCorp, College Station, Texas, USA). A two-sided p value of <0.05 was considered as statistically significant.

RESULTS

Demographics

A total of 564,798 patients with one or more traumatic rib fractures or flail chest were included from the NTDB. The overall median age was 53 (IQR 39–67) years and the majority (n=390,101, 69.1%) were male. Subgroup analyses identified 253,564 (44.9%) patients with polytrauma, 161,579 (28.6%) elderly patients, 350,898 (62.1%) patients with isolated thoracic trauma and 23,388 (4.1%) with flail chest. Blunt chest injury accounted for 95.5% (n=539,422) of rib fractures, penetrating chest injury accounted for 2.9% (n=16,179). The demographic characteristics for the entire group and subgroups are enumerated in Table 1.

Injury-related characteristics

Motor vehicle accidents were the most common mechanism of injury for rib fractures (n=237,995, 51.6%). Even higher rates of motor vehicle accidents were observed in the subgroups of patients with polytrauma (n=130,039, 62.4%) and flail chest (n=11,458, 60.3%). The most common mechanism of injury in elderly patients were falls from heights or stairs (n=67,675, 51.9%), assault accounted for all penetrating chest injury.

Among all patients, the most common concomitant pulmonary injury was pneumothorax (n=148,216, 26.2%) followed by pulmonary contusion (n=143,096, 25.3%) and then hemothorax (n=35,898, 6.4%). Concomitant pulmonary injuries were also more prevalent in patients with polytrauma, flail chest and after blunt chest trauma.

Of the entire cohort, the median number of rib fractures was 3 (IQR 2–6). Two per cent (n=11,433) had open rib fractures and in 4.1% a manifest flail chest was present. The number of patients with a flail chest was higher in the polytrauma group (n=18,227, 7.2%), compared with the non-polytrauma group (n=5,161, 1.7%). After penetrating chest injury, the majority of patients sustained 1 (n=9,401, 58.4%) or 2 (n=3,617, 22.5%) fractured ribs. The injury characteristics and the distribution of the number of rib fractures are shown in Table 1.

Table 1. Demographics, injury-related characteristics, and interventions of patients with traumatic rib fractures.

		Polytrauma (ISS >16)		Elderly (> 65 years)		Isolated thoracic trauma		Flail chest		Type of Injury	
Variable	Total cohort	Yes	No	Yes	No	Yes	No	Yes	No	Blunt	Penetrating
All, No. (%)	564,798	253,564 (44.9)	311,234 (55.1)	161,579 (28.6)	403,219 (71.4)	350,898 (62.1)	213,900 (37.8)	23,388 (4.1)	541,410 (95.9)	539,422 (95.5)	16,179 (2.9)
Age at trauma	53 (39-67)	50 (34-63)	56 (43-70)	76 (70-82)	46 (33-55)	350,898	50 (34-64)	55 (45-66)	53 (39-67)	54 (40-67)	29 (23-41)
Male sex	390,101 (69.1)	180,082 (71.0)	210,019 (67.5)	90,521 (56.0)	299,580 (74.3)	241,872 (68.9)	148,033 (69.3)	17,528 (74.9)	372,573 (68.8)	368,796 (63.4)	14,481 (89.5)
Mechanism of injury											
Motor vehicle accident	237,995 (51.6)	130,039 (62.4)	107,956 (42.6)	49,591 (38.1)	188,404 (56.9)	128,905 (45.1)	109,090 (62.0)	11,458 (60.3)	226,537 (51.2)	237,995 (54.6)	0 (0)
Fall from height/stairs	129,577 (28.1)	38,618 (18.5)	90,939 (35.9)	67,675 (51.9)	61,882 (18.7)	92,781 (32.5)	36,776 (20.9)	3,974 (21.0)	125,583 (28.4)	129,577 (29.7)	0 (0)
Pedestrian	11,955 (2.6)	4,777 (2.3)	7,178 (2.8)	2,078 (1.6)	9,877 (3.0)	8,215 (2.9)	3,740 (2.1)	518 (2.7)	11,437 (2.6)	11,955 (2.7)	0 (0)
Assault	16,173 (3.5)	8,611 (4.1)	7,562 (3.0)	499 (0.4)	15,674 (4.7)	10,213 (3.6)	5,960 (3.4)	78 (0.4)	16,095 (3.6)	0 (0)	16,173 (100)
Struck-by	16,819 (3.6)	5,593 (2.7)	11,226 (4.4)	2,045 (1.6)	14,774 (4.5)	12,166 (4.3)	4,653 (2.6)	523 (2.8)	16,296 (3.7)	16,819 (3.9)	0 (0)
Other	49,049 (10.6)	20,738 (10.0)	28,311 (11.2)	8,399 (6.4)	40,650 (12.3)	33,224 (11.6)	15,825 (9.0)	2,457 (12.9)	46,592 (10.5)	39,846 (9.1)	0 (0)
Type of Injury,											
Blunt	539,422 (95.5)	241,344 (95.2)	298,078 (95.8)	159,344 (98.6)	380,078 (94.3)	334,500 (95.3)	204,922 (95.8)	22,904 (97.9)	516,518 (95.4)	539,422 (100)	0 (0)
Penetrating	16,179 (2.9)	8,615 (3.4)	7,564 (2.4)	500 (0.3)	15,679 (3.9)	10,261 (2.9)	5,963 (2.8)	78 (0.01)	16,101 (3.0)	0 (0)	16,179 (100)
AIS											
Head	0 (0-1)	0 (0-3)	0 (0-0)	0 (0-1)	0 (0-2)	0 (0-0)	2 (0-4)	0 (0-0)	0 (0-1)	0 (0-2)	0 (0-0)
Thorax	3 (2-3)	3 (3-4)	3 (2-3)	3 (2-3)	3 (2-4)	3 (2-3)	2 (2-4)	3 (3-4)	3 (2-3)	3 (2-3)	3 (3-4)
Abdomen	0 (0-1)	0 (0-2)	0 (0-0)	0 (0-0)	0 (0-1)	0 (0-0)	0 (0-3)	0 (0-2)	0 (0-1)	0 (0-1)	0 (0-2)
Extremities	0 (0-2)	0 (0-2)	0 (0-0)	0 (0-2)	0 (0-2)	0 (0-0)	1 (0-3)	1 (0-2)	0 (0-2)	0 (0-2)	0 (0-1)
ISS	14 (9-22)	22 (18-29)	10 (8-13)	13 (9-18)	14 (10-22)	10 (9-14)	22 (17-29)	24 (17-33)	14 (9-21)	14 (9-22)	17 (10-26)
Polytrauma (ISS > 16	253,564 (44.9)	253,564 (100)	0 (0)	56,704 (35.1)	196,860 (48.8)	76,466 (21.8)	177,098 (82.8)	18,227 (77.9)	255,044 (43.5)	241,344 (95.3)	298,078 (95.8)
GCS	15 (15-15)	15 (13-15)	15 (15-15)	15 (15-15)	15 (15-15)	15 (15-15)	15 (14-15)	15 (10-15)	15 (15-15)	15 (15-15)	15 (12-15)
Comorbidity											
Congestive heart failure	14,692 (2.6)	4,657 (1.8)	10,035 (3.2)	11,115 (6.9)	3,577 (0.9)	10,319 (2.9)	4,373 (2.0)	474 (2.0)	14,218 (2.6)	14,485 (2.7)	62 (0.4)
Hypertension	170,045 (30.1)	63,762 (25.1)	106,283 (34.1)	91,395 (56.6)	78,650 (19.5)	115,550 (32.9)	54,473 (25.5)	7,298 (31.2)	162,747 (30.1)	166,539 (30.8)	1,259 (7.8)
Diabetes Mellitus	69,798 (12.4)	26,593 (10.5)	43,205 (13.9)	35,766 (22.1)	34,032 (8.4)	47,111 (13.4)	22,687 (10.6)	3,123 (13.4)	66,675 (12.3)	68,482 (12.7)	443 (2.7)

Table 1. Demographics, injury-related characteristics, and interventions of patients with traumatic rib fractures. (continued)

		Polytrauma (ISS >16)		Elderly (> 65 years)		Isolated thoracic trauma		Flail chest		Type of Injury	
Variable	Total cohort	Yes	No	Yes	No	Yes	No	Yes	No	Blunt	Penetrating
Respiratory disease	42,764 (7.6)	15,221 (6.0)	27,543 (8.8)	20,250 (12.5)	22,514 (5.6)	29,956 (8.5)	12,808 (6.0)	1,811 (7.7)	40,953 (7.6)	41,465 (7.7)	631 (3.9)
Obesity	30,621 (5.4)	14,734 (5.8)	15,887 (5.1)	7,992 (4.9)	22,629 (5.6)	18,573 (5.3)	12,048 (5.6)	1,765 (7.5)	28,856 (5.3)	29,946 (5.6)	395 (2.4)
Smoker	96,579 (17.1)	42,469 (16.7)	54,110 (17.4)	11,319 (7.0)	85,155 (21.1)	61,515 (17.5)	35,064 (16.4)	3,678 (15.7)	92,901 (17.2)	91,716 (17.0)	3,123 (0.0)
Number of rib fractures											
1	116,689 (21.6)	36,984 (15.7)	79,705 (26.0)	27,748 (17.9)	88,941 (23.0)	71,636 (21.2)	45,053 (22.2)	-	116,689 (21.6)	105,076 (20.3)	9,401 (58.4)
2	88,243 (16.3)	29,200 (12.4)	59,043 (19.3)	24,835 (16.0)	63,408 (16.4)	56,649 (14.7)	31,594 (15.6)	-	88,243 (16,3)	83,072 (16.1)	3,617 (22.5)
3	69,765 (12.9)	27,988 (11.9)	41,777 (13.4)	22,003 (14.2)	47,762 (12.4)	47,023 (12.2)	22,742 (11.2)	-	69,765 (12.9)	67,518 (13.1)	1,115 (6.9)
4	75,373 (13.9)	35,792 (15.2)	39,581 (12.9)	23,077 (14.9)	52,296 (13.5)	50,054 (12.9)	25,319 (12.5)	-	75,373 (13.9)	73,678 (14.3)	561 (3.5)
5	41,466 (7.7)	19,928 (8.5)	21,538 (7.0)	12,807 (8.3)	28,659 (7.4)	27,354 (7.1)	14,112 (7.0)	-	41,466 (7.7)	40,681 (7.9)	198 (1.2)
> 6	149,874 (27.7)	85,332 (36.3)	64,429 (21.1)	44,386 (28.7)	105,488 (27.3)	133,838 (34.6)	64,150 (31.6)	-	149,758 (26.5)	146,493 (28.4)	1,209 (7.5)
Flail chest	23,388 (4.1)	18,227 (7.2)	5,161 (1.7)	6,723 (4.2)	16,665 (4.1)	12,458 (3.6)	10,861 (5.1)	23,388 (100)	0 (0)	22,904 (4.2)	78 (0.5)
Open rib fractures	11,433 (2.0)	6,776 (2.7)	4,657 (1.5)	444 (0.3)	10,969 (2.7)	6,879 (2.0)	4,554 (2.1)	31 (0.1)	11,402 (2.1)	2,643 (0.5)	8,680 (53.6)
Concomitant injuries											
Pulmonary contusion	143,096 (25.3)	90,926 (35.9)	52,170 (16.8)	24,659 (15.3)	118,437 (29.4)	78,102 (22.3)	64,994 (30.4)	11,256 (48.1)	131,840 (24.4)	138,792 (25.7)	2,364 (14.6)
Pneumothorax	148,216 (26.2)	78,287 (30.9)	69,929 (22.5)	30,679 (19.0)	117,537 (29.1)	91,874 (26.2)	56,342 (26.3)	8,756 (37.4)	139,460 (25.8)	144,418 (26.8)	1,270 (7.8)
Hemothorax	35,898 (6.4)	21,114 (8.3)	14,784 (4.8)	10,944 (6.8)	24,954 (6.2)	21,166 (6.0)	14,732 (6.9)	3,513 (15.0)	32,385 (6.0)	34,298 (6.4)	1,020 (6.3)
Sternum fracture	43,134 (7.6)	25,162 (9.9)	17,972 (5.8)	14,308 (8.9)	28,826 (7.1)	24,202 (6.9)	18,932 (8.9)	2,680 (11.5)	40,454 (7.5)	42,368 (7.9)	342 (2.1)
Interventions											
Epidural analgesia	2,505 (0.4)	1,202 (0.4)	1,303 (0.4)	890 (0.5)	1,615 (0.4)	1,834 (0.5)	671 (0.3)	332 (1.4)	2,173 (0.4)	2,456 (0.5)	7 (0.01)
Thoracotomy	4,397 (0.8)	3,427 (1.4)	970 (0.3)	698 (0.4)	3,699 (0.9)	2,060 (0.6)	2,337 (1.1)	658 (2.8)	3,739 (0.7)	3,210 (0.6)	1,130 (7.0)
Rib fixation	25,338 (4.5)	17,102 (6.8)	8,236 (2.6)	3,655 (2.3)	21,683 (5.4)	11,052 (3.5)	14,286 (6.7)	2,939 (12.6)	22,399 (4.1)	24,966 (4.6)	147 (0.9)

Abbreviations: AIS, Abbreviated Injury Scale; ISS, Injury Severity score; GCS, Glasgow Coma Scale.

** Numbers may not add up to total number of patients due to missing values*

All categorical and dichotomous variables are presented as number (%)

All continuous variables are presented as median (interquartile range)

Interventions

Epidural analgesia was administered in 0.4% (n=2,505) of all patients and a thoracotomy was performed in 0.8% (n=4,397). Rib fixation was performed in 4.5% (n=25 388) of the entire cohort, with a higher incidence observed among patients with polytrauma (n=17,102, 6.8%), and those who sustained a flail chest (n=2,939, 12.6%) (Table 1).

In-hospital outcomes and complications

Overall, the median LOS was 5 (IQR 3–9) days and 279,615 patients (49.5%) were admitted to the ICU, with a median ILOS of 4 (IQR 2–8) days. Among these patients, 146,191 (25.9%) required IMV, with a median duration of 4 (IQR 2–11) days. The in-hospital mortality rate was 5.6% (n=31,524) and the most common complication encountered in this cohort was pneumonia (n=28,841, 5.1%). The in-hospital outcomes and complications are presented in Tables 2 and 3, respectively.

With respect to our subgroups, patients with polytrauma as well as patients with a flail chest were more likely to be transferred to the ICU. In the polytrauma group, 69.1% (n=175,120) of patients were ultimately admitted to the ICU, while this was 33.7% (n=104,772) in the non-polytrauma group. The incidence of ICU admission among patients with flail chest was 71.4% (n=16,695) and 48.6% (n=263,197) for those without. The incidence of ICU admission was higher after penetrating chest injury (n=9,769, 60.4%), compared with blunt chest injury (n=265,716, 49.2%).

Additionally, the need for intubation with subsequent IMV was higher among the patients with polytrauma (41.3% vs 13.3%), and patients with flail chest (47.7% vs 24.9%). The total length of ICU stay and duration of IMV was prolonged in the flail chest group, while no differences were found between other subgroups. The highest mortality rate was found in patients with flail chest (n=3,039, 13.0%), polytrauma (n=26,898, 10.6%) and elderly patients (n=12,239, 7.6%). The mortality rate after blunt chest injury was 5.3% (n=29,014), while this was 12.1% (n=1,964) after penetrating chest injury. A lower mortality rate was observed in patients with isolated thoracic trauma (n=7,347, 2.1%).

The overall incidence of complications was also higher in both patients with polytrauma and flail chest. The most frequent complication was pneumonia with 5.1% (n=28,841) in the total cohort. Higher rates were observed among patients with polytrauma (8.9% vs 2.0%) and patients with flail chest (13.7% vs 4.7%). A lower incidence of pneumonia was observed among patients with isolated thoracic trauma (2.6% vs 9.2%). There was no clear difference in the occurrence of complications in the elderly.

Multivariable analyses

The results of multivariable logistic regression on mortality are shown in Table 4. Variables that were independently associated with a higher risk of mortality were: age, male sex, ISS score, GCS score, pre-existing comorbidity (congestive heart failure, diabetes mellitus, respiratory disease and obesity), number of rib fractures, open rib fractures, the presence of a concomitant hemothorax or sternum fracture and thoracotomy. Patients who underwent a thoracotomy had a 3.92 times higher

Table 2. In-hospital outcomes of patients with traumatic rib fractures.

		Polytrauma (ISS > 16)		Elderly (> 65 years)		Isolated thoracic trauma		Flail chest		Type of Injury	
	Total patients	Yes	No	Yes	No	Yes	No	Yes	No	Blunt	Penetrating
Outcome	n = 564,798	n = 253,564	n = 311,234	n = 161,579	n = 403,219	n = 350,898	n = 213,900	n = 23,388	n = 541,410	n = 539,422	n = 16,179
HLOS	5 (3-9)	7 (4-14)	4 (2-6)	5 (3-9)	5 (2-9)	4 (2-7)	7 (4-15)	9 (4-17)	5 (3-9)	5 (3-9)	6 (2-12)
ICU admission	279,615 (49.5)	175,120 (69.1)	104,772 (33.7)	80,424 (49.8)	199,138 (49.5)	128,932 (36.7)	150,960 (70.6)	16,695 (71.4)	263,197 (48.6)	265,716 (49.2)	9,769 (60.4)
ILOS	4 (2-8)	4 (2-10)	3 (2-5)	4 (2-7)	4 (2-8)	3 (2-5)	4 (2-10)	6 (3-15)	3 (2-7)	4 (2-8)	3 (2-7)
Need for IMV	146,191 (25.9)	104,712 (41.3)	41,479 (13.3)	35,975 (22.3)	110,216 (27.3)	55,010 (15.7)	91,181 (42.6)	11,151 (47.7)	135,040 (24.9)	136,811 (25.4)	6836 (42.3)
Duration IMV	4 (2-11)	5 (2-12)	3 (1-7)	5 (2-12)	4 (2-11)	3 (2-9)	5 (2-12)	8 (3-15)	4 (2-11)	5 (2-12)	2 (1-6)
Mortality	31,524 (5.6)	26,898 (10.6)	4,626 (1.5)	12,239 (7.6)	19,285 (4.8)	7,347 (2.1)	24,177 (11.3)	3,039 (13.0)	28,485 (5.3)	29,014 (5.3)	1,964 (12.1)

Abbreviations: HLOS, Hospital Length of Stay; ICU, Intensive Care Unit; ILOS, Intensive Care Unit Length of Stay; IMV, Invasive Mechanical Ventilation.
All categorical and dichotomous variables are presented as number (%)
All continuous variables are presented as median (interquartile range)

Table 3. Complications of patients with traumatic rib fractures.

		Polytrauma (ISS > 16)		Elderly (> 65 years)		Isolated thoracic trauma		Flail chest		Type of Injury	
	Total patients	Yes	No	Yes	No	Yes	No	Yes	No	Blunt	Penetrating
Outcome	n = 564,798	n = 253,564	n = 311,234	n = 161,579	n = 403,219	n = 350,898	n = 213,900	n = 23,388	n = 541,410	n = 539,422	n = 16,179
Pneumonia	28,841 (5.1)	22,578 (8.9)	6,263 (2.0)	7,917 (4.9)	20,924 (5.2)	9,178 (2.6)	19,663 (9.2)	3,203 (13.7)	25,638 (4.7)	27,594 (5.1)	779 (4.8)
ARDS	11,488 (2.0)	9,190 (3.6)	2,314 (0.7)	3,127 (1.9)	8,361 (2.1)	3,590 (1.0)	7,898 (3.7)	1,360 (5.8)	10,128 (1.9)	10,917 (2.0)	391 (2.4)
DVT	9,895 (1.8)	8,022 (3.2)	1,873 (0.6)	2,649 (1.6)	7,246 (1.8)	2,647 (0.8)	7,248 (3.4)	1,043 (4.5)	8,852 (1.6)	9,435 (1.7)	337 (2.1)
Pulmonary embolism	4,341 (0.7)	3,200 (1.3)	1,141 (0.4)	1,040 (0.6)	3,301 (0.8)	1,459 (0.4)	2,882 (1.3)	376 (1.6)	3,965 (0.7)	4,130 (0.8)	158 (1.0)
Myocardial Infarction	1,993 (0.4)	1,264 (0.5)	729 (0.2)	1,288 (0.8)	705 (0.2)	841 (0.2)	1,152 (0.5)	160 (0.7)	1,833 (0.3)	1,993 (0.4)	30 (0.2)
Cardiac arrest with CPR	8,380 (1.5)	7,007 (2.8)	1,373 (0.4)	2,871 (1.8)	5,509 (1.4)	2,311 (0.7)	6,069 (2.8)	944 (4.0)	7,436 (1.4)	7,787 (1.4)	482 (3.0)

Abbreviations: ARDS, Acute Respiratory Distress Syndrome; CPR, Cardiopulmonary Resuscitation; DVT, Deep Vein Thrombosis.
All data are presented as mean (%)

mortality risk (OR 3.92, 95% CI 3.45 to 4.32, p<0.001). Patients with open rib fractures had a 1.84 times higher mortality risk compared with patients with closed rib fractures (OR 1.84, 95% CI 1.69 to 2.01, p<0.001). Patients with congestive heart failure had a 1.85 times higher mortality risk (OR 1.85, 95% CI 1.72 to 1.99, p<0.001), and the presence of a concomitant hemothorax was associated with a 1.41 times higher mortality risk (OR 1.41, 95% CI 1.34 to 1.48, p<0.001). A lower mortality risk was observed among patients who received rib fixation (OR 0.18, 95% CI 0.16 to 0.21, p<0.001) and epidural analgesia (OR 0.49, 95% CI 0.35 to 0.68, p<0.001).

Table 4. Multivariable analysis on mortality.

Variable	OR	95% confidence interval			*p*-value
Age					
18-29	Ref	-	-	-	-
30-39	1.09	1.03	-	1.16	0.005
40-49	1.35	1.28	-	1.43	<0.001
50-59	1.91	1.80	-	2.02	<0.001
60-69	2.98	2.81	-	3.17	<0.001
70-79	5.58	5.24	-	5.94	<0.001
80-89	10.7	10.1	-	11.4	<0.001
Male sex	1.19	1.16	-	1.24	<0.001
ISS	1.07	1.06	-	1.07	<0.001
GCS score	1.28	1.28	-	1.29	<0.001
Comorbidity					
Congestive heart failure	1.85	1.72	-	1.99	<0.001
Hypertension	0.88	0.85	-	0.92	<0.001
Diabetes mellitus	1.24	1.18	-	1.30	<0.001
Respiratory disease	1.35	1.28	-	1.43	<0.001
Obesity	1.17	1.09	-	1.25	<0.001
Smoker	0.66	0.62	-	0.69	<0.001
Number of rib fractures	1.05	1.04	-	1.06	<0.001
Open rib fractures	1.84	1.69	-	2.01	<0.001
Concomitant injuries			-		
Pulmonary contusion	0.94	0.91	-	0.97	<0.001
Pneumothorax	0.85	0.82	-	0.88	<0.001
Hemothorax	1.41	1.34	-	1.48	<0.001
Sternum fracture	1.15	1,20	-	1.21	<0.001
Rib fixation	0.18	0.16	-	0.21	<0.001
Thoracotomy	3.92	3.45	-	4.32	<0.001
Epidural analgesia	0.49	0.35	-	0.68	<0.001

Abbreviations: GCS, Glasgow Coma Scale; ISS, Injury Severity Score; OR, Odds ratio.

DISCUSSION

The present study aimed to describe the epidemiology, injury characteristics and in-hospital outcomes of patients with traumatic rib fractures. Data were reported for polytrauma, elderly, isolated thoracic trauma, flail chest and type of injury (blunt vs penetrating) as it was hypothesized that these subgroups should be considered as different entities. To our knowledge, with the inclusion of 564,798 patients using the NTDB, this study consists of one of the largest cohorts to establish normative data and in-hospital outcomes of patients with traumatic rib fractures.

In this study, we demonstrated that traumatic rib fractures must be considered as a surrogate marker of severe injury, as about half of our cohort consisted of patients with polytrauma. Among these patients, significant worse outcomes were observed with respect to mortality, number of complications and other in-hospital outcomes, such as admission to the ICU and need for mechanical ventilation. These results are in accordance with previous studies. As stated in a study by Ziegler and Agarwal, rib fractures are a reflection of severe chest trauma, and of associated injuries.[1] In their study, they reported that 96% of the 7,147 patients had associated extra-thoracic injuries. Additionally, a large multicenter study by Chrysou et al reported that the mortality in patients with polytrauma with blunt chest trauma was mainly determined by the severity of associated head injuries.[7] No correlation was found between severity of chest injury and mortality. In line with these findings, our results showed that about 20% of the patients with polytrauma had a GCS score lower than 8, corresponding to severe head injury. Therefore, the mortality in patients with thoracic trauma appears to be highly dependent on the severity of the extra-thoracic injuries. Furthermore, a large prospective cohort study by Lin et al, including 1,333 patients, described that the associated injuries in patients with polytrauma with flail chest were of a greater importance than the thoracic factors, with respect to ICU admission and prolonged duration of ICU care.[15] As shown in our study, patients with isolated thoracic trauma had significantly better outcomes regarding mortality and complications, compared with our polytrauma group. Consequently, as previously emphasized by Sirmali et al, the ISS seem to be of great importance for the evaluation of trauma severity as well as for the accurate decision making in the subsequent treatment.[17]

The estimated mortality among patients with traumatic rib fractures varies within the current literature, ranging from 10% to 25%.[1,18] In our study, we described an overall unadjusted mortality rate of 5%. As we pointed out, there was a vast difference in mortality rates between the different subgroups that we studied. The highest mortality rate was observed among patients with flail chest (13.0%), followed by patients with polytrauma (10.6%) and elderly patients (7.6%). Furthermore, with this study we emphasized the increased lethality of penetrating chest injury. The difference in mortality between these subgroups might explain the varying mortality rates reported within the current literature (10%–25%).[1,18] Future research could compare treatment outcomes and mortality rates according to different age groups, flail chest and severity of associated injuries, to determine the optimal treatment of patients with traumatic rib fractures.

Over the past years, several studies have reported risk factors that are associated with mortality in patients with rib fractures after blunt chest trauma.[14] However, the current literature is inconclusive, as contradictory outcomes have been reported. In the current study, age, male gender, ISS, GCS score, pre-existent comorbidities, number of rib fractures, open rib fractures, thoracotomy and the presence of a concomitant hemothorax or sternum fracture were independently associated with a higher risk of mortality in our multivariable regression model. With respect to these findings, it should be noted that several factors had relatively small ORs. So, although statistically significant in our analysis, the clinical relevance might be debatable and should be seen in a wider context.

An unexpected finding in our analysis was that the risk factors of smoking, pulmonary contusion and pneumothorax were inversely correlated with mortality. This could be due to potential confounding or collinearity between our included variables. Another explanation is that there might be an increased vigilance for patients with concomitant pulmonary injuries resulting in more intensive monitoring or care. Furthermore, it has been described that smoking might significantly reduce the number of complications and mortality in severely injured patients, which is known as the 'smoker's paradox'.[19] Similar outcomes have been described among patients with cardiovascular disease.[20] However, the potential protective mechanisms behind this phenomenon and its clinical implications are not well established.

The number of rib fractures, as a risk factor that is associated with mortality, remains an important topic of discussion.[11,13,21] In previous studies, it has been suggested that the number of rib fractures could be considered as an important predictor for overall trauma severity and mortality.[5,9–13] One of the first NTDB studies conducted by Flagel et al reported that the number of rib fractures was directly correlated with higher pulmonary complications and mortality.[13] Six or more rib fractures were considered as an important threshold for mortality, since the incidence increased from 1.8% to 6.8%. A recent study by Shulzhenko et al showed similar results and reported that in elderly patients the threshold of mortality was eight or more fractured ribs.[11] However, other studies have shown opposite results and reported that not the number of rib fractures was associated with worse outcomes, but that age, ISS or a flail chest were independent risk factors for mortality.[14,21,22] Whitson et al showed, in a large NTDB study, that the total number of rib fractures was not an independent predictor for either in-hospital morbidities or mortality.[21] Although, the number of rib fractures was independently associated with the mortality in our multivariable analysis, it did not seem to have a large effect on the overall mortality risk (OR 1.05, 95% CI 1.04 to 1.06, $p<0.001$).

In line with the current literature, our study showed that age is an important independent predictor for mortality in patients with traumatic rib fractures. However, an interesting and unexpected finding of this study was that the total length of hospital stay in the elderly patients did not appear to be longer than their younger counterparts. Moreover, the need for critical care support in the ICU was not higher among the elderly patients, and, in fact, it turned out that they were even less likely to be mechanically ventilated compared with patients younger than 65 years (22% vs 27%). This could be explained by the fact that the elderly patients less frequently sustained polytrauma and that the incidence of concomitant pulmonary injuries was also considerably lower.

Patients with flail chest tend to have significantly worse outcomes than those diagnosed with multiple rib fractures.[23,24] The stability of the chest wall appears to be an important prognostic factor for mortality, and flail chest is often associated with high impact trauma.[23] In accordance with previous results, our large-scale data demonstrated that there is a clear difference between patients with or without flail chest. The flail chest group was associated with a significant higher incidence of respiratory complications, an increased duration of hospital and ICU stay and they were more likely to be intubated and mechanically ventilated. Furthermore, the mortality rate was nearly 2.5 times higher in patients with flail chest than in those without. These results explain why studies on patients with flail chest showed promising results for rib fixation whereas rib fixation has not shown to be beneficial for patients with solely multiple rib fractures yet. Therefore, patients with flail chest should be considered as an independent entity and surgical treatment might play a pivotal role in improving outcome for these patients.[25]

This study should be interpreted in the light of several limitations. First, the NTDB is subject to missing data and under-reporting, as it is based on the voluntary supply of the contributing trauma centers.[26] Hence, complications may have been underestimated. Second, interesting information such as indication for ICU admission or cause of mortality cannot be extracted from the NTDB. Third, although it is well-known that adequate pain relief is the cornerstone in the treatment of rib fractures, the number of patients with epidural analgesia was low. However, we expect that this might be underestimated due to miscoding and missing data. Fourth, with this study we could only report on the in-hospital outcomes, as we did not have any information about the long-term outcomes.

In conclusion, traumatic rib fractures are a marker of severe injury as about half of patients were patients with polytrauma. Furthermore, half of all patients were admitted to an ICU, with a quarter requiring invasive mechanical ventilatory support. This study primarily shows that patients with rib fractures are a very heterogeneous group with a considerable difference in epidemiology, injury characteristics and in-hospital outcomes. Future studies should recognize these differences and treatment should be evaluated accordingly. Worse outcomes were predominantly seen in patients with polytrauma and flail chest.

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Part II

Pain management of traumatic rib fractures

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

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Eur J Trauma Emerg Surg 2019

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.

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 recommended 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.

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

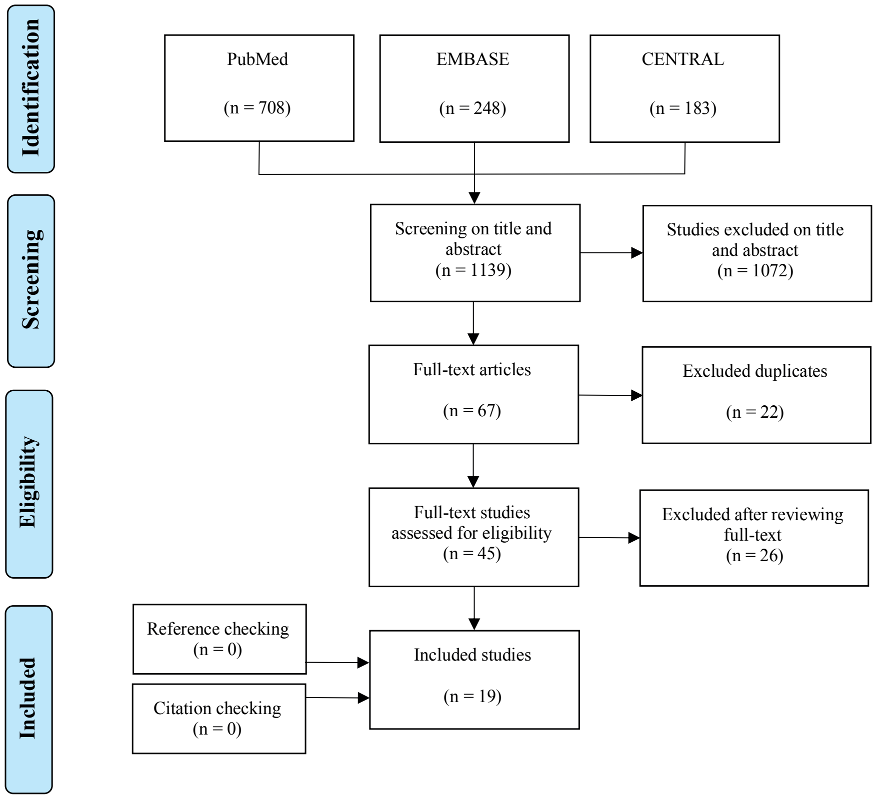
A published protocol for this review does not exist. No ethical committee approval was necessary for this literature review.

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 interventions for blunt chest trauma with traumatic rib fractures. Three different electronic databases (PubMed, EMBASE and CENTRAL) were used to perform a systematic search. The search strategy included keywords and MeSH or Emtree terms relating to traumatic rib fractures, analgesic interventions, pain management and complications. The full search syntax is provided in Appendix 1. The search was not restricted by date or any other limits.

After screening of all titles and abstracts of the identified studied, full texts were obtained of the remaining relevant studies. Two reviewers (JP, DS) read the full-text articles, removed duplicates and made a final selection of relevant studies. Reference lists of retrieved articles were checked and citation tracking was performed using Web of Science, to identify articles not found in the original search. Figure 1 shows a flowchart of the search strategy.

Figure 1. PRISMA flow diagram representing the search and screen process of articles describing analgesic interventions in patients with traumatic rib fractures.



Manuscripts were eligible for inclusion if published in English, French or Dutch language and available in full-text. Studies describing mixed cohorts of patients with blunt chest trauma, including traumatic rib fractures, were also eligible for inclusion. Animal studies, abstracts for conferences, studies including patients below 16 years of age, case reports and studies with less than five patients were excluded. There were no further restrictions for inclusion. Authors were approached if additional information was needed or if full-text was not available.

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 2, 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 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, Tau^2 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 x 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 checking. A flow chart of the complete selection procedure is shown in Figure. 1.

Quality assessment

The total MINORS score of the included articles are listed in Appendix 2. 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 described 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 compared epidurals, with only opioids as drugs, with intravenous analgesia.[19,24,29] Three studies[22,25,26] compared epidural analgesia with intercostal blocks, three studies compared epidural analgesia with paravertebral blocks[6,30,31], one study[32] compared paravertebral blocks with intravenous analgesia and one study[23] compared intercostal blocks with intravenous analgesia. The characteristics of the included studies are shown in Appendix 3.

Epidural analgesia versus intravenous analgesia

The results of the studies comparing epidural with intravenous analgesia are summarized in Appendix 4. Meta-analyses are shown in Figure 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 described lower pain scores at all intervals of the study period in the group that received epidural analgesia ($p < 0.05$).[16] Significant lower pain scores on coughing were found in the first 24 h in the epidural group ($p < 0.05$). One study 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.[20] One 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.[28] One study 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 ($p = 0.08$).[21] 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, 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] The average number of days on the ICU was lower in the epidural group (6.4 ± 3.7) compared with the intravenous group (8.7 ± 6.5), again pooled analysis showed no significant differences [95% CI, MD −2.20 (−4.92, 0.53), $I^2 = 93\%$ $p = 0.11$]. Five studies reported on the duration of mechanical ventilation.[8,16,17,24,27] Four studies were eligible for pooled analysis because the data of one study were not available.[8,17,24,27] 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 showed no significant differences between the groups [95% CI, MD −5.09 (−11.76, 1.58), $I^2 = 90\%$, $p = 0.14$].

Ten studies reported on the occurrence of pulmonary complications.[8,16–21,24,28,29] 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 5. Meta-analyses are shown in Appendix Figure 1. 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 reported on pain scores (Table 1).[22,26] One study described solely pain scores of the group that received intercostal blocks.[26] 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, epidural analgesia provides better control of pain than the intercostal modality.[22] The mean VAS scores that were observed during

Figure 2. Forest plot of the length of **a)** hospital stay **b)** intensive care unit stay **c)** mechanical ventilation (epidural vs intravenous) **d)** forest plot of the pulmonary complications (epidural vs intravenous).

Figure 2a.

Study or Subgroup	Epidural Mean	Epidural SD	Epidural Total	Intravenous Mean	Intravenous SD	Intravenous Total	Weight	Mean Difference IV, Random, 95% CI
1.2.1 RCT								
Bulger et al. 2004	18	16	22	16	13	24	8.1%	2.00 [−6.47, 10.47]
Mackersie et al. 1991	8.7	4.2	15	7.1	6.2	17	13.2%	1.60 [−2.03, 5.23]
Moon et al. 1999	11	6.1	13	9.6	6.2	11	11.8%	1.40 [−3.54, 6.34]
Ullman et al. 1989	14.85	2.2	15	47.69	14.7	13	8.5%	−32.84 [−40.91, −24.77]
Subtotal (95% CI)			**65**			**65**	**41.6%**	**−6.69 [−19.81, 6.42]**
Heterogeneity: Tau^2 = 168.09; Chi^2 = 62.57, df = 3 (P < 0.00001); I^2 = 95%								
Test for overall effect: Z = 1.00 (P = 0.32)								
1.2.2 Observational								
Kieninger et al. 2005	8.6	4.6	53	5.6	5.1	134	15.0%	3.00 [1.49, 4.51]
Waqar et al. 2013	19	3.1	47	21	4.1	38	15.0%	−2.00 [−3.58, −0.42]
Wu et al. 1999	12	6.1	25	12.3	7.1	39	13.6%	−0.30 [−3.57, 2.97]
Yeh et al. 2012	7	5.19	34	5	4.44	153	14.8%	2.00 [0.12, 3.88]
Subtotal (95% CI)			**159**			**364**	**58.4%**	**0.73 [−1.86, 3.32]**
Heterogeneity: Tau^2 = 5.87; Chi^2 = 22.26, df = 3 (P < 0.0001); I^2 = 87%								
Test for overall effect: Z = 0.55 (P = 0.58)								
Total (95% CI)			**224**			**429**	**100.0%**	**−1.84 [−5.34, 1.66]**
Heterogeneity: Tau^2 = 20.68; Chi^2 = 89.05, df = 7 (P < 0.00001); I^2 = 92%								
Test for overall effect: Z = 1.03 (P = 0.30)								
Test for subgroup differences: Chi^2 = 1.18, df = 1 (P = 0.28), I^2 = 15.5%								

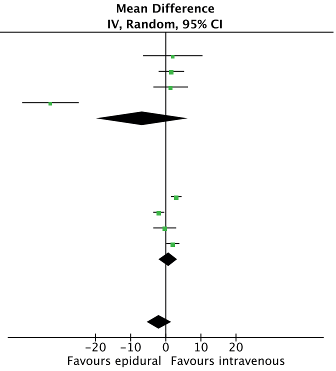


Figure 2b.

Study or Subgroup	Epidural Mean	Epidural SD	Epidural Total	Intravenous Mean	Intravenous SD	Intravenous Total	Weight	Mean Difference IV, Random, 95% CI
1.1.1 RCT								
Ahmed et al. 2015	9.5	1.6	10	12.8	2.8	10	14.3%	−3.30 [−5.30, −1.30]
Bulger et al. 2004	10	15	22	12	26	24	3.8%	−2.00 [−14.14, 10.14]
Moon et al. 1999	4.3	4	13	4.1	5.1	11	12.0%	0.20 [−3.52, 3.92]
Ullman et al. 1989	5.93	1.4	15	18.69	5.2	13	13.2%	−12.76 [−15.67, −9.85]
Subtotal (95% CI)			**60**			**58**	**43.3%**	**−4.85 [−11.18, 1.47]**
Heterogeneity: Tau^2 = 34.18; Chi^2 = 37.70, df = 3 (P < 0.00001); I^2 = 92%								
Test for overall effect: Z = 1.51 (P = 0.13)								
1.1.2 Observational								
Baker et al. 2017	4.6	4.4	6	5.6	6.7	159	12.1%	−1.00 [−4.67, 2.67]
Waqar et al. 2013	12	2.4	47	14	3.5	38	15.0%	−2.00 [−3.31, −0.69]
Wu et al. 1999	4.4	4.1	25	2.5	3.5	39	14.4%	1.90 [−0.05, 3.85]
Yeh et al. 2012	1	2.22	34	0	0.74	153	15.3%	1.00 [0.24, 1.76]
Subtotal (95% CI)			**112**			**389**	**56.7%**	**0.06 [−1.86, 1.98]**
Heterogeneity: Tau^2 = 2.89; Chi^2 = 18.20, df = 3 (P = 0.0004); I^2 = 84%								
Test for overall effect: Z = 0.06 (P = 0.95)								
Total (95% CI)			**172**			**447**	**100.0%**	**−2.20 [−4.92, 0.53]**
Heterogeneity: Tau^2 = 12.46; Chi^2 = 101.77, df = 7 (P < 0.00001); I^2 = 93%								
Test for overall effect: Z = 1.58 (P = 0.11)								
Test for subgroup differences: Chi^2 = 2.13, df = 1 (P = 0.14), I^2 = 53.0%								

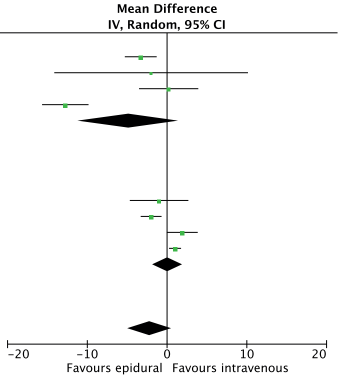


Figure 2c.

Study or Subgroup	Epidural Mean	Epidural SD	Epidural Total	Intravenous Mean	Intravenous SD	Intravenous Total	Weight	Mean Difference IV, Random, 95% CI
1.3.1 RCT								
Ahmed et al. 2015	6	2	10	9	3	10	29.7%	−3.00 [−5.23, −0.77]
Bulger et al. 2004	8	16	22	9	26	24	15.0%	−1.00 [−13.37, 11.37]
Ullman et al. 1989	3.07	1.3	15	18.23	8.1	13	27.1%	−15.16 [−19.61, −10.71]
Subtotal (95% CI)			**47**			**47**	**71.8%**	**−6.99 [−16.66, 2.67]**
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	28.2%	0.20 [−3.39, 3.79]
Subtotal (95% CI)			**6**			**159**	**28.2%**	**0.20 [−3.39, 3.79]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.11 (P = 0.91)								
Total (95% CI)			**53**			**206**	**100.0%**	**−5.09 [−11.76, 1.58]**
Heterogeneity: Tau^2 = 37.66; Chi^2 = 30.38, df = 3 (P < 0.00001); I^2 = 90%								
Test for overall effect: Z = 1.49 (P = 0.14)								
Test for subgroup differences: Chi^2 = 1.87, df = 1 (P = 0.17), I^2 = 46.5%								

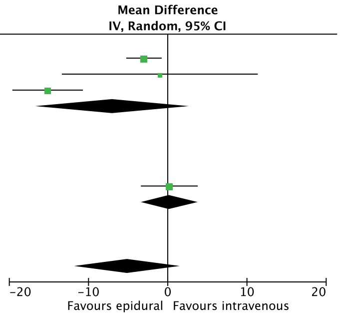
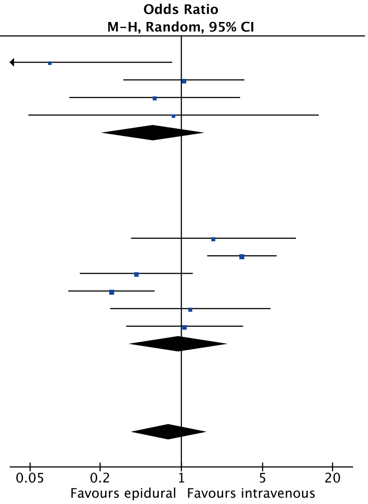


Figure 2d.

Study or Subgroup	Epidural Events	Epidural Total	Intravenous Events	Intravenous Total	Weight	Odds Ratio M-H, Random, 95% CI
1.4.1 RCT						
Ahmed et al. 2015	4	10	9	10	6.0%	0.07 [0.01, 0.84]
Bulger et al. 2004	14	22	15	24	11.4%	1.05 [0.32, 3.48]
Mackersie et al. 1991	11	15	14	17	8.8%	0.59 [0.11, 3.20]
Ullman et al. 1989	1	15	1	13	4.8%	0.86 [0.05, 15.22]
Subtotal (95% CI)		**62**		**64**	**30.9%**	**0.58 [0.21, 1.61]**
Total events	30		39			
Heterogeneity: Tau² = 0.24; Chi² = 3.78, df = 3 (P = 0.29); I² = 21%						
Test for overall effect: Z = 1.05 (P = 0.30)						
1.4.2 Observational						
Baker et al. 2017	3	6	55	159	9.1%	1.89 [0.37, 9.68]
Kieninger et al. 2005	38	53	58	134	14.1%	3.32 [1.67, 6.61]
Waqar et al. 2013	6	47	10	38	11.8%	0.41 [0.13, 1.26]
Wisner et al. 1990	7	52	64	167	13.3%	0.25 [0.11, 0.59]
Wu et al. 1999	3	25	4	39	9.3%	1.19 [0.24, 5.85]
Yeh et al. 2012	4	34	17	153	11.6%	1.07 [0.33, 3.40]
Subtotal (95% CI)		**217**		**690**	**69.1%**	**0.95 [0.35, 2.55]**
Total events	61		208			
Heterogeneity: Tau² = 1.17; Chi² = 24.88, df = 5 (P = 0.0001); I² = 80%						
Test for overall effect: Z = 0.10 (P = 0.92)						
Total (95% CI)		**279**		**754**	**100.0%**	**0.79 [0.37, 1.66]**
Total events	91		247			
Heterogeneity: Tau² = 0.91; Chi² = 29.71, df = 9 (P = 0.0005); I² = 70%						
Test for overall effect: Z = 0.63 (P = 0.53)						
Test for subgroup differences: Chi² = 0.47, df = 1 (P = 0.49), I² = 0%						



hospitalization were 2.2 ± 0.74 at rest and 3.05 ± 0.88 with cough in the epidural group, respectively 3.3 ± 1.01 and 4.95 ± 0.99 in the intercostal group.

Three studies reported on the length of hospital stay.[22,25,26] The average number of days of hospitalization was 7.1 ± 2.3 with epidural analgesia and 6.0 ± 2.7 with intercostal blocks. One study was not included for pooled analysis because the standard deviations were not reported.[26] 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 reported on the length of ICU stay, pooled analysis showed no significant differences [95% CI, MD −0.37 (−0.93, 0.19), I^2 = 0%, p = 0.20].[22,25]

Epidural analgesia versus paravertebral block

The results of the studies comparing epidural analgesia with paravertebral blocks are summarized in Appendix 6. Meta-analyses are shown in Appendix Figure 2. 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 reported on the length of hospital and ICU stay.[6,30,31] The average number of days of hospitalization was 8.3 ± 1.7 with epidural analgesia and 8.6 ± 2.6 with paravertebral blocks, respectively, 4.5 ± 2.1 and 4.6 ± 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].

Table 1. Results of studies reporting on pain relief.

First author	Pain assessment tool	Outcome (mean ± SD)		
Epidural analgesia versus 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 hours in epidural group ($p < 0.05$)		
Wu et al.	Standardized form (0-5)[a]	Baseline	4 [3,4] vs 4 [3,4], $p < 0.82$	
		After 8h	2 [2,1] vs 3 [2,4], $p < 0.001$	
		After 24h	1 [1,2] vs 3 [3,4], $p < 0.001$	
		After 48h	2 [1,2] vs 3 [2,3], $p < 0.001$	
		After 72h	1 [1,2] vs 3 [2,3], $p < 0.001$	
Moon et al.*	Verbal rating scale (0-10)[b]	First 24h	5.8 vs 7.5, $p < 0.05$	
		After 48h	6.0 vs 6.3	
		After 72h	3.8 vs 6.2, $p < 0.05$	
Mackersie et al.*	Visual analogue scale (0-100)[b]	Percentage change in VAS score:		
		At rest	-32 ± 24 vs -27 ± 27, $p < 0.05$	
		Coughing and deep breathing	-42 ± 25 vs -25 ± 26, $p < 0.05$	
			At rest:	Coughing:
		Pre-analgesia	56 vs 62	88 vs 89
		Post-analgesia	24 vs 37	45 vs 63
		After 48h	28 vs 38	51 vs 53
		After 72h	19 vs 26	42 vs 58
Epidural analgesia versus 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 ± 1.01	
		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:	Coughing:
		Pre-analgesia	7.5	9.4
		Post-analgesia	2.6	3.6
		No comparison with epidural group		

Epidural analgesia versus 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)[b]	No significant differences in mean VAS scores at rest ($p = 0.426$) and on coughing ($p = 0.721$)		
			At rest:	Coughing:
		Baseline	66 vs 66	97 vs 97
		After 0.5h	13 vs 13	31 vs 44
		After 24h	17 vs 7	42 vs 34
		After 72h	12 vs 9	32 vs 32
Intercostal block versus intravenous analgesia				
Hwang et al.	Visual analogue scale (0-10)		At rest:	
		Baseline	9.43 vs 8.16	
		Post-analgesia	5.39 vs 7.42, p = 0.007	
		After 24h	5.04 vs 6.16, p = 0.024	
		After 7 days	3.65 vs 3.81, p = 0.944	
Paravertebral block versus intravenous analgesia				
Yeying et al.*	Visual analogue scale (0-10)		At rest:	Coughing:
		Baseline	7.6 ± 2.2 vs. 7.8 ± 2.1	7.9 ± 2.0 vs 8.0 ± 2.2
		After 1h	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 24h	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 48h	2.8 ± 0.9 vs 3.0 ± 1.0	3.3 ± 0.8 vs 3.5 ± 0.9, $p < 0.05$
		After 72h	2.1 ± 0.5 vs 2.2 ± 0.6	2.7 ± 0.6 vs 2.8 ± 0.7, $p < 0.05$

Abbreviations: CINB, continuous intercostal nerve block; h, hour; SD, standard deviation; VAS, visual analogue scale; vs, versus.
**RCT, [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 compared intravenous analgesia with intercostal blocks.[23] The average number of hospital days and the VAS pain scores were reported, and are summarized in Appendix 7, 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 compared paravertebral blocks with intravenous analgesia.[32] The mortality and the VAS pain scores were reported, and are summarized in Appendix 8, 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 9. 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 significant differences ($p < 0.05$) were found in the improvement of pain in favor of epidural analgesia when compared with intravenous analgesia.[16,20,28] In one study, the reduction of pain appeared to be more definite in the group that received epidural analgesia.[21]

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., found a significant increased intervention effect for the reduction of pain, in favor of epidural analgesia, when compared with the paravertebral or intercostal modality.[10] 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., 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.[11] 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. and Carrier et al., we included observational studies.[10,11] Therefore, we were able to include several (new) studies resulting in a larger patient database.[16–20,23,25–27,29–32]

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 using mixed cohorts of patients, in which the analgesic interventions used in the control group were not extractable, were also excluded in our study.[4,47,49,50] 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, 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.[15,51,52] 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, where 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 and collegues.[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 ribcage. 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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Appendix 1. 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]) AND (anesthesia[Title/Abstract] OR anaesthesia[Title/Abstract] OR analgesia[Title/Abstract] OR block[Title/Abstract] OR blocks[Title/Abstract]) OR analgesics[Title/Abstract])) OR ("Pain"[Mesh] OR ((pain[Title/Abstract] OR pains[Title/Abstract]) AND (manag*[Title/Abstract] OR alleviat*[Title/Abstract] OR control*[Title/Abstract] OR reduc*[Title/Abstract] OR treat* OR therap*[Title/Abstract] OR scor*[Title/Abstract]))))	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 anaesthesia:ab,ti OR analgesia:ab,ti OR analgesics ab,ti OR block:ab,ti OR blocks:ab,ti OR 'anaesthesia'/exp OR 'epidural anesthesia' OR 'intravenous regional anesthesia'/exp OR 'intercostal nerve block'/exp)	248
CENTRAL	Rib fracture	183

Appendix 2. Quality assessment of the included studies by 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	1	2	2	2	2	1	2	2	2	2	2	2	2
Inclusion of consecutive patients	1	0	0	2	1	1	2	1	0	0	2	2	2	2	0	0	0	2	0
Prospective collection of data	0	2	0	0	0	0	0	2	2	0	0	0	2	2	0	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	1	1	0	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	2	1	1	2	1
Loss to follow-up less than 5%	2	2	0	2	2	2	2	1	2	0	2	2	2	2	0	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
Adequate control group	2	2	2	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	2	1	0	2	2	2	2
Baseline equivalence of groups	1	2	1	1	1	1	1	2	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	1	2	2	2	2
Total MINORS score	**15**	**17**	**11**	**16**	**15**	**17**	**16**	**17**	**16**	**12**	**16**	**17**	**18**	**18**	**11**	**14**	**18**	**23**	**13**

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

Appendix 3. Baseline characteristics

Study	Country	Design, Setting	Patient characteristics		Intervention
			Inclusion criteria	Exclusion criteria	
Epidural analgesia versus intravenous analgesia					
Baker et al. 2016	UK	R, Level I trauma center	≥ 16 years ≥ 1 thoracic fractures (ribs, sternum, scapular and clavicular fractures)	Patients who died within 24h of admission to hospital and patients with penetrating injuries.	Continuous epidural analgesia, *containing bupivacaine and fentanyl*
Ahmed et al. 2015	India	RCT, ICU	18-55 years ≥ 3 rib fractures with flail segment required mechanical ventilation	Acute spine fracture, pre-existing spine deformity, severe traumatic brain or spinal cord injury, unstable pelvic fracture or open abdomen, ongoing cardiac instability or coagulopathy, and active chest wall infection.	Thoracic epidural analgesia, *4 mL of 0.125% bupivacaine bolus followed by 4 mL/h of 2 μg/kg fentanyl as adjuvant*
Waqar et al. 2013	Paki-stan	R, Surgical ICU	> 18 years ≥ 3 rib fractures	Contraindications to epidural catheter, pregnancy, allergy to local anesthetics or opioids, and associated injuries like intracranial hematoma.	Thoracic epidural *analgesia, bupivacaine*
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*
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
Bulger et al. 2004	USA	RCT, Level I trauma center	> 18 years ≥ 3 rib fractures	Acute spine fracture or pre-existing spine deformity, severe traumatic brain or spinal cord injury, or severe altered mental status, unstable pelvic fracture or open abdomen, active chest wall infection, and acute thoracic aortic transection.	Thoracic epidural analgesia, *bupivacaine, morphine and fentanyl*
Wu et al. 1999	USA	R, NR	> 18 years ≥ 3 rib fractures Following motor vehicle crash	NR	Thoracic epidural analgesia, *0.125 to 0.25% bupivacaine and 2.5 μg/kg fentanyl*

Comparator	Patients		Male, n (%)		Age (mean ± SD)		ISS (mean ± SD)	
	INT	COM	INT	COM	INT	COM	INT	COM
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
Intravenous analgesia, *fentanyl 2 μg/kg*	10	10	7(70%)	8(80%)	39.8±8.8	36.7±10.6	25±7	28±7
Intravenous opioid analgesia	47	38	35 (75%)	29 (76%)	54±17	45±22	23.6±10.3	21.0±6.7
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
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
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
Intravenous morphine, *delivered by PCA*	25	39	13(52%)	20(51%)	56±17	45±22	21.6±10.3	21.9±6.7

Appendix 3. Baseline characteristics (continued)

Study	Country	Design, Setting	Patient characteristics		Intervention
			Inclusion criteria	Exclusion criteria	
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*
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	Pregnancy, history of substance abuse, psychiatric disorder, axial spine injury, chronic pain or chronic us of analgesics, and painful extremity injury.	Continuous epidural analgesia, *fentanyl bolus 1.0 µg/kg followed by continuous administration at an initial rate of 0.5 mg/kg/hour*
Wisner et al. 1990	USA	R, NR	≥ 60 Admission diagnosis of either rib fracture or sternal fracture	NR	Epidural analgesia, *morphine sulfate bolus or continuous infusions of fentanyl*
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	NR	Thoracic epidural analgesia, *loading dose fentanyl 100 µg with morphine 5 mg, and continuous morphine 70 µg/ml*
Epidural analgesia versus intercostal block					
Britt et al. 2015	USA	R, Level II trauma center	> 18 years ≥ 2 rib fractures	NR	Epidural analgesia, *bupivacaine 0.1% with 5 µg/mL fentanyl*
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, fever and systemic or epidural infection.	Thoracic epidural analgesia, *bupivacaine 0.125 and 1 mg morphine every 8 hours, and pethidine 0.5 ml PRN*

Comparator	Patients		Male, n (%)		Age (mean ± SD)		ISS (mean ± SD)	
	INT	COM	INT	COM	INT	COM	INT	COM
Intravenous analgesia, *intravenous morphine 0.1mg/kg loading doses followed by morphine 1mg/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
Continuous intravenous, *fentanyl bolus 5 μg/cc followed by continuous administration at an initial rate of 0.5 mg/kg/hour*	15	17	NR	NR	49.3±19	47.8±14	20±7.6	16.0±7.2
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
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
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
Intercostal nerve block, *bupivacaine 0.25% every 8 hours, and pethidine 0.5 ml PRN*	30	30	28(95%)	27(90%)	45.5±15.4	64.5±7.2	NR	NR

Appendix 3. Baseline characteristics (continued)

Study	Country	Design, Setting	Patient characteristics		Intervention
			Inclusion criteria	Exclusion criteria	
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 versus paravertebral block					
Shapiro et al. 2017	USA	R, Level II trauma center	≥ 2 unilateral rib fractures	Bilateral rib fractures	Epidural analgesia
Malekpour et al. 2017[a]	USA	R, NR	> 18 years > 1 rib fracture	Patients with sternum, larynx, and trachea fractures.	Epidural analgesia
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, pre-existing spinal deformity, use of anticoagulants or coagulopathy.	Continuous thoracic epidural
Paravertebral block versus intravenous analgesia					
Yeying et al. 2017	China	RCT, Level I trauma center	≥ 18 years ≥ 3 unilateral rib fractures	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 anaesthetics.	Paravertebral block, *250 ml 0.2% ropivacaine 5mL/h, with a 5 ml bolus dose, and lockout interval of 15 minutes*
Intercostal block versus intravenous analgesia					
Hwang et al. 2014	Korea	R, NR	≥ 1 rib fracture	NR	Conventional (iv PCA and/or fentanyl patch) + continuous intercostal nerve block (CINB)

Abbreviations: 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; P, prospective cohort study; RCT, randomized controlled trial; R, retrospective; SD, standard deviation; TEA, thoracic epidural analgesia; TPVB, thoracic paravertebral block; UK, United Kingdom; USA, United States of America.

[a] *Patient characteristics before propensity matching*

Comparator	Patients		Male, n (%)		Age (mean ± SD)		ISS (mean ± SD)	
	INT	COM	INT	COM	INT	COM	INT	COM
Epidural analgesia	102	75	NR	NR	69	68	14	15
Paravertebral analgesia, *bupivacaine 0.5%*	31	79	NR	NR	61.4±18.1	68.7±18.1	NR	NR
Paravertebral block	1073	1110	740 (69%)	706 63.9%)	58±16.3	54.5±17.8	17 (11-22)	14 (10-22)
Thoracic paravertebral	15	15	12(80%)	12(80%)	38.9±14.9	40.4±14.8	15.9±7.1	13.6±5.6
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 minutes*	45	45	29 64,4%)	68,9%)	39.1±8.9	41.2±9.7	14.2±5.1	13.7±5.5
Conventional pain control (iv PCA and/or fentanyl patch)	23	31	44 81,4%)		48.5±NR		NR	NR

Appendix 4. Results of studies comparing epidural analgesia with intravenous analgesia.

Study	Patients		Mortality		Mechanical ventilation		Hospital LOS		ICU LOS	
	EPI	IV	EPI	IV	EPI	IV	EPI	IV	EPI	IV
Baker et al.	6	159	0 (0%)	1 (16.7%)	3.5±4.4	3.3±4.6	17.6±22.6[a]		4.6±4.4	5.6±6.7
Ahmed et al.	10	10	0 (0%)	1 (10%)	6±2	9±3	NR	NR	9.5±1.6	12.8±2.8
Waqar et al.	47	38	2 (4%)	1 (2,6%)	NR		19±3.1	21±4.1	12±2.4	14±3.5
Yeh et al.	34	153	NR	NR	NR	NR	7 (5-12)[b]	5 (4-10)[b]	1 (0-3)[b]	0 (0-1)[b]
Kieninger et al.	53	134	5 (2,6%) NR		NR	NR	8.6±4.6	5.6±5.1	NR	NR
Bulger et al.	22	24	2 (9%)	1 (4,2%)	8±16	9±26	18±16	16±13	10±15	12±26
Wu et al.	25	39	0 (0%)	0 (0%)	NR	NR	12.0±6.1	12.3±7.1	4.4±4.1	2.5±3.5
Moon et al.	13	11	0 (0%)	0 (0%)	NR	NR	11±6.1	9.6±6.2	4.3±4.0	4.1±5.1
Mackersie et al.	15	17	0 (0%)	0 (0%)	NR	NR	8.7±4.2	7.1±6.2	NR	NR
Wisner et al.	52	167	2 (4%)	26 (16%)	4.4±0.7		NR	NR	NR	NR
Ullman et al.	15	13	NR	NR	3.1±1.3	18.2±8.1	14.9±2.2	47.7±4.7	5.9±1.4	18.7±5.2

Abbreviations: ARDS, acute respiratory distress syndrome; EPI, epidural group; ICU, Intensive Care Unit; IV, intravenous group; LOS, length of stay; NR, not reported
[a] Average of all studied groups, including patients receiving epidural analgesia, PCA, combination of epidural and PCA, and interval administered analgesia (included oral, intramuscular, subcutaneous and narcotic agents given intermittently or Pro Re Nata).[b] Data presented as median (interquartile range)

Pulmonary complications		Other complications	
EPI	IV	EPI	IV
Pneumonia n = 3 (50%) Respiratory tract infection n = 1 (16.7%)	Pneumonia n = 55 (34.6%) Respiratory tract infection n = 12 (7.5%)	NR	NR
Pneumonia n = 2 (20%) ARDS n = 2 (20%)	Pneumonia n = 4 (40%) ARDS n = 5 (50%)	Hypotension n = 2 (20%) Bradycardia n =1 (10%)	Hypotension n = 0 (0%) Bradycardia n = 0 (0%)
Pneumonia n = 6 (13%)	Pneumonia n=10 (26%)	Cardiac n = 2 (4%)	Cardiac n = 1 (2,6%)
Overall n = 4 (11,8%)	Overall N = 17 (11%)	Overall n = 7 (20,6%)	Overall n = 25 (16,3%)
Overall n = 38 (72%)	Overall n = 58 (43%)	NR	NR
Pneumonia n = 4 (18%) ARDS n = 10 (45%)	Pneumonia n = 9 (38%) ARDS n = 6 (25%)	Pruritus n = 5 (27%) Transient motor block n = 2 (9%) Catheter site inflammation or superficial infection n = 1 (5%)	Pruritus n = 5 (21%) Nausea/vomiting n = 6 (25%) Depressed level of consciousness n = 1 (4%)
Pneumonia n = 3 (12%)	Pneumonia n = 4 (10%)	Cardiac n =1 (4%) Neurologic n=1 (4%)	Cardiac n = 5 (13%) Neurologic n = 7 (18%)
NR	NR	NR	NR
Pneumonia n = 0 (0%) Atelectasis n = 11 (73%)	Pneumonia n = 0 (0%) Atelectasis n = 14 (82%)	Nausea/ vomiting n = 7 (46%) Itching/rash n = 2 (13%)	Nausea/vomiting n = 5 (29%) Itching/rash n = 4 (23%)
Pneumonia n = 4 (8%) ARDS n = 3 (6%) Effusion n = 0 (0%) Pneumothorax n = 0 (0%) Lung collapse n = 0 (0%)	Pneumonia n = 32 (19%) ARDS n = 24 (14%) Effusion n = 2 (1%) Pneumothorax n = 2 (1%) Lung collapse n = 4 (2%)	Major complications n = 0 (0%) Delayed respiratory depression n = 0 (0%) Erythema at catheter site n = 2 (4%) Urinary retention n = 0 (0%)	NR
None	None	Urinary retention n = 2 (13,3%)	None

Appendix 5. Results of studies comparing epidural analgesia with intercostal block.

Study	Patients		Mortality		Mechanical ventilation		Hospital LOS		ICU LOS		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	Pneumonia or ventilator-dependent respiratory failure n = 8 (12.5%)	Pneumonia or ventilator-dependent respiratory failure n = 8 (12.5%)	NR	NR
Hashemzadeh et al.	30	30	NR	NR	NR	NR	5.7±2.0	7.7±3.7	1.6±1.0	1.9±1.4	No intergroup difference regarding incidence of respiratory complications		NR	NR
Truitt et al.	75	102	NR	NR	NR	NR	5.9	2.9	NR	NR	NR	NR	NR	NR

Abbreviations: 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*

Appendix 6. Results of studies comparing epidural analgesia with paravertebral block

Study	Patients		Mortality		Mechanical ventilation		Hospital LOS		ICU LOS		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	2.13±1.9	3.14±2.8	NR	NR	0 (0%)	0 (0%)
Malekpour et al.	557	557	8 (1.4%)	12 (2.2%)	4±4.4	5±6.6	8±4.4	8±5.9	5±3.7	4±4.4	Pneumonia n = 40 (7.2%)	Pneumonia n = 40 (7.2%)	NR	NR
Mohta et al.	15	15	0 (0%)	0 (0%)	NR	NR	10.1±3.5	11.7±5.5	6.3±1.6	6.8±4.2	Pneumonia n = 1 (6.7%) Delayed pleural effusion n = 1 (6.7%)	Pneumonia n = 2 (13.3%) Delayed pleural effusion n = 0 (0%)	Hypotension n = 6 (40%)	Hypotension n = 2 (13.3%)

Abbreviations: EPI, epidural group; PVB, paravertebral group; ICU, intensive care unit; LOS, length of hospital stay; NR, not reported.

Appendix 7. Results of studies comparing intercostal block with intravenous analgesia.

Study	Patients		Mortality		Mechanical ventilation		Hospital LOS		ICU LOS		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

Abbreviations: IB, intercostal block group; IV, intravenous group; ICU, intensive care unit; LOS, length of hospital stay; NR, not reported.

Appendix 8. Results of studies comparing paravertebral block with intravenous analgesia.

Study	Patients		Mortality		Mechanical ventilation		Hospital LOS		ICU LOS		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%)

Abbreviations: EPI, epidural group; ICU, intensive care unit; LOS, length of hospital stay; NR, not reported, PVB, paravertebral group.

Appendix 9. 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 versus 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; 1.42]	-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 versus 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*

Appendix Figure 1. Forest plot of the length of **a** hospital stay **b** intensive care unit stay (epidural vs intercostal).

Figure a.

Study or Subgroup	Epidural Mean	Epidural SD	Epidural Total	Intercostal Mean	Intercostal SD	Intercostal Total	Weight	Mean Difference IV, Random, 95% CI
2.2.1 RCT								
Hashemzadeh et al. 2011	5.7	1.97	30	7.65	3.72	30	56.3%	−1.95 [−3.46, −0.44]
Subtotal (95% CI)			**30**			**30**	**56.3%**	**−1.95 [−3.46, −0.44]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.54 (P = 0.01)								
2.2.2 Observational								
Britt et al. 2015	9.7	9.9	45	7.49	6.18	64	43.7%	2.21 [−1.05, 5.47]
Subtotal (95% CI)			**45**			**64**	**43.7%**	**2.21 [−1.05, 5.47]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.33 (P = 0.18)								
Total (95% CI)			**75**			**94**	**100.0%**	**−0.13 [−4.18, 3.91]**

Heterogeneity: $Tau^2 = 6.97$; $Chi^2 = 5.14$, df = 1 (P = 0.02); $I^2 = 81\%$
Test for overall effect: Z = 0.06 (P = 0.95)
Test for subgroup differences: $Chi^2 = 5.14$, df = 1 (P = 0.02), $I^2 = 80.6\%$

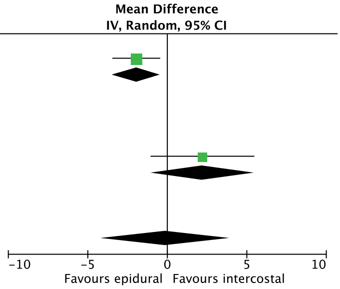
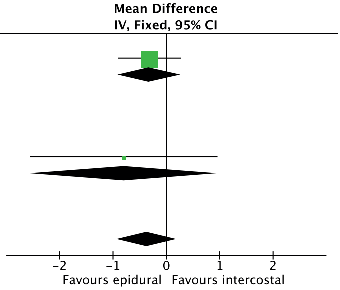


Figure b.

Study or Subgroup	Epidural Mean	Epidural SD	Epidural Total	Intercostal Mean	Intercostal SD	Intercostal Total	Weight	Mean Difference IV, Fixed, 95% CI
2.1.1 RCT								
Hashemzadeh et al. 2011	1.58	0.95	30	1.9	1.35	30	89.9%	−0.32 [−0.91, 0.27]
Subtotal (95% CI)			**30**			**30**	**89.9%**	**−0.32 [−0.91, 0.27]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.06 (P = 0.29)								
2.1.2 Observational								
Britt et al. 2015	3.7	4.4	45	4.5	4.9	64	10.1%	−0.80 [−2.56, 0.96]
Subtotal (95% CI)			**45**			**64**	**10.1%**	**−0.80 [−2.56, 0.96]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.89 (P = 0.37)								
Total (95% CI)			**75**			**94**	**100.0%**	**−0.37 [−0.93, 0.19]**

Heterogeneity: $Chi^2 = 0.26$, df = 1 (P = 0.61); $I^2 = 0\%$
Test for overall effect: Z = 1.29 (P = 0.20)
Test for subgroup differences: $Chi^2 = 0.26$, df = 1 (P = 0.61), $I^2 = 0\%$



Appendix Figure 2. Forest plot of the length of **a** hospital stay **b** intensive care unit stay (epidural vs paravertebral).

Figure a.

Study or Subgroup	Epidural Mean	Epidural SD	Epidural Total	Paravertebral Mean	Paravertebral SD	Paravertebral Total	Weight	Mean Difference IV, Fixed, 95% CI
4.1.1 RCT								
Mohta et al. 2009	10.1	3.5	15	11.7	5.5	15	2.7%	−1.60 [−4.90, 1.70]
Subtotal (95% CI)			**15**			**15**	**2.7%**	**−1.60 [−4.90, 1.70]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.95 (P = 0.34)								
4.1.2 Observational								
Malekpour et al. 2017	8	4.4	557	8	5.9	557	77.9%	0.00 [−0.61, 0.61]
Shapiro et al. 2017	6.77	2.6	31	6.08	3.69	79	19.4%	0.69 [−0.53, 1.91]
Subtotal (95% CI)			**588**			**636**	**97.3%**	**0.14 [−0.41, 0.68]**
Heterogeneity: Chi^2 = 0.98, df = 1 (P = 0.32); I^2 = 0%								
Test for overall effect: Z = 0.49 (P = 0.62)								
Total (95% CI)			**603**			**651**	**100.0%**	**0.09 [−0.45, 0.63]**
Heterogeneity: Chi^2 = 2.01, df = 2 (P = 0.37); I^2 = 1%								
Test for overall effect: Z = 0.33 (P = 0.74)								
Test for subgroup differences: Chi^2 = 1.04, df = 1 (P = 0.31), I^2 = 3.6%								

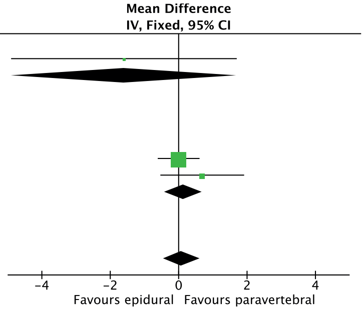
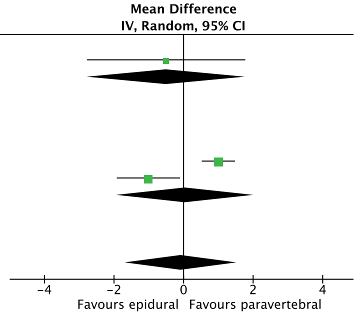


Figure b.

Study or Subgroup	Epidural Mean	Epidural SD	Epidural Total	Paravertebral Mean	Paravertebral SD	Paravertebral Total	Weight	Mean Difference IV, Random, 95% CI
4.2.1 RCT								
Mohta et al. 2009	6.3	1.6	15	6.8	4.2	15	22.7%	−0.50 [−2.77, 1.77]
Subtotal (95% CI)			**15**			**15**	**22.7%**	**−0.50 [−2.77, 1.77]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.43 (P = 0.67)								
4.2.2 Observational								
Malekpour et al. 2017	5	3.7	557	4	4.4	557	40.4%	1.00 [0.52, 1.48]
Shapiro et al. 2017	2.13	1.9	31	3.14	2.8	79	36.9%	−1.01 [−1.92, −0.10]
Subtotal (95% CI)			**588**			**636**	**77.3%**	**0.03 [−1.93, 2.00]**
Heterogeneity: Tau^2 = 1.88; Chi^2 = 14.69, df = 1 (P = 0.0001); I^2 = 93%								
Test for overall effect: Z = 0.03 (P = 0.97)								
Total (95% CI)			**603**			**651**	**100.0%**	**−0.08 [−1.68, 1.52]**
Heterogeneity: Tau^2 = 1.60; Chi^2 = 15.51, df = 2 (P = 0.0004); I^2 = 87%								
Test for overall effect: Z = 0.10 (P = 0.92)								
Test for subgroup differences: Chi^2 = 0.12, df = 1 (P = 0.73), I^2 = 0%								



5 | Epidural analgesia for severe chest trauma: an analysis of current practice on the efficacy and safety.

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Crit Care Res Pract 2019

ABSTRACT

Background Adequate pain control is essential in the treatment of patients with traumatic rib fractures. Although epidural analgesia is recommended in international guidelines, the use remains debatable and is not undisputed. The aim of this study was to describe the efficacy and safety of epidural analgesia in patients with multiple traumatic rib fractures.

Methods A retrospective cohort study was performed. Patients with ≥3 rib fractures following blunt chest trauma who received epidural analgesia between January 2015 and January 2018 were included. The main outcome parameters were the success rate of epidural analgesia and the incidence of medication-related side effects and catheter-related complications.

Results A total of 76 patients were included. Epidural analgesia was successful in a total of 45 patients (59%), including 22 patients without and in 23 patients with an additional analgesic intervention. In 14 patients (18%), epidural analgesia was terminated early without intervention due to insufficient sensory blockade (n = 4), medication-related side effects (n = 4), and catheter-related complications (n = 6). In 17 patients (22%), the epidural catheter was removed after one or multiple additional interventions due to insufficient pain control. Minor epidural-related complications or side effects were encountered in 36 patients (47%). One patient had a major complication (opioid intoxication).

Conclusion Epidural analgesia was successful in 59% of patients; however, 30% needed additional analgesic interventions. As about half of the patients had epidural-related complications or side effects, it remains debatable whether epidural analgesia is a sufficient treatment modality in patients with multiple rib fractures.

INTRODUCTION

Thoracic trauma is frequently encountered in the emergency department and is responsible for 10% to 15% of all trauma admissions.[1] Traumatic rib fractures represent an important injury following blunt thoracic trauma and are identified in 10% to 40% of all trauma patients.[1–3] Rib fractures are associated with severe injury and carry a significant morbidity and mortality rate.[2,4] Factors associated with higher mortality rates are an increased number of rib fractures, advanced age, and concomitant injuries.[1,2,5,6] Furthermore, preexistent (pulmonary) comorbidities have shown to be of significant influence on the outcome.[7]

Adequate pain control is key in the management of rib fractures. Pain associated with rib fractures and other thoracic injury can lead to inefficient ventilation resulting in respiratory complications, need for mechanical ventilation, and prolonged recovery.[2,8] Consequently, multiple analgesic modalities have been described in the last few decades, including epidural catheters, intravenous narcotics, and intercostal, paravertebral, or interpleural blocks. However, epidural analgesia remains the recommended method according to the management guidelines of the Eastern Association for the Surgery of Trauma (EAST).[9]

The use of epidural analgesia remains an important topic of discussion. Over the past decades, several studies reported on beneficial outcomes of epidural analgesia and encouraged the use of epidural analgesia over other analgesic modalities.[1,6,10–16] However, there is growing evidence questioning its advantages over other analgesic modalities in the management of severely injured trauma patients.[4,17–19] Furthermore, the current evidence is of low quality, and therefore, the recommendation of the EAST is conditional.[9]

Epidural analgesia may be insufficient due to the high risk of failure and catheter-related problems. In previous studies on the use of epidural analgesia after surgery, failure rates have been reported up to 47%.[20] Furthermore, the use of epidural analgesia is limited by a number of contraindications, such as hypotension and respiration depression, which is even of greater influence on polytrauma patients.[21]

Further research on the use of epidural analgesia is needed. There is limited literature regarding the efficacy and complications of epidural analgesia in thoracic trauma. Therefore, the aim of this retrospective cohort study was to describe the efficacy and risk of complications of epidural analgesia for patients with multiple traumatic rib fractures.

METHODS

Study Design and Participants

A single-center retrospective cohort study was conducted in the University Medical Center Utrecht, a level 1 trauma center in the Netherlands. To analyze current practice, all adult patients with three or more rib fractures following blunt chest trauma who were admitted between January 2015 and January 2018 were eligible for inclusion. Patients who received epidural analgesia according to clinical documentation in the electronic patient file were included. Data collection was performed with the use of the Dutch National Trauma Registry, a national prospective database containing all trauma patients admitted to the emergency department in the Netherlands. In multitrauma patients, all concomitant injuries were graded using the abbreviated injury scale (AIS).[22] Patients were excluded in case the injury with the highest AIS was not located in the thorax since pain control of such injuries cannot be achieved by thoracic epidural analgesia. Other exclusion criteria included the need for immediate mechanical ventilation upon admission and/or transfer to or from another hospital. A waiver of consent was approved by our institutional review board.

Epidural Analgesia Indication and Procedure

According to our hospital's pain protocol, epidural analgesia was indicated for patients with three or more fractured ribs with insufficient pain control despite the use of paracetamol, nonsteroidal anti-inflammatory drugs, and morphine. Epidural analgesia was also indicated in case of an increased risk of respiratory insufficiency due to pre-existent comorbidities. Indication for epidural analgesia was made primarily in the emergency department, or secondarily, after admission in the surgical ward. The degree of pain was assessed according to the Numerical Rating Scale (NRS) pain score. The NRS is an 11-point scale to measure pain intensity, ranging from 0 (no pain) to 10 (worst imaginable pain).[23]

Contraindications for epidural analgesia included patient refusal, vertebral fractures, spinal cord injury, traumatic brain injury, Glasgow Coma Scale < 15, unstable pelvic fracture, hemodynamic instability, local infection at the insertion site, or coagulopathy. Epidural catheter placement was performed by anesthesiologists at the level of the thoracic injury. A loss of resistance technique was used to guide a 17-gauge Tuohy needle. After reaching the epidural space, a test dose of 3 ml lidocaine 2% was administered to exclude intravascular or intrathecal positioning. Following appropriate catheter insertion, an initial bolus dose with local anesthetics was administered and a continuous epidural infusion was started with a mixture of bupivacaine 2.5 mg/ml and morphine 0.04 mg/ml. The initial infusion rate was 4ml/hr. According to the patient's response and degree of pain relief, the infusion rate was gradually increased up to a maximum of 6 ml/kg/h. If the epidural block is still not provided with satisfactory pain relief with sufficient dermatomal coverage despite a maximum administration of epidural analgesia, the epidural mixture was diluted 50% with a mixture of bupivacaine 1.25 mg/ml and morphine 0.02 mg/ml. The maximum infusion rate after dilution was 12 ml/hr. All patients received paracetamol in combination with a nonsteroidal anti-inflammatory drug (e.g., diclofenac or ibuprofen), unless contraindications were present. A urinary catheter was inserted in all cases and remained in place during administration of epidural analgesia.

The NRS scores were measured every 8 hours by the ward nurses. A specialized pain team visited the patients daily to evaluate the adequacy of sensory block, side effects, and complications. Additionally, data regarding catheter placement difficulties, duration of infusion, number of top-ups, need for additional pain medication, reason for epidural catheter termination, and conversion to another analgesic modality were recorded. A top-up was defined as an additional bolus administration of 3 ml lidocaine 2% or bupivacaine 0.25% to provide or restore a sufficient sensory block.

Baseline Characteristics and Outcome Measures

Data were retrieved from a prospective database and completed by checking the electronic patient files. Baseline characteristics included patient demographics (i.e., age, gender, and relevant co-morbidities), trauma mechanism, injury severity score (ISS) and AIS scores, concomitant injuries, and rib fracture-related characteristics including number and place of fractured ribs, presence of flail segment, bilateral involvement, dislocation, presence of dorsal fracture, first rib involvement, fractures in upper/middle/lower part of the thorax, and indication for rib fixation. Fracture characteristics were evaluated with the use of computed tomography scans.

The primary outcome measure was the success rate of epidural analgesia during the first 5 days of administration. Successful application of epidural analgesia was defined as follows: (1) sufficient pain control or sensory block and (2) no early termination due to medication-related side effects, or catheter-related complications. Epidural analgesia was also classified as successful in case the catheter was removed within the first 5 days due to satisfactory pain, or if necessary for early mobilization. A distinction has been made between success with or without an additional analgesic intervention. Analgesic interventions included epidural top-up/bolus, adjustment of epidural analgesia, and/or administration of intravenous analgesia. Insufficient pain control was defined, according to the hospital pain protocol, as ongoing severe pain (NRS $\geq$ 7) with the maximum administration of paracetamol, nonsteroidal anti-inflammatory drugs, and morphine.[23] Insufficient block was defined as any present sensory block that provided insufficient coverage for the corresponding thoracic injury. Minor medication-related side effects included hypotension, nausea, urinary retention, and pruritus. Major side effects included respiratory depression and intoxication. Minor catheter-related complications included primary placement failure, dislocation, disconnection, occlusion, loosened filter, and leakage. Major complications included focal neurologic deficit, epidural abscess, and hematoma.

Secondary outcome measures included the rate of other complications, length of stay in the intensive care unit (ICU) and hospital, duration of mechanical ventilation, and mortality (in-hospital and 30 days after discharge). Respiratory complications included pneumonia, need for intubation, atelectasis, acute respiratory distress syndrome, and the need of tracheotomy. Pneumonia was defined by presence of clinical symptoms (coughing, fever, and desaturation) requiring antibiotic treatment, regardless of a negative or positive culture. Diagnosis was confirmed by examination of a chest radiograph. Atelectasis was defined as collapse or incomplete expansion of pulmonary parenchyma confirmed on a chest radiograph or computed tomography scan. Acute respiratory distress syndrome was defined by severe hypoxemia with a PaO2/FIO ratio smaller than 100 mmHg.

Statistical Analysis

Data were described using frequencies and percentages for dichotomous and categorical variables, mean and standard deviation (SD) for normally distributed continuous data, and median and interquartile range (IQR) for non-normally distributed continuous data.

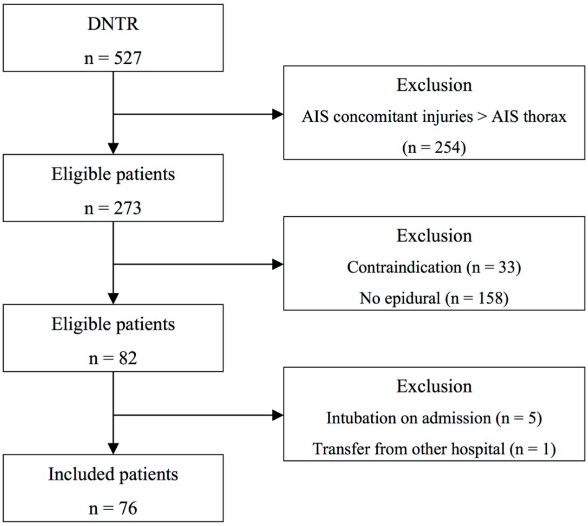
To assess possible rib fracture characteristics independently associated with epidural analgesia failure, a multivariable logistic regression was performed. Subgroup analysis was performed for success of epidural analgesia on in-hospital outcome measures. Statistical significance was defined as $p < 0.05$. All statistical analyses were performed using Stata® 13.0 (StataCorp LP, College Station, TX, USA).

RESULTS

Patients

A total of 527 patients were identified with the Dutch National Trauma Registry. Ultimately, 76 patients who received epidural analgesia were included in this study (Figure 1).

Figure 1. Flowchart representing the selection process of the included patients.



The included patients had a mean age of 58 (SD 14) years and were predominantly male (n = 61, 80%). The median ISS was 14 (IQR 10-17) (Table 1). The mean number of rib fractures was 7 (SD 3), bilateral fractures occurred in 15 patients (20%), and 12 patients (24%) had a flail segment. Sixty-five patients (86%) had one or more fractured rib(s) in the upper thorax (costae 1 to 4), 74 patients (97%) in the middle thorax (costae 5 to 8), and 38 patients (50%) in the lower thorax (costae 9 to 12). Operative rib fixation was performed in 28 patients (37%) (Table 2).

Table 1. Baseline characteristics of patients with epidural analgesia for multiple traumatic rib fractures

Variable	Total
	n = 76
Age (mean ± SD)	58 ± 14
Sex (n, %)	
Male	61 (80)
Female	15 (20)
Trauma mechanism (n, %)	
Motor-vehicle	21 (28)
Bicycle	17 (22)
Fall	19 (25)
Assault	1 (1)
Other	18 (24)
ISS (median, IQR)	14 (10-17)
AIS (median, IQR)	
Head	0 (0-0)
Face	0 (0-0)
Chest	3 (3-3)
Abdomen	0 (0-0)
Extremity	0 (0-2)
External	1 (0-1)
GCS (median, IQR)	15 (15-15)
Concomitant injuries (n, %)	
Lung contusion	25 (33)
Pneumothorax	30 (39)
Hematothorax	8 (11)

Abbreviations: AIS, Abbreviated Injury Scale; GCS, Glasgow Coma Scale; ISS, Injury Severity Score; IQR, interquartile range; n, number; SD, standard deviation.

Sixty-five patients (86%) received an epidural catheter primarily upon time of admission. In 11 patients (14%), catheter placement occurred secondarily during admission since sufficient pain control could not be achieved.

Efficacy of Epidural Analgesia

As demonstrated in the flowchart in Figure 2, epidural analgesia was successful in the first 5 days in a total of 45 patients (59%). In 22 patients (29%), no intervention was needed, and in 23 patients (30%), an additional intervention was needed, which included administration of intravenous morphine in 4 patients (5%), an epidural top-up in 9 patients (12%), or a combination in 10 patients (13%). In 14 patients (18%), epidural analgesia was terminated before day 5 due to insufficient sensory blockade (n = 4), medication-related side effects (n = 4), and catheter-related complications (n = 6). In 17 patients (22%), the epidural catheter was removed after one or multiple additional interventions due to insufficient pain control.

Table 2. Fracture characteristics

Variable	Total
	n = 76
Number of rib fractures (mean ± SD)	7 ± 3
Bilateral rib fractures (n, %)	15 (20)
Location rib fracture (n, %)	
Costae 1-4	65 (86)
Costae 5-8	74 (97)
Costae 9-12	38 (50)
First rib fracture (n, %)	21 (28)
Flail segment (n, %)	12 (24)
Displacement (n, %)	31 (41)
Dorsal fracture (n, %)	54 (71)
Rib fixation (n, %)	28 (37)

Abbreviations: IQR, interquartile range; n, number; SD, standard deviation.

Side Effects and Complications

Medication-related side effects and catheter-related complication were encountered in 37 patients (49%) (Table 3). Minor medication-related side effects were reported in 28 patients (37%) and included nausea (n = 10, 13%), pruritus (n = 10, 13%), and hypotension with need of vasopressin support (n = 7, 9%). One patient (1%) experienced a major side effect due to morphine intoxication with severe systemic effects, most likely because of co-administration of transdermal fentanyl. Minor catheter-related complications occurred in 9 patients (12%) and included primary placement failure (n = 2, 3%), accidental dislocation (n = 1, 1%), disconnection (n = 3, 4%), occlusion (n = 1, 1%), loosened filter (n = 1, 1%), and leakage (n = 1, 1%), and in one patient (1%), epidural medication was administered intravenously. No major complications occurred.

The epidural catheter was removed in only 5% of all patients due to one of the medication-related side effects, and in only 8% of all patients due to a catheter-related complication. All other medication-related side effects could be remedied by adjusting the medication.

Additional Analyses

A multivariable analysis was performed to identify rib fracture characteristics that were independently associated with epidural analgesia failure. The following rib fracture-related characteristics were included in our analysis: number of rib fractures, bilateral involvement, dislocation, first rib involvement, presence of dorsal fracture(s), and location of fractures (upper, middle, or lower part of thorax). No rib fracture characteristics appeared to be independently associated with epidural analgesia failure.

Table 4 shows the in-hospital outcomes stratified by the success rate of epidural analgesia. Two patients died in the group of unsuccessful epidural analgesia. One patient died in the ICU due to sepsis with multiorgan failure, and in one patient, the probable cause of death was a bilateral pneumonia. There were no further differences between the in-hospital outcome measures and success rate of epidural analgesia.

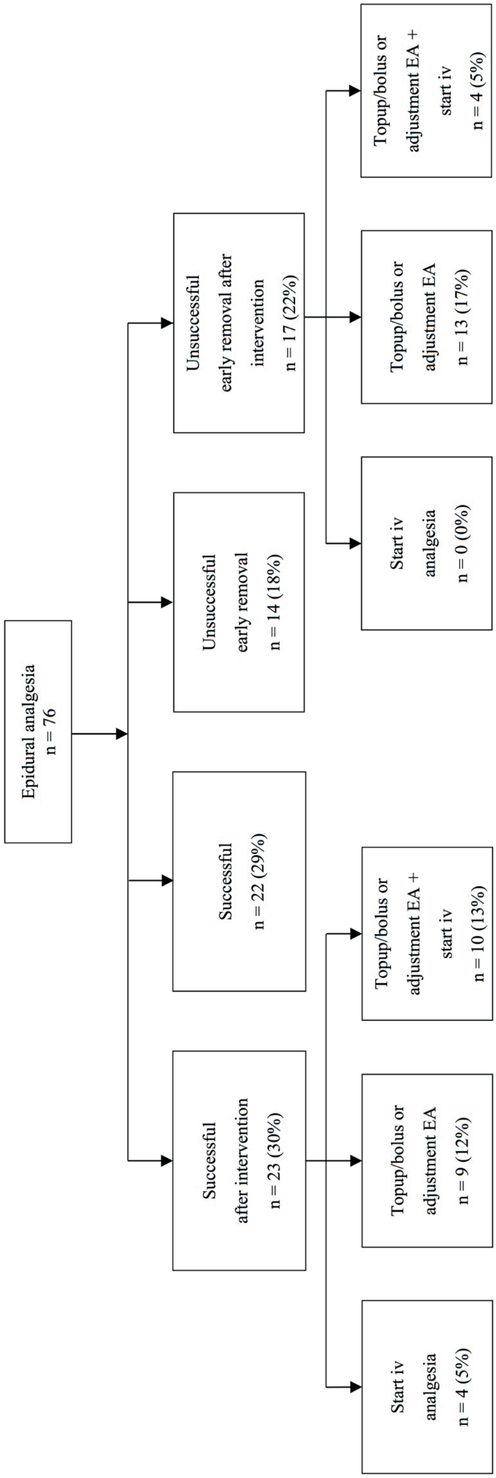


Figure 2. Flowchart representing the efficacy of epidural analgesia in patients with traumatic rib fractures.

Table 3. Side effects and complications

Variable	Total
	n = 37
Medication-related (n, %)	
Hypotension	7 (9)
Nausea	10 (13)
Pruritus	10 (13)
Intoxication	1 (1)
Catheter-related (n, %)	
Primary placement failure	2 (3)
Dislocation	1 (1)
Disconnection	3 (4)
Occlusion	1 (1)
Loosened filter	1 (1)
Leakage	1 (1)
Focal neurologic deficits	0 (0)

Abbreviations: n, number

Table 4. In hospital outcome measures in patients with successful or unsuccessful epidural analgesia.

Variable	Successful	Unsuccessful
	n = 45	n = 31
Hospital length of stay (median, IQR)	10 (7-12)	10 (8-17)
Intensive care length of stay (median, IQR)	0 (0-0)	0 (0-0)
Duration of mechanical ventilation (median, IQR)	0 (0-0)	0 (0-0)
Respiratory complications (n, %)		
Pneumonia	6 (13)	3 (10)
Atelectasis	4 (9)	2 (6)
ARDS	0 (0)	1 (3)
Mortality (n, %)		
During admission	0 (0)	2 (6)
Post-discharge 30 days	0 (0)	0 (0)

Abbreviations: ARDS, Acute Respiratory Distress Syndrome; IQR, interquartile range; n, number; SD, standard deviation.

DISCUSSION

International guidelines recommend epidural analgesia in patients with traumatic rib fractures. However, the evidence regarding the effects and safety of epidural analgesia remains inconclusive.[9] The aim of this study was to report on the success rate of epidural analgesia in patients with multiple rib fractures in the current practice. Epidural analgesia was successful in 59% of patients. Nonetheless, more than half of these patients needed additional interventions to achieve sufficient pain control. Epidural-related minor complications or side effects occurred in 49% of patients; however, this ultimately led to catheter removal in only 10% of all cases.

Previous studies on epidural analgesia after different types of surgery, reported incidence rates of epidural analgesia failure ranging from 13% to 47%.[20] A study by Ready included 25,000 patients who received postoperative epidural analgesia, reporting a failure rate of 32% in thoracic epidural analgesia and 27% in lumbar epidural analgesia. Similar to our findings, the most common reasons for epidural failure reported in the literature are unsatisfactory analgesia- or catheter-related complications such as early catheter dislodgment, leakage, or occlusion.[24,25]

About half of the patients in our study had complications or side effects after epidural analgesia. The majority were minor medication-related side effects such as pruritus, nausea, and hypotension. Other complications reported in the literature include bradycardia, respiratory depression, or decreased consciousness, and catheter-related complications such as epidural hematoma or abscess.[26] In our study, an opioid intoxication due to administration of both epidural and transdermal opioids was encountered in one patient. The incidence of catheter-related complications was 12% in this study, which is similar to the reported incidences in the current literature.[27] Ultimately, this resulted in removal of the epidural catheter in 8% of all cases. Therefore, it must be taken into account that risk of failure of the epidural catheter placement is an important contributing factor on the overall success rate.

The question whether epidural analgesia is beneficial over other analgesic modalities in patients with traumatic rib fractures is debatable.[9,17,28] A large multicenter retrospective cohort study of Gage et al. demonstrated a significant reduction in mortality in patients with multiple rib fractures who received epidural analgesia.[10] Similar findings were reported by Flagel et al., who examined the use of epidural analgesia in patients with multiple rib fractures, using the National Trauma Databank.[1] In a randomized controlled trial, Bulger et al. compared the effect of epidural analgesia with intravenous analgesia in patients with more than three rib fractures.[6] They concluded that epidural analgesia resulted in a decrease of incidence of pneumonia and duration of mechanical ventilation. However, they remarked that the feasibility of this analgesic modality is limited by numerous contraindications. In contrast, a recent matched-cohort study of McKendy et al. showed that patients with one or more fractured ribs who received epidural analgesia were associated with higher rates of respiratory complications and an increased hospital length of stay compared to patients who received other analgesic interventions.[19] They stated that possible explanations for a failed application of epidural analgesia were lack of experience with the use of epidural analgesia and inability of early mobilization. In response to this matched-cohort study of McKendy et al., Amaral Saxe and Jensen performed the same analyses on a similar-sized cohort using a database at their institution.[19,29] However, they found the opposite outcomes and reported a significant reduction in mortality in favor of patients receiving epidural analgesia.[29]

In a recent systematic review and meta-analysis of both observational studies and randomized controlled trials, effects of epidural analgesia were compared with other analgesic modalities in patients with one or more traumatic rib fractures. Nineteen studies were included, representing a total of 2801 patients. This study showed that epidural analgesia provided better pain relief than other analgesic modalities, although few studies reported on pain scores. No beneficial effects from epidural analgesia could be demonstrated for the outcome measures hospital and intensive care unit length of stay, duration of mechanical ventilation, respiratory complications, and mortality.[28]

Several difficulties are associated with the use of epidural analgesia in patients with traumatic rib fractures that are insufficiently highlighted in current practice while important information for decision-making. According to a recent systematic review, incidences of epidural-related complications are poorly reported.[28] Also, there are insufficient data on failure rates, need for additional interventions (e.g., epidural top-ups), duration of sufficient epidural analgesia, and need for additional (escape) medication. Furthermore, patients with multiple rib fractures are often polytrauma patients with concomitant injuries making these patients frequently not eligible for epidural analgesia. Moreover, it remains unclear to what extent outcomes are affected by other concomitant injuries.

This study had several limitations. First, due to the retrospective nature of this study, results are subject to missing data and underreporting. Pain perspective is an important outcome measure; however, this could not be accurately assessed due to missing data. Therefore, we could not provide an overall presentation of the pain scores of this cohort. Additionally, there were insufficient data to calculate the daily used intravenous morphine. However, the number of patients who received additional intravenous opioids has been described. Second, patients were selected using the AIS thorax which might have resulted in a specific subgroup of patients limiting generalizability of the study results. Third, the number of included patients was relatively small. So, although we did not identify a significant difference in mortality between patients with or without successful epidural analgesia, it must be considered that this might be due to a limited power.

Finally, the available literature reporting on the efficacy of epidural analgesia in patients with multiple traumatic rib fractures remains scarce; therefore, this study contributes to the current literature and discussion of optimal management of these patients.

CONCLUSION

Epidural analgesia was successful in 59% of patients; however, 30% needed additional analgesic interventions. As about half of the patients had epidural-related complications or side-effects, it remains debatable whether epidural analgesia is a sufficient treatment modality in patients with multiple rib fractures. Future research could focus on other regional analgesic modalities that are more effective and less susceptible to complications.

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Part III

Operative management of traumatic rib fractures

6 | Fixation of flail chest or multiple rib fractures: current evidence and how to proceed. A systematic review and meta-analysis.

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ABSTRACT

Purpose The aim of this systematic review and meta-analysis was to present current evidence on rib fixation and to compare effect estimates obtained from randomized controlled trials (RCTs) and observational studies.

Methods MEDLINE, Embase, CENTRAL, and CINAHL were searched on June 16th 2017 for both RCTs and observational studies comparing rib fixation versus nonoperative treatment. The MINORS criteria were used to assess study quality. Where possible, data were pooled using random effects meta-analysis. The primary outcome measure was mortality. Secondary outcome measures were hospital length of stay (HLOS), intensive care unit length of stay (ILOS), duration of mechanical ventilation (DMV), pneumonia, and tracheostomy.

Results Thirty-three studies were included resulting in 5874 patients with flail chest or multiple rib fractures: 1255 received rib fixation and 4619 nonoperative treatment. Rib fixation for flail chest reduced mortality compared to nonoperative treatment with a risk ratio of 0.41 (95% CI 0.27, 0.61, $p < 0.001$, $I^2 = 0\%$). Furthermore, rib fixation resulted in a shorter ILOS, DMV, lower pneumonia rate, and need for tracheostomy. Results from recent studies showed lower mortality and shorter DMV after rib fixation, but there were no significant differences for the other outcome measures. There was insufficient data to perform meta-analyses on rib fixation for multiple rib fractures. Pooled results from RCTs and observational studies were similar for all outcome measures, although results from RCTs showed a larger treatment effect for HLOS, ILOS, and DMV compared to observational studies.

Conclusions Rib fixation for flail chest improves short-term outcome, although the indication and patient subgroup who would benefit most remain unclear. There is insufficient data regarding treatment for multiple rib fractures. Observational studies show similar results compared with RCTs.

INTRODUCTION

Rib fractures are very common in patients with thoracic trauma and nowadays still associated with significant morbidity and mortality due to the underlying injuries to the lung and heart resulting in more pulmonary complications.[1–4] Compared to multiple rib fractures, flail chest is associated with a worse outcome due to a higher incidence of respiratory compromise and concomitant injuries.[5,6]

A combination of adequate pain control, respiratory assistance, and physiotherapy is considered the gold standard in management of rib fractures.[3] Over the past decades, there has been a growing interest in rib fixation for flail chest and for multiple rib fractures, however, there is no consensus regarding the indication and patient selection for rib fixation.

In the field of (orthopedic) trauma surgery, there is increasing scientific evidence that inclusion of observational studies could add value to meta-analyses without decreasing quality of the results.[7–10] Adding observational studies result in larger sample sizes and might enable the evaluation of small treatment effects, subgroups, and infrequent outcome measures while also providing information about the generalizability of the results.[11]

The aim of this systematic review and meta-analysis was 1) to present current evidence on outcome after rib fixation compared to nonoperative treatment for both flail chest and multiple rib fractures and 2) to compare effect estimates obtained from RCTs and observational studies.

METHODS

This review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and the Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines.[12,13] A published protocol for this review does not exist. Ethical committee approval did not apply to this study.

Search strategy and eligibility criteria

A structured literature search was conducted in MEDLINE, Embase, CENTRAL and CINAHL on June 16th, 2017 for both randomized controlled trials (RCTs) and observational studies comparing operative to nonoperative treatment of traumatic rib fractures. The search was not restricted by publication date, language, or other limits. The full search syntax is provided in Appendix 1.

All obtained studies from the literature search were independently screened for eligibility based on title and abstract by two reviewers (RBB, JP). Exclusion criteria were animal studies, abstracts of conferences, case-reports, reviews, inclusion of patients younger than 18 years, and studies written in another language than English, French, Dutch or German. Disagreement regarding study selection was resolved by discussion with a third reviewer (RMH). References of included studies were manually screened and citation tracking was conducted using Web of Science to identify additional relevant studies.

Data extraction

Data were extracted by two independent reviewers (RBB, JP), using a data extraction file. Extracted data included first author, year of publication, study period, study design, country, fracture type, number of fractured ribs, number of included patients, number of patients with flail chest or multiple rib fractures (according to the definition used by the original study), age, gender, type of operative treatment, type of nonoperative treatment, duration of follow-up, loss to follow-up, Injury Severity Score (ISS), Abbreviated Injury Scale (AIS), Glasgow Coma Scale (GCS), hemothorax, pneumothorax, pulmonary contusion, type of implant in operative group, mortality during hospitalization, hospital length of stay (HLOS), intensive care unit length of stay (ILOS), duration of mechanical ventilation (DMV), incidence of pneumonia, need for tracheostomy, complications, revision surgery, and implant removal.

Outcome measures

The primary outcome measure was mortality during hospitalization. Secondary outcome measures were HLOS, ILOS, DMV, incidence of pneumonia, need for tracheostomy, complications, revision surgery, and implant removal.

Quality assessment

The Methodological Index for Non-Randomized Studies (MINORS) score was used to assess the included studies.[14] The MINORS is a critical appraisal instrument developed to assess the methodological quality of observational surgical studies. Other quality assessment tools focus on a specific study design while the MINORS is externally validated on RCTs and is therefore a suitable instrument for meta-analyses of different study designs. The MINORS score ranges from 0 to 24 and a higher score reflects better quality. Studies were independently assessed by two reviewers (RBB, JP) using the MINORS criteria and disagreement was resolved by discussion with a third reviewer (RMH). Additional details on the MINORS criteria and scoring system are set out in Appendix 2.

Statistical analysis

Statistical analyses were performed using Review Manager (RevMan, Version 5.3.5 Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014). Data were converted to a mean with standard deviation (SD) using different methods as described in the Cochrane Handbook for Systematic Reviews of Interventions.[15]

Different studies based on the same patient cohort were included only once in the analysis.[16,17] Studies reporting on specific patient subgroups were split and included separately for meta-analysis, if sufficient information was reported; Qiu et al. distinguished between the presence or absence of a flail chest and Voggenreiter et al. made subgroups based on the presence or absence of pulmonary contusion.[18,19] Results from both RCTs and observational studies were pooled in the primary analysis.

Meta-analysis was performed if outcome measures of two or more studies were available. For continuous outcome measures, the inverse variance weighted random effects model was used to estimate the pooled difference in the outcome measure for fixation versus no fixation, with corresponding 95% confidence interval (CI). For dichotomous outcomes, we applied the Mantel–Haenszel method and pooled results are presented as risk ratios (RR) with 95% CI. Heterogeneity between studies was assessed by visual inspection of the forest plots and by estimating statistical measure for heterogeneity, i.e., the I^2 statistic. Inspection of a funnel plot of the study-specific difference in the primary outcome measure against its standard error was done to detect potential publication bias. A two-sided p value < 0.05 was considered statistically significant.

Subgroup and sensitivity analyses

In subgroup analysis, we stratified by study design and pooled effects of RCTs were compared with pooled effects of observational studies. For the analysis of study quality only studies with an arbitrarily chosen MINORS score of 16 or higher were included, similar to previously published meta-analyses in orthopedic trauma surgery studying both study designs. [8,10,20] To assess the impact of improvement in intensive care management over time, we performed a sensitivity analysis including only studies published in the last 5 years. Different methods were used to include studies with zero events in one or both arms of the outcome measure. To assess the sensitivity of the analyses to the choice of the method of analysis, also the crude methods, DerSimonian– Laird method with correction, the inverse variance with and without correction for zero event data, and the Peto method were applied and results were compared for consistency.[21]

RESULTS

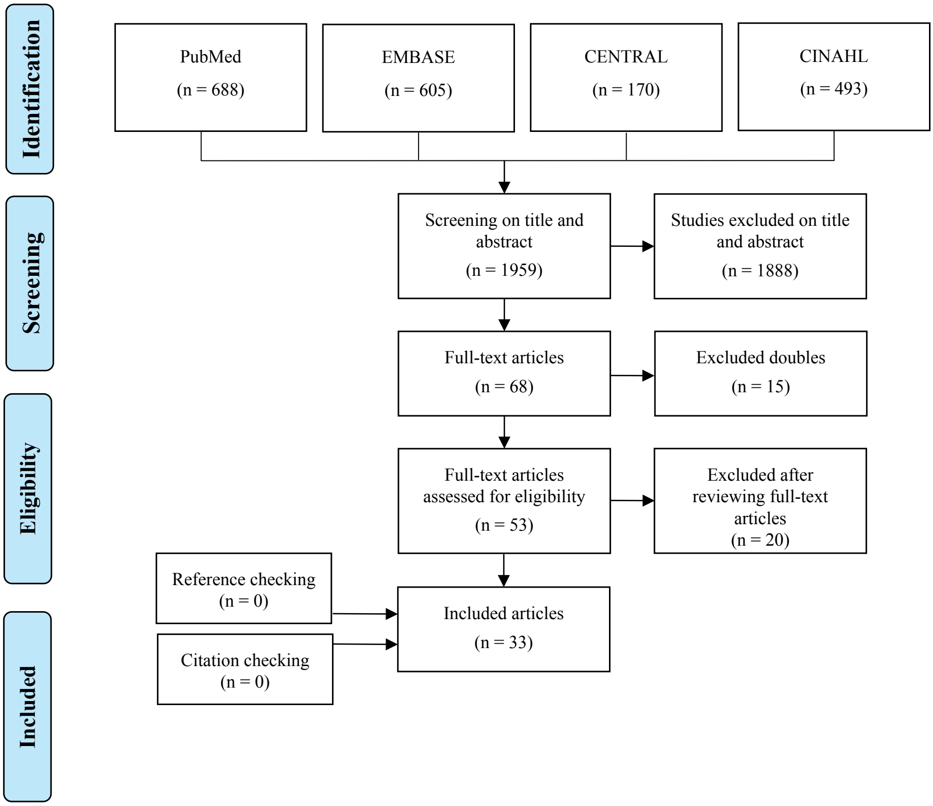
Search

The flowchart of the literature search is presented in Figure 1. Ultimately, 33 studies were included.[16–19,22–50] There were three RCTs, two prospective cohort studies, 14 retrospective cohort studies, and 14 case–control studies.

Patient characteristics

The studies included for meta-analysis included 5874 patients; 1255 received rib fixation and 4619 received nonoperative treatment. In the majority of the studies (n = 20), patients were surgically treated with plates (Tables 1 and Table 2). Other surgical methods were K-wires and Judet or Adkins struts. Nonoperative treatment consisted generally of 'best medical treatment' and included adequate pain management, lung physiotherapy and respiratory support. The weighted average age was 52.9 years and 73% of patients were male. The weighted average of the number of rib fractures was 6.9 in the rib fixation group and 6.0 in the nonoperative group with a weighted mean ISS of 21.2 and 22.4, respectively.

Figure 1. Flowchart of the literature search.



Quality assessment

The average MINORS score of the included studies was 15.4 (SD 2.7; range 9–21). The MINORS score for RCTs was 20 (SD 1.0; range 19–21) and for observational studies 14.9 (SD 2.4; range 9–21). An overview of the study-specific MINORS score is provided in Appendix 3.

Mortality

Twenty-five studies (n = 4826) reported on mortality (Appendix 4).[18,19,22,23,25,27,28,30,32–34,36–50]. Rib fixation resulted in a significant reduction of mortality compared to nonoperative treatment with a risk ratio (RR) of 0.41 (95% CI 0.27, 0.61, $p < 0.001$, $I^2 = 0\%$) (Figure 2). Different methods of incorporating studies in the meta-analysis with zero-event data in one or both arms yielded similar results (Appendix 5). When stratified by study design, RCTs showed a RR 0.57 (95% CI 0.13, 2.52, $p = 0.46$, $I^2 = 0\%$) vs. RR 0.40 (95% CI 0.26, 0.60, $p < 0.001$, $I^2 = 0\%$) in observational studies (Table 3). Figure 3 shows a funnel plot of the odds ratio and standard error of the included studies using the mortality rate; there was no important asymmetry observed.

Table 1. Baseline characteristics of the included studies comparing rib fixation versus nonoperative treatment of traumatic rib fractures.

Study	Study design	Country		Number of patients	Follow-up (months)	Age (years, range or ± SD)	Male (%)	Number of fractured ribs	ISS-score
Dehghan 2018	RC	Canada	RF:	77	NR	52 ± 18	55 (76)	NR	NR
			NOM:	1631		58 ± 18	1176 (72)		
Ali-Osman 2018	RC	USA	RF:	64	NR	68.5 [63-74]	41 (64)	7 [5.25-9]	17.5 [9-25}
			NOM:	135		72 [66-81]	73 (54)	5 [3-7.25]	14 [8-24]
Wijffels 2018	CC	Netherlands	RF:	20	NR	60 [41-69]	15 (75)	9 [8-11]	31 [21-48]
			NOM:	20		57 [44-69]	15 (75)	10 [9-14]	32 [21-41]
Kane 2018	RC	USA	RF:	116	NR	58.3 ± 14.4	NR	NR	21.6 (9.1)
			NOM:	1000		46.9 ± 29.3			16.1 (11.4)
Fitzgerald 2017	CC	USA	RF:	23	NR	68 (63–89)	NR	NR	21 (16-26)
			NOM:	50		75 (65–97)			19 (14-23)
Farquhar 2016	CC	Canada	RF:	19	21.9 ± 13.2	53 ± 14	15 (79)	NR	31.4 ± 9.6
			NOM:	36	16.0 ± 12.1	57 ± 16	25 (69)		29.3 ± 8.1
Pieracci 2016	PC	USA	NOM:	35	16.0 [10.0, 23.0]	50 + 15	24 (69)	9.0 [6.0, 13.0]	22.0 [17.0,38.0]
Defreest 2016	RC	USA	RF:	41	28.3 (9–69)	51 (19–80)	32 (78)	11.2 (6-19)	27.5 (16-48)
			NOM:	45	13.0 (3–43)	56 (23–89)	39 (87)	10.6 (6-23)	29.3 (16-66)
Uchida 2016	CC	Japan	RF:	10	NR	63 [51,72]	7 (70)	5 [4, 8]	NR
			NOM:	10		57 [53,75]	7 (70)	5 [2, 7]	
Velasquez 2016	CC	USA	RF:	20	6 [4,10]	51 [41,63]	NR	5 [4, 8]	9 [9,16]
			NOM:	20	16 [11,22]	45 [36,55]		5 [4.6, 5]	13 [9,17]
Qiu a 2016	RC	China	RF:	21	NR	35 ± 13	15 (48)	6.0 ± 1.3	NR
			NOM:	17		36 ± 14	12 (71)	5.9 ± 1.3	
Qiu b 2016	RC	China	RF:	65	NR	38 ± 12	46 (71)	3.2 ± 1.2	NR
			NOM:	59		36 ± 12	42 (71)	3.5 ± 1.2	
Jayle 2015	CC	France	RF:	10	21.7 ± 7.8	48 ± 11	8 (80)	7.7 ± 2.4	21.7 ± 7.80

Table 1. Baseline characteristics of the included studies comparing rib fixation versus nonoperative treatment of traumatic rib fractures. (continued)

Study	Study design	Country		Number of patients	Follow-up (months)	Age (years, range or ± SD)	Male (%)	Number of fractured ribs	ISS-score
			NOM:	10	32.3 ± 19.3	51 ± 13	8 (80)	6.6 ± 2.9	32.3 ± 19.3
Zhang Y 2015	RC	China	RF:	24	38 [33, 54.25]	43 [34,50]	19 (79)	11.5 [8, 15.3]	38 [34,43]
			NOM:	15	60 [38, 99.75]	47 [35,55]	14 (93)	11 [7, 16]	38 [35,43]
Zhang X 2015	CC	China	RF:	23	419,4 ± 107.1	58 ± 12	21 (72)	7.8 ± 1.5	NR
			NOM:	29	419,4 ± 107.1	60 ± 10	16 (70)	7.4 ± 1.7	
Wada 2015	CC	Japan	RF:	84	33 (24-45)	NR	59 (70)	NR	NR
			NOM:	336	42 (23-58)		225 (76)		
Wu 2015	PC	China	RF:	75	15.3 ± 6.4	52 ± 5	75 (100)	8.1 (6-12)	NR
			NOM:	89	26.5 ± 6.9	51 ± 3	89 (100)	7.9 (6-11)	
Majercik 2015	CC	USA	RF:	137	11.4 + 5.7	56 ± 16	110 (80)	6.5 ± 2.0	21 ± 10.7
			NOM:	274	12.3 + 9.1	55 ± 20	56 (80)	4.6 ± 2.3	22 ± 11.8
Xu 2015	RC	China	RF:	17	NR	36 ± 14	12 (71)	6.8 ± 2.1	21.8 ± 7.8
			NOM:	15		39 ± 12	12 (80)	7.4 ± 1.6	24.0 ± 8.0
Granhed 2014	CC	Sweden	RF:	60	NR	NR	53 (77)	7.5 (2-14)	21.7 ± 10.7
			NOM:	153		NR	NR	NR	30.9 ± 13.3
Doben 2014	CC	USA	RF:	10	21.6 (8-59)	47 ± 15	9 (90)	8.3 (4-20)	26.3 ± 9.5
			NOM:	11	28.5 (6-50)	57 ± 17	7 (64)	9.2 (6-16)	35.7 ± 12.7
Marasco 2013	RCT	Australia	RF:	23	90	58 ± 17	20 (87)	11.0 ± 3.1	35.0 ± 11.4
			NOM:	23	90	59 ± 10	20 (87)	11.3 ± 4.7	30.0 ± 6.3
Khandelwal 2011	PC	India	RF:	31	30	47	40 (66)	3.1	NR
			NOM:	29	30	45	NR	3.3	NR
Moya 2011	CC	USA	RF:	16	18 ± 12	45 ± 16	14 (88)	8 ± 4	24 ± 7
			NOM:	32	16 ± 11	47 ± 14	26 (81)	8 ± 3	25 ± 9
Althausen 2011	CC	USA	RF:	22	17.84 ± 4.51	48	17 (74)	5.9	25.1
			NOM:	28	NR	51	23 (79)	7.3	24.3

Table 1. Baseline characteristics of the included studies comparing rib fixation versus nonoperative treatment of traumatic rib fractures. (continued)

Study	Study design	Country		Number of patients	Follow-up (months)	Age (years, range or ± SD)	Male (%)	Number of fractured ribs	ISS-score
Solberg 2009	RC	USA	RF:	9	16.1 ± 6.7	39 ± 17	6 (67)	NR	24.9 ± 6.5
			NOM:	7	12.0 ± 2.3	41 ± 13	5 (71)		24.8 ± 6.2
Nirula 2006	CC	USA	RF:	30	NR	52	NR	NR	25.7
			NOM:	30		50			27.5
Granetzny 2006	RCT	Germany	RF:	20	2	41 ± 8	17 (85)	4.4	16.8 ± 3.5
			NOM:	20	2	36 ± 15	16 (80)	4.0	18.0 ± 5,1
Balci 2004	RC	Turkey	RF:	27	NR	35 ± 8	20 (74)	NR	21.0 ± 7.4
			NOM:	37		31 ± 10	28 (76)		18.4 ± 8.1
Tanaka 2002	RCT	Japan	RF:	18	360	43 ± 12	12 (67)	8,2 ± 3.3	33 ± 11
			NOM:	19	360	46 ± 9	14 (74)	8.2 ± 2.6	30 ± 8
Voggenreiter a 1996	RC	Germany	RF:	10	NR	55 ± 8	NR	NR	31.0 ± 7.0
			NOM:	18		44 ± 19			36.6 ± 12.3
Voggenreiter b 1996	RC	Germany	RF:	10	NR	50 ± 16	NR	NR	37.0 ± 7.9
			NOM:	4		48 ± 27			37.8 ± 19.5
Ahmed 1995	RC	UAE	RF:	26	(3-9)	20-60 (range)	23 (88)	NR	NR
			NOM:	38	(3-9)	10-60 (range)	36 (95)		
Kim 1981	RC	France	RF:	18	NR	NR	NR	NR	NR
			NOM:	142					
Aubert 1981	RC	France	RF	224	NR	NR	NR	NR	NR
			NOM:	NR					

Abbreviations: CC case control; PC prospective cohort; RC retrospective cohort; RCT randomized controlled trial; RF rib fixation; UAB United Arab Emirates; USA, United States of America; NOM nonoperative treatment; NR not reported.

Table 2. Treatment characteristics of the included studies comparing operative versus nonoperative management of traumatic rib fractures.

Study	Treatment groups	Included fractures	Flail chest in surgery group	Indication for surgery
Dehghan 2018	NR	FC	77 (100%)	NR
Ali-Osman 2018	RF: Plates + screws NOM: Aggressive pain management	FC + MRF	NR	Displaced rib fractures, uncontrolled pain, rib crepitus with breathing
Wijffels 2018	RF: Plates + intramedullary nails NOM: Supportive management	FC	20 (100%)	Flail chest
Kane 2018	RF: NR NOM: Multimodal analgesia protocol	FC + MRF	75 (65%)	3 consecutively displaced rib fractures plus FEV1 and FVC less than 50% predicted
Fitzgerald 2017	RF: Plates + screws NOM: NR	FC + MRF	NR	NR
Farquhar 2016	RF: Plates + screws NOM: Standard conservative treatment	FC	19 (100%)	FC (≥ 3 fractures), displaced, segmental rib fractures with respiratory insufficiency
Pieracci 2016	RF: Titanium plates + screws NOM: Standard conservative treatment	FC + MRF	28 (80%)	FC (≥ 3 fractures), ≥ 3 displaced fractures; ≥ 30% thorax volume loss, failure treatment within first 72h
Defreest 2016	RF: Titanium locking plates + screws NOM: NR	FC	41 (100%)	Failure to wean, intractable pain, or respiratory failure
Uchida 2016	RF: Titanium plates + locking screws NOM: Conservative management + chest strap	FC + MRF	NR	Flail segment, massive dislocation, >15mm fracture overlapping, or pain
Velasquez 2016	RF: Thoracic Osteosynthesis System (STRATOS) NOM: NR	FC + MRF	NR	FC (>3 fractures), ≥ 3 ribs fractured + respiratory failure, intractable pain, thorax deformity, or displacement
Qiu a 2016	RF: AO standard plates + cancellous screws NOM: NR	FC	21 (100%)	NR
Qiu b 2016	RF: AO standard plates + cancellous screws NOM: NR	MRF	0 (0%)	NR
Jayle 2015	RF: Titanium plates + screws NOM: NR	FC	10 (100%)	FC (≥ 3 fractures)
Zhang Y 2015	RF: ORIF NOM: NR	FC + PC	24 (100%)	NR
Zhang X 2015	RF: Claw-type titanium plates NOM: Standard conservative treatment	FC	23 (100%)	FC (≥ 3 fractures)
Wada 2015	RF: ORIF NOM: NR	FC + MRF	84 (100%)	NR

Table 2. Treatment characteristics of the included studies comparing operative versus nonoperative management of traumatic rib fractures. (continued)

Study	Treatment groups	Included fractures	Flail chest in surgery group	Indication for surgery
Wu 2015	RF: Nickel titanium alloy devices	FC + MRF	31 (41%)	FC (≥ 3 fractures), ≥ 3 rib fractures, dislocation, thorax deformity, or chest cavity active bleeding
	NOM: Conservative management + chest strap			
Majercik 2015	RF: Plates + locking screws	FC + MRF	101 (75%)	FC, severely displaced fractures, intractable pain, failure to wean, or combination of these
	NOM: Standard conservative management			
Xu 2015	RF: Titanium locking plates	FC	17 (100%)	NR
	NOM: Standard conservative management			
Granhed 2014	RF: Titanium plates + intramedullary splints	FC + MRF	56 (93%)	Impaired saturation in spite of oxygen administration; intractable pain
	NOM: NR			
Xu 2015	RF: Titanium locking plates	FC	17 (100%)	NR
	NOM: Standard conservative management			
Granhed 2014	RF: Titanium plates + intramedullary splints	FC + MRF	56 (93%)	Impaired saturation in spite of oxygen administration; intractable pain
	NOM: NR			
Doben 2014	RF: Plates + intramedullary nails	FC	10 (100%)	Failure of nonoperative management
	NOM: Standard conservative management			
Marasco 2013	RF: Inion resorbable plates + bicortical screws	FC	23 (100%)	FC (≥ 3 fractures) and ventilator dependent without prospect of weaning within 48h
	NOM: Mechanical ventilator management			
Khandelwal 2011	RF: Titanium plates + screws	FC + MRF	2 (5.3%)	NRS score > 7 on 10 days after trauma
	NOM: NR			
Moya 2011	RF: Titanium or steel plates	FC + MRF	9 (56%)	intractable pain, ≥ 2 severely displaced rib fractures with pain, and respiratory failure
	NOM: NR			
Althausen 2011	RF: Locking plates + locking screws	FC	22 (100%)	FC with displacement, failure to wean, respiratory failure, or need of thoracotomy
	NOM: NR			
Solberg 2009	RF: Titanium plates	FC	9 (100%)	superolateral chest wall deformity
	NOM: Ventilatory pneumatic stabilization			
Nirula 2006	RF: Adkin struts	FC + MRF	15 (50%)	FC, intractable pain, bleeding, and inability to wean
	NOM: NR			
Granetzny 2006	RF: K-wires and/or stainless-steel wire	FC	20 (100%)	FC (≥ 3 rib fractures) with paradoxical chest wall movement
	NOM: Strapping and packing			

Table 2. Treatment characteristics of the included studies comparing operative versus nonoperative management of traumatic rib fractures. (continued)

Study	Treatment groups	Included fractures	Flail chest in surgery group	Indication for surgery
Balci 2004	RF: Suture and traction NOM: Endotracheal intubation	FC	27 (100%)	FC with paradoxical chest wall movement, respiratory failure, dyspnea, and insufficient blood gas
Tanaka 2002	RF: Judet struts NOM: Internal pneumatic stabilization	FC	18 (100%)	FC (≥ 6 fractures) with respiratory failure requiring mechanical ventilation and failure to wean
Voggenreiter a 1996	RF: ASIF reconstruction plates NOM: Standard conservative management	FC without PC	10 (100%)	FC and thoracotomy for other injury, respiratory failure, paradoxical chest wall movement, or deformity
Voggenreiter b 1996	RF: ASIF reconstruction plates NOM: Standard conservative management	FC + PC	10 (100%)	FC and thoracotomy for other injury, respiratory failure, paradoxical chest wall movement, severe deformity
Ahmed 1995	RF: K-wires NOM: Endotracheal intubation	FC	26 (100%)	NR
Kim 1981	RF: Judet struts NOM: Internal pneumatic stabilization	FC	18 (100%)	NR
Aubert 1981	RF: Osteosynthesis NOM: Ventilator assistance, physiotherapy	FC	22 (100%)	NR

Abbreviations: RF rib fixation; NOM nonoperative management; NR not reported; FC flail chest; MRF multiple rib fractures; PC pulmonary contusion.

Hospital stay length of stay

Twenty-one studies (n = 4770) reported on length of hospital stay (Appendix 4).[16,17,23,25,26,31–35,37–45,47,50,51] Rib fixation did not result in a significant reduction of HLOS compared to nonoperative treatment with a mean difference of −1.46 days (95% CI −4.31, 1.39, $p = 0.32$, $I^2 = 96\%$) (Appendix 6). When stratified by study design, the pooled mean difference of RCTs (−8.33 days; 95% CI −14.6, −2.1; $p < 0.001$, $I^2 = 46\%$) was greater compared to observational studies (−0.77; 95% CI −3.72, 2.18; $p = 0.61$, $I^2 = 97\%$) (Table 3).

ICU length of stay

Twenty-six studies (n = 4520) reported on length of ICU stay (Appendix 4).[16–18,22–26,28,30–33,35–44,47,50,51] Rib fixation resulted in a significant reduction of ILOS compared to nonoperative treatment with a mean difference of −2.0 (95% CI −3.61, −0.38, $p = 0.02$, $I^2 = 85\%$) (Appendix 7). When stratified by study design, RCTs showed a greater difference compared to observational studies (Table 3).

Table 3. Subgroup & sensitivity analyses of studies included in a meta-analysis of rib fractures comparing rib fixation versus nonoperative treatment for patients with a flail chest.

Analysis description	Mortality			HLOS			ILOS		
	n	RR (95% CI)	P value	n	MD (95% CI)	P value	n	MD (95% CI)	P value
All studies	25	0.41 (0.27, 0.61)	p<0.001	21	-1.46 (-4.31, 1.39)	0.32	26	-2.00 (-3.61, -0.38)	0.02
Subgroup analysis									
RCT	3	0.57 (0.13, 2.52)	0.46	2	-8.33 (-14.60, -2.07)	0.009	3	-6.37 (-9.72, -3.03)	p<0.001
Observational studies	22	0.40 (0.26, 0.60)	p<0.001	19	-0.77 (-3.72, 2.18)	0.61	23	-1.53 (-3.21, 0.15)	0.07
Sensitivity analysis									
High-quality studies	13	0.71 (0.35, 1.44)	0.34	15	-3.53 (-7.27, 0.21)	0.06	17	-2.83 (-4.75, -0.91)	0.004
Studies after 2012	17	0.43 (0.25, 0.77)	0.004	16	-0.64 (-3.98, 2.69)	0.71	19	-1.51 (-3.40, 0.37)	0.12
Analysis description	DMV			Pneumonia			Tracheostomy		
	n	MD (95% CI)	P value	n	RR (95% CI)	P value	n	MD (95% CI)	P value
All studies	27	-4.01 (-5.58, -2.45)	p<0.001	25	0.59 (0.42, 0.83)	p<0.001	16	0.59 (0.39, 0.90)	0.01
Subgroup analysis									
RCT	3	-5.88 (-11.32, -0.44)	0.03	3	0.36 (0.15, 0.85)	0.02	2	0.38 (0.14, 1.02)	0.05
Observational studies	23	-3.79 (-5.46, -2.11)	p<0.001	22	0.63 (0.44, 0.92)	0.02	14	0.63 (0.40, 1.01)	0.05
Sensitivity analysis									
High-quality studies	17	-3.87 (-6.06, -1.68)	0.000	16	0.55 (0.37, 0.82)	0.004	10	0.57 (0.41, 0.80)	0.001
Studies after 2012	18	-3.27 (-5.11, -1.43)	0.000	16	0.73 (0.50, 1.06)	0.10	12	0.73 (0.47, 1.14)	0.16

Abbreviations: RCT randomized controlled trial; RR risk ratio; MD mean difference; CI confidence interval; n no. of studies; RR risk ratio; MD mean difference.

Figure 2. Mortality in a systematic review of rib fractures comparing operative to nonoperative treatment.

Study or Subgroup	Surgery Events	Surgery Total	Conservative Events	Conservative Total	Weight	Risk Ratio M-H, Random, 95% CI
1.1.1 Observational						
Ahmed 1995	2	20	11	19	8.6%	0.17 [0.04, 0.68]
Ali-Osman 2018	1	64	13	135	4.0%	0.16 [0.02, 1.21]
Aubert 1981	3	22	54	224	13.9%	0.57 [0.19, 1.66]
Balci 2004	3	27	10	37	11.4%	0.41 [0.12, 1.35]
Defreest 2016	1	41	5	45	3.7%	0.22 [0.03, 1.80]
Dehghan 2018	2	77	160	1631	8.5%	0.26 [0.07, 1.05]
Farquhar 2016	1	19	1	36	2.2%	1.89 [0.13, 28.63]
Fitzgerald 2017	0	23	2	50	1.8%	0.42 [0.02, 8.51]
Kane 2018	1	116	53	1000	4.2%	0.16 [0.02, 1.17]
Kim 1981	1	18	60	142	4.4%	0.13 [0.02, 0.89]
Pieracci 2016	0	35	0	35		Not estimable
Qiu a 2016	1	21	2	17	3.0%	0.40 [0.04, 4.09]
Uchida 2016	0	10	0	10		Not estimable
Velasquez 2016	0	20	2	20	1.8%	0.20 [0.01, 3.92]
Voggenreiter a 1996	0	10	7	18	2.1%	0.12 [0.01, 1.83]
Voggenreiter b 1996	3	10	1	4	4.3%	1.20 [0.17, 8.38]
Wada 2015	3	84	6	336	8.7%	2.00 [0.51, 7.83]
Wijffels 2018	2	20	1	20	3.0%	2.00 [0.20, 20.33]
Wu 2015	1	75	4	89	3.4%	0.30 [0.03, 2.60]
Xu 2015	0	17	1	15	1.7%	0.30 [0.01, 6.77]
Zhang X 2015	0	23	0	29		Not estimable
Zhang Y 2015	0	24	2	15	1.8%	0.13 [0.01, 2.50]
Subtotal (95% CI)		**776**		**3927**	**92.6%**	**0.40 [0.26, 0.60]**
Total events	25		395			
Heterogeneity: Tau² = 0.00; Chi² = 17.52, df = 18 (P = 0.49); I² = 0%						
Test for overall effect: Z = 4.32 (P < 0.0001)						
1.1.2 RCT						
Granetzny 2006	2	20	3	20	5.7%	0.67 [0.12, 3.57]
Marasco 2013	0	23	1	23	1.6%	0.33 [0.01, 7.78]
Tanaka 2002	0	18	0	19		Not estimable
Subtotal (95% CI)		**61**		**62**	**7.4%**	**0.57 [0.13, 2.52]**
Total events	2		4			
Heterogeneity: Tau² = 0.00; Chi² = 0.15, df = 1 (P = 0.70); I² = 0%						
Test for overall effect: Z = 0.74 (P = 0.46)						
Total (95% CI)		**837**		**3989**	**100.0%**	**0.41 [0.27, 0.61]**
Total events	27		399			
Heterogeneity: Tau² = 0.00; Chi² = 17.94, df = 20 (P = 0.59); I² = 0%						
Test for overall effect: Z = 4.36 (P < 0.0001)						
Test for subgroup differences: Chi² = 0.21, df = 1 (P = 0.64), I² = 0%						

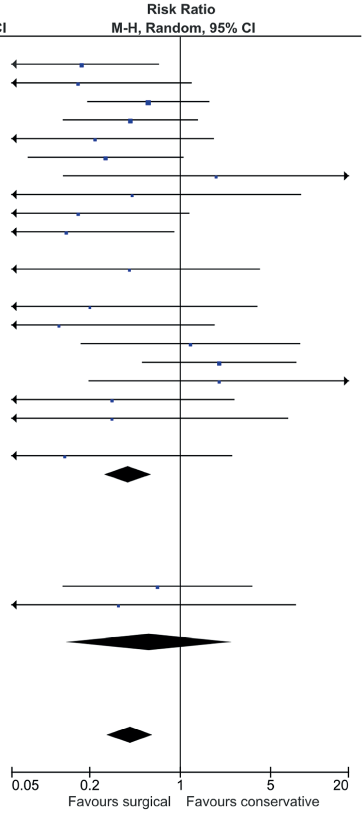
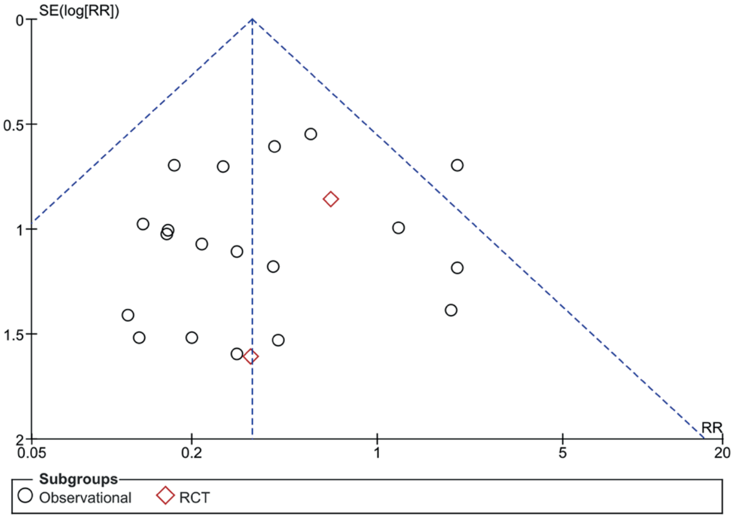


Figure 3. Funnel plot of studies included in a meta-analysis reporting mortality rates after operative or nonoperative treatment of rib fractures (RR risk ratio, SE standard error).



Duration of mechanical ventilation

Twenty-seven studies (n = 2063) reported on duration of mechanical ventilation (Appendix 4).[16–19,22–28,30–32,35–42,45–47,49–51] Rib fixation resulted in a significant reduction of days on mechanical ventilation compared to nonoperative treatment with a mean difference of −4.01 (95% CI −5.58, −2.45, $p < 0.001$, $I^2 = 91\%$) (Appendix 8). When stratified by study design, RCTs showed a greater difference compared to observational studies (Table 3).

Pneumonia

Twenty-five studies (n = 4485) reported on the incidence of pneumonia (Appendix 4).[16–19,22,24–26,28,30–33,37–39,41–44,47,50,51] Rib fixation resulted in a significant reduction of pneumonia compared to nonoperative treatment with a risk ratio of 0.59 (95% CI 0.42, 0.83, $p = 0.002$, $I^2 = 79\%$) (Appendix 9). When stratified by study design both subgroups showed similar results (Table 3).

Tracheostomy

Fourteen studies (n = 1541) reported on the need of tracheostomy (Appendix 4).[16–18,22,25,26,28,30,32,34,36–38,45,50] Rib fixation resulted in a significant reduction of tracheostomies compared to nonoperative treatment with a risk ratio of 0.59 (95% CI 0.36, 0.90, $p = 0.01$, $I^2 = 72\%$) (Appendix 10). When stratified by study design both subgroups showed similar results (Table 3).

Other outcome measures

Nine studies (n = 1174) reported on implant removal; five studies reported zero events and four studies reported implant removal ranging from 1.5 to 4.9% (Appendix 4).[17,26,28,36–38,40,45,48] Eleven studies reported on wound infection; five studies reported zero events and six studies reported a wound infection rate ranging from 1.7 to 25%.[18,23,24,26–30,46] Other short and/or long-term complications were poorly reported and described mainly respiratory complications.

Sensitivity analyses

In sensitivity analysis for study quality, results did not change significantly except for HLOS which increased in favor of rib fixation in studies with higher quality with a mean difference of −3.53 (95% CI −7.27, −0.21, $p = 0.06$) (Table 3). Results from studies published after 2012 did not show a reduced HLOS, ILOS, incidence of pneumonia or need for tracheostomy after rib fixation (Table 3).

DISCUSSION

In this systematic review and meta-analysis of RCTs and observational studies, rib fixation for patients with flail chest resulted in lower mortality, shorter ILOS and DMV, lower pneumonia rate, and lower need for tracheostomy. Pooled results from RCTs and observational studies were similar for all studied outcome measures although results from RCTs showed a larger treatment effect for

HLOS, ILOS, and DMV. Results from recent studies showed lower mortality and shorter DMV after rib fixation, but there were no significant differences for the other outcome measures. The implant removal rate ranged from 1.5 to 4.9%. There were not enough studies of only patients with multiple rib fractures to perform meta-analyses on rib fixation for this patient population.

This meta-analysis included a large number of studies demonstrating the potential short-term benefit of rib fixation over nonoperative treatment for flail chest. Most often the indication for rib fixation was the presence of flail chest and to a lesser extent respiratory failure or intractable pain. Even though almost all studies included patients with flail chest, in many cases it was unclear whether it was a radiological or clinical flail chest making results harder to interpret. It is important to distinguish between these subgroups as respiratory compromise as well as injury severity is thought to mark important differences and influence outcome. The heterogeneous indication and patient populations reported on in the literature mask the exact indication and patient subgroup that would benefit most from rib fixation and consequently the adaptation of rib fixation in current practice.

Very few studies are available investigating patients with multiple rib fractures without flail chest. In a retrospective study, Qiu et al. performed separate analysis on patients with multiple rib fractures without flail segment and showed good short-term results and an earlier return to 'normal activity' after rib fixation.[18] Another notable study on multiple rib fractures was from Khandelwal et al. who described a prospective cohort of patients with multiple rib fractures where most patients had two or three rib fractures and only two (5.3%) had a flail chest.[29] They reported a significant reduction of pain and earlier return to work after rib fixation. No other studies have reported on rib fixation compared to nonoperative treatment focused on multiple rib fractures even though this is the largest subgroup of patients seen in daily practice.

In this review, we have included both RCTs and observational studies and show similar results for all outcome measures between both designs. Concato et al., Benson et al., and Ioannides et al. have provided an empirical basis for the comparison of RCTs and observational studies and showed results from these different designs can be remarkably similar, but can be rather different as well.[52–54] Although, treatment effects can be similar across studies regardless of design, genuine differences in treatment effects between different patient populations may be masked by biases in observational studies. Pooling results across different design could then lead to incorrect inferences. The judgement about validity of pooling results from different designs should be made on a case-by-case basis, since for instance the potential for confounding bias is context- and research-specific. Still, within the field of (orthopedic) trauma surgery there is growing evidence showing the potential of observational studies in meta-analyses leading to more robust conclusions without decreasing quality of the results.[7–9]

Interestingly, RCTs in this study showed a larger treatment effect for some of the outcome measures as compared to observational studies. It is thought that observational studies tend to overestimate treatment effect which is possibly the result of the surgeon introducing a selection bias by choosing the optimal patient or publication bias.[55,56] The three RCTs available on this subject all had very strict inclusion and exclusion criteria resulting in specific patient groups where treatment effects could be demonstrated yet with limited generalizability.[22,23,50] In observational studies, usually with less strict inclusion and exclusion criteria, an unclear indication together with other serious concomitant injuries can result in a selection of patients including patients who would benefit more from nonoperative treatment. A wrong patient selection can reduce measured treatment effects after rib fixation which could explain differences found between RCTs and observational studies in this specific topic. Additionally, differences in timing of the surgical procedure between studies might have introduced bias in comparability as early surgical stabilization is associated with favorable outcomes.[57] However, data regarding timing of surgery were not sufficiently reported in the included studies to further explore these effects. Finally, improvement of intensive care management over time could have attributed to differences in treatment effects as shown by our sensitivity analysis. In more recent studies only mortality and DMV improved after rib fixation, but there was no difference for the other outcome measures.

This study had some limitations. First, the results may be altered by missed studies in the literature search or by publication bias. However, we performed an extensive search using multiple databases with citation and reference checking of included studies. A funnel plot of the primary outcome measure did not suggest bias due to selective publication. Therefore, we are confident that we have a representative overview of the current literature. Second, we did not distinguish between studies with both flail chest and multiple rib fractures and studies including only flail chest patients. Very few patients with multiple rib fractures were included in these studies. Therefore, we think results from these studies translate to flail chest patients and should not be excluded from analyses. Still, cautious interpretation of study results is necessary as the variety of definitions used in the included studies might have resulted in a high in-between study variability of patient samples.

More research is needed to further identify the right indication and right patient for rib fixation. As previously mentioned, RCTs in this heterogenic population are very difficult to perform and for adequate subgroup analyses sufficiently large sample sizes are needed. In the rapidly developing area of surgery, RCTs can be expensive, time consuming, and often have limitations in terms of generalizability and small sample sizes due to strict inclusion and exclusion criteria.[58,59] Observational studies show similar results as compared to RCTs and might be an achievable first step in gathering high-quality evidence. Currently a large prospective multicenter database is created in the Netherlands including both patients with flail chest and multiple rib fractures from multiple level-1 trauma centers, aiming to answer the above questions with the use of large sample sizes and long-term follow-up.[60]

CONCLUSION

Rib fixation significantly improves short-term outcome for patients with flail chest, although the indication and patient subgroup who would benefit most from this treatment remain unclear. There is not enough data regarding patients with multiple rib fractures without flail segment. Observational studies show similar results as compared to RCTs and might be an achievable first step in gathering high-quality evidence. Larger prospective studies are required to investigate proper indications and relevant outcome after rib fixation.

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Appendix 1. Search syntax representing the used search strings in the different databases.

Database	Syntax
PubMed (n = 698)	("Rib Fractures"[Mesh] OR rib fracture* OR "flail chest"[Mesh]) AND (surgical management OR fixation OR plating OR orif)
EMBASE (n = 847)	((('rib fracture'/exp OR (rib NEAR/1 fracture*):ab,ti OR 'flail chest':ab,ti) AND ('fracture treatment'/exp OR orif:ab,ti OR fixation:ab,ti OR plating:ab,ti)
CENTRAL (n = 207)	("rib fracture*" OR "flail chest")
CINAHL (n = 612)	("rib fracture*")

Appendix 2. MINORS assessment criteria

Criteria	**2**	**1**	**0**
A clearly stated aim	Aim or hypothesis including outcomes have been reported	Aim or hypothesis have been reported without a clear outcome	Not reported
Inclusion of consecutive patients	Explicit inclusion and exclusion criteria have been reported	Unclear or poor description inclusion and exclusion criteria have been reported	Not reported
Prospective collection of data	Prospective	Retrospective	Not reported
Endpoints appropriate to the aim of the study	Outcomes are appropriate to the aim of the study	Outcomes are not appropriate to the aim of the study	Not reported
Unbiased assessment of the study endpoint	Blind evaluation of objective outcomes and double-blind evaluation of subjective outcomes	One or more outcomes have been blinded	No blinding / not reported
Follow-up period appropriate to the aim of the study	≥ 1 year	< 1 year	Not reported
Loss to follow-up less than 5%	≤ 5%	> 5% and ≤ 20%	Not reported / >20%
Prospective calculation of the study size	Power analysis has been performed	Explanation for the number of included patients without a power analysis	Not reported / not performed
An adequate control group	Plate or intramedullary fixation compared with a conservative treatment	Not applicable	Not reported
Contemporary groups	Study group and controls have been managed during the same time period	Study group and controls have not been managed during the same time period	Not reported / unclear discription
Baseline equivalence of groups	Baseline characteristics have been described for both groups and are comparable	Baseline characteristics have not been described thoroughly or are not comparable	Not reported
Adequate statistical analyses	Statistical analysis has been described including the type of test	Inadequate statistical analysis	Not reported

Appendix 3. Quality assessment of all included studies in a systematic review of rib fractures comparing operative to nonoperative treatment.

Criteria	Aubert 1981	Kim 1981	Ahmed 1995	Voggenreiter 1996	Tanaka 2002	Balci 2004	Granetzny 2005	Nirula 2006	Solberg 2009	Althausen 2011	Moya 2011	Khandelwal 2011	Marasco 2013	Doben 2014	Granhed 2014	Xu 2015	Majercik a + b 2015	Wu 2015	Wada 2015	Zhang X 2015	Zhang Y 2015	Jayle 2015	Qiu 2016	Velasquez 2016	Uchida 2016	DeFreest 2016	Pieracci 2016	Farquhar 2016	Fitzgerald 2017	Dehghan 2018	Ali-Osman 2018	Wijffels 2018	Kane 2018
A Clearly stated aim	2	2	2	2	2	2	2	2	1	2	2	1	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Inclusion of consecutive patients	2	1	2	2	2	2	2	0	2	2	1	2	2	2	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	0
Prospective collection of data	1	1	1	1	2	1	2	1	1	1	1	2	2	1	1	1	1	2	1	1	1	1	1	1	1	1	2	1	0	0	0	0	0
Endpoints appropriate to the aim of the study	2	2	2	2	2	2	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	1	2	2	1
Unbiased assessment of the study endpoint	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Follow-up period appropriate to the aim of the study	2	1	1	1	2	0	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	1	2	2	2	2
Loss to follow-up less than 5%	1	1	2	0	2	0	2	0	0	0	2	2	1	2	0	0	2	0	0	0	1	0	0	2	0	2	1	2	1	0	1	1	0
Prospective calculation of the study size	0	0	0	0	0	0	0	0	0	2	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
An adequate control group	0	0	0	0	2	1	2	2	1	1	1	1	2	1	1	0	2	2	2	2	0	2	0	1	2	1	2	1	2	1	1	2	1
Contemporary groups	1	1	1	2	2	1	2	2	2	2	1	2	2	1	0	2	2	2	2	2	2	1	1	1	2	1	1	1	1	1	1	1	1
Baseline equivalence of groups	0	0	1	2	2	1	1	1	2	2	2	0	2	2	0	2	1	2	2	2	2	2	2	2	2	2	1	1	2	1	1	2	1
Adequate statistical analyses	2	2	0	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	1	2	2	1
Total quality score MINORS	**13**	**11**	**12**	**14**	**20**	**12**	**19**	**13**	**15**	**18**	**16**	**17**	**21**	**17**	**12**	**15**	**18**	**17**	**17**	**16**	**16**	**16**	**14**	**17**	**17**	**17**	**17**	**16**	**15**	**11**	**14**	**16**	**9**

Appendix 4. Results of the included studies comparing operative versus non-operative management of traumatic rib fractures.

Study	Treatment groups	Mortality	Hospital LOS	ICU LOS	Duration of mechanical ventilation	Pneumonia	Tracheostomy
Dehghan 2018	Operative	2 (2.6%)	21 ± 20	15 ± 13	NR	45 (48%)	17 (22%)
	Non-operative	160 (9.8%)	17 ± 26	13 ± 15		614 (38%)	182 (11%)
Ali-Osman 2018	Operative	1 (1.6%)	12 [9-16]	6 [3-10]	3 [1-15]	5 (7.8%)	NR
	Non-operative	13 (9.6%)	4.8 [2.9-8.4]	4 [3-7]	4 [1-10]	16 (12%)	
Wijffels 2018	Operative	2 (10%)	21 [12-33]	5 [3-13]	4 [2-10]	7 (35%)	NR
	Non-operative	1 (5%)	23 [17-42]	12 [3-29]	18 [12-26]	16 (80%)	NR
Kane 2018	Operative	1 (0.9%)	12 [10-14]	3 [0-6]	NR	7 (6%)	10 (8.6%)
	Non-operative	13 (1.3%)	5 [3-9]	0 [0-3]		59 (6%)	45 (4.5%)
Fitzgerald 2017	Operative	0 (0%)	18 (14-23)	12 (7-17)	NR	0 (0%)	NR
	Non-operative	2 (4%)	17 (10-23)	8 (5-11)		7 (14%)	
Farquhar 2016	Operative	1 (5,3%)	21.9 ± 13.2	7.4 ± 6.7	6.1 ± 5.9	12 (63%)	NR
	Non-operative	1 (2,8%)	16.0 ± 12.1	3.7 ± 6.0	3.1 ± 5.5	8 (22%)	
Pieracci 2016	Operative	0 (0%)	13.0 [9.0, 21.0]	6.0 [3.0, 10.0]	0 [0.0, 8.0]	7 (20%)	5 (14%)
	Non-operative	0 (0%)	16.0 [10.0, 23.0]	9.0 [4.0, 15.0]	5.0 [0, 18]	11 (31%)	16 (46%)
Defreest 2016	Operative	1 (2,4%)	28.3 (9-69)	14.0 (0-43)	9.3 (0-39)	11 (27%)	10 (24%)
	Non-operative	5 (11,1%)	13.0 (3-43)	8.0 (0-43)	5.8 (0-39)	10 (22%)	8 (18%)
Uchida 2016	Operative	0 (0%)	NR	6.5 [3, 9]	5.5 [1, 8]	2 (20%)	1 (10%)
	Non-operative	0 (0%)		12 [8, 14]	9 [7, 12]	9 (90%)	3 (30%)
Velasquez 2016	Operative	0 (0%)	6 [4, 10]	4.5 [1, 8]	2 [1, 3]	3 (15%)	NR
	Non-operative	2 (10%)	16 [11, 22]	8 [6, 10.5]	10 [6, 16]	13 (65%)	
Qiu a 2016	Operative	1 (4,8%)	NR	7.2 ± 1.7	5.7 ± 1.4	NR	2 (9,5%)
	Non-operative	2 (11,8%)		10.3 ± 2.3	9.1 ± 3.6		8 (47%)
Qiu b 2016	Operative	0 (0%)	11.1 ± 1.9	NR	NR	3 (4,6%)	NR
	Non-operative	0 (0%)	15.9 ± 2.8			10 (17%)	
Jayle 2015	Operative	NR	21.7 ± 7.8	9.0 ± 4.3	3.1 ± 5.2	4 (40%)	NR
	Non-operative	NR	32.3 ± 19.3	12.3 ± 8.5	5.9 ± 9.4	3 (30%)	
Zhang Y 2015	Operative	0 (0%)	38 [33, 54.25]	4.5 [21.3, 30.7]	12 [7.5, 17.8]	16 (67%)	12 (50%)
	Non-operative	2 (13,3%)	60 [38, 99.75]	21.5 [18, 33.5]	7 [4, 14]	7 (47%)	7 (9,7%)
Zhang X 2015	Operative	0 (0%)	NR	5.5 ± 6.4	4.1 ± 6.1	NR	NR
	Non-operative	0 (0%)		14.2 ± 6.5	14 ± 7.6		
Wada 2015	Operative	3 (3,6%)	33 [22, 45]	NR	NR	NR	10 (12%)
	Non-operative	6 (1,8%)	42 [23, 58]				68 (20%)
Wu 2015	Operative	1 (1,3%)	15.3 ± 6.4	8.2 ± 4.3	3.7 ± 1.4	5 (6,7%)	4 (5,3%)
	Non-operative	4 (4,5%)	26.5 ± 6.9	14.6 ± 3.2	9.5 ± 4.3	17 (19%)	7 (7,9%)
Majercik 2015	Operative	NR	11.4 ± 5.7	4.6 ± 5.6	0 [0, 3]	12 (8,8%)	8 (5,8%)
	Non-operative		12.3 ± 9.1	5.9 ± 7.7	0 [0, 4]	55 (20%)	30 (11%)
Xu 2015	Operative	0 (0%)	NR	15.9 ± 5.0	10.5 ± 3.7	10 (59%)	2 (12%)
	Non-operative	1 (6,7%)		19.6 ± 5.0	13.7 ± 4.4	12 (93%)	6 (40%)

Appendix 4. Results of the included studies comparing operative versus non-operative management of traumatic rib fractures. (continued)

Study	Treatment groups	Mortality	Hospital LOS	ICU LOS	Duration of mechanical ventilation	Pneumonia	Tracheostomy
Granhed 2014	Operative	2 (3,3%)	NR	NR	2.7 (0-21)	0 (0%)	NR
	Non-operative	NR			9.0 (1-76)	NR	
Doben 2014	Operative	N/A	21.6 (8-59)	12.5 (5-21)	8.2 (0-30)	NR	NR
	Non-operative	0 (0%)	28.5 (6-50)	15.3 (5-22)	18.0 (4-40)		
Marasco 2013	Operative	0 (0%)	20 [18, 28]	13.5 [9.9, 15.8]	6.3 ± 3.4	11 (48%)	9 (3,9%)
	Non-operative	1 (4,3%)	25 [18, 38]	18.7 [13.4, 26.9]	7.5 ± 5.4	17 (74%)	16 (7,0%)
Khandelwal 2011	Operative	NR	NR	NR	NR	NR	NR
	Non-operative						
Moya 2011	Operative	NR	18 ± 12	9 ± 8	7 ± 8	5 (31%)	NR
	Non-operative		16 ± 11	7 ± 10	6 ± 10	12 (38%)	
Althausen 2011	Operative	NR	11.9 ± 7.8	7.6 ± 7.4	4.2 ± 6.6	1 (4,5%)	3 (3,9%)
	Non-operative		19.0 ± 12.6	9.7 ± 9.2	9.7 ± 9.2	7 (25%)	11 (3,9%)
Solberg 2009	Operative	NR	NR	5.4 ± 1.5	1.9 ± 1.1	0 (0%)	NR
	Non-operative			21 ± 13.6	13.3 ± 5.3	3 (43%)	
Nirula 2006	Operative	NR	18.8 ± 1.8	12.1 ± 1.2	6.5 ± 1.3	NR	NR
	Non-operative		21.1 ± 3.9	14.1 ± 2.7	11.2 ± 2.6		
Granetzny 2006	Operative	2 (10%)	11.7 ± 10.1	9.6 ± 12.0	2 ± 8.9	NR	NR
	Non-operative	3 (15%)	23.1 ± 10.1	14.6 ± 12.0	12 ± 8.9		
Balci 2004	Operative	3 (1,11%)	18.3 ± 7.6	NR	3.1 ± 1.8	NR	0 (0%)
	Non-operative	10 (27,0%)	19.2 ± 7.2	NR	7.2 ± 5.8		7 (19%)
Tanaka 2002	Operative	0 (0%)	NR	16.5 ± 7.4	10.8 ± 3.4	4 (22%)	3 (17%)
	Non-operative	0 (0%)		26.8 ± 13.2	18.3 ± 7.4	17 (90%)	15 (79%)
Voggenreiter a 1996	Operative	0 (0%)	NR	NR	6.5 ± 7.0	1 (10%)	NR
	Non-operative	7 (38,9%)			26.7 ± 29.0	5 (28%)	
Voggenreiter b 1996	Operative	3 (30%)	NR	NR	30.8 ± 33.7	4 (40%)	NR
	Non-operative	1 (25%)			29.3 ± 22.5	2 (50%)	
Ahmed 1995	Operative	2 (10%)	NR	9	3.9	NR	3 (15%)
	Non-operative	11 (57,9%)		21	15		14 (74%)
Kim 1981	Operative	1 (5,9%)	NR	NR	24 ± 15	NR	NR
	Non-operative	60 (42,2%)			22.1 ± 13.5	7 (4,9%)	
Aubert 1981	Operative	3 (13,6%)	NR	NR	NR	NR	NR
	Non-operative	54 (24,1%)					135 (60%)

Abbreviations: RF rib fixation; NOM nonoperative management; NR not reported; FC flail chest; MRF multiple rib fractures; PC pulmonary contusion.

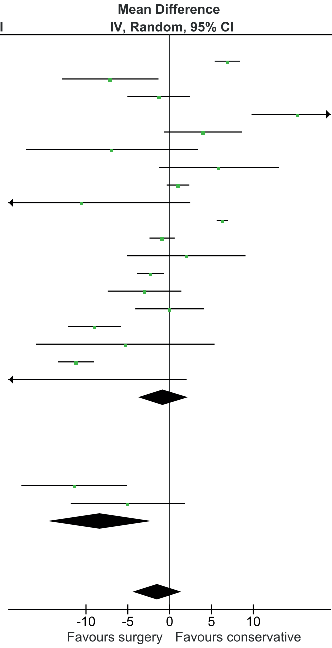
Appendix 5. Impact of different methods to handle zero-event data in a meta-analysis of operative versus nonoperative treatment of rib fractures and mortality.

Method	Observational studies	RCT	Total
	OR (95% CI)	OR (95% CI)	OR (95% CI)
Mantel-Haenzel*	0.43 (0.27 – 0.69)	0.57 (0.13 – 2.52)	0.44 (0.28 – 0.69)
Crude	0.21 (0.13 – 0.35)	0.49 (0.09 – 2.79)	0.22 (0.14 – 0.35)
Inverse variance - no correction	0.41 (0.23 – 0.73)	0.63 (0.09 – 4.24)	0.43 (0.25 – 0.74)
Inverse variance - with correction	0.39 (0.23 – 0.65)	0.59 (0.13 – 2.68)	0.41 (0.25 – 0.66)
DerSimonian Laird with correction	0.37 (0.17 – 0.79)	0.58 (0.11 – 3.23)	0.39 (0.20 – 0.78)
Peto	0.28 (0.16 – 0.49)	0.50 (0.07 – 3.47)	0.29 (0.17 – 0.50)

* *Method used in meta-analysis; OR odds-ratio; CI confidence interval*

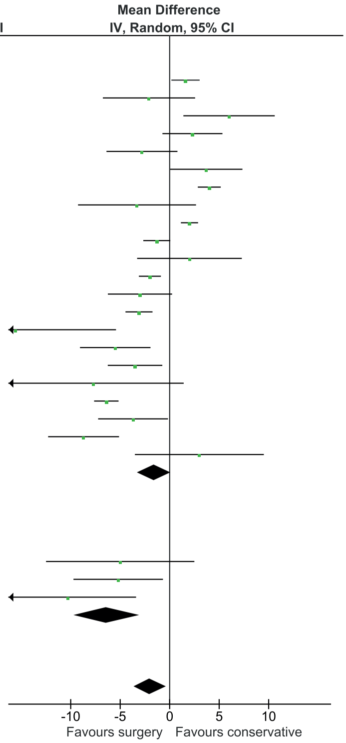
Appendix 6. Hospital length of stay in a systematic review of rib fractures comparing operative to nonoperative treatment.

	Surgery			Conservative				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
1.2.1 Observational								
Ali-Osman 2018	12.3	5.2	64	5.4	4.1	135	5.9%	6.90 [5.45, 8.35]
Althausen 2011	11.9	7.79	22	19	12.64	28	4.8%	-7.10 [-12.80, -1.40]
Balci 2004	18.3	7.6	27	19.6	7.2	37	5.4%	-1.30 [-4.99, 2.39]
Defreest 2016	28.3	15	41	13	10	45	4.9%	15.30 [9.86, 20.74]
Dehghan 2018	20.6	19.9	77	16.6	25.4	1631	5.2%	4.00 [-0.61, 8.61]
Doben 2014	21.6	12.75	10	28.5	11	11	3.4%	-6.90 [-17.13, 3.33]
Farquhar 2016	21.9	13.2	19	16	12.1	36	4.3%	5.90 [-1.23, 13.03]
Fitzgerald 2017	18	2.25	23	17	3.25	50	5.9%	1.00 [-0.29, 2.29]
Jayle 2015	21.7	7.8	10	32.2	19.3	10	2.7%	-10.50 [-23.40, 2.40]
Kane 2018	12	3	116	5.7	4.4	1000	6.0%	6.30 [5.69, 6.91]
Majercik 2015	11.4	5.7	137	12.3	9.1	274	5.9%	-0.90 [-2.34, 0.54]
Moya 2011	18	12	16	16	11	32	4.4%	2.00 [-5.01, 9.01]
Nirula 2006	18.8	1.8	30	21.1	3.9	30	5.9%	-2.30 [-3.84, -0.76]
Pieracci 2016	13	8.9	35	16	9.6	35	5.2%	-3.00 [-7.34, 1.34]
Velasquez 2016	6	4.4	20	6	8.1	20	5.3%	0.00 [-4.04, 4.04]
Wada 2015	33	6.4	84	42	25.92	336	5.6%	-9.00 [-12.09, -5.91]
Wijffels 2018	22	15.6	20	27.3	18.5	20	3.3%	-5.30 [-15.91, 5.31]
Wu 2015	15.3	6.6	75	26.5	6.9	89	5.8%	-11.20 [-13.27, -9.13]
Zhang Y 2015	38	15.7	24	60	45.7	15	1.1%	-22.00 [-45.96, 1.96]
Subtotal (95% CI)			**850**			**3834**	**90.9%**	**-0.77 [-3.72, 2.18]**
Heterogeneity: Tau² = 34.35; Chi² = 523.49, df = 18 (P < 0.00001); I² = 97%								
Test for overall effect: Z = 0.51 (P = 0.61)								
1.2.2 RCT								
Granetzny 2006	11.7	10.1	20	23.1	10.1	20	4.6%	-11.40 [-17.66, -5.14]
Marasco 2013	20	7.4	23	25	14.8	23	4.5%	-5.00 [-11.76, 1.76]
Subtotal (95% CI)			**43**			**43**	**9.1%**	**-8.33 [-14.60, -2.07]**
Heterogeneity: Tau² = 9.43; Chi² = 1.85, df = 1 (P = 0.17); I² = 46%								
Test for overall effect: Z = 2.61 (P = 0.009)								
Total (95% CI)			**893**			**3877**	**100.0%**	**-1.46 [-4.31, 1.39]**
Heterogeneity: Tau² = 35.38; Chi² = 548.90, df = 20 (P < 0.00001); I² = 96%								
Test for overall effect: Z = 1.00 (P = 0.32)								
Test for subgroup differences: Chi² = 4.58, df = 1 (P = 0.03), I² = 78.2%								



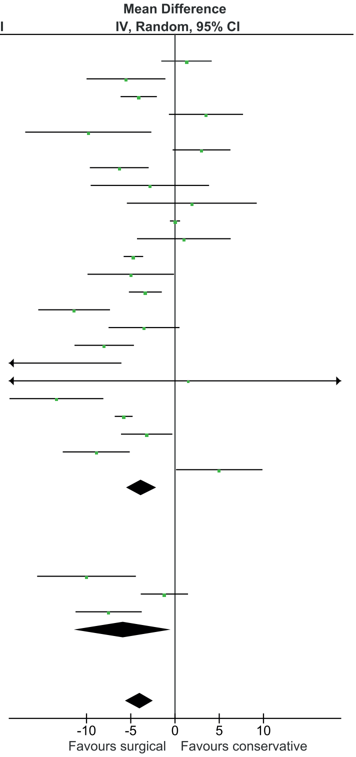
Appendix 7. Intensive care length of stay in a systematic review of rib fractures comparing operative to nonoperative treatment.

	Surgery			Conservative				Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**
1.3.1 Observational								
Ahmed 1995	9	0	20	21	0	19		Not estimable
Ali-Osman 2018	6.3	5.2	64	4.7	3	135	5.1%	1.60 [0.23, 2.97]
Althausen 2011	7.59	7.43	22	9.68	9.18	28	3.7%	-2.09 [-6.69, 2.51]
Defreest 2016	14	10.75	41	8	10.8	45	3.7%	6.00 [1.44, 10.56]
Dehghan 2018	14.9	12.9	77	12.6	15.3	1631	4.5%	2.30 [-0.68, 5.28]
Doben 2014	12.5	4	10	15.3	4.25	11	4.2%	-2.80 [-6.33, 0.73]
Farquhar 2016	7.4	6.7	19	3.7	6	36	4.2%	3.70 [0.11, 7.29]
Fitzgerald 2017	12	2.5	23	8	1.5	50	5.2%	4.00 [2.90, 5.10]
Jayle 2015	9	4.3	10	12.3	8.5	10	3.1%	-3.30 [-9.20, 2.60]
Kane 2018	3	4.4	116	1	2.2	1000	5.2%	2.00 [1.19, 2.81]
Majercik 2015	4.6	5.6	137	5.9	7.7	274	5.1%	-1.30 [-2.61, 0.01]
Moya 2011	9	8	16	7	10	32	3.4%	2.00 [-3.23, 7.23]
Nirula 2006	12.1	1.2	30	14.1	2.7	30	5.2%	-2.00 [-3.06, -0.94]
Pieracci 2016	6	5.2	35	9	8.1	35	4.4%	-3.00 [-6.19, 0.19]
Qiu a 2016	7.19	1.67	21	10.29	2.31	17	5.1%	-3.10 [-4.41, -1.79]
Solberg 2009	5.4	1.5	9	21	13.6	7	1.7%	-15.60 [-25.72, -5.48]
Uchida 2016	6.5	4	10	12	4	10	4.2%	-5.50 [-9.01, -1.99]
Velasquez 2016	4.5	5.2	20	8	3.3	20	4.6%	-3.50 [-6.20, -0.80]
Wijffels 2018	7	7.4	20	14.7	19.3	20	2.0%	-7.70 [-16.76, 1.36]
Wu 2015	8.2	4.3	75	14.6	3.2	89	5.1%	-6.40 [-7.58, -5.22]
Xu 2015	15.9	5	17	19.6	5	15	4.2%	-3.70 [-7.17, -0.23]
Zhang X 2015	5.5	6.4	23	14.2	6.5	29	4.2%	-8.70 [-12.23, -5.17]
Zhang Y 2015	24.5	7	24	21.5	11.5	15	2.9%	3.00 [-3.46, 9.46]
Subtotal (95% CI)			**839**			**3558**	**91.0%**	**-1.53 [-3.21, 0.15]**
Heterogeneity: Tau² = 12.57; Chi² = 301.16, df = 21 (P < 0.00001); I² = 93%								
Test for overall effect: Z = 1.79 (P = 0.07)								
1.3.2 RCT								
Granetzny 2006	9.6	12	20	14.6	12	20	2.5%	-5.00 [-12.44, 2.44]
Marasco 2013	13.5	4.4	23	18.7	10	23	3.8%	-5.20 [-9.66, -0.74]
Tanaka 2002	16.5	7.4	18	26.8	13.2	19	2.7%	-10.30 [-17.15, -3.45]
Subtotal (95% CI)			**61**			**62**	**9.0%**	**-6.37 [-9.72, -3.03]**
Heterogeneity: Tau² = 0.00; Chi² = 1.66, df = 2 (P = 0.44); I² = 0%								
Test for overall effect: Z = 3.74 (P = 0.0002)								
Total (95% CI)			**900**			**3620**	**100.0%**	**-2.00 [-3.61, -0.38]**
Heterogeneity: Tau² = 12.80; Chi² = 314.29, df = 24 (P < 0.00001); I² = 92%								
Test for overall effect: Z = 2.43 (P = 0.02)								
Test for subgroup differences: Chi² = 6.44, df = 1 (P = 0.01), I² = 84.5%								



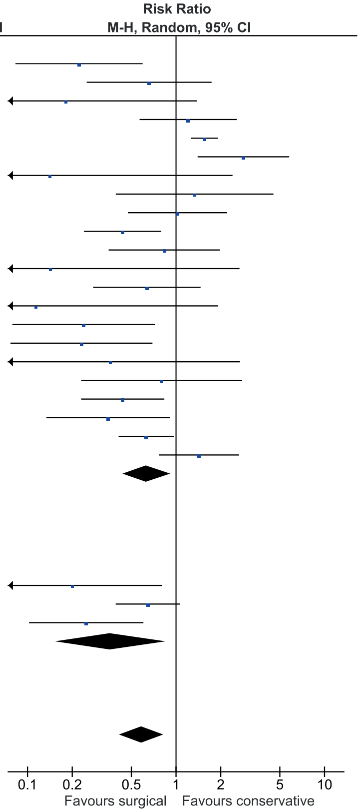
Appendix 8. Duration of mechanical ventilation in a systematic review of rib fractures comparing operative to non-operative treatment

	Surgery			Conservative				Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**
1.4.1 Observational								
Ali-Osman 2018	6.3	10.4	64	5	6.7	135	4.5%	1.30 [-1.49, 4.09]
Althausen 2011	4.14	6.66	22	9.68	9.18	28	3.7%	-5.54 [-9.93, -1.15]
Balci 2004	3.1	1.8	27	7.2	5.8	37	4.8%	-4.10 [-6.09, -2.11]
Defreest 2016	9.3	9.75	41	5.8	9.75	45	3.8%	3.50 [-0.63, 7.63]
Doben 2014	8.2	7.5	10	18	9	11	2.5%	-9.80 [-16.86, -2.74]
Farquhar 2016	6.1	5.9	19	3.1	5.5	36	4.3%	3.00 [-0.20, 6.20]
Granhed 2014	2.7	5.25	60	9	18.8	153	4.2%	-6.30 [-9.56, -3.04]
Jayle 2015	3.06	5.19	10	5.9	9.35	10	2.7%	-2.84 [-9.47, 3.79]
Kim 1981	24	15	18	22.1	13.5	142	2.4%	1.90 [-5.38, 9.18]
Majercik 2015	0	2.22	137	0	2.96	274	5.2%	0.00 [-0.51, 0.51]
Moya 2011	7	8	16	6	10	32	3.3%	1.00 [-4.23, 6.23]
Nirula 2006	6.5	1.3	30	11.2	2.6	30	5.1%	-4.70 [-5.74, -3.66]
Pieracci 2016	0	5.92	35	5	13.3	35	3.5%	-5.00 [-9.82, -0.18]
Qiu a 2016	5.71	1.35	21	9.06	3.58	17	4.9%	-3.35 [-5.15, -1.55]
Solberg 2009	1.9	1.1	9	13.3	5.3	7	3.9%	-11.40 [-15.39, -7.41]
Uchida 2016	5.5	5.18	10	9	3.7	10	3.9%	-3.50 [-7.45, 0.45]
Velasquez 2016	2	1.33	20	10	7.4	20	4.2%	-8.00 [-11.30, -4.70]
Voggenreiter a 1996	6.5	7	10	26.7	29	18	1.0%	-20.20 [-34.28, -6.12]
Voggenreiter b 1996	30.8	33.7	10	29.3	22.5	4	0.3%	1.50 [-28.87, 31.87]
Wijffels 2018	5.3	5.9	20	18.7	10.4	20	3.3%	-13.40 [-18.64, -8.16]
Wu 2015	3.7	1.4	75	9.5	4.3	89	5.1%	-5.80 [-6.75, -4.85]
Xu 2015	10.5	3.7	17	13.7	4.4	15	4.4%	-3.20 [-6.04, -0.36]
Zhang X 2015	4.1	6.1	23	13	7.6	29	4.0%	-8.90 [-12.62, -5.18]
Zhang Y 2015	12	7.59	24	7	7.4	15	3.5%	5.00 [0.18, 9.82]
Subtotal (95% CI)			**728**			**1212**	**88.3%**	**-3.79 [-5.46, -2.11]**
Heterogeneity: Tau² = 12.39; Chi² = 272.23, df = 23 (P < 0.00001); I² = 92%								
Test for overall effect: Z = 4.44 (P < 0.00001)								
1.4.2 RCT								
Granetzny 2006	2	8.9	20	12	8.9	20	3.2%	-10.00 [-15.52, -4.48]
Marasco 2013	6.3	3.4	23	7.5	5.4	23	4.5%	-1.20 [-3.81, 1.41]
Tanaka 2002	10.8	3.4	18	18.3	7.4	19	4.0%	-7.50 [-11.18, -3.82]
Subtotal (95% CI)			**61**			**62**	**11.7%**	**-5.88 [-11.32, -0.44]**
Heterogeneity: Tau² = 18.99; Chi² = 12.42, df = 2 (P = 0.002); I² = 84%								
Test for overall effect: Z = 2.12 (P = 0.03)								
Total (95% CI)			**789**			**1274**	**100.0%**	**-4.01 [-5.58, -2.45]**
Heterogeneity: Tau² = 12.28; Chi² = 288.28, df = 26 (P < 0.00001); I² = 91%								
Test for overall effect: Z = 5.03 (P < 0.00001)								
Test for subgroup differences: Chi² = 0.52, df = 1 (P = 0.47), I² = 0%								



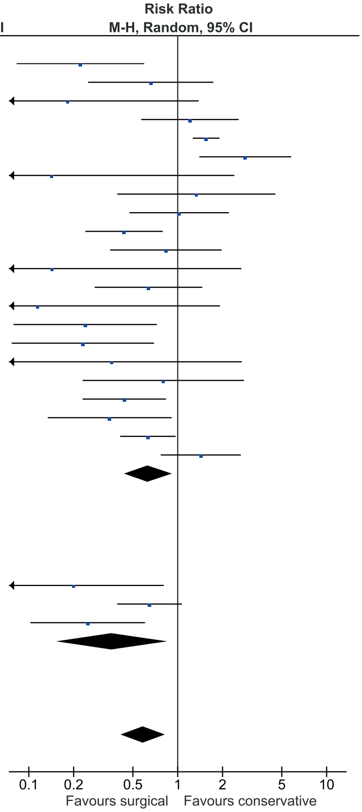
Appendix 9. Pneumonia in a systematic review of rib fractures comparing operative to nonoperative treatment.

Study or Subgroup	Surgery Events	Surgery Total	Conservative Events	Conservative Total	Weight	Risk Ratio M-H, Random, 95% CI
1.5.1 Observational						
Ahmed 1995	4	36	19	38	4.2%	0.22 [0.08, 0.59]
Ali-Osman 2018	5	64	16	135	4.2%	0.66 [0.25, 1.72]
Althausen 2011	1	22	7	28	2.0%	0.18 [0.02, 1.37]
Defreest 2016	11	41	10	45	4.9%	1.21 [0.57, 2.54]
Dehghan 2018	45	77	614	1631	6.2%	1.55 [1.27, 1.89]
Farquhar 2016	12	19	8	36	5.0%	2.84 [1.41, 5.73]
Fitzgerald 2017	0	23	7	50	1.2%	0.14 [0.01, 2.38]
Jayle 2015	4	10	3	10	3.5%	1.33 [0.40, 4.49]
Kane 2018	7	116	59	1000	4.8%	1.02 [0.48, 2.19]
Majercik 2015	12	137	55	274	5.3%	0.44 [0.24, 0.79]
Moya 2011	5	16	12	32	4.6%	0.83 [0.35, 1.96]
Nirula 2006	0	30	3	30	1.1%	0.14 [0.01, 2.65]
Pieracci 2016	7	35	11	35	4.6%	0.64 [0.28, 1.45]
Solberg 2009	0	9	3	7	1.2%	0.11 [0.01, 1.91]
Uchida 2016	2	10	9	9	3.9%	0.24 [0.08, 0.72]
Velasquez 2016	3	20	13	20	3.9%	0.23 [0.08, 0.69]
Voggenreiter a 1996	1	10	5	18	2.0%	0.36 [0.05, 2.67]
Voggenreiter b 1996	4	10	2	4	3.5%	0.80 [0.23, 2.76]
Wijffels 2018	7	20	16	20	5.2%	0.44 [0.23, 0.83]
Wu 2015	5	75	17	89	4.3%	0.35 [0.14, 0.90]
Xu 2015	10	17	14	15	5.8%	0.63 [0.41, 0.96]
Zhang Y 2015	16	24	7	15	5.3%	1.43 [0.78, 2.63]
Subtotal (95% CI)		**821**		**3541**	**86.8%**	**0.63 [0.44, 0.92]**
Total events	161		910			
Heterogeneity: Tau² = 0.48; Chi² = 97.79, df = 21 (P < 0.00001); I² = 79%						
Test for overall effect: Z = 2.43 (P = 0.02)						
1.5.2 RCT						
Granetzny 2006	2	20	10	20	3.1%	0.20 [0.05, 0.80]
Marasco 2013	11	23	17	23	5.6%	0.65 [0.40, 1.06]
Tanaka 2002	4	18	17	19	4.5%	0.25 [0.10, 0.60]
Subtotal (95% CI)		**61**		**62**	**13.2%**	**0.36 [0.15, 0.85]**
Total events	17		44			
Heterogeneity: Tau² = 0.37; Chi² = 5.92, df = 2 (P = 0.05); I² = 66%						
Test for overall effect: Z = 2.32 (P = 0.02)						
Total (95% CI)		**882**		**3603**	**100.0%**	**0.59 [0.42, 0.83]**
Total events	178		954			
Heterogeneity: Tau² = 0.49; Chi² = 115.31, df = 24 (P < 0.00001); I² = 79%						
Test for overall effect: Z = 3.03 (P = 0.002)						
Test for subgroup differences: Chi² = 1.38, df = 1 (P = 0.24), I² = 27.6%						



Appendix 10. Tracheostomy in a systematic review of rib fractures comparing operative to nonoperative treatment.

Study or Subgroup	Surgery Events	Surgery Total	Conservative Events	Conservative Total	Weight	Risk Ratio M-H, Random, 95% CI
1.5.1 Observational						
Ahmed 1995	4	36	19	38	4.2%	0.22 [0.08, 0.59]
Ali-Osman 2018	5	64	16	135	4.2%	0.66 [0.25, 1.72]
Althausen 2011	1	22	7	28	2.0%	0.18 [0.02, 1.37]
Defreest 2016	11	41	10	45	4.9%	1.21 [0.57, 2.54]
Dehghan 2018	45	77	614	1631	6.2%	1.55 [1.27, 1.89]
Farquhar 2016	12	19	8	36	5.0%	2.84 [1.41, 5.73]
Fitzgerald 2017	0	23	7	50	1.2%	0.14 [0.01, 2.38]
Jayle 2015	4	10	3	10	3.5%	1.33 [0.40, 4.49]
Kane 2018	7	116	59	1000	4.8%	1.02 [0.48, 2.19]
Majercik 2015	12	137	55	274	5.3%	0.44 [0.24, 0.79]
Moya 2011	5	16	12	32	4.6%	0.83 [0.35, 1.96]
Nirula 2006	0	30	3	30	1.1%	0.14 [0.01, 2.65]
Pieracci 2016	7	35	11	35	4.6%	0.64 [0.28, 1.45]
Solberg 2009	0	9	3	7	1.2%	0.11 [0.01, 1.91]
Uchida 2016	2	10	9	9	3.9%	0.24 [0.08, 0.72]
Velasquez 2016	3	20	13	20	3.9%	0.23 [0.08, 0.69]
Voggenreiter a 1996	1	10	5	18	2.0%	0.36 [0.05, 2.67]
Voggenreiter b 1996	4	10	2	4	3.5%	0.80 [0.23, 2.76]
Wijffels 2018	7	20	16	20	5.2%	0.44 [0.23, 0.83]
Wu 2015	5	75	17	89	4.3%	0.35 [0.14, 0.90]
Xu 2015	10	17	14	15	5.8%	0.63 [0.41, 0.96]
Zhang Y 2015	16	24	7	15	5.3%	1.43 [0.78, 2.63]
Subtotal (95% CI)		**821**		**3541**	**86.8%**	**0.63 [0.44, 0.92]**
Total events	161		910			
Heterogeneity: Tau² = 0.48; Chi² = 97.79, df = 21 (P < 0.00001); I² = 79%						
Test for overall effect: Z = 2.43 (P = 0.02)						
1.5.2 RCT						
Granetzny 2006	2	20	10	20	3.1%	0.20 [0.05, 0.80]
Marasco 2013	11	23	17	23	5.6%	0.65 [0.40, 1.06]
Tanaka 2002	4	18	17	19	4.5%	0.25 [0.10, 0.60]
Subtotal (95% CI)		**61**		**62**	**13.2%**	**0.36 [0.15, 0.85]**
Total events	17		44			
Heterogeneity: Tau² = 0.37; Chi² = 5.92, df = 2 (P = 0.05); I² = 66%						
Test for overall effect: Z = 2.32 (P = 0.02)						
Total (95% CI)		**882**		**3603**	**100.0%**	**0.59 [0.42, 0.83]**
Total events	178		954			
Heterogeneity: Tau² = 0.49; Chi² = 115.31, df = 24 (P < 0.00001); I² = 79%						
Test for overall effect: Z = 3.03 (P = 0.002)						
Test for subgroup differences: Chi² = 1.38, df = 1 (P = 0.24), I² = 27.6%						



7 | Complications and outcome after rib fracture fixation: A systematic review.

Peek J, *Beks RB, Hietbrink F, Heng M, De Jong MB, Beeres FJP, Leenen LPH, Groenwold RHH, Houwert RM.*

J Trauma Acute Care Surg 2020

ABSTRACT

Background In recent years, there has been a growing interest in operative treatment for multiple rib fractures and flail chest. However, to date, there is no comprehensive study that extensively focused on the incidence of complications associated with rib fracture fixation. Furthermore, there is insufficient knowledge about the short- and long-term outcomes after rib fracture fixation.

Methods This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines. The MEDLINE, EMBASE, and Cochrane databases were searched to identify studies reporting on complications and/or outcome of surgical treatment after rib fractures. Complications were subdivided into (1) surgery- and implant-related complications, (2) bone-healing complications, (3) pulmonary complications, and (4) mortality.

Results Forty-eight studies were included, with information about 1,952 patients who received rib fracture fixation because of flail chest or multiple rib fractures. The overall risk of surgery- and implant-related complications was 10.3%, with wound infection in 2.2% and fracture-related infection in 1.3% of patients. Symptomatic nonunion was a relatively uncommon complication after rib fixation (1.3%). Pulmonary complications were found in 30.9% of patients, and the overall mortality was 2.9%, of which one third appeared to be the result of the thoracic injuries and none directly related to the surgical procedure. The most frequently used questionnaire to assess patient quality of life was the EuroQol-5D (EQ-5D) (n = 4). Four studies reporting on the EQ-5D had a weighted mean EQ-5D index of 0.80 indicating good quality of life after rib fracture fixation.

Conclusion Surgical fixation can be considered as a safe procedure with a considerably low complication risk and satisfactory long-term outcomes, with surgery- and implant-related complications in approximately 10% of the patients. However, the clinically most relevant complications such as infections occur infrequently, and the number of complications requiring immediate (surgical) treatment is low.

INTRODUCTION

Rib fractures are the most common injuries following blunt chest trauma and are identified in approximately 10% of all trauma patients.[1,2] Rib fractures are considered to be a surrogate marker of severe injury and are often accompanied by serious intra- and extra-thoracic injuries.[3-5] Furthermore, rib fractures represent an important burden of disease as they are associated with chronic pain, long-term disability and impaired quality of life.[6-8] An increased number of fractured ribs and higher age are associated with even worse outcomes.[5,9,10]

Traditionally, supportive care has been the standard approach in patients with fractured ribs, consisting of adequate pain control, respiratory support, and physiotherapy. In recent years, stimulated by technological advancements there has been a growing interest in operative treatment for multiple rib fractures and flail chest.[11] Previous randomized controlled trials suggest that surgical treatment of flail chest in selected patients may reduce the duration of hospital length of stay (HLOS), intensive care length of stay (ILOS), days on mechanical ventilation (DMV), mortality, and the incidence of pneumonia.[12-15] A systematic review of randomized controlled trials (RCT) as well as observational studies reported similar results for patients with a flail chest, but was not able to show improved in-hospital outcomes for patients with multiple rib fractures.[16]

Reported complications after plate fixation for rib fractures include nonunion, infection, bleeding, and implant-related complications such as irritation and implant failure. However, there is no comprehensive study that focused on the incidence and consequences of complications associated with rib fracture fixation. Furthermore, there is insufficient knowledge about the short- and long-term outcomes after rib fracture fixation.

Therefore, the aim of this systematic review was to report on the incidence of complications associated with rib fracture fixation and to determine the short- and long-term outcomes after surgery.

METHODS

This systematic review was performed in adherence to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[17] A published review protocol does not exist for this study. Ethical committee approval was not required.

Search strategy and selection criteria

A systematic literature search (lastly updated on January 1st, 2020) was conducted in the MEDLINE, EMBASE, and Cochrane electronic databases to identify studies reporting on complications and/or outcomes of surgical treatment after rib fractures. Single arm studies reporting on outcome of a surgical treatment as well as comparison studies to either another operative or non-operative treatment were eligible for inclusion. The search syntax used for the different databases is provided in Appendix 1.

After duplicates were removed, two reviewers (JP and RBB) independently screened all titles and abstracts for relevance. A full-text assessment was performed for studies potentially suitable for inclusion. Exclusion criteria were studies describing patients with non-traumatic rib fractures (e.g. as a result of cardiopulmonary resuscitation, osteoporosis, bone malignancy, or nonunion), a language other than English, no availability of full text, and letters, abstracts of conferences, animal studies or case reports. Non-consecutive case series and studies insufficiently reporting on indication of surgery or the surgical procedure were also deemed ineligible for inclusion. References were checked and citation tracking was performed using Web of Science to identify articles not found in the original search. Discrepancies concerning the search, eligibility of full-text studies, and quality assessment were resolved by consensus or by discussion with a third author (RHM).

Data extraction

Data were retrieved independently by two authors (JP and RBB) following a predefined extraction file. The following data were extracted: first author, year of publication, study design, country, number of patients, age, sex, total follow-up time, number of fractured ribs, fracture type (i.e. multiple rib fractures; flail chest, or combined), Injury Severity Score (ISS), Abbreviated Injury Scale (AIS) thorax, indication for surgery, time until surgery, type of plate or fixation material used, number of fixated ribs, complications, and short- or long-term outcomes. The complications and outcomes were defined and reported as mentioned in the original studies. The indication for surgery was subdivided in the following categories: flail chest, (multiple) dislocated rib fractures, pain, thorax deformity, failure to wean, other, or a combination of these indications. Follow-up studies and studies reporting on the same patient cohorts were merged and presented together. Studies that distinguished between flail chest and multiple rib fractures were reported separately in case sufficient information on both groups was provided.

Outcome measures

The primary outcome measure was the occurrence of complications following surgical fixation of multiple rib fractures or flail chest. Complications were subdivided into surgery- and implant-related complications, bone-healing complications, pulmonary complications, and mortality. Surgery-related complications included bleeding, wound infection, fracture-related infection and revision surgery. Implant-related complications included breakage, mechanical failure, numbness of the chest wall, and irritation. Bone-healing complications were defined as nonunion and malunion of the rib fractures that were fixated. Pulmonary complications included pneumonia, excess pleural fluid, hemothorax, (tension) pneumothorax, pleural empyema, need for tracheostomy, and Acute Respiratory Distress Syndrome (ARDS). Mortality was subdivided into two categories; overall mortality and mortality due to the thoracic injury.

The secondary outcome measure was the outcome after rib fracture fixation. The outcomes were considered as short-term outcomes (< 12 months) and long-term outcomes ($\geq$ 12 months) based on the average follow-up time.

Quality assessment

Two reviewers (JP and RBB) independently assessed the methodological quality of the included studies using the Methodological Index for Non-Randomized Studies (MINORS).[18] The MINORS is a validated tool designed to assess the methodological quality of non-randomized surgical studies and is applicable for both comparative and non-comparative studies. Since we were only interested in the surgical groups, for the included comparative studies only the surgical treatment arms were considered. Therefore, the total score was based on the first eight questions with a maximum score of 16 points.

Statistical analysis

Data were described and presented using weighted descriptive statistics with mean and standard deviation for normally distributed data and median and interquartile range for non-normally distributed data.[19]

RESULTS

Search

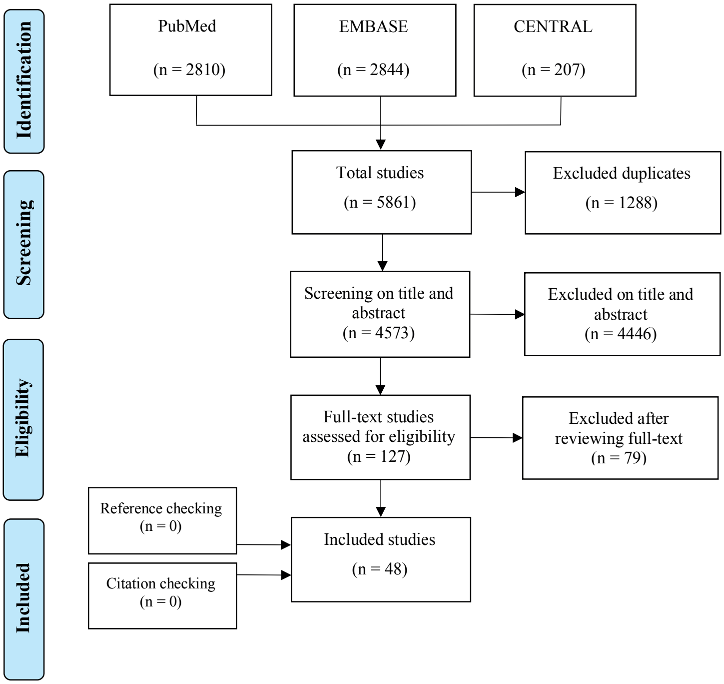
A flowchart of the literature search and the study selection is shown in Figure 1. A total of 48 studies were included in this systematic review.[12,13,15,20–64] Of these, all studies reported on complications and 11 studies reported on the short- or long-term outcomes after rib fixation. Studies were mainly excluded because the outcome of interest was not reported. Three studies reporting on the same patient cohort were merged.[30,32,45] Three other studies subdivided their cohort into flail chest and multiple rib fractures and were therefore reported separately.[36,40,63]

Baseline characteristics

The included studies represented a total of 1952 patients, of which the baseline characteristics are presented in Table 1. The weighted overall mean age was 53 (range, 15 - 93) years, 67% was male, and the weighted mean ISS score was 26 (range, 9 – 66). Twenty studies reported on patients with a flail chest, 3 studies reported on patients with multiple rib fractures, and combined cohorts were described in 23 studies. Overall, the mean weighted number of fractured ribs was 8 (range, 3 - 19).

In the majority of studies, the indication for surgical treatment consisted of a combination of (multiple) rib fractures and severe fracture displacement, uncontrolled persistent pain, thorax deformity, and/or failure to wean from mechanical ventilation. In 19 studies, surgical fixation was solely indicated if a flail chest was present. Most patients were surgically treated by plate fixation or a combination of plates and splints. Other surgical methods were K-wires, absorbable pates, titanium elastic nails, or splints only. The mean weighted time to surgery was 4 days. The mean weighted number of ribs fixated was 4, and the ratio between the total number of fixated and the number of fractured ribs was 0.5.

Figure 1. PRISMA flow diagram representing the search and screen process of articles describing complications of rib fracture fixation.



Quality assessment

An overview of the total MINORS score of the included studies are summarized in Appendix 2. The mean MINORS score was 10.8, ranging from 8 to 20 points.

Surgery- and implant-related complications

Forty-five studies reported on surgery- and implant-related complications (n = 1690), which are presented in Appendix 3. The overall risk of surgery- and implant-related complications was 10.3% (n = 173). Among the surgery- and implant-related complications, the most common complication was revision surgery (24.9%, n = 43), followed by wound infection (17.9%, n = 31), fracture-related infection (12.1%, n = 21), and intra- or postoperative bleeding (6.9%, n = 12). This means that the absolute risk of these complications among patients who received rib fracture fixation after rib fractures were 2.9% (revision surgery), 2.2% (wound infection), 1.4% (intra- or post-operative bleeding), and 1.3% (fracture-related infection) (Table 2). Of the patients that required revision surgery (n = 43), this was performed because of implant removal (81.4%, n = 35), persistent pneumothorax or empyema (9.3%, n = 4), nonunion (2.3%, n = 1), or due to other reasons (7.0%, n = 3). Implant removal (n = 35) was performed because of implant irritation (45.7%, n = 16), fracture-related infection (34.3%, n = 12), nonunion (5.7%, n = 2), or due to other reasons (14.3%, n = 5). The most common implant-related complication was implant irritation with an overall complication risk of

Table 1. Baseline characteristics of included studies describing complications of rib fracture fixation.

Author and year	Study Design	Country	Fracture Type	Patients, No. (%)	Male, No. (%)	Age, Mean (SD), y	ISS, Mean (SD)	Fractured ribs, Mean (SD)	Follow-up, Mean (SD), d
Pieracci et al, 2019[64]	RCT/PC	USA	Multiple rib	51	39 (77)	55	13	7	NA
Akil et al, 2019[50]	PC	Germany	Multiple rib	50	18 (36)	63 (30-98)[a]	NA	4 (2-8)[b]	487 (91)
Liu et al, 2019[15]	RCT	China	Flail chest	25	21 (84)	45 (22-58)[b]	29 (22-36)[b]	NA	21 (17-25)[a,‡]
Marasco et al, 2019[59]	RC	Australia	Flail chest	67	51 (76)	59 (17)	24 (14-30)[b]	NA	730
Walters et al, 2019[61]	CC	UK	Combined	56	41 (73)	54 (17)	28 (11)	NA	536 (289)
Su et al, 2019[60]	RC	Taiwan	Combined	33	26 (79)	62 (19-92)[c]	20 (9-24)[c]	5 (4-8)[c]	NA
Ali-Osman et al, 2018[62]	RC	USA	Combined	64	41 (64)	69 (63-74)[b]	18 (9-25)[b]	7 (5-9)[b]	12 (9-16)[b]
Beks et al, 2018A[63]	RC	Netherlands	Multiple rib	99	81 (82)	56 (47-64)[b]	21 (16-29)[b]	7 (6-10)[b]	1607 (1242-2155)[b]
Beks et al, 2018B[63]	RC	Netherlands	Flail chest	67	52 (78)	57 (48-69)[b]	24 (18-34)[b]	10 (8-12)[b]	1132 (877-1863)[b]
Iqbal et al, 2018[20]	RC	UK	Combined	102	66 (65)	62 (20-93)[c]	18	6 (3-10)[c]	91
Kane et al, 2018[21]	RC	USA	Combined	116	NA	58 (14)	22 (9)	NA	12 (10-14)[b,‡]
Liu et al, 2018[22]	RC	China	Combined	59	34 (31)	NA	NA	6 (2.1)	183
Michelitsch et al, 2018[23]	RC	Switzerland	Combined	23	17 (74)	56 (49-63)[b]	21 (16-29)[b]	NA	840 (365-2070)[a]
Wijffels et al, 2018[24]	CC	Netherlands	Flail chest	23	15 (65)	60 (40-69)[b]	29 (20-41)[b]	10 (9-14)[b]	20 (13-30)[b,‡]
Fitzgerald et al, 2017[25]	CC	USA	Combined	23	NA	68 (63-89)a	21 (16-26)[a]	NA	122
Kocher et al, 2017[26]	RC	Germany	Flail chest	61	44 (72)	68 (36-87)[a]	33	10 (4)	782 (408)
Schulz-Drost et al, 2017[27]	PC	Germany	Flail chest	15	9 (60)	59 (18)	NA	NA	84
Song et al, 2017[28]	RC	China	Combined	25	18 (72)	60 (13)	NA	8 (4)	587 (310)
DeFreest et al, 2016[31]	RC	USA	Flail chest	41	19 (46)	51 (19-80)[b]	28 (16-48)[a]	11 (6-19)[b]	28 (9-69)[a,‡]
Farquhar et al, 2016[33]	CC	Canada	Flail chest	19	15 (79)	53 (14)	31 (10)	NA	22 (13)[‡]
Granhed et al, 2014*[30,32,45]	PC	Sweden	Combined	60	44 (73)	57 (19-86)[a]	22 (11)	8 (2-14)[a]	365
Marasco et al, 2016[34]	RC	Australia	Multiple rib	14	14 (100)	52 (32-77)[a]	NA	7 (4-14)[c]	183
Pieracci et al, 2016[35]	PC	USA	Combined	35	30 (86)	51 (15)	22 (17-26)[b]	9 (7-11)	13 (9-21)[b,‡]
Qiu et al, 2016A[36]	RC	China	Multiple rib	21	15 (71)	35 (13)	NA	NA	NA
Qiu et al, 2016B[36]	RC	China	Flail chest	65	46 (71)	38 (12)	NA	NA	NA

Table 1. Baseline characteristics of included studies describing complications of rib fracture fixation. (continued)

Author and year	Study Design	Country	Fracture Type	Patients, No. (%)	Male, No. (%)	Age, Mean (SD), y	ISS, Mean (SD)	Fractured ribs, Mean (SD)	Follow-up, Mean (SD), d
Tarng et al, 2016[37]	RC	Taiwan	Combined	12	11 (92)	47 (14)	21 (4)	7 (1)	639 (548-730)[a]
Taylor et al, 2016[38]	CC	USA	Flail chest	88	59 (67)	54 (17)	24 (11)	9 (4)	NA
Thiels et al, 2016[39]	RC	USA	Combined	122	89 (73)	60 (16)	17 (13-22)[b]	7 (5-9)[b]	222 (97-398)[b]
Uchida et al, 2016[29]	CC	Japan	Combined	10	7 (70)	63 (51-72)[b]	NA	5 (5-7)[b]	NA
Zhang X et al, 2015[41]	RC	China	Flail chest	23	16 (79)	58 (12)	NA	8 (2)	426 (108)
Zhang Y et al, 2015[43]	CC	China	Flail chest	24	19 (79)	43 (34-50)[b]	38 (34-43)[b]	12 (8-15)[b]	38 (33-54)[c‡]
Doben et al, 2014[44]	CC	USA	Flail chest	10	9 (90)	47 (15)	26 (10)	8 (4-20)[a]	183
Wiese et al, 2014A[40]	PC	Switzerland	Multiple rib	26	19 (73)	52 (47-68)[b]	NA	6 (5-10)[b]	183
Wiese et al, 2014B[40]	PC	Switzerland	Flail chest	68	55 (81)	NA	NA	8 (6-11)[c]	183
Bottlang et al, 2013[46]	PC	USA	Flail chest	20	NA	51 (29-70)[a]	28 (16-66)[a]	9 (4-15)	183
Marasco et al, 2013[13]	RCT	Australia	Flail chest	23	20 (87)	58 (17)	35 (11)	11 (3)	91
Muhm et al, 2013[47]	RC	Germany	Combined	21	15 (71)	59 (36-87)[c]	36 (18)	9 (4)	32 (14)[‡]
Althausen et al, 2011[49]	CC	USA	Flail chest	22	17 (77)	48	25	6	543 (137)
Khandelwal et al, 2011[51]	PC	India	Combined	31	NA	47	NA	3	30
Sellers et al, 2011[48]	RC	UK	Combined	10	7 (70)	50 (28-83)[c]	29 (16-41)[c]	NA	NA
Campbell et al, 2009[52]	RC	Australia	Combined	32	23 (70)	53 (40-64)[b]	26 (10)	9 (6-13)[b]	480
Marasco et al, 2009[53]	PC	Australia	Flail chest	10	6 (60)	59 (13)	33 (8)	NA	91
Mayberry et al, 2009[54]	RC	USA	Combined	46	36 (78)	50 (15-85)[a]	30 (12)	8 (3)	800 (840)
Solberg et al, 2009[55]	RC	USA	Flail chest	9	3 (33)	39 (17)	25 (7)	NA	487
Richardson et al, 2007[56]	RC	USA	Multiple rib	5	NA	41 (33-58)[a]	NA	8 (7-9)[c]	1460 (365-3650)[a]
Granetzny et al, 2005[12]	RCT	Germany	Flail chest	20	17 (85)	41 (8)	17 (4)	4	60
Lardinois et al, 2001[57]	PC	Germany	Flail chest	66	56 (85)	53 (21-82)[a]	NA	6 (4-11)[a]	183
Mouton et al, 1997[58]	PC	Swiss	Flail chest	23	21 (91)	52 (22-81)[a]	NA	NA	840

Abbreviations: CC, Case Control; D, Days; ISS, Injury Severity Score; NA, Not Available; No., Number; PC, Prospective Cohort; RC, Retrospective Cohort; RCT, Randomized Controlled Trial; SD, Standard Deviation; UK, United Kingdom; USA, United States of America; Y, Years.

[a] Mean (Range), [b] Median (Interquartile Range), [c] Median (Range), [‡] Based on total hospital length of stay, *Merged data

7.4% (n = 65). Numbness of the chest wall was reported in only three studies, ranging from 0 to 16% (27,28,52). Breakage or mechanical failure was reported in only one patient (0.1%).

Bone-healing complications

Twenty-four studies reported on bone-healing complications (n = 911), which are presented in Appendix 3. The overall risk of symptomatic rib nonunion after surgical fixation was 1.3% (n = 12) (Table 2). Malunion was not reported by the included studies.

Pulmonary complications

Forty studies reported on pulmonary complications (n = 1655), which are presented in Appendix 4. The overall risk of pulmonary complications was 30.9% (n = 511). Among the pulmonary complications, the most common complication was pneumonia (54.2%, n = 277), followed by need for tracheostomy (29.7%, n = 152), ARDS (3.7%, n = 19), pneumothorax (3.1%, n = 16), and hemothorax (2.1%, n = 11). This means that the absolute risk of these pulmonary complications after rib fracture fixation were 17.9% (pneumonia), 15.2% (need for tracheostomy), 2.6% (ARDS), 2.2% (pneumothorax), and 1.6% (hemothorax) (Table 2).

Table 2. Complications of rib fracture fixation.

Complication classification	Studies, No.	Patients, No.	Incidence, No. (%)
Surgery- and implant-related complications			
Bleeding	24	849	12 (1.4)
Wound infection	36	1394	31 (2.2)
FRI	41	1608	21 (1.3)
Revision surgery	38	1507	43 (2.9)
Breakage	35	1278	0 (0)
Mechanical failure	35	1278	1 (0.1)
Irritation	22	939	65 (6.9)
Bone-healing complications			
Nonunion	24	911	12 (1.3)
Malunion	22	867	0 (0)
Pulmonary complications			
Pneumonia	34	1546	277 (17.9)
Excess pleural fluid	14	673	16 (2.4)
Hemothorax	15	695	11 (1.6)
Pneumothorax	16	728	16 (2.2)
Tension pneumothorax	15	669	15 (2.2)
Empyema	15	677	5 (0.7)
Tracheostomy	23	997	152 (15.2)
ARDS	15	725	19 (2.6)

Abbreviations: ARDS, Acute Respiratory Distress Syndrome; FRI, Fracture Related Infection; No., Number.

Mortality

Forty-one studies reported on the mortality (n = 1725) with an overall mortality risk of 2.9% (n = 50) (Appendix 3). Fourteen studies distinguished between the cause of mortality and reported that 27.0% of the patients died as a result of an underlying injury or complication related to the thoracic injury. The main causes of mortality were respiratory failure due to ARDS or pneumonia.

Outcomes

Eleven studies reported on short- or long-term outcome after rib fracture fixation using many different patient-reported outcome measures (PROMs). The most frequently used questionnaire was the EQ-5D for patient quality of life in four studies reporting a weighted mean EQ-5D index of 0.80 indicating good quality of life. Details of the different questionnaires reported by the studies are presented in Table 3.

Table 3. Long- and short-term outcomes after rib fracture fixation.

Author and year	Follow-up, Mean (SD), m	Patients, No. (%)		PROM	Outcome, Mean (SD)	
		Surg	Cons		Surg	Cons
Long-term outcomes (≥12 months)						
Marasco et al, 2019[59]	24	59	177	GOSE	5.5 (5.1-6.0)[c]	6.0 (5.7-6.2)[c]
				SF MMC	52.5 (49.3-55.7)[c]	51.9 (50.1-53.6)[c]
				SF PCS	38.4 (34.9-42.0)[c]	42.2 (40.3-44.1)[c]
Walters et al, 2019[61]	19 (10)	36	25	EQ-5D-5L index	0.6 (0.3)	0.6 (0.3)
Beks et al, 2018A[63]	53 (41-71)[b]	63	NA	EQ-5D-5L index	0.8 (0.6-0.9)[b]	NA
				EQ-VAS	73 (65-80)[b]	NA
Beks et al, 2018B[63]	37 (29-61)[b]	40	NA	EQ-5D-5L index	0.9 (0.6-1.0)[b]	NA
				EQ-VAS	75 (63-85)	NA
Granhed et al, 2014*[30,32,45]	12	45	NA	EQ-5D-3L index	0.9	NA
				EQ-VAS	90 (30-100)[a]	NA
Farquhar et al, 2016[33]	Unspecified	11	18	EQ-VAS	65 (45.7-84.2)[c]	67.2 (56.3-78.0)[c]
Mayberry et al, 2009[54]	26 (27)	46	NA	Rand-36 General Health	70 (23)	NA
				Rand-36 Physical Function	76 (28)	NA
Campbell et al, 2009[52]	34 (16)	20	NA	AQoL	0.6 (0.4)	NA
Short-term outcomes (<12 months)						
Pieracci et al, 2019[64]	2	NA	NA	QOL - American Chronic Pain Association	10	7
Bottlang et al, 2013[46]	6	15	NA	Rand-36 General Health	53 (21)	NA
				Rand-36 Physical Function	54 (31)	NA
Xu et al, 2015[42]	0.5	15	17	APACHE II	6.5 (1.8)	10.1 (4.7)
Marasco et al, 2013[13]	6	19	18	SF-36 PCS	33.6 (9.8)	35.2 (10.7)

Abbreviations: AQoL, Assessment of Quality of Life Instrument; Cons, Conservative, EQ-5D-5L, EuroQol-5D-5L; GOSE, Glasgow Outcome Scale Extended; NA, not applicable; PROM, Patient Reported Outcome Measure; SF-MMC, Short-Form Physical Component Summary, SF-36, Short-Form 36; Surg, Surgery.

[a] Mean (Range), [b] Median (Interquartile Range), [c] Median (Range), *Merged data

DISCUSSION

The aim of this systematic review was to report on the incidence of complications associated with rib fixation after rib fractures and to determine clinical outcomes and quality of life following surgery. Results of this study showed that rib fixation can be considered as a safe procedure with a considerably low complication risk and satisfactory long-term outcomes.

The present study demonstrated that the incidence of surgery- and implant-related complications of rib fixation was relatively low. Revision surgery showed to be the most frequently encountered complication and was reported in 2.9% of all cases. Wound infection was reported in 2.2% of all patients. The majority of these patients were treated successfully with systemic antibiotic treatment. Furthermore, fracture-related infection showed to be a relatively uncommon complication of rib fracture fixation and occurred in only one percent of all patients. In the current literature, significantly higher rates, ranging from 5% to 20%, have been observed after open and internal fixation for other fracture types.[39,65] Even though the implant-related complications after rib fixation reported in this systematic review seemed to be relatively low, it must be noted that these complications remain a relevant problem associated with a significant morbidity. Infections may result in compromised fracture healing, chronic osteomyelitis, prolonged antibiotic therapy, or reduced functionality, and often necessitates extensive radical debridement with implant removal.[66] Indeed, as showed in the current study, revision surgery with or without implant removal was required in one-third of all patients with an infection.

Another important finding of this study was that implant-related irritation after rib fracture fixation might be a relevant and possibly underestimated problem. Twenty-two studies showed that the risk of implant-related irritation after rib fracture fixation was 6.9%. However, there was a wide variety in the number of patients with implant-related irritation between the included studies, ranging from 0% to 53%. An explanation for this variety, is that there was only one long-term follow-up study using a standardized questionnaire concerning implant-related irritation and removal accounting for 75% of all patients with implant-related irritation in this systematic review.[63] Therefore, it is expected that the total incidence of implant-related irritation is underestimated because of insufficient reporting. Another explanation is that about two-third of the included studies had a follow-up time of less than a year, which might be too short to determine these complications. Future studies should therefore focus on the use of an implant-related irritation and removal questionnaire, for example, as described by Hulsmans and collegues.[67]

Pneumonia appeared to be the most important pulmonary complication among patients with rib fractures. In previous studies, it has been reported that pain associated with rib fractures can lead to insufficient ventilation and impaired airway clearance. Consequently, patients are at greater risk of acquiring (acute) pulmonary infections.[68] Therefore, the main purpose of rib fixation is to restore the integrity and stability of the chest wall, reduce pain, and thus diminish the risk of pulmonary complications. A recent systematic review of Beks et al, showed that rib fixation resulted in a significant reduction of pneumonia compared to those who were treated conservatively (Risk Ratio 0.59, 95% CI 0.42-0.83, $p = 0.002$).[16] The mean weighted incidence of pneumonia among patients who underwent surgery and those treated conservatively was 20% and 26%, respectively. Rib fixation resulted also in significantly lower rates of tracheostomy and a reduction of days on mechanical ventilation in favor of the operative group. However, although rib fixation might improve the outcomes in terms of pulmonary complications, the current study showed that the pulmonary complications remain a major problem, even among patients who underwent rib fixation.

Previous studies showed that multiple rib fractures are associated with a significant morbidity, including chronic pain, long-term disability, and impaired quality of life.[6,7,14,59,69] However, it remains unclear to what extent rib fracture fixation can be beneficial in quality of life. In this systematic review, eight studies reported on the long-term (≥ 12 months) outcomes after rib fracture fixation, of which three were comparative studies. Different outcomes were observed and there was a great heterogeneity between the patient reported outcome measures used in the included studies. A recent comparison study of Marasco et al used the Short-Form 12 questionnaire to evaluate the quality of life and reported on significant worse outcomes after rib fixation.[59] However, an important limitation of this study was that the severity of the thoracic injuries was not taken into consideration. This is of great influence on the results as it has been shown that the number and location of fractured ribs are associated with worse quality of life.[69] Two other comparative studies used the EQ-5D-5L questionnaire, and described that surgical fixation had no effect on the long-term quality of life when compared to the non-operative patients.[61,63] Beks et al reported that the EQ-5D index after rib fixation was comparable to the Dutch reference population and that there were no differences in EQ-5D index scores between patients with flail chest and multiple rib fractures.[63] An explanation for this finding was that patients with flail chest and multiple rib fractures had comparable injury severity scores and there was no distinction between radiological and clinical flail chest. Caragounis et al showed similar results in a one-year follow up study of both flail chest and multiple rib fractures patient.[30] Campbell et al reported that the quality of life was lower compared to the reference population, which might be explained by the higher ISS score of the surgery group.[52] Although outcomes have been described heterogeneously, overall quality of life after rib fixation was considered high compared to population based reference values.

Several potential limitations of this systematic review must be acknowledged. First, results might be affected by missed studies. However, a large comprehensive search was performed using multiple databases and citations and references were checked. Therefore, the potential risk of missing studies was low. Second, the complication rates after rib fixation reported in different studies could have been affected by the use of different definitions. For example, a considerable heterogeneity was observed regarding the definitions used for pneumonia. Furthermore, clear definitions of the implant- and surgery-related complications were often lacking. Therefore, in future studies improvements can be made by consistently using unambiguous definitions for complications, for example the Clavien-Dindo classification for surgical complications.[70] Third, the bone-healing complications requiring revision surgery may be underestimated as only a small number of studies adequately reported on these complications, thus implicating reporting bias. Fourth, it has been suggested that early fixation might result in a reduction of complications. However, due to insufficient data we were not able to adjust for the time until surgery. Fifth, many studies reporting on the long-term outcomes after rib fracture fixation differed concerning the used patient reported outcome measures, patient cohorts, and average follow-up time, and therefore, outcomes were overall difficult to compare.

Over the past years, there has been an increased interest in surgical fixation and many studies reported on the in-hospital and long-term outcomes of rib fracture fixation. Although favorable results have been reported after surgical fixation, no comprehensive study reported on the complications associated with rib fixation. Patients should be counseled that surgical- and implant-related complications occur in approximately one in ten patients. However, the clinically most relevant complications (i.e. wound infection, fracture-related infection, and nonunion) occur infrequently and the number of complications requiring immediate (surgical) treatment is low. In conclusion, this systematic review helps to provide better insight into the complication profile of surgical fixation of fractured ribs and contributes to the discussion regarding the optimal treatment of patients with rib fractures.

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Appendix 1. Search syntax representing the used search strings in the different databases

Database	Syntax
PubMed (n = 2810)	(((((fractur* [Title/Abstract]) AND ((ribs [Mesh]) OR rib* [Title/Abstract]))) OR ((((rib fractures [Mesh]) OR flail chest [Mesh]) OR rib fractur* [Title/Abstract]) OR “flail chest” [Title/Abstract]))) AND ((((((((fracture treatment [Mesh]) OR surgical treatment [Mesh]) OR surgical management [Mesh]) OR surgical procedure, operative [Mesh]) OR ORIF [Title/Abstract]) OR plat* [Title/Abstract]) OR surg* [Title/Abstract]) OR fix* [Title/Abstract])
EMBASE (n = 2844)	((‘ribs’/exp OR ‘ribs*’:ab,ti) AND ‘fractur*’:ab,ti OR ‘rib fractur*’:ab,ti OR ‘rib fractures’/exp OR ‘flail chest’/exp OR ‘flail chest’:ab,ti) AND (‘fracture treatment’ OR orif:ab,ti OR ‘plat*’:ab,ti OR ‘surg*’:ab,ti OR ‘fix*’:ab,ti)
CENTRAL (n = 207)	(“rib fracture*” OR “flail chest”)

Appendix 2. Quality assessment according to the MINORS criteria

MINORS criteria	Pieracci et al, 2019[64]	Akil et al, 2019[50]	Liu et al, 2019[15]	Marasco et al, 2019[59]	Su et al, 2019[60]	Walters et al, 2019[61]	Ali-Osman et al, 2018[62]	Beks et al, 2018 A&B[63]	Iqbal et al, 2018[20]	Kane et al, 2018[21]	Liu et al, 2018[22]	Michelitsch et al, 2018[23]	Wijffels et al, 2018[24]	Fitzgerald et al, 2017[25]	Kocher et al, 2017[26]	Schulz-Drost et al, 2017[27]	Song et al, 2017[28]	DeFreest et al, 2016[31]	Farquhar et al, 2016[33]	Granhed et al, 2014[30,32,45]	Marasco et al, 2016[34]	Pieracci et al, 2016[35]	Qiu et al, 2016 A&B[36]	Taylor et al. 2016[38]	Tarng et al, 2015
A clearly stated aim*	2	2	2	2	2	2	2	2	2	2	1	2	2	2	2	1	2	2	2	2	2	2	2	2	2
Inclusion of consecutive patients	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Prospective collection of data	2	2	2	1	2	2	1	1	1	2	1	1	1	1	1	2	1	1	1	2	1	2	1	1	0
Endpoints appropriate to the aim of study	2	2	2	2	2	2	2	2	2	2	1	2	2	1	2	2	2	2	2	2	1	2	2	2	2
Unbiased assessment of the study endpoint	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0
Follow-up period appropriate to the aim of the study	1	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	0	2	2	2	1	1	2
Loss to follow-up less than 5%	1	2	2	1	2	1	2	1	2	1	2	1	2	1	2	2	2	2	1	1	2	1	0	0	2
Prospective calculation of the study size	2	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Adequate control group	2	-	-	-	-	-	0	-	0	-	-	-	-	-	0	-	0	0	-	0	0	-	-	0	-
Contemporary groups	2	-	-	-	-	-	0	-	0	-	-	-	-	-	0	-	0	0	-	0	0	-	-	0	-
Baseline equivalence of groups	2	-	-	-	-	-	0	-	0	-	-	-	-	-	0	-	0	0	-	0	0	-	-	0	-
Adequate statistical analyses	2	-	-	-	-	-	0	-	0	-	-	-	-	-	0	-	0	0	-	0	0	-	-	0	-
Total MINORS score	**20**	**12**	**14**	**10**	**12**	**11**	**10**	**10**	**11**	**11**	**9**	**10**	**12**	**10**	**11**	**11**	**11**	**11**	**8**	**11**	**10**	**11**	**8**	**8**	**10**

Continued

Appendix 2. (Continued)

MINORS criteria	Thiels et al, 2016[39]	Uchida et al, 2016[29]	Xu et al, 2015[42]	Zhang X et al, 2015[41]	Zhang Y et al, 2015[43]	Doben et al, 2014[44]	Wiese et al, 2014 A&B[40]	Bottlang et al, 2013[46]	Marasco et al, 2013[13]	Muhm et al, 2013[47]	Althausen et al, 2011[49]	Khandelwal et al, 2011[51]	Sellers et al, 2011[48]	Campbell et al, 2009[52]	Marasco et al, 2009[53]	Mayberry et al, 2009[54]	Solberg et al, 2009[55]	Richardson et al, 2007[56]	Granetzny et al, 2005[12]	Lardinois et al, 2001[57]	Mouton et al, 1997[58]
A clearly stated aim*	2	2	2	2	2	2	2	2	2	2	2	1	2	2	2	1	1	2	2	2	2
Inclusion of consecutive patients	2	2	2	2	2	2	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2
Prospective collection of data	1	1	1	1	1	1	2	2	2	1	1	2	1	1	2	1	1	1	2	2	2
Endpoints appropriate to the aim of study	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	1	2	2	2
Unbiased assessment of the study endpoint	1	1	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0
Follow-up period appropriate to the aim of the study	2	2	1	2	2	2	0	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Loss to follow-up less than 5%	1	2	2	0	2	2	1	1	2	2	0	2	2	1	1	1	0	2	2	2	2
Prospective calculation of the study size	0	0	0	0	0	0	0	0	2	0	2	2	0	0	0	0	0	0	0	0	0
Adequate control group	-	-	0	0	0	-	-	-	-	0	-	-	-	-	-	0	-	0	0	-	0
Contemporary groups	-	-	0	0	0	-	-	-	-	0	-	-	-	-	-	0	-	0	0	-	0
Baseline equivalence of groups	-	-	0	0	0	-	-	-	-	0	-	-	-	-	-	0	-	0	0	-	0
Adequate statistical analyses	-	-	0	0	0	-	-	-	-	0	-	-	-	-	-	0	-	0	0	-	0
Total MINORS score	**11**	**12**	**10**	**9**	**11**	**11**	**9**	**11**	**14**	**11**	**11**	**13**	**11**	**10**	**11**	**9**	**8**	**10**	**12**	**12**	**12**

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, 1 point if one of the PICO criteria has not been satisfied, 0 points if not reported according to the PICO model

Appendix 3. Surgery- and implant-related complications, bone-healing complications, and mortality[#].

Author and year	Surgery-related complications				Implant-related complications			Bone-healing complications		Mortality
	Bleeding	Wound infection	Fracture-related infection	Revision surgery	Breakage	Mechanical failure	Irritation	Nonunion	Malunion	
Pieracci et al, 2019[64]	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	NA	NA	0 (0)
Akil et al, 2019[50]	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Liu et al, 2019[15]	0 (0)	0 (0)	0 (0)	NA	0 (0)	0 (0)	NA	0 (0)	0 (0)	4 (16)
Marasco et al, 2019[59]	NA	NA	NA	NA	NA	NA	NA	NA	NA	1 (1.5)
Su et al, 2019[60]	NA	NA	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	NA	NA	2 (6.1)
Walters et al, 2019[61]	NA	NA	NA	NA	NA	NA	NA	NA	NA	1 (1.8)
Ali-Osman et al, 2018[62]	NA	1 (1.6)	0 (0)	NA	NA	NA	NA	NA	NA	1 (1.6)
Beks et al, 2018A[63]	1 (1.5)	0 (0)	3 (3.0)	5 (5.1)	0 (0)	0 (0)	28 (44.0)	NA	NA	3 (3)
Beks et al, 2018B[63]	1 (1.5)	1 (1.5)	2 (3.0)	5 (7.5)	0 (0)	0 (0)	21 (53.0)	NA	NA	6 (9)
Iqbal et al, 2018[20]	0 (0)	1 (1.0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	4 (3.9)
Kane et al, 2018[21]	NA	NA	NA	NA	NA	NA	NA	NA	NA	1 (0.9)
Liu et al, 2018[22]	NA	NA	0 (0)	1 (1.7)	0 (0)	0 (0)	1 (1.9)	NA	NA	NA
Michelitsch et al, 2018[23]	0 (0)	0 (0)	0 (0)	4 (17.4)	0 (0)	0 (0)	NA	0 (0)	NA	0 (0)
Wijffels et al, 2018[24]	2 (9)	3 (13.0)	0 (0)	0 (0)	NA	NA	NA	NA	NA	2 (9)
Fitzgerald et al, 2017[25]	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	NA	NA	NA	0 (0)
Kocher et al, 2017[26]	0 (0)	1 (1.6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (4.9)
Schulz-Drost et al, 2017[27]	NA	0 (0)	0 (0)	1 (6.7)	0 (0)	0 (0)	NA	0 (0)	0 (0)	0 (0)
Song et al, 2017[28]	8 (32.0)	NA	NA	2 (8.0)	NA	NA	2 (8)	0 (0)	0 (0)	NA
DeFreest et al, 2016[31]	0 (0)	0 (0)	2 (4.9)	5 (12.2)	0 (0)	0 (0)	0 (0)	NA	NA	1 (2.4)
Farquhar et al, 2016[33]	NA	NA	NA	0 (0)	NA	NA	NA	NA	NA	1 (5.0)
Granhed et al, 2014*[30,32,45]	0 (0)	0 (0)	1 (1.7)	3 (5.0)	0 (0)	0 (0)	1 (1.7)	NA	NA	3 (5)
Marasco et al, 2016[34]	NA	NA	NA	2 (14.3)	0 (0)	0 (0)	0 (0)	2 (14.3)	0 (0)	0 (0)

Appendix 3. Surgery- and implant-related complications, bone-healing complications, and mortality#. (continued)

Author and year	Surgery-related complications				Implant-related complications			Bone-healing complications		Mortality
	Bleeding	Wound infection	Fracture-related infection	Revision surgery	Breakage	Mechanical failure	Irritation	Nonunion	Malunion	
Pieracci et al, 2016[35]	NA	NA	1 (2.9)	1 (2.9)	0 (0)	1 (2.9)	NA	NA	NA	0 (0)
Qiu et al, 2016A[36]	NA	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	NA	0 (0)	0 (0)	0 (0)
Qiu et al, 2016B[36]	NA	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	NA	0 (0)	0 (0)	1 (4.8)
Tarng et al, 2016[37]	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Taylor et al, 2016[38]	NA	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1.1)	0 (0)	2 (2.3)
Thiels et al, 2016[39]	NA	1 (0.8)	5 (4.1)	5 (4.1)	NA	NA	NA	0 (0)	0 (0)	1 (0.8)
Uchida et al, 2016[29]	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	NA	NA	0 (0)
Xu et al, 2015[42]	NA	NA	0 (0)	NA	0 (0)	0 (0)	NA	NA	NA	0 (0)
Zhang X et al, 2015[41]	NA	0 (0)	1 (4.3)	2 (8.7)	0 (0)	0 (0)	6 (26.1)	NA	NA	NA
Zhang Y et al, 2015[43]	NA	6 (25.0)	NA	NA	NA	NA	NA	NA	NA	0 (0)
Doben et al, 2014[44]	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	NA	NA	N/A
Wiese et al, 2014A[40]	NA	NA	0 (0)	NA	NA	NA	NA	NA	NA	0 (0)
Wiese et al, 2014B[40]	NA	NA	2 (2.9)	2 (2.9)	NA	NA	NA	NA	NA	1 (1.5)
Bottlang et al, 2013[46]	0 (0)	1 (5)	1 (5.0)	1 (5.0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Marasco et al, 2013[13]	NA	NA	NA	NA	NA	NA	NA	3 (14.3)	NA	0 (0)
Muhm et al, 2013[47]	0 (0)	0 (0)	0 (0)	0 (0)	NA	NA	NA	NA	NA	2 (9.5)
Althausen et al, 2011[49]	NA	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	NA
Khandelwal et al, 2011[51]	NA	3 (9.7)	0 (0)	NA	0 (0)	0 (0)	NA	NA	NA	0 (0)
Sellers et al, 2011[48]	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Campbell et al, 2009[52]	0 (0)	5 (15.6)	0 (0)	1 (3.1)	0 (0)	0 (0)	NA	1 (3)	0 (0)	1 (3)
Marasco et al, 2009[53]	0 (0)	1 (10.0)	1 (10.0)	0 (0)	0 (0)	0 (0)	NA	2 (20)	0 (0)	0 (0)
Mayberry et al, 2009[54]	0 (0)	0 (0)	2 (4.3)	1 (2.2)	0 (0)	0 (0)	1 (2.2)	3 (6.5)	0 (0)	NA

Appendix 3. Surgery- and implant-related complications, bone-healing complications, and mortality[#]. (continued)

Author and year	Surgery-related complications				Implant-related complications			Bone-healing complications		Mortality
	Bleeding	Wound infection	Fracture-related infection	Revision surgery	Breakage	Mechanical failure	Irritation	Nonunion	Malunion	
Solberg et al, 2009[55]	NA	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	NA	NA	NA	NA
Richardson et al, 2007[56]	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	NA	0 (0)	0 (0)	0 (0)
Granetzny et al, 2005[12]	NA	4 (20.0)	0 (0)	NA	NA	NA	NA	NA	NA	2 (10.0)
Lardinois et al, 2001[57]	NA	2 (3.0)	0 (0)	0 (0)	0 (0)	0 (0)	NA	0 (0)	0 (0)	7 (11.0)
Mouton et al, 1997[58]	0 (0)	1 (4.3)	0 (0)	2 (8.7)	0 (0)	0 (0)	5 (21.7)	0 (0)	0 (0)	2 (8.7)

Abbreviations: NA, Not Available

[#] *All data presented as numbers with percentages*

* *Merged data*

Appendix 4. Pulmonary complications after rib fracture fixation

Author and year	Pneumonia	Excess pleural fluid	Hemothorax	Pneumothorax	Tension pneumothorax	Pleural empyema	Tracheostomy	ARDS
Pieracci et al, 2019[64]	1 (2)	NA	NA	NA	NA	NA	NA	NA
Akil et al, 2019[50]	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Liu et al, 2019[15]	12 (48.0)	NA	NA	NA	NA	NA	10 (40.0)	7 (28.0)
Su et al, 2019[60]	7 (21.2)	NA	NA	NA	NA	NA	NA	NA
Ali-Osman et al, 2018[62]	5 (7.8)	6 (9.3)	0 (0)	1 (1.6)	0 (0)	0 (0)	NA	0 (0)
Beks et al, 2018A[63]	32 (32.0)	3 (3.0)	2 (2.0)	2 (2.0)	2 (2.0)	0 (0)	9 (9.0)	3 (3.0)
Beks et al, 2018B[63]	26 (39.0)	3 (4.5)	2 (3.0)	2 (3.0)	1 (1.0)	1 (1.5)	7 (10.0)	2 (3.0)
Iqbal et al, 2018[20]	29 (28.4)	0 (0)	0 (0)	1 (1)	0 (0)	0 (0)	12 (11.8)	0 (0)
Kane et al, 2018[21]	7 (6.0)	NA	NA	NA	NA	NA	10 (8.6)	NA
Liu et al, 2018[22]	NA	NA	7 (3.5)	7 (13.5)	NA	NA	NA	NA
Michelitsch et al, 2018[23]	NA	NA	0 (0)	NA	NA	NA	NA	NA
Wijffels et al, 2018[24]	8 (35.0)	NA	NA	NA	NA	0 (0)	NA	NA
Kocher et al, 2017[26]	5 (8.2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	16 (26.2)	1 (1.6)
Schulz-Drost et al, 2017[27]	0 (0)	NA	NA	2 (13.3)	NA	NA	NA	NA
DeFreest et al, 2016[31]	11 (26.8)	NA	NA	1 (2.4)	NA	3 (7.3)	10 (24.4)	2 (4.9)
Farquhar et al, 2016[33]	12 (63.0)	NA	NA	NA	NA	NA	NA	NA
Fitzgerald et al, 2017[25]	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Granhed et al, 2014*[30,32,45]	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	NA	0 (0)
Pieracci et al, 2016[35]	7 (20)	NA	NA	NA	NA	NA	7 (20)	NA
Qiu et al, 2016A[36]	3 (4.6)	NA	NA	NA	NA	NA	0 (0)	NA
Qiu et al, 2016B[36]	1 (4.8)	NA	NA	NA	NA	NA	2 (9.5)	NA
Tarng et al, 2016[37]	NA	NA	NA	NA	NA	NA	0 (0)	NA
Taylor et al, 2016[38]	16 (18.2)	NA	NA	NA	NA	NA	21 (23.9)	NA
Thiels et al, 2016[39]	19 (15.6)	NA	NA	NA	NA	NA	NA	NA
Uchida et al, 2016[29]	2 (20.0)	NA	0 (0)	0 (0)	0 (0)	0 (0)	1 (10.0)	0 (0)
Xu et al, 2015[42]	10 (58.8)	NA	NA	NA	NA	NA	2 (11.8)	NA
Zhang X et al, 2015[41]	7 (30.4)	NA	NA	NA	NA	NA	11 (47.8)	NA
Zhang Y et al, 2015[43]	16 (66.7)	3 (12.5)	NA	NA	NA	NA	12 (50.0)	NA
Wiese et al, 2014A[40]	0 (0)	NA	NA	NA	NA	NA	NA	NA
Wiese et al, 2014B[40]	4 (5.9)	NA	NA	NA	NA	NA	NA	NA
Bottlang et al, 2013[46]	6 (30.0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Marasco et al, 2013[13]	11 (48.0)	NA	NA	NA	NA	NA	9 (39.0)	NA
Muhm et al, 2013[47]	12 (57.1)	NA	NA	NA	NA	NA	10 (47.6)	NA
Althausen et al, 2011[49]	1 (4.6)	NA	NA	NA	NA	NA	3 (13.6)	NA
Campbell et al, 2009[52]	3 (9.0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Mayberry et al, 2009[54]	NA	1 (2.2)	NA	NA	NA	NA	NA	NA

Appendix 4. Pulmonary complications after rib fracture fixation (continued)

Author and year	Pneumonia	Excess pleural fluid	Hemothorax	Pneumothorax	Tension pneumothorax	Pleural empyema	Tracheostomy	ARDS
Solberg et al, 2009[55]	0 (0)	NA	NA	NA	NA	NA	NA	NA
Richardson et al, 2007[56]	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	NA	0 (0)
Granetzny et al, 2005[12]	NA	0 (0)	0 (0)	0 (0)	0 (0)	1 (5)	NA	NA
Lardinois et al, 2001[57]	5 (7.6)	NA	NA	NA	NA	NA	NA	4 (6.1)

Abbreviations: ARDS, Acute Respiratory Distress Syndrome; NA, Not Available

[#] All data presented as numbers with percentages

* Merged data

8 | The evaluation of pulmonary function after rib fixation for multiple rib fractures and flail chest: a retrospective study and systematic review of the current evidence.

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ABSTRACT

Purpose The primary aim of this retrospective cohort study was to evaluate the pulmonary function after rib fixation for patients with multiple rib fractures and flail chest. Secondary, a systematic review was performed to give an overview of the current literature and to allow comparison with our results.

Methods All adult (≥ 18 years) patients who underwent rib fixation for multiple rib fractures or flail chest between 2010 and 2018 and who received a control pulmonary function test during the postoperative follow-up at our level-1 trauma center were retrospectively reviewed. Secondary, the PubMed, EMBASE and Cochrane databases were searched to identify studies reporting on the pulmonary function after rib fixation. The primary outcome parameters were the forced vital capacity (FVC), forced expiratory volume in 1 second (FEV_1), FEV_1/FVC ratio, maximum vital capacity (VC_{max}), total lung capacity (TLC), residual volume (RV), and RV/TC ratio.

Results Of the 103 patients who underwent rib fixation, a total of 61 (59%) patients underwent a pulmonary function test in our hospital and were ultimately included. In the majority of patients all pulmonary function parameters fell within the normal range of the reference values. Obstructive impairment was predominantly seen in patients with pre-existing chronic obstructive pulmonary disease (COPD). Patients with multiple rib fractures had better recovery compared to those with a flail chest. The systematic review included a total of 15 studies and showed comparable results.

Conclusion The present study demonstrates that rib fixation for multiple rib fractures or flail chest results in adequate recovery of the pulmonary function within three months after surgery. In addition, based on the current literature, further gradual improvement to maximum pulmonary values appears to occur during the first 12 months after rib fixation.

INTRODUCTION

Thoracic trauma is considered the second leading cause of death among the trauma population.[1] Rib fractures are the most frequently encountered injuries sustained after blunt thoracic trauma and are identified in 10% of all polytrauma patients.[2] Rib fractures carry a significant morbidity and mortality as they are mostly accompanied by severe concomitant injury to the lung or other organs.[3-5] Mortality rates reported range between 10% to 20%, depending on risk factors such as age, underlying injuries, number of fractured ribs, and the presence of a flail segment.[4,6]

Rib fractures can lead to severe pain and a loss of the chest wall integrity, resulting in insufficient ventilation, ineffective clearance of secretions, and atelectasis. Furthermore, in patients with a clinical flail chest, the paradoxical movement of the flail segment can affect the ventilation even more.[7] Consequently, there is an increased risk of pneumonia, respiratory failure, and prolonged mechanical ventilation.[3]

Adequate restoration of the pulmonary function is key in the management of rib fractures to prevent respiratory complications and prolonged mechanical ventilation. Previously, patients with rib fractures were treated conservatively with a combination of adequate pain relief, respiratory support, and aggressive pulmonary toilet. Nowadays, in the current clinical practice, surgical fixation has increasingly been applied and aims to restore the chest wall integrity, alleviate pain, and improve the pulmonary function.[8] However, even though previous studies reported on favorable outcomes after rib fixation in patients with flail chest, literature on the impact of rib fixation on the pulmonary function is scarce.[9]

Therefore, the primary aim of this retrospective cohort study was to evaluate the pulmonary function after rib fixation for patients with multiple rib fractures and flail chest. Secondary, a systematic review was performed to give an overview of the current literature and to allow comparison with our results.

METHODS

Retrospective study

This study was approved by the institutional review board (EKNZ 2019-00618) and was conducted according to the Declaration of Helsinki. The article was written in adherence to the STROBE statement guidelines for reporting observational studies.[10]

Study design and participants

A single-center retrospective cohort study was performed at a level-1 trauma center in Switzerland. All patients who underwent rib fixation for multiple rib fractures or flail chest after blunt chest trauma between 2010 and 2018 and who received a control pulmonary function test during the postoperative follow-up were eligible for inclusion. Patients transferred to an outside facility after their surgical treatment, and those who did not receive a control pulmonary function test during their follow-up care were excluded. Furthermore, patients with non-traumatic rib fractures (e.g. after cardiopulmonary resuscitation, bone malignancy, or nonunion) and patients younger than 18 years were also not eligible for inclusion.

Patients were identified in our institutional patient data registry using *Swiss Classification of Surgical Intervention* (CHOP) procedure codes for rib fixation and *International Classification of Diseases Ninth Revision* (ICD-9) codes for rib fractures. Data were retrieved from the electronic patient documentation and the German (TraumaRegister DGU®) and Swiss Trauma Registry (STR). These trauma registries contain prospectively gathered data on demographics, mechanism of trauma, sustained injuries, and in-hospital outcomes of level-1 trauma centers.

Surgical- and postoperative treatment

The indication for rib fixation was based on clinical and radiological assessment by a trauma and thoracic surgeon. Primary indications for surgery included flail chest, severely dislocated fractures, and severe chest wall deformity. Secondary indications were failure to wean from mechanical ventilation or uncontrolled persistent pain despite maximum administration of epidural, intravenous or parenteral analgesia. All procedures were performed by one of two experienced surgeons using intramedullary splints, locking plates (MatrixRib, Synthes®, Switzerland), or a combination of both.

All patients who underwent rib fixation were treated following a standardized management protocol including multimodal systemic pain management and chest physiotherapy during hospitalization, and a pulmonary function test with a control radiograph at least three months after surgery. Spirometry and body plethysmography were performed in a standardized manner using the Jaeger Master Screen Pro (CareFusion, GmbH, Hoechberg, Germany).

Explanatory variables and outcome measures

Data on demographics (i.e. age and sex), American Society of Anesthesiologists (ASA) Score, preexistent comorbidities (i.e. asthma, chronic obstructive pulmonary disease, congestive heart failure, myocardial infarction, and diabetes mellitus), body mass index (BMI), smoking status, mechanism of injury, injury severity score (ISS), Glasgow Coma Scale (GCS) at admission, concomitant injuries (i.e. pulmonary contusion, pneumothorax, hemothorax, and sternum fracture), and fracture- and surgery-related characteristics were obtained. BMI was only considered if reported within a range of six months prior to the surgery. Smoking was considered positive if the patient was a current smoker at the time of hospital admission. Fractures and concomitant pulmonary injuries were evaluated and classified with the use of computed tomography (CT) scans. Dislocation was defined as displacement of the fracture parts of one shaft width or greater. Multiple rib fractures were defined as three or more unilateral rib fractures. Flail chest was defined as three or more consecutive rib fractures in at least two places with or without clinical signs of paradoxical chest wall movement.

The in-hospital characteristics that were obtained included length of hospital stay (HLOS), intensive care unit length of stay (ILOS), duration of mechanical ventilation (DMV), need for tracheostomy, incidence of respiratory complications (e.g. acute respiratory distress syndrome (ARDS), empyema, pneumonia, and postoperative excess pleural fluid or pneumothorax), incidence of surgery-related complications (e.g. bleeding, wound infection, fracture-related infection, and revision surgery), and implant-related complications (e.g. breakage, mechanical failure, nonunion, and implant removal). ARDS was defined by severe hypoxemia with a PaO2/FiO2 ratio less than or equal to 100 mmHg. Pneumonia was defined by the appearance of clinical signs and symptoms (temperature >38.5, coughing, and decreased oxygen saturation) requiring antimicrobial therapy, with or without positive mucus cultures. Excess pleural fluid was defined by excessive accumulation of fluid in the pleural space on chest radiograph or computed tomography scan requiring (additional) thoracic drainage.

The primary outcome measure of this study was the pulmonary function measured by spirometry and body-plethysmography and expressed as forced vital capacity (FVC), forced expiratory volume in 1 second (FEV_1), peak expiratory flow (PEF), FEV_1/FVC ratio, maximum vital capacity (VC_{max}), total lung capacity (TLC), residual volume (RV), RV/TC ratio, and the percentage of the predicted individual's FEV_1 (FEV_1% predicted), FVC (FVC% predicted), PEF (PEF% predicted), VC (VC% predicted), TLC (TLC % predicted), RV (RV% predicted). The predicted values were based on a healthy reference population with similar age, sex, and height. Obstructive pulmonary impairment was defined as a $FEV_1/FVC < 70\%$ of predicted and restrictive pulmonary impairment was defined as a $FVC < 80\%$ of predicted. A combined obstructive and restrictive pulmonary impairment was defined as a $FEV_1/FVC < 80\%$ and $FVC < 90\%$.

Statistical analysis

All analyses were performed separately for patients with flail chest and patients with multiple rib fractures. Discrete data were presented as frequencies with percentages. Normally distributed continuous data were presented as means with standard deviation (SD) and non-normally distributed continuous data as medians with interquartile range (IQR). The Shapiro-Wilk test and Q-Q plots were used to assess the distribution of continuous variables. A two-sided p-value < 0.05 was considered statistically significant. All statistical analyses were performed using Stata® 14.0 (StataCorp LP, College Station, TX, USA).

Systematic review

Following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines a systematic literature search was conducted in the PubMed, EMBASE, and Cochrane databases by two independent reviewers (JP and RB).[11] Randomized controlled trials (RCTs) as well as observational studies that reported on the pulmonary function after rib fixation for rib fractures were included. Abstracts for conferences, biomechanical studies, case reports, and studies including patients below 18 years of age were excluded. No further restrictions were applied. Citation tracking and reference screening was performed. The search syntax and the quality assessment of the included studies are provided in appendix 1 and 2, respectively.

The following data was extracted from the included studies: author, year of publication, study design, number of patients, fracture type, timing of pulmonary function test, and the pulmonary outcomes (i.e. FVC, FEV_1, VC and TLC). Data were pooled if outcomes were reported by at least three studies. For pooled analysis, all continuous variables were converted to means and standard deviations if sufficient data were provided, according to the methods described in the Cochrane Handbook for Systematic Reviews for Interventions.[12]

RESULTS

Retrospective study

Between 2010 and 2018, a total of 103 consecutive patients underwent rib fixation for multiple rib fractures or flail chest after blunt chest trauma. Of these, 61 (59%) patients underwent a pulmonary function test during their postoperative follow-up in our hospital and were ultimately included in this study. Thirty-eight (62%) patients had multiple rib fractures and 23 (38%) patients sustained a flail chest. The median time until surgery was 2 days (IQR 1-5) and the mean time between surgery and the pulmonary function test was 3 months (range 3-4).

Multiple rib fractures

The median age of patients with multiple rib fractures was 60 (IQR 54-75) years and 82% (n = 31) were male. Pre-existent lung diseases were present in 4 (11%) patients, all four had COPD (Table 1). The median number of fractured ribs was 7 (IQR 5-8) and the median ISS score was 20 (IQR 16-24) with a median AIS thorax of 4 (IQR 3-4) (Table 1 & 2). Concomitant pulmonary injuries suffered by patients with multiple rib fractures included pulmonary contusion in 34% (n = 13), pneumothorax in 79% (n = 30), and hemothorax in 45% (n = 17) (Table 1).

The median HLOS was 16 (IQR 12-20) days and 19 patients (50%) were admitted to the ICU with a median ILOS of 1 (IQR 1-4) day. Eight percent (n = 3) required mechanical ventilation and the total duration of ventilation of these patients was 4 (IQR 2-6) days. Respiratory complications that occurred during hospital admission included excess pleural fluid in three (8%) patients, pneumonia in one (3%) patient, and one (3%) patient had a new pneumothorax postoperatively and required an additional chest tube. There were no patients who needed a tracheostomy and no surgery- or implant-related complications occurred. The mortality rate was 0%. The in-hospital outcomes and complications are shown in Table 3.

The mean FVC three months after surgery was 3.8 (SD 1.3) liters, which corresponded to a predicted FVC of 96.0% (SD 22.1). The mean FEV_1 was 2.9 (SD 1.0) liters with a predicted FEV_1 of 93.0% (SD 22.4), and the FEV_1/FVC ratio was 0.8 (SD 0.1). A FEV_1/FVC ratio below 0.70 was found in 3 (7.9%) patients, of which all had pre-existing COPD. The outcomes of the pulmonary function tests are shown in Table 4.

Table 1. Baseline characteristics of patients who received rib fixation for with multiple rib fractures or flail chest.

Variable	Total cohort	Multiple rib fractures	Flail chest
	n = 61	n = 38	n = 23
Age at trauma, median (IQR)	60 (55-75)	60 (54-75)	67 (55-75)
Sex, n (%)			
Male	50 (82)	31 (82)	19 (83)
Female	11 (18)	7 (18)	4 (17)
ASA score, n (%)			
1	10 (16)	7 (18)	3 (13)
2	27 (44)	15 (40)	12 (52)
≥ 3	24 (39)	16 (42)	8 (35)
Pre-existent comorbidity, n (%)			
Asthma	2 (3)	0 (0)	2 (9)
COPD	9 (15)	4 (11)	4 (17)
Congestive heart failure	4 (7)	3 (8)	1 (4)
Myocardial infarction	5 (8)	4 (11)	1 (4)
Diabetes Mellitus	8 (13.1)	3 (8)	5 (22)
BMI, median (IQR)	26 (24-29)	26 (24-29)	27 (24-28)
Smoker, n (%)	15 (25)	9 (24)	6 (27)
Trauma-mechanism, n (%)			
Motor vehicle	4 (7)	2 (5)	2 (9)
Motor bike	9 (15)	5 (13)	4 (17)
Fall from height/stairs	26 (43)	15 (40)	11 (48)
Bicycle	13 (21)	9 (24)	4 (17)
Other	9 (15)	7 (18)	2 (9)
AIS, median (IQR)			
Head	0 (0-2)	0 (0-2)	0 (0-3)
Thorax	4 (4-4)	4 (3-4)	4 (4-4)
Abdomen	0 (0-0)	0 (0-0)	0 (0-0)
Extremities	0 (0-2)	0 (0-2)	2 (0-2)
ISS, median (IQR)	20 (17-25)	20 (16-24)	24 (20-29)
GCS, median (IQR)	15 (15-15)	15 (15-15)	15 (15-15)
Concomitant injuries, n (%)			
Pulmonary contusion	28 (46)	13 (34)	15 (65)
Pneumothorax	46 (75)	30 (79)	16 (70)
Hemothorax	33 (54)	17 (45)	16 (70)
Sternum fracture	10 (16)	2 (5)	8 (35)
Base excess, median (IQR)	0.1 (-1.0 to 1.6)	0 (-1.0 to 1.7)	0 (-2.0 to 1.5)
Epidural catheter n (%)	43 (72)	25 (66)	18 (82)

Abbreviations: AIS, Abbreviated Injury Scale; GCS, Glasgow Coma Scale; n, number; SD, standard deviation; ISS, Injury Severity Score; IQR, interquartile range.

Table 2. Fracture characteristics of patients who received rib fixation for with multiple rib fractures or flail chest.

Variable	Total cohort	Multiple rib fractures	Flail chest
	n = 61	n = 38	n = 23
Number of rib fractures, median (IQR)	8 (5-10)	7 (5-8)	10 (8-12)
Bilateral rib fractures, n (%)	9 (15)	3 (8)	6 (26)
Location rib fractures, n (%)			
Ribs 1 - 4	46 (75)	25 (66)	21 (91)
Ribs 5 - 8	60 (98)	37 (97)	23 (100)
Ribs 9 - 12	47 (77)	27 (71)	20 (87)
Dislocation, n (%)	52 (85)	32 (84)	20 (87)
Dorsal fracture, n (%)	45 (74)	28 (74)	17 (74)

Abbreviations: n, number; IQR, interquartile range

Table 3. In-hospital outcomes and respiratory complications of patients who received rib fixation for multiple rib fractures or flail chest.

Variable	Total cohort	Multiple rib fractures	Flail chest
	n = 61	n = 38	n = 23
Hospital length of stay, median (IQR)	17 (13-21)	16 (12-20)	18 (14-21)
Admission to intensive care unit, n (%)	39 (64)	19 (50)	20 (87)
Intensive care length of stay, median (IQR)	2 (1-4)	1 (1-4)	2 (1-7)
Need for mechanical ventilation, n (%)	12 (20)	3 (8)	9 (39)
Duration of mechanical ventilation, median (IQR)	4 (2-8)	4 (2-6)	3 (2-10)
Tracheostomy, n (%)	2 (3)	0 (0)	2 (9)
Respiratory complications, n (%)			
ARDS	0 (0)	0 (0)	0 (0)
Empyema	0 (0)	0 (0)	0 (0)
Excess pleural fluid	4 (7)	3 (8)	1 (4)
Pneumonia	8 (13)	1 (3)	7 (30)
Pneumothorax	3 (5)	1 (3)	1 (4)

Abbreviations: ARDS, acute respiratory distress syndrome; n, number; IQR, interquartile range

Flail chest

The median age of patients with flail chest was 67 (IQR 55-75) years and 83% (n = 19) were male (Table 1). Pre-existent lung diseases were present in 6 (26%) patients, of which 2 had asthma and 4 had COPD. The median number of fractured ribs was 10 (IQR 8-12) and the median ISS score was 24 (IQR 20-29) with a median AIS thorax of 4 (IQR 4-4) (Table 1 & 2). Concomitant pulmonary injuries suffered by patients with flail chest included pulmonary contusion in 65% (n = 15), pneumothorax in 70% (n = 16), and hemothorax in 70% (n = 16) (Table 1).

The median HLOS was 18 (IQR 14-21) days and 20 (87%) patients were admitted to the ICU with a median ILOS of 2 (IQR 1-7) days. Thirty-nine (n = 9) percent required mechanical ventilation and the total duration of ventilation of these patients was 3 (IQR 2-10) days. Respiratory complications that occurred during hospital admission included pneumonia in 7 patients (30%) and 2

Table 4. Pulmonary function 3-months after rib fixation for multiple rib fractures or flail chest.

Lung function test	Total cohort	Multiple rib fractures	Flail chest
	n = 61	n = 38	n = 23
Spirometry			
FVC			
FVC, L	3.6 ± 1.2	3.8 ± 1.3	3.3 ± 1.0
FVC, % of predicted	90.2 ± 20.5	96.0 ± 22.1	80.7 ± 21.5
FEV_1			
FEV_1, L	2.6 ± 0.9	2.9 ± 1.0	2.3 ± 0.8
FEV_1, % of predicted	83.8 ± 21.3	93.0 ± 22.4	75.6 ± 16.7
PEF			
PEF, L	6.9 ± 2.5	7.5 ± 2.6	6.6 ± 1.7
PEF, % of predicted	88.3 ± 26.5	97.3 ± 27.8	85.9 ± 20.1
FEV1/FVC, ratio	0.7 ± 0.1	0.8 ± 0.1	0.7 ± 0.1
Body-plethysmography			
VC_{max}			
VC_{max}, L	3.7 ± 1.2	3.9 ± 1.3	3.6 ± 0.9
VC_{max}, % of predicted	91.9 ± 19.5	97.0 ± 23.0	88.9 ± 16.9
TLC			
TLC, L	6.1 ± 1.5	6.2 ± 1.6	6.1 ± 1.3
TLC, % of predicted	92.8 ± 20.6	97.0 ± 18.0	94.0 ± 17.3
RV			
RV, L	2.4 ± 0.8	2.2 ± 0.6	2.6 ± 0.9
RV, % of predicted	104.1 ± 30.9	98.5 ± 22.0	110.6 ± 31.2
RV/TLC			
RV/TLC, ratio	0.4 ± 0.1	0.4 ± 0.1	0.4 ± 0.1

Abbreviations: FEV1, Forced Expiratory Volume in 1 Second; FVC, Forced Vital Capacity; L, Liter; RV, Residual Volume; TLC, Total Lung Capacity; VCmax, Maximum Vital Capacity

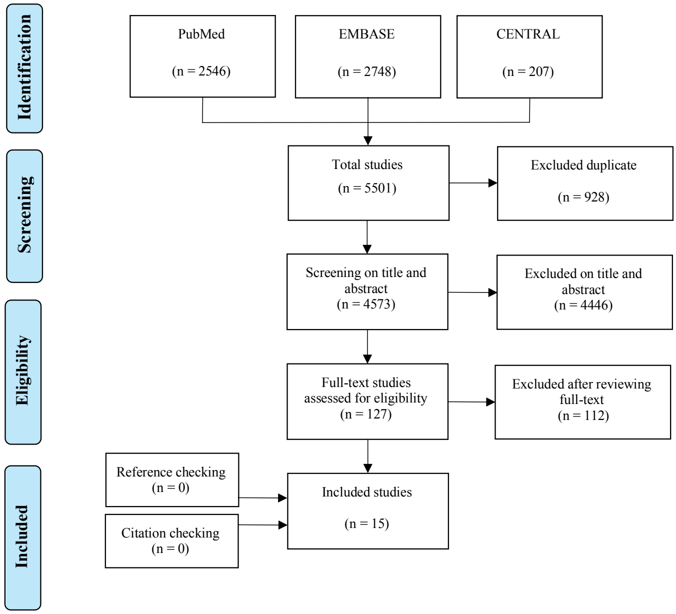
patients (9%) needed a tracheostomy. There were no surgery- or implant-related complications. The mortality rate was 0% (Table 3).

The mean FVC three months after surgery was 3.3 (SD 1.0) liters, which corresponded to a predicted FVC of 80.7%. The mean FEV_1 was 2.3 (SD 0.8) liters with a predicted FEV_1 value of 75.6% (SD 16.7), and the FEV_1/FVC ratio was 0.7 (SD 0.1). A FEV_1/FVC ratio below 0.70 was found in 6 (26.0%) patients, of which 4 had pre-existing COPD. (Table 4).

Systematic review

Figure 1 shows a flowchart of the literature search and study selection. Ultimately, a total of 15 studies met the inclusion criteria.[13-27] There were 3 RCT's and 12 observational studies, of which 9 were single arm studies that solely reported on the lung function after rib fixation. The included studies represented a total of 560 patients.

Figure 1. PRISMA flow diagram representing the search and screen process of articles describing the pulmonary function after rib fixation for multiple rib fractures or flail chest.



Outcomes of the included studies are presented in Table 5. Among the included studies, the timing of the control pulmonary function test varied between 1 day to 12 months postoperatively. Seven studies reported on the FVC three months postoperatively, with a mean weighted FVC of 82.8% (SD 14.8) of predicted.[13,19,22,24–27] Three studies reported on the FVC 12 months postoperatively, with a mean weighted FVC of 99.4% (SD 20.4) of predicted.[13,19,26] Six studies reported on the FEV_1 three months postoperatively, with a mean weighted FEV_1 of 77.8% (SD 15.6) of predicted.[13,22,24-27] Three studies reported on the TLC three months postoperatively, with a mean weighted TLC of 88.0% (SD 18.4) of predicted.[24,26,27]

DISCUSSION

The primary aim of this retrospective cohort study was to evaluate the pulmonary function after rib fixation in patients with multiple rib fractures and flail chest. Secondarily, a systematic review was conducted to provide a comprehensive overview of the literature and to allow comparison with the current cohort. The results of the present cohort study showed that adequate restoration of the pulmonary function was established three months after rib fixation. In the majority of patients, the pulmonary function parameters fell within the normal range of the reference values. Obstructive impairment was predominantly seen in patients with pre-existing COPD. Patients with multiple rib fractures had better recovery compared to those with a flail chest.

Table 5. Literature overview including studies reporting on post-operative pulmonary function after rib fixation for multiple rib fractures or flail chest.

Author and year	Study design	No.	Fracture type	Timing of pulmonary function test	Pulmonary outcome (% of predicted)			
					FVC	FEV_1	VC	TLC
Surgical versus conservative treatment								
Fagevik Olsén 2016	RCS	31/30	Combined	Unspecified	103 ± 20 vs. 111 ± 29	NR	NR	NR
Marasco 2013	RCT	17/17	Flail chest	3-months	77.9 ± 15.7 vs 84.8 ± 14.0	74.3 ± 15.0 vs 80.2 ± 18.3	NR	84.0 ± 24.4 vs 88.2 ± 23.4
Zhang 2015	RCS	23/29	Flail chest	Post-op	NR	1.58 ± 0.1 vs. 1.42 ± 0.1	NR	NR
Granetzny 2005	RCT	20/20	Flail chest	2-months	75.0 ± 5.4 vs. 66.5 ± 6.5	75.5 ± 8.7 vs. 75.0 ± 0.4	NR	90.7 ± 4.2 vs. 85.8 ± 11.3
Tanaka 2002	RCT	18/19	Flail chest	Post-op 1-month 3-months 12-months	44 vs. 41 69 vs. 53 85 vs. 65 96 vs. 81	NR	NR	NR
Balci 2004	RCS	24/47	Flail chest	1-month	Overall: (68-78) no significant difference	NR	NR	NR
Surgical treatment only								
Ali-osman 2018	RCS	43	Combined	Pre-op Post-op, day 5	36.1 ± 16.7 49.1 ± 17.3	35.1 ± 17.5 47.6 ± 17.6	NR	NR
Caragounis 2016	PCS	34	Multiple rib fractures	3-months 6-months 12-months	86.2 ± 19.4 93.1 ± 20.7 105.9 ± 17.5	79.4 ± 22.7 81.8 ± 25.3 80.4 ± 29.6	NR	NR
Nickerson 2016	RCS	11	Combined	1-month 3-months 12-months	72 [51-91] 83 [52-99] 85 [65-105]	64 [39-90] 75 [43-97] 71 [53-99]	73 [49-92] 86 [52-99] 86 [68-105]	85.5 [50-99] 90 [83-108] 94 [79-101]
Moslam 2015	PCS	40	Combined	Pre-op 3-months	69.28 ± 5.9 78.55 ± 5.5	68.07 ± 4.7 78.97 ± 5.5	NR	NR
Wiese 2014	PCS	75	Combined	6-months	88 [79, 95]	NR	NR	NR
Jayle 2014	PCS	10	Flail chest	3-months	90.2 ± 13.2	77.6 ± 12.1	NR	93.1 ± 7.6
Bottlang 2013	PCS	16	Flail chest	3-months 6-months	84 85	77 79	NR	NR
Said 2013	PCS	20	Flail chest	Pre-op Post-op 3-months	0.9 [0.1-3.0] 1.8 [1.3-4.0] 2.7 [1.4-7.0]	NR	NR	NR
Lardinois 2001	PCS	50	Flail chest	6-months	NR	NR	NR	TLC ≥ 85% (n=45, 90%) TLC < 85% (n=5, 10%)

Abbreviations: AIS, Abbreviated Injury Scale; GCS, Glasgow Coma Scale; No, Number of participants; SD, standard deviation; ISS, Injury Severity Score; IQR, interquartile range; PCS, Prospective Cohort Study; RCS, Retrospective Cohort Study; RCT, Randomized controlled trial.
All data are presented as Mean ± Standard Deviation or as Median [Interquartile Range]

Previous studies showed that blunt chest trauma can cause severe deteriorating of the pulmonary function with predominantly a restrictive pattern due to loss of the chest wall integrity and the underlying concomitant pulmonary injuries.[16,18] A significant decrease in the VC and FVC up to 40-50% of their predicted values has been reported in the first weeks after trauma.[7,19,28,29] The results of the present cohort study demonstrate that normalization of the pulmonary parameters occurs predominantly within the first three months after surgery, which appears to be consistent with prior research. In a pooled analysis of studies included in this systematic review, the mean weighted values of the FVC and TLC showed to be above 80% of predicted at three months postoperatively, reflecting a non-compromised pulmonary function. Additionally, three studies reporting on the long-term pulmonary outcome after rib fixation demonstrated a further gradual improvement during the first three to twelve months after surgery.[13,19,26] This might implicate that even though a considerable improvement in pulmonary function can be observed within the first few months, the underlying concomitant pulmonary injuries associated with traumatic rib fractures require a substantial recovery time. In a prospective study on prolonged respiratory dysfunction after chest trauma, Kishikawa et al. reported that the presence of a concomitant pulmonary contusion in patients with a flail chest was independently associated with worse pulmonary outcomes six months after injury. Fibrous changes in the lung parenchyma, indicating persistent lung damage, were present on computed tomography scans even years after injury.[30]

Rib fixation has increasingly gained in popularity over the past few decades.[31] A recent systematic review demonstrated that surgical fixation for flail chest resulted in significantly better in-hospital outcomes compared to non-operative treatment.[9] However, fewer studies exist on the short- and long-term clinical outcomes after rib fixation. Based on the results of our systematic review reporting on pulmonary function, it might be suggested that patients who underwent rib fixation have a better pulmonary outcome than those treated non-operatively. Tanaka et al. examined the FEV_1 on different intervals during a one-year follow-up and reported significantly better outcomes in the operative group.[19] Likewise, Zhang et al. described a significant better FEV_1 immediately after surgery.[20] Granetzny et al. reported on the pulmonary function at a two-months follow-up and reported significant higher values of the FVC and TLC in favor of the surgical group, but found no difference in the FEV_1.[18] Nevertheless, there were also a few studies that failed to show a beneficial effect of rib fixation on the pulmonary outcome.[17,21,27] However, several potential limitations must be considered that may have affected their results. For example, in a long-term follow-up study by Fagevik-Olsen et al, the time between trauma and follow-up varied widely between their study groups.[21] As they used a historical control group, the pulmonary function tests of the conservative group were performed 2.5-6 years after trauma, whilst this was 1-2.5 years in the operative group. In another study, Marasco et al. reported that there were no discernible differences in the measured FVC, FEV_1, and TLC at three months after rib fixation.[27] However, a major difference with respect to this study is that they used biodegradable plates. As these absorbable plates maintain only about 40% of their strength after three months, it has been suggested that this type of plate might weaken before complete fracture healing.

The improvement in pulmonary function after rib fixation might be explained by multiple factors. Surgical fixation of the fractured ribs initially ensures the restoration of the chest wall integrity and contributes to reduce chest pain, which is necessary for adequate ventilation and effective clearance of secretions.[16,18] Furthermore, it has been demonstrated that rib fixation for flail chest is associated with a significant reduction in the duration of mechanical ventilation and a lower incidence of pulmonary complications such as pneumonia, atelectasis, and ARDS.[9,19] Therefore, one might suggest that surgical fixation results in earlier recovery of the pulmonary function due to a shortened ventilation time and fewer pulmonary complications. Lastly, rib fixation has been shown to have a positive influence on the most important long-term sequelae associated with rib fractures, such as chronic pain, chest wall stiffness, impaired breathing excursions, and chest wall deformity.[32,34]

Another interesting finding of the present study is that patients with multiple rib fractures appeared to have a better pulmonary recovery than patients with a flail chest. This might be explained by the fact that flail chest is generally associated with both more severe thoracic and extra-thoracic injuries. In the current cohort study, this was reflected by a higher median ISS, a higher percentage of concomitant thoracic injuries (e.g. pulmonary contusion, hemothorax, and sternum fracture), and a higher number of fractured ribs in patients with a flail chest. Subsequently, flail chest was associated with worse in-hospital outcomes, such as longer HLOS and ILOS, more patients requiring mechanical ventilation, and a higher rate of respiratory complications. Therefore, these findings suggest that patients with flail chest are often more severely injured which requires a longer recovery time.

Several limitations of this retrospective cohort study and systematic review must be acknowledged. First, due to the retrospective nature, data on the long-term pulmonary outcome were not available as well as data on subjective patient reported outcomes such as dyspnea, pain, quality of life, or other respiratory complaints. Furthermore, only patients who underwent rib fixation for multiple rib fractures or flail chest received a control pulmonary function test in our institution. Therefore, no comparison could be made with patients who were treated conservatively. Third, a relatively large portion of the eligible patients did not receive their pulmonary function test in our hospital. However, since we are a level-1 trauma center many patients (and tourists) are referred back to the local hospitals or rehabilitation centers for their aftercare. This could have resulted in a selection bias. However, since the baseline characteristics and in-hospital outcomes showed no difference with respect to the included patients, the current results are considered representative of the entire cohort. Third, in this systematic review there was a large heterogeneity concerning the reported pulmonary parameters and the timing of pulmonary function testing, which limits comparison of results. Comparison of results was further limited as only few studies reported on all pulmonary function parameters after rib fixation, as performed in our study.

CONCLUSION

The present study demonstrates that rib fixation for multiple rib fractures or flail chest results in adequate recovery of the pulmonary function within three months after surgery. Flail chest injuries, however, are associated with more severe pulmonary lesions and prolonged HLOS and ILOS. In addition, based on the current literature, further gradual improvement to maximum pulmonary values appears to occur during the first 12 months after rib fixation. Furthermore, surgical fixation of rib fractures seems to lead to a better pulmonary function and a shorter recovery time compared conservative treatment.

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Appendix 1. Search syntax used in the PubMed, EMBASE and Central databases to identify studies reporting on the pulmonary function after rib fixation.

Database	Syntax
PubMed (n = 2546)	(((((fractur* [Title/Abstract]) AND ((ribs [Mesh]) OR rib* [Title/Abstract]))) OR ((((rib fractures [Mesh]) OR flail chest [Mesh]) OR rib fractur* [Title/Abstract]) OR "flail chest" [Title/Abstract]))) AND ((((((((fracture treatment [Mesh]) OR surgical treatment [Mesh]) OR surgical management [Mesh]) OR surgical procedure, operative [Mesh]) OR ORIF [Title/Abstract]) OR plat* [Title/Abstract]) OR surg* [Title/Abstract]) OR fix* [Title/Abstract])
EMBASE (n = 2748)	((‘ribs’/exp OR ‘ribs*’:ab,ti) AND ‘fractur*’:ab,ti OR ‘rib fractur*’:ab,ti OR ‘rib fractures’/exp OR ‘flail chest’/exp OR ‘flail chest’:ab,ti) AND (‘fracture treatment’ OR orif:ab,ti OR ‘plat*’:ab,ti OR ‘surg*’:ab,ti OR ‘fix*’:ab,ti)
CENTRAL (n = 207)	("rib fracture*" OR "flail chest")

Appendix 2. Quality assessment according to the MINORS criteria of studies reporting on the pulmonary function after rib fixation for multiple rib fractures or flail chest.

MINORS criteria	Ali-osman 2018	Caragounis 2016	Fagevik-Olsén 2016	Nickerson 2016	Moslam 2015	Zhang 2015	Jayle 2014	Wiese 2014	Bottlang 2013	Marasco 2013	Said 2013	Granetzny 2005	Balci 2004	Tanaka 2002	Lardinois 2001
A clearly stated aim*	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2
Inclusion of consecutive patients	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2
Prospective collection of data	0	2	1	1	2	1	1	2	2	2	2	2	1	2	2
Endpoints appropriate to the aim of study	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Unbiased assessment of the study endpoint	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Follow-up period appropriate to the aim of the study	2	2	2	2	2	2	2	2	2	2	2	2	0	2	2
Loss to follow-up less than 5%	1	1	1	1	2	0	0	0	1	1	2	2	0	2	2
Prospective calculation of the study size	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0
Adequate control group	1	-	2	-	-	2	2	-	-	2	-	2	1	2	-
Contemporary groups	1	-	2	-	-	2	1	-	-	2	-	2	1	2	-
Baseline equivalence of groups	1	-	2	-	-	2	2	-	-	2	-	1	1	2	-
Adequate statistical analyses	2	-	2	-	-	2	2	-	-	2	-	2	2	2	-
Total MINORS score	**14**	**11**	**18**	**10**	**11**	**16**	**16**	**10**	**11**	**21**	**12**	**19**	**12**	**20**	**12**

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, 1 point if one of the PICO criteria has not been satisfied, 0 points if not reported according to the PICO model.*

9 | Long-term quality of life and functional outcome after rib fracture fixation.

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ABSTRACT

Purpose The primary aim of this study was to assess the long-term quality of life and functional outcome after rib fracture fixation for patients with multiple rib fractures or flail chest. Secondarily, this study sought to identify risk factors associated with the quality of life.

Methods A retrospective cohort study with a follow-up by questionnaire was performed at a level-1 trauma center in Switzerland. All adult patients with three or more rib fractures treated with rib fixation between 2010 and 2018 were eligible for inclusion. All outcomes were independently assessed for patients with multiple rib fractures and patients with a flail chest. The outcome measures were quality of life, level of dyspnea, return to work, implant irritation, and implant removal after a minimum of 12 months of follow-up. Quality of life was assessed using the EuroQol five-dimensional-five-level questionnaire (EQ-5D-5L) and level of dyspnea was determined with the modified Medical Research Council dyspnea (mMRC) scale.

Results The survey was completed by 74 out of 102 patients (73%) at a median follow-up of 26 months (IQR 15-37). The median EQ-5D utility index score was 0.91 (0.89-1.0), which was equivalent to the reference population (0.902, p = 0.523). The vast majority of patients experienced 'no problems' or 'slight problems' in any of the EQ-5D-5L dimensions. The complication rate associated with rib fracture fixation was low, implant-related irritation was the most common long-term sequela and occurred in 31% of patients. In multivariable regression analyses total length of stay on the intensive care unit (ICU-LOS) was independently associated with a worse quality of life.

Conclusions Patients who underwent rib fracture fixation for multiple rib fractures or flail chest after severe chest trauma experienced a good quality of life at least one year after surgery. A longer ICU-LOS was independently associated with impaired quality of life. In addition, there were no significant differences in the long-term quality of life and functional outcome between patients with multiple rib fractures and a flail chest. Implant-related irritation was the most important long-term sequela and occurred in one third of patients.

INTRODUCTION

Thoracic trauma remains an important cause of morbidity and mortality among the trauma population.[1] Rib fractures are the most frequently encountered injuries after thoracic trauma, accounting for approximately 10% to 15% of all trauma-related hospital admissions.[2,3] Fractured ribs are presumed to be a surrogate marker of severe injury, as most patients sustain critical additional injuries.[1,4]

Rib fractures are also associated with a significant morbidity and disability on the long term. These injuries can cause long-lasting physical impairment, dyspnea, and delayed return to work, resulting in a diminished quality of life.[5-7] In addition, previous studies have shown that up to a quarter of patients with fractured ribs experience enduring chest pain even one year or more after their injury.[6,7]

In the current clinical practice, surgical treatment is increasingly performed in patients with rib fractures, as it is assumed that restoration of the chest wall integrity can improve pain and preserve the normal mechanics of breathing. Although recent evidence suggests that rib fracture fixation can lead to improvement in pulmonary function, a lower incidence of (pulmonary) complications, and a shorter hospital and intensive care unit (ICU) length of stay in selected patients, a definitive consensus on which patients should be operated has not yet been ascertained.[8-10] Contributing to the difficulty in establishing the optimal treatment for patients with rib fractures is that there is limited evidence with respect to the long-term quality of life and functional outcome after rib fracture fixation.

Therefore, the primary aim of this study was to assess the long-term quality of life and functional outcome after rib fracture fixation for patients with multiple rib fractures or flail chest. Secondarily, this study sought to identify risk factors with impaired quality of life.

METHODS

The Medical Ethical Review Board granted approval for this study under protocol number EKNZ 2019-00618 and informed consent was obtained from all subjects. This article was written according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.[11]

Study design and participants

A retrospective cohort study with a follow-up by questionnaire was performed at a level-1 trauma center in Switzerland. All adult patients with three or more rib fractures or a flail chest treated with rib fixation between January 2010 and December 2018 were eligible for inclusion. Eligible patients were identified using *International Classification of Diseases Ninth Revision (ICD-9)* diagnosis codes for rib fractures and *Swiss Classification of Surgical Intervention (CHOP)* procedural codes for rib fixation in an electronic search of the medical files. Inclusion criteria were age 18 years and older and three or more rib fractures as a result of blunt thoracic trauma followed by rib fixation. Patients who were deceased, resided in a foreign country, or unable to fulfill the questionnaire at follow-up were excluded from analysis. In addition, patients were excluded if there was no availability of a CT-scan of the chest or if the patient was transferred to or from another hospital. All eligible patients were invited to participate in this study by a recruitment letter.

Surgery characteristics

The main indications for rib fixation were flail chest with paradoxical chest movement (clinical flail chest), severe chest wall deformity, failure to wean from mechanical ventilation, or intractable pain despite epidural, intravenous, or oral pain treatment. A muscle sparing minimal invasive approach was performed to fix the fractured ribs using the MatrixRIB system (Depuy Synthes). Preferably three bi-cortical screws were placed on each side of the fracture and if no plate could be inserted due to anatomical boundaries, intramedullary splints were used. The number of fixated ribs depended on the anatomical boundaries and possibility to regain chest wall stability during respiration. If ribs were fractured in more than one place initially only one fracture was fixed, but if needed to augment stability, both fractures were addressed.

Outcome measures and explanatory variables

Data on explanatory variables were retrieved from the German (TraumaRegister DGU®) and the Swiss Trauma Registry (STR) as well as the electronic patient documentation. The following baseline characteristics were obtained: age at trauma, sex, American Society of Anesthesiologists (ASA) classification, smoking status, mechanism of trauma, Body Mass Index (BMI), Abbreviated Injury Scale (AIS) score, Injury Severity Score (ISS), number of rib fractures, presence of bilateral rib fractures, rib fractures in the upper (rib 1 to 4), middle (rib 5 to 8), lower (rib 9 to 12) third or dorsal side of the thorax, displacement (a shaft width displacement in the transversal plane), the presence of a flail segment (three or more consecutive rib fractures in at least two places with or without clinical signs of paradoxical chest wall movement), concomitant injuries including pneumothorax, hemothorax, pulmonary contusion, and sternum fracture, and need for emergency surgery upon time of arrival (e.g. thoracotomy, laparotomy, or craniotomy). The surgery-related characteristics included time from injury until surgery, duration of surgery, surgical approach, number of ribs fixated, the ratio of fixated ribs and fractured ribs (fixated ribs/fractured ribs), and side of rib fixation.

The outcome measures were subdivided into in-hospital and long-term outcomes. The in-hospital outcomes were total hospital length of stay (HLOS) in days, ICU admission (yes or no), ICU length of stay (ICU-LOS) in days, need for mechanical ventilation (yes or no), duration of invasive mechanical ventilation (IMV) in days, incidence of surgery- and implant-related complications (e.g. intra- or postoperative bleeding, infection, and migration or failure of the implant material), reoperations, incidence of disturbed fracture healing (e.g. delayed union, nonunion, and malunion), incidence of pulmonary complications (e.g. pneumonia and acute respiratory distress syndrome [ARDS]), and mortality. Infections were subdivided into 1) superficial wound infections and 2) fracture-related infections according to the diagnostic criteria established by Metsemakers and colleagues.[12] Pneumonia was defined as having clinical signs (fever, dyspnea, coughing, desaturation) requiring antibiotic treatment with or without positive sputum cultures. ARDS was defined by severe hypoxemia with a PaO2/FIO2 smaller than 100 mmHg.

The long-term outcome measures were quality of life, level of dyspnea, return to work, implant irritation, and implant removal after a minimum of 12 months of follow-up. Quality of life was assessed using the EuroQol five-dimensional-five-level questionnaire (EQ-5D-5L) and the EuroQol Visual Analogue Scale (EQ-VAS).[13,14] The EQ-5D-5L is a validated questionnaire designed to measure patient's general health status and scores the severity of problems (ranging from no problems to severe problems) in the following five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. The EQ-5D-5L health states were converted into a single EQ-5D (utility) index score using a scoring algorithm. A higher score reflects a better patient reported quality of life, with an index value of 1 representing full health.[13,15] In addition, the outcome scales of all dimensions were dichotomized into the subgroups 'no problems' and 'problems', with this last subgroup ranging from 'mild problems' to 'severe problems and being unable to perform certain activities'. The EQ-VAS is a patient's subjective measurement of generic health ranging from 0 and 100, where higher scores represent better subjective health experience. The level of dyspnea was measured with the modified Medical Research Council dyspnea (mMRC) scale which is a five-category scale that characterizes the level of dyspnea with physical activity where higher scores corresponds with more dyspnea.[16] In addition to the questionnaires, patients were asked whether they were able to return to their preinjury level of work and were categorized as follows: 1) not able to work, 2) able but not on their pre-injury level, and 3) on the same level as before their injury. Implant irritation and implant removal were assessed using a previously described algorithm by Hulsmans and colleagues.[17] Implant irritation was defined as a local pain, tenderness or discomfort at the implant site. If implant irritation was present, patients were asked whether their complaints required implant removal.

Statistical analysis

All analyses were performed separately for patients with flail chest and patients with multiple rib fractures.

Data were presented using absolute numbers with percentages (%) for dichotomous and categorical variables, means with standard deviations (SD) for normally distributed variables, medians with interquartile ranges (IQR) for non-normally distributed data. The Shapiro-Wilk test and Q-Q plots were performed to assess the distribution of continuous variables.

The differences in baseline characteristics were compared between responders and non-responders. All outcome variables were reported separately for patients with multiple rib fractures and flail chest. For analysis of continuous variables, the independent *t*-test and the Mann-Whitney *U* test were used for normally and non-normally distributed data, respectively. The Pearson's chi-square test was used for categorical data and the Fisher's exact test was used in case of a cell count of 5 or less. Since a validated EQ-5D reference value set has not yet been established for the Swiss population, the EQ-5D utility index score was obtained using the EQ-5D German index tariff. The EQ-5D utility index scores of the study population were compared with the reference value of the German population using the independent *t*-test.

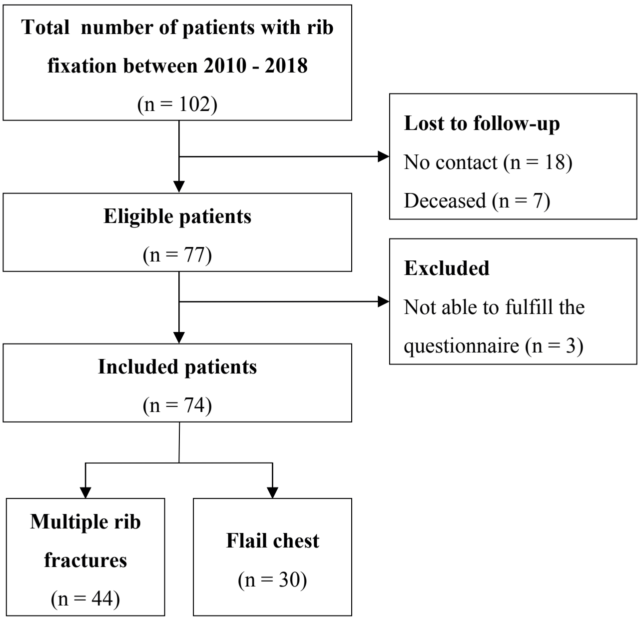
Bivariate linear regression analyses were performed to assess individual factors affecting the EQ-5D-5L utility index score and the EQ-VAS. Multivariable linear regression analyses were performed to identify factors independently associated with these outcomes. For multivariable analyses, independent variables were substantively selected based on the expected clinical relationship with each of the outcome variables.

All analyses were performed with Stata® 14.0 (StataCorp LP, College Station, TX, USA); a *p*-*v*alue of less than 0.05 was considered significant.

RESULTS

Figure 1 shows a flowchart of the inclusion process. A total of 102 patients with multiple rib fractures or flail chest met the inclusion criteria. Of these patients, 18 could not be contacted anymore, 7 were deceased, and 3 were not able to fulfill the questionnaire due to dementia or cognitive impairment. Ultimately, a total of 74 patients (73%) completed the questionnaire and were included for analysis.

Figure 1. Flowchart representing the selection of included patients.



The baseline characteristics are shown in Table 1. There were no significant differences observed between responders and non-responders. Of the entire cohort, the median age at trauma was 62 years (IQR 54-75) and 86 patients (84%) were male. The mean ISS was 24 (IQR 20-29) with a me-

Table 1. Baseline characteristics

Characteristics	Entire cohort n = 102	Responders n = 74	Non-responders n = 28	*p-value*
Age at trauma, median (IQR)	62 (54-75)	63 (54-74)	59 (53-75)	0.845
Male sex, n (%)	86 (84)	63 (85)	23 (82)	0.711
ASA class, n (%)				0.053
1	19 (19)	15 (20)	4 (14)	
2	43 (42)	36 (49)	7 (25)	
≥ 3	40 (39)	23 (31)	17 (61)	
Smoker, n (%)	21 (21)	15 (20)	6 (21)	0.897
Mechanism of trauma, n (%)				0.382
Motor vehicle accident	42 (41)	31 (42)	11 (39)	
Fall from height / stairs	27 (26)	17 (23)	10 (36)	
Other	33 (32)	26 (35)	7 (25)	
AIS score, median (IQR)				
Head	0 (0-2)	0 (0-2)	0 (0-3)	0.566
Face	0 (0-0)	0 (0-0)	0 (0-0)	0.481
Thorax	4 (4-4)	4 (4-4)	4 (4-4)	0.676
Abdomen	0 (0-0)	0 (0-0)	0 (0-2)	0.437
Extremities	0 (0-2)	1 (0-2)	0 (0-2)	0.515
ISS, median (IQR)	24 (20-29)	24 (20-29)	20 (17-29)	0.656
No. of rib fractures, median (IQR)	8 (5-10)	8 (5-10)	7 (5-11)	0.583
Bilateral rib fractures, n (%)	20 (20)	15 (20)	5 (18)	0.784
Level rib fractures, n (%)				
Upper	77 (75)	57 (77)	20 (71)	0.557
Middle	99 (97)	73 (97)	27 (96)	0.817
Lower	69 (68)	49 (66)	20 (71)	0.616
Displacement, n (%)	88 (86)	63 (85)	25 (89)	0.587
Dorsal fractures, n (%)	75 (74)	56 (76)	19 (68)	0.424
Flail segment, n (%)	39 (38)	30 (41)	9 (32)	0.436
Concomitant injuries, n (%)				
Pneumothorax	72 (71)	55 (74)	17 (61)	0.178
Hemothorax	60 (59)	43 (57)	17 (63)	0.610
Pulmonary contusion	48 (47)	34 (46)	14 (50)	0.714
Sternum fracture	15 (15)	12 (16)	3 (11)	0.484
Emergency surgery, n (%)	11 (11)	9 (12)	2 (7)	0.466

Abbreviations: AIS, Abbreviated Injury Scale; ASA Class, American Society of Anesthesiologists Classification; GCS, Glasgow Coma Scale; n, number; SD, standard deviation; ISS, Injury Severity Score; IQR, Interquartile Range.

dian AIS thorax of 4 (IQR 4-4). The median number of rib fractures was 8 (IQR 5-10). Seventy-five percent of patients had rib fractures in the upper level (rib 1 to 4) of the thorax, 75 patients (74%) had dorsally located fractures, and 39 patients (38%) sustained a flail chest. Emergency surgery was required in 11 patients (11%), of which 5 patients (5%) underwent a laparotomy and 4 patients (4%) underwent a thoracotomy.

Table 2. In-hospital and long-term outcomes after rib fracture fixation.

Characteristics	Entire cohort	Multiple rib fractures	Flail chest	*p-value*
In-hospital outcomes	**n = 102**	**n = 63**	**n = 39**	
Length of stay, median (IQR)				
Hospital	16 (12-21)	17 (12-21)	16 (13-19)	0.928
Intensive care	2 (1-6)	3 (1-7)	2 (1-6)	0.753
Intensive care unit admission, n (%)	75 (74)	40 (63)	35 (90)	**0.003**
Need for mechanical ventilation, n (%)	31 (30)	14 (22)	17 (44)	**0.025**
Days on mechanical ventilation, median (IQR)	4 (2-10)	6 (3-14)	3 (2-10)	0.223
Complications, n (%)				
ARDS	1 (1)	1 (2)	0 (0)	0.618
Pneumonia	20 (20)	9 (14)	11 (28)	0.085
Tracheostomy	10 (10)	5 (8)	5 (12)	0.500
Infection	2 (2)	1 (2)	1 (3)	0.621
Mortality, n (%)	0 (0)	0 (0)	0 (0)	n/a
Long-term outcomes	**n = 74**	**n = 44**	**n = 30**	
EQ-5D utility index score, n (%)	0.91 (0.89-1.0)	0.91 (0.89-1.0)	0.91 (0.83-1.0)	0.801
EQ-VAS, n (%)	80 (60-95)	78 (60-95)	80 (70-90)	0.630
Problems in dimension, n (%)				
Mobility	47 (46)	30 (48)	17 (44)	0.692
Self-care	37 (36)	23 (37)	14 (36)	0.950
Usual activities	45 (44)	28 (44)	17 (44)	0.933
Pain / discomfort	63 (62)	42 (67)	21 (54)	0.195
Anxiety/depression	43 (42)	29 (46)	14 (36)	0.314
mMRC dyspnea scale (n, %)				0.788
0	60 (81)	35 (80)	25 (83)	
1	8 (11)	6 (14)	2 (7)	
2	2 (3)	1 (2)	1 (3)	
3	4 (5)	2 (5)	2 (7)	
4	0 (0)	0 (0)	0 (0)	
Implant irritation (n, %)	23 (31)	15 (34)	8 (27)	0.498
Implant removal (n, %)	0 (0)	0 (0)	0 (0)	n/a
Follow-up in months, median (IQR)	26 (15-37)	27 (17-39)	23 (13-36)	0.351

Abbreviations: ARDS, Acute Respiratory Distress Syndrome; EQ-5D, Euroqol 5-Dimensions; EQ-VAS, EuroQol Visual Analogue Scale; IQR, Inter Quartile Range; mMRC, modified Medical Research Council; n, Number.

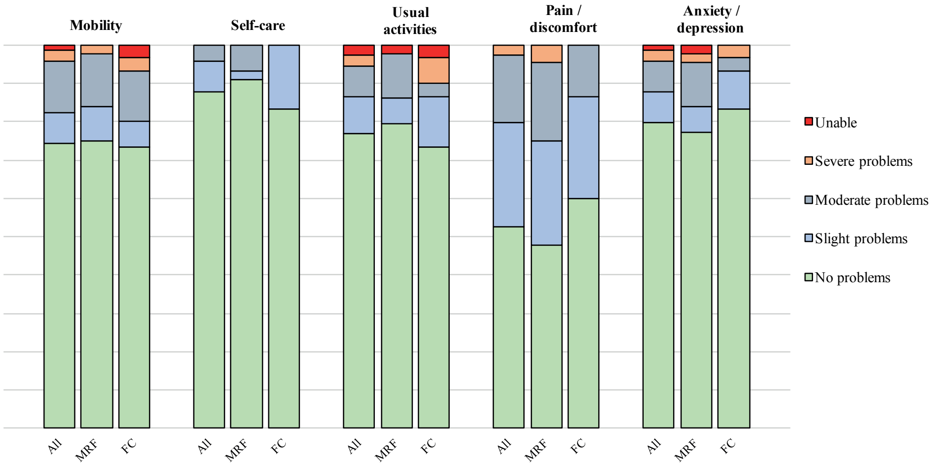
The surgery-related characteristics are shown in Appendix 1. The median time from injury to rib fixation was 3 days (IQR 1-6). All patients were treated with plate osteosynthesis, 51 patients (50%) were additionally treated with intramedullary splints. The median number of fixated ribs was significantly higher in the group of patients with a flail chest compared to those with multiple rib fractures (5 versus 4, $p = 0.003$). Furthermore, the number of patients who received bilateral rib fixation was also significantly higher among patients with a flail chest (90% versus 0%, $p = 0.019$).

The in-hospital and long-term outcomes of the entire cohort and specified for multiple rib fractures and flail chest are depicted in Table 2. The median HLOS and ICU-LOS were comparable between both groups, with a median of 16 days (IQR 12-21) and 2 days (IQR 1-6), respectively. Significant disadvantage of the flail chest group was observed with respect to ICU admission (90% versus 63%, $p = 0.003$) and need for mechanical ventilation (44% versus 22%, $p = 0.025$). The most common complication was pneumonia (20%), ARDS occurred in 1 patient (1%). Superficial wound infections occurred in 2 patients (2%), there were no cases of fracture-related infections. Revision surgery was performed in 1 patient (1%) due to a persisting thoracic hematoma. There were no implant-related complications and adequate healing of the fractures occurred in all patients. The overall mortality was 0%.

The questionnaires were completed after a median follow-up of 26 months (IQR 15-37) (Table 2). No significant differences were observed with respect to the long-term outcomes between the subgroups of patients with multiple rib fractures and flail chest. The median EQ-5D utility index score of the entire cohort was 0.91 (0.89-1.0), which was not significantly different from the mean score of the reference population (0.902; $p = 0.523$). The corresponding EQ-VAS score was 80 (IQR 60-95). The most frequently reported responses for the EQ-5D-5L dimensions were 'no problems' or 'slight problems', an overview of the responses for each EQ-5D-5L dimension is presented in Figure 2. The severity of dyspnea during exercise reported by the mMRC dyspnea scale was categorized as 0 (only breathless with strenuous exercise) in the vast majority of patients (81%). Six patients (8%) experienced 'mild' to 'severe' complaints of dyspnea. Eighty-three percent of the patients that were employed before their injury reported to be able to work on their preinjury level. However, 9 patients (20%) were not able to work on the same level as before their injury and 7 patients (16%) were not able to work anymore. The median time between rib fixation and return to work was 12 weeks (IQR 8-20). Implant irritation was found in 23 patients (31%). Two patients (2%) considered implant removal due to the severity of their complaints. However, eventually no patients required implant removal during our follow-up.

In bivariate analysis, AIS thorax ($p = 0.030$), ISS ($p = 0.008$), total number of rib fractures ($p = 0.028$), need for mechanical ventilation ($p < 0.001$), ICU-LOS ($p < 0.001$), and pneumonia ($p = 0.001$) were associated with a reduced long-term quality of life as measured with the EQ-5D-5L (Appendix 2). For the health-related quality of life according to the EQ-VAS, there was a significant relationship with ASA classification ($p = 0.003$), ISS ($p = 0.015$), need for mechanical ventilation ($p = 0.001$), ICU-LOS ($p = 0.006$), and pneumonia ($p = 0.001$).

Figure 2. EQ5D-5L scores of patients with multiple rib fractures (MRF) and flail chest (FC) after rib fracture fixation.



In multivariable analysis, a longer ICU-LOS (regression coefficient [β] -0.010, 95% Confidence Interval [CI] -0.017 to -0.003; p = 0.008) was independently associated with a lower EQ-5D utility index (Table 3). Factors independently associated with a lower EQ-VAS were a higher ASA classification (β -8.245, 95% CI -14.871 to -1.619, p = 0.016) and a longer ICU-LOS (β -1.198, 95% CI -1.917 to -0.479, p = 0.002).

Table 3. Multivariable analysis

Characteristics	β coefficient	95% CI			*p*-value
EQ-5D-5L					
Age	0.009	-0.003	-	0.005	0.680
ASA class	0.018	-0.048	-	0.084	0.591
BMI	-0.000	-0.009	-	0.085	0.997
ISS	0.001	-0.005	-	0.007	0.765
Number of rib fractures	-0.006	-0.021	-	0.009	0.417
Flail segment	0.044	-0.064	-	0.152	0.415
Need for mechanical ventilation	-0.070	-0.190	-	0.051	0.247
Intensive care length of stay	-0.010	-0.017	-	0.003	**0.008**
EQ-VAS					
Age	0.132	-0.303	-	0.568	0.542
ASA class	-8.245	-14.871	-	-1.619	**0.016**
BMI	0.243	-0.613	-	1.101	0.567
ISS	0.112	-0.488	-	0.711	0.708
Number of rib fractures	0.777	-0.737	-	2.291	0.304
Flail segment	1.248	-9.658	-	12.154	0.817
Need for mechanical ventilation	-5.540	-17.652	-	6.572	0.359
Intensive care length of stay	-1.198	-1.917	-	-0.479	**0.002**

Abbreviations: ASA Class, American Society of Anesthesiologists Classification; BMI, Body Mass Index; EQ-VAS, EuroQol Visual Analogue Scale; ISS, Injury Severity Score.

DISCUSSION

With the present study, the long-term quality of life and functional outcome were assessed in patients who sustained severe thoracic injury with multiple rib fractures or a flail chest, requiring rib fracture fixation. The quality of life at a follow-up of at least one year postoperatively was considered good compared to the reference population. The vast majority of patients experienced a good recovery and reported 'no problems' or 'slight problems' in any of the five domains tested with the EQ-5D-5L. Furthermore, the complication rate associated with rib fracture fixation was low with implant-related irritation being the most common long-term sequela in 31% of the patients, without the need of any re-intervention.

A recent systematic review showed that in the current literature a varying range of outcome measures has been used to report on the health-related quality of life and functional outcome after surgical treatment of rib fractures.[18] Similar to the present study, four previous studies used the EQ-5D-5L to determine the quality of life. Most recently, Beks et al. presented the long-term results of 166 patients with multiple rib fractures ($\geq$ 3 rib fractures) or a flail chest at a follow-up ranging from 1 to 7.5 years after surgery.[19] In accordance to our findings, their patients with multiple rib fractures as well as those treated for a flail chest appeared to have a good recovery, with an EQ-5D utility index comparable to the Dutch reference population. Importantly, although the ISS and the number of fractured ribs were higher among flail chest patients, there was no significant difference in the long-term outcomes compared to patients with multiple rib fractures. In a study of Caragounis et al., patients' quality of life, as measured with the EQ-5D utility index, progressively increased from 0.78 to 0.93 in the first year after surgery.[20] Interestingly, they found that the greatest improvement tended to occur between 6 weeks and 3 months postoperatively. Therefore, we assume that our follow-up duration is appropriate to assess the long-term outcomes after rib fracture fixation. Furthermore, in a retrospective cohort study of Mayberry et al., quality of life was assessed using the Research and Development-36 (RAND-36) survey in patients who required surgical fixation for severe chest wall injuries.[21] They found that patients' health status after surgery was equivalent or even better compared to the general population.

Although the long-term quality of life after rib fracture fixation appeared to be good in our patient population, several studies have not been able to show any quality of life benefit of rib fracture fixation over conservative treatment. In a prospective follow-up study of Walters et al., no significant differences were observed with respect to patient-reported outcome measures including quality of life, pain, and overall satisfaction between patients who received rib fracture fixation an those who were not operated.[22] However, the interpretation of their results was limited due to a low response rate. Additionally, in a retrospective cohort study of Marasco et al., quality of life measured over 24 months after surgery did not differ among the operative and non-operative group.[23] Nevertheless, the authors noted that the rib fracture related characteristics, such as total number of fractured ribs, thoracic level of rib fractures, and degree of displacement, were not taken into account. Therefore, as these factors were expected to be of influence on the decision to operate, selection bias could have affected their results. In conclusion, despite strong indications that rib fracture fixation might be beneficial in the long-term with respect to quality of life, high quality evidence is still needed to determine the difference in outcomes between surgical and non-surgical management.

Knowledge about the course of quality of life, functional outcome, and pain after rib fracture fixation might be of great value to guide patients on what to expect of their recovery. Furthermore, establishing evidence regarding factors predicting the outcome could facilitate identification of patients at risk of an impaired or delayed recovery. Despite the fact that evidence on these factors is scarce in the current literature, a previous study has shown that the total number of fractured ribs and fractures in the lower segment of the thorax might negatively predict patients' quality of life.[24] Nevertheless, the overall injury severity and the severity of the thoracic injuries were not associated with a worse outcome. These results mirror our findings, as the injury-related characteristics such as total ISS, AIS thorax, and presence of a flail chest appeared not to be of influence on the EQ-5D-5L. In addition, only the total ICU-LOS was independently associated with a diminished quality of life in multivariable regression analyses. Taking these results into account, one might suggest that although flail chest patients should be considered as a different entity with more severe intra- and extra-thoracic injuries leading to worse in-hospital outcomes, surgical fixation might restore the chest wall anatomy resulting in a good long-term recovery comparable to patients who sustained rib fractures without a flail chest.

Operative treatment of rib fractures has been associated with complications such as wound- or fracture-related infections, bone-healing complications, implant irritation, and the need for revision surgery. A recent systematic review showed that the overall risk of surgery- and implant-related complications was 10.3%.[18] However, the incidence of the clinically most important complications such as wound- or fracture-related infections was relatively low, indicating that rib fracture fixation is a safe procedure. Nevertheless, it has been shown that implant irritation might be a very important but potentially underestimated problem, as only few studies reported on this outcome. Implant-related irritation varied widely between 0% to 53% among the included studies.[18] In the present study, implant-related irritation was considered the most import long-term sequela after rib fracture fixation and occurred in about one-third of patients. However, none of the patients required re-intervention or removal of the implant material. A potential explanation for the high rate of patients which experience implant irritation is that ribs are subject to continual movement during respiration, in combination with the narrow anatomical boundaries in which the osteosynthesis material is inserted. As implant-related irritation can result in enduring chest pain, patients should be counseled accordingly.

A number of limitations need to be acknowledged. This study was a retrospective cohort study with a follow-up by questionnaire. Therefore, we were not able to report on the course of patients' recovery during standardized times in the follow-up. Furthermore, although we demonstrated that the quality of life after rib fracture fixation appeared to be good, no comparison was made with a conservatively treated control group, which would have increased the understanding of the impact surgical fixation has on patient-reported quality of life and functional outcomes. In addition, it must be noted that implant-related irritation is a subjective reporting in which patients mostly experience a local discomfort at the site of surgery. Nevertheless, it remains unclear whether this is solely related to the implant material or if other factors such as scar tissue formation, injury pattern, or loss of compliance of the thoracic wall are of influence. However, in our previous study, no restrictive lung function impairment was found after rib fracture fixation.[8] Finally, despite that with 102 patients this study is one of the larger studies reporting on the quality of life after rib fracture fixation, our multiple regression analyses were restricted by the number of predictors that could be incorporated.

CONCLUSION

In conclusion, the results of this study showed that patients who underwent rib fracture fixation for multiple rib fractures or flail chest after severe chest trauma experienced a good quality of life at least one year after surgery. A longer ICU-LOS was independently associated with an impaired quality of life. In addition, there were no significant differences in the long-term quality of life and functional outcome between patients with multiple rib fractures and a flail chest. Implant-related irritation was the most important long-term sequela and occurred in one third of patients.

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10 | General discussion and future perspectives

GENERAL DISCUSSION

This thesis was designed to provide insight in the epidemiology and outcome of rib fractures and to determine and evaluate the different treatment strategies for these trauma patients. In this chapter, the results of the studies included in this thesis will be discussed and placed into perspective of the current evidence. The research in this thesis is the result of an international collaboration between the departments of traumatology of the University Medical Center Utrecht in the Netherlands, Massachusetts General Hospital in the United States, and the Lucerne Cantonal Hospital in Switzerland.

EPIDEMIOLOGY AND OUTCOME

Epidemiology is generally regarded as the basic science of public health research.[1] In the field of trauma surgery, epidemiological studies are indispensable as they can be used to determine the incidence of specific injuries, to assist in the recognition of high-risk patient populations, and to allow benchmarking and comparisons across institutions, regions, or countries.[2,3] Furthermore, knowledge on the epidemiology and outcome of trauma patients is important to define relevant research questions and to monitor trends and outcomes, such as the overall incidence and mortality rates, over time.

While research on rib fractures and their treatment has received much attention over the past years, data with regard to the epidemiology of and outcome after rib fractures have been found to be outdated as they mainly originate from the beginning of this century.[4] Furthermore, although previous literature suggests that different subgroups of patients with traumatic rib fractures can be distinguished who are at increased risk of developing complications or other adverse outcomes, only very limited data are available to assist in identifying potential high-risk patient populations. Therefore, in order to provide benchmark data on the incidence and outcomes of rib fractures and to determine these outcomes for different subgroups of patients, this thesis included two nationwide epidemiological studies using the Dutch Trauma Registry (DTR) and the National Trauma Data Bank (NTDB). The DTR and NTDB are the largest trauma registries of the Netherlands and the United States, respectively.

According to our nationwide study with the DTR (**Chapter 2**), it was demonstrated that rib fractures are still a relevant and frequently occurring injury associated with a significant morbidity and mortality. Six percent of all hospitalized trauma patients appeared to sustain one or more fractured ribs and the absolute incidence rate of rib fractures requiring hospital admission among the Dutch population was 29 per 100,000 person-years. Furthermore, we found that the incidence rate of rib fractures in the elderly was even higher with 72 per 100,000 person-years, which illustrates the high clinical impact of rib fractures on the elderly population. Hence, given the considerable morbidity and mortality of rib fractures in these patients, it could be argued that rib fractures may impose the largest burden of disease after hip fractures in the elderly trauma patient. Furthermore, with the increasing aging population, it is to be expected that the incidence of elderly patients with fractured ribs requiring clinical care will increase. Although our epidemiological study included in **Chapter 2** is one of the very few existing studies reporting on the absolute incidence of rib fractures, it should be acknowledged that the reported incidence rates solely refer to the patients who are ultimately admitted to the hospital. Therefore, the true incidence of rib fractures in the general Dutch population is likely to be even higher than reported.

In **Chapter 2** and **Chapter 3** of this thesis, we also illustrated the extensive clinical heterogeneity among patients with rib fractures and emphasized the importance of subgroup identification. Furthermore, in line with previous literature, our subgroup analysis showed that rib fractures should be regarded as a surrogate marker of severe injury.[5,6] Approximately one-third of patients were polytrauma patients sustaining multiple critical associated injuries to the head, abdomen, or extremities. In this subgroup, significant worse outcomes were found concerning the number of complications, overall mortality, and other in-hospital outcomes, such as the need for mechanical ventilation and intensive care unit admission.

Another important subgroup of patients with an increased risk of complications and adverse outcomes are those sustaining a flail chest. Although the incidence of flail chest showed to be relatively low, representing approximately 4% of all rib fracture patients, this injury is often life-threatening, either by itself or in conjunction with other injuries. A flail chest is generally caused by a high impact trauma to the chest wall. Therefore, the vast majority of patients sustain additional life-threatening intra-thoracic injuries to the lungs, heart, or critical blood vessels, which increases the risk of death. Besides, due to the severity of the trauma, almost all flail chest patients also suffer from severe injuries outside the thoracic compartment. As a result, a flail chest should be recognized as a different entity and must be distinguished from patients with multiple rib fractures without a flail segment.

THE VALUE OF TRAUMA REGISTRIES FOR CLINICAL SCIENTIFIC RESEARCH

Historically, the establishment and implementation of trauma registries arose from the need to critically monitor the performance of trauma systems.[7] Systematic collection of injury data allowed to determine whether patients were properly triaged or transferred to a designated trauma center and to evaluate the overall quality of trauma care provided.[2,3,8] However, in the current clinical practice, trauma registries are not only used to monitor the performance of trauma care and improve its quality but are also increasingly used for scientific research. For example, as shown in **Chapter 2** and **Chapter 3**, trauma registries can be of great value to establish benchmark data on the epidemiology and in-hospital outcomes of trauma patients. In addition, in recent years, trauma registries are also increasingly used to monitor the effectiveness of (new) clinical interventions, to compare treatment strategies and outcomes within a hospital or against other institutions, or to guide and evaluate trauma prevention programs.

One of the most appealing aspects of registry studies is the large sample size, with the possibility to perform subgroup analysis. Furthermore, randomized controlled trials, which are presumed the gold standard for evaluating the effectiveness of interventions, are often very difficult, if not impossible, to conduct in the setting of acute trauma.[9] Therefore, observational research, including registry studies, are a great promise to evaluate and, ultimately, improve the quality of trauma care.[10] Nevertheless, results from trauma registry studies must be interpreted with caution as it has become apparent that trauma registries have its own set of challenges with respect to the quality and representativeness of its data.[2] To answer the question whether or not trauma registries can be adequately used for clinical scientific research, three aspects of the quality of registry data should be considered: 1) representativeness of patients, 2) completeness of data, 3) accuracy of data.

First, representativeness refers to the important challenge for trauma registries to ensure that all eligible patients are ultimately included in the registry. As shown in **Chapter 2,** one of the major issues of most trauma registries is that they systematically exclude patients who died on-site and those declared dead upon time of arrival, patients who are discharged home after treatment on the emergency department, and patients admitted to the hospital for a reason other than their traumatic injury. However, this does not necessarily have to constitute a problem, as long as the included patients are representative of the target group to be studied. Second, completeness of collected data refers to the number of variables that are finally included in the registry for a single case. An important shortcoming of many trauma registries is that they are often subject to a substantive amount of missing data. Adequate reporting of pre-hospital values (e.g. vital parameters, Glasgow Coma Scale, intubation on-scene, pre-trauma quality of life), and subsequently, incorporation of these data in the registry have proven to be a common problem among trauma registries. Furthermore, trauma is by nature an unexpected affair in which patients or their informants are often unable to provide information with respect to the medical history, current comorbidities, or otherwise. Third, accuracy of data refers to how precisely the data in a trauma registry correspond to the data from the medical records. Correct registration of the collected values is of undeniable importance to provide reliable data for research purposes. In general, trauma registries are maintained by trauma registrars who manually collect, encode, and enter data concerning patient demographics, injury-related characteristics, pre-hospital care, and in-hospital outcomes. Since diagnosis coding requires interpretation of the injury-related characteristics and because the data input is still often done with human effort, registry data is subject to coding errors.

In conclusion, the question whether or not trauma registries are suitable for research purposes cannot simply be answered. To ensure high-quality research, it is important to be aware of the abovementioned shortcomings of registry data. Therefore, with these limitations borne in mind, it is clear that the suitability and applicability of registry data strongly depends on the specific purpose or research question that is being pursued. In addition, to further strengthen the value of registry-based studies and to ensure fair (international) inter-registry comparisons, we believe that trauma registries should aim to reduce the number of missing data and increase the inter-registry comparability by standardizing variables across all trauma networks.

PAIN MANAGEMENT

Pain associated with rib fractures can be severe and disabling.[11–13] More importantly, it is well known that ineffective pain management significantly increases the likelihood of developing pulmonary complications, which is caused by several mechanisms.[14] First, the thoracic pain associated with rib fractures may lead to hypoventilation, consequently resulting in ineffective coughing, retention of secretions, and ultimately, atelectasis. Second, rib fractures can compromise the integrity of the chest wall, which may alter the normal breathing mechanism, especially in patients suffering from a clinical flail chest. Third, the frequently encountered concomitant injuries to the lungs, such as a pulmonary contusion or hemothorax, may negatively affect the pulmonary gas exchange.[15] As such, in order to reduce the risk of pulmonary complications, prompt evaluation and adequate pain management has traditionally been considered as the cornerstones in the treatment of rib fractures.[16]

Adequate pain management can be challenging in patients with rib fractures and the optimal treatment has been an important topic of debate as high quality studies are still scarce.[17] A variety of analgesic modalities have been described for the treatment of the rib fracture associated pain, including oral anti-inflammatory analgesics or opioids, intravenous narcotics, or regional techniques such as thoracic epidurals.[17–19] Furthermore, other regional techniques, including paravertebral and intercostal blocks, have recently gained in popularity as they appear to have a lower risk of complications and seem to affect the hemodynamics in a lesser extent.[20,21] Nevertheless, despite that the level of evidence is limited, thoracic epidurals have remained the recommended modality in patients with rib fractures following blunt chest trauma.

Given the paucity of data regarding pain management for rib fractures, this thesis aimed to provide an overview of the current analgesic modalities and to compare the single modalities independently with each other. In **Chapter 4**, our findings supported the viewpoint that epidural analgesia provides better pain relief compared to a systemic intravenous approach. Nonetheless, with respect to the secondary outcomes (i.e. mortality, pulmonary complications, hospital and intensive care unit length of stay), our meta-analysis failed to show any beneficial effect of treatment with thoracic epidurals compared to the other analgesic modalities. As mentioned above, the clinical heterogeneity among patients with rib fractures might have played a pivotal role in the assessment of the treatment effects of the different analgesic modalities. It could be argued that the relationship between the analgesic intervention and the secondary outcome parameters was largely influenced by multiple factors other than the type of analgesia, for example the number and severity of the concomitant intra- and extra-thoracic injuries. In addition, it must be noted that the overall quality evidence was low. Of the studies reporting on pain, patient samples were overall small, pain assessment scales varied widely, and exact pain scores were often not or poorly reported. Furthermore, despite that information on the type of medication administered and the analgesia-related side effects and complications can be important for decision-making, knowledge on these topics is very limited. Thus, although epidural analgesia seemed to be superior with respect to the management of pain, the quality of the available evidence is low and, therefore, precludes strong recommendations.

Notwithstanding the fact that in the current clinical practice epidural analgesia is widely used, there is still a lack of understanding of the efficacy and safety of epidural analgesia in patients with traumatic rib fractures. In **Chapter 5** we aimed to report on the success rate of epidural analgesia and the incidence of medication-related side effects and catheter-related complications. This study showed that epidural catheters were successful in 59% of patients. However, 30% of patients required additional analgesic interventions to achieve sufficient pain control. The minor epidural-related complications occurred in about half of patients, but this ultimately resulted in catheter removal in only 10% of all cases. Another important remark with respect to the feasibility of epidural analgesia, which is thought to be important for decision-making, is the high number of contra-indications. As epidural analgesia is often contraindicated in patients with multiple fractured ribs or a flail chest due to high extent of concomitant injuries, its applicability is limited, particularly in polytrauma patients. Therefore, future research on the optimal pain treatment remains necessary as high-quality studies are scarce. Besides, studies on other regional techniques that are more widely applicable in severely injured patients with rib fractures and less susceptible to complications is highly desirable.

OPERATIVE MANAGEMENT

While non-operative treatment has traditionally been the golden standard in rib fracture treatment (**Part II**), it comes with several challenges and as such new treatment strategies are still being explored. In the modern-day clinical practice, the use of rib fixation has rapidly increased over the last years and it is expected that this trend will continue as it has been received with great enthusiasm in many trauma centers.[4] Although previous randomized controlled trials reported a significant positive treatment effect of surgical fixation, the available evidence mainly focused on patients suffering from a clinical flail chest, instead of all patients with multiple rib fractures, which thus limits its generalizability.[22–24] Despite rib fixation showing promising results in selected patients, there is a growing debate about the exact indication and patient selection for this operation, as there is no consensus as to which patients would benefit. Besides, while important in the decision-making process, the long-term outcomes and complication risk of surgical fixation have received little attention. Therefore, throughout **Part III** of this thesis we focused on the value of surgical fixation in the treatment of rib fractures.

In **Chapter 6,** we endeavored to determine the treatment effect of rib fixation in both patients with a flail chest and multiple rib fractures. By including randomized controlled trials as well as observational studies, we aimed to improve the generalizability of the results and increase the power of our study. In this systematic review and meta-analysis, we have shown that rib fixation for patients with flail chest resulted in lower mortality, shorter HLOS, ILOS and DMV, lower pneumonia rate, and lower incidence of tracheostomy. However, as only very few studies were available investigating patients with multiple rib fractures without a flail chest, we were not able to perform any meta-analyses for this patient population.

In **Chapter 7,** the complication risk and long-term outcomes were assessed in a systematic review of the current literature. In this study we have shown that surgical fixation can be considered as a safe procedure with a considerably low complication risk and satisfactory long-term outcomes. Surgery- an implant- related complications appeared to occur in approximately 10% of patients. However, the clinically most relevant complications, such as infections, occurred infrequently, and the number of complications requiring immediate (surgical) treatment tended to be low.

Apart from the negative short-term impact of rib fractures on patients' health, long-lasting physical impairment, dyspnea, and delayed return to work have been described in non-surgically treated patients.[13,25–27] In **Chapter 8** and **Chapter 9** we reported on the pulmonary function and long-term quality of life after rib fracture fixation, respectively. **Chapter 8** demonstrated that rib fixation for multiple rib fractures or flail chest results in adequate recovery of the pulmonary function within 3 months after surgery. Based on our systematic review, surgical fixation of rib fractures appeared to result in a better pulmonary function and a shorter recovery time compared to conservative treatment, presumably because rib fixation restores the chest wall integrity and reduces the associated pain, leading to improved ventilation and a reduction in pulmonary complications. **Chapter 9** showed that patients who underwent rib fracture fixation for multiple rib fractures or flail chest after severe chest trauma experienced a good quality of life at least one year after surgery. However, implant-related irritation showed to be a common long-term sequela of this procedure and occurred in one third of patients.

FUTURE PERSPECTIVES: HOW TO PROCEED?

While this thesis has addressed a number of important questions concerning the epidemiology, treatment and outcome of patients with traumatic rib fractures, there are many avenues left to explore. Although surgical fixation seems to acquire an increasingly important role in the management of rib fractures, the question which patients should be operated on remains unanswered. In order to avoid overtreatment, high-quality prospective research on the indication and patient selection is still highly desirable and future studies should focus on establishing a simple and efficient clinical algorithm to determine the eligibility for operative treatment. In addition, given the extensive clinical heterogeneity of this patient population, it is strongly recommended to evaluate the outcomes and determine the effects of rib fixation for different patient subgroups. Besides the question of 'who' should be operated on, future studies should also focus on the optimal timing of surgery. Even though early fixation is preferred in the current clinical practice as it is thought to improve the in-hospital outcomes, more evidence is required to support this hypothesis.

Despite the growing interest in rib fracture fixation by trauma surgeons and researchers, it is most likely that in the future the vast majority of patients will still be treated non-operatively. Therefore, further research on the different analgesic modalities remains important as we have shown that the current evidence is scarce, often inconsistent, and of low quality. Furthermore, despite several decades of research regarding the use of various analgesic modalities in the field of thoracic surgery, the paucity of literature concerning pain management in patients sustaining blunt chest trauma is remarkable. However, applying findings from such studies to trauma patients is hardly possible, as the benefits and risks have not yet been thoroughly verified for this patient population. As such, well-designed prospective studies are still warranted to assess the optimal pain management strategies in patients with rib fractures following blunt chest trauma. Besides, while in this thesis it is suggested that epidural analgesia can provide adequate pain relief in patients with traumatic rib fractures, it appeared to be insufficient in a substantial number of patients due to the high probability of failure and the high number of contraindications. Therefore, future studies should explore alternative regional analgesic techniques that are safe, efficient, and widely applicable in polytrauma patients sustaining rib fractures. In addition, in order to enable fair comparison between the various analgesic modalities, it is of great importance that future studies will assess pain using a universal pain assessment tool and also report on the supplemental opioid intake and incidence of complications.

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Part IV
Appendices

Dutch summary (Nederlandse samenvatting)
Acknowledgements (Dankwoord)
List of publications
Curriculum vitae auctoris

DUTCH SUMMARY

Achtergrond

Trauma is wereldwijd een van de belangrijkste doodsoorzaken en is geassocieerd met een hoge morbiditeit. In Nederland overlijden jaarlijks ongeveer 5,000 mensen ten gevolge van traumatisch letsel na een ongeval.

Thoraxletsel is de derde meest voorkomende oorzaak van trauma-gerelateerde mortaliteit en ziekenhuisopname binnen de algehele populatie traumapatiënten. Ongeveer 25% van alle trauma-gerelateerde sterfgevallen zijn toe te wijden aan een of meerdere letsels van de thorax. Thoraxtrauma omvat een breed spectrum aan letsels. Dit varieert van geïsoleerde fracturen van de ossale structuren waaruit de thoraxwand is opgebouwd, tot aan letsel van de intra-thoracaal gelegen organen zoals longen, hart- en bloedvaten.

Ribfracturen zijn de meest voorkomende letsels ten gevolge van thoraxtrauma en worden naar schatting gezien in 10% tot 30% van alle trauma patiënten. Ribfracturen komen voor in verschillende mate van ernst, uiteenlopend van een enkelvoudige fractuur tot aan multipele (drie fracturen of meer) ribfracturen met of zonder een fladdersegment. Een klinische fladderthorax kan worden beschouwd als de uiterste zijde van het spectrum en wordt gedefinieerd als een letsel waarbij drie of meer opeenvolgende ribben zijn gebroken op tenminste twee plaatsen. Hierdoor kan een fladdersegment ontstaan die gedurende de respiratie een tegengestelde (paradoxale) beweging maakt ten opzichte van de rest van de thoraxwand.

Ondanks het veelvuldig voorkomen van ribfracturen, zijn de data omtrent de huidige epidemiologie, incidentie en ziekenhuisuitkomsten sterk verouderd. Tevens blijkt uit de klinische praktijk dat ribfracturen voorkomen in een zeer heterogene patiëntenpopulatie, waarbij de uitkomsten (bijv. totale ziekenhuisduur, noodzaak tot intubatie en beademing, intensive care opname en risico op pulmonale complicaties of mortaliteit), sterk afhankelijk zijn van zowel 1) patiënt-gerelateerde factoren (o.a. leeftijd, geslacht en pre-existente comorbiditeiten) als 2) trauma-gerelateerde factoren (o.a. aantal ribfracturen en ernst van begeleidend letsel). Echter, in de huidige literatuur wordt hier veelal onvoldoende rekening mee gehouden. De doelstelling van **Deel 1** van dit proefschrift is om de huidige epidemiologie, letselkenmerken en ziekenhuisuitkomsten van patiënten met traumatische ribfracturen te beschrijven en om verschillende risicogroepen met elkaar te vergelijken.

Ribfracturen zijn klinisch zeer relevante letsels aangezien deze geassocieerd zijn met een hoge morbiditeit en mortaliteit en veelal gepaard gaan met ernstige pijnklachten op zowel korte als lange termijn. Zelfs enkelvoudige (niet gedislokeerde) ribfracturen zijn geassocieerd met langdurige invaliderende pijnklachten en een verminderde kwaliteit van leven. De mortaliteit en morbiditeit geassocieerd met ribfracturen zijn onder andere afhankelijk van het aantal ribfracturen, leeftijd, de ernst van het begeleidend letsel en de aanwezigheid van een fladderthorax.

Thoracale pijn ten gevolge van ribfracturen kan leiden tot een verandering in de ademmechaniek en onvermogen tot adequaat ophoesten van sputum met als gevolg een insufficiënte ademhaling. Dientengevolge is er een sterk verhoogd risico op het ontwikkelen van sputumstase, atelectase en secundair hieraan pneumonie. Bovendien heeft het overgrote deel van de patiënten met ribfracturen begeleidend pulmonaal letsel, zoals longcontusie, pneumothorax of hemothorax, hetgeen het risico op pulmonale complicaties verhoogd. Ongeveer een derde van de patiënten met (multipele) ribfracturen ontwikkelt een pneumonie tijdens ziekenhuisopname. In het uiterste geval kan dit leiden tot een verstoorde ventilatie/perfusie verhouding en hypoxemie, met als gevolg respiratoire insufficiëntie waarbij intubatie en invasieve beademing op de intensive care noodzakelijk wordt.

Ribfracturen worden van oudsher hoofdzakelijk conservatief behandeld. Adequate pijnstilling in combinatie met longfysiotherapie en (niet-) invasieve beademing vormen daarbij de hoeksteen van de behandeling, gericht op het voorkomen van pulmonale complicaties en het bewerkstelligen van comfort. De acute pijnbestrijding van ribfracturen kan worden beschouwd als een gezamenlijke verantwoordelijkheid die idealiter wordt uitgevoerd door een multidisciplinair team bestaande uit chirurgen, anesthesiologen, fysiotherapeuten en verpleegkundigen. In de huidige klinische praktijk is er een breed scala aan pijnbestrijdingsmodaliteiten beschikbaar die kunnen worden toegepast om de pijn bij patiënten met ribfracturen te verlichten, bijvoorbeeld: thoracale epidurale analgesie, intraveneuze (patiënt gecontroleerde) analgesie, intercostale-, paravertebrale- of interpleurale blokkade, orale opioïden, of een combinatie van de verschillende technieken. In **Deel 2** van dit proefschrift worden de verschillende pijnmodaliteiten met elkaar vergeleken.

In de afgelopen jaren is er een groeiende interesse in het operatief behandelen van patiënten met multipele ribfracturen en fladderthorax door middel van ribfixatie. De eerste gerandomiseerde studies naar ribfixatie bij patiënten met een fladderthorax hebben positieve effecten laten zien, met een significante daling ten aanzien van de noodzaak tot invasieve behandeling, een vermindering van het aantal intensive care dagen, minder pijn en een lagere incidentie van de pulmonale complicaties. Alhoewel op basis van de literatuur het in steeds meer traumacentra de tendens is om ook patiënten met multipele ribfracturen vaker vroegtijdig operatief te behandelen, bestaat er nog geen consensus over de exacte indicatie van ribfixatie. Tot op heden is het onduidelijk welke patiënten het meest gebaat zijn bij operatieve behandeling. **Deel 3** van dit proefschrift richt zich op de waarde van chirurgische fixatie bij de behandeling van ribfracturen.

Proefschrift

Deel 1 – Epidemiologie en uitkomsten

In **deel 1** van dit proefschrift wordt gebruik gemaakt van de nationale data van de Landelijke Traumaregistratie (LTR) en de National Trauma Databank (NTDB) om de epidemiologie, letselkenmerken en uitkomsten van ribfracturen te beschrijven. De LTR en NTDB zijn de grootste traumaregistraties van respectievelijk Nederland en de Verenigde Staten.

In **hoofdstuk 2** laten de resultaten van de LTR zien dat ribfracturen nog steeds relevante en veel voorkomende letsels zijn na trauma. Zes procent van alle gehospitaliseerde traumapatiënten had één of meer ribfracturen en de algehele incidentie betrof 29 per 100.000 persoonsjaren. De incidentie van ribfracturen bij patiënten van 65 jaar en ouder betrof 72 per 100.000 persoonsjaren, hetgeen de hoge klinische impact van ribfracturen op de oudere populatie illustreert. De gemiddelde opnameduur betrof 7 dagen en de 30-dagen mortaliteit was 6.9%.

De resultaten van **hoofdstuk 3** bevestigen de ernstige morbiditeit waarmee ribfracturen gepaard gaan. De data van de NTDB laten zien dat 50% van alle gehospitaliseerde patiënten met ribfracturen uiteindelijk opname behoefde op de intensive care. Invasieve beademing was daarbij noodzakelijk in 25% van alle patiënten.

Hoofdstuk 2 en **hoofdstuk 3** laten tevens zien dat ribfracturen een belangrijke marker zijn voor ernstig letsel aangezien 30% tot 45% van de patiënten kunnen worden gecategoriseerd als polytrauma patiënten (Injury Severity Score $\geq$ 16) met ernstig intra- en/of extra-thoracaal letsel. Tevens laten de subgroepanalyses zien dat er een substantiële heterogeniteit is binnen de populatie traumapatiënten met ribfracturen waarbij grote verschillen kunnen worden geobserveerd tussen polytrauma patiënten, ouderen en patiënten met een fladderthorax.

Op basis van de resultaten kan worden gesuggereerd dat een fladderthorax dient te worden beschouwd als een afzonderlijke entiteit, gezien dit letsel geassocieerd is met een significant verhoogd risico op (pulmonale) complicaties, intensive care opname, intubatie en langdurige ziekenhuisopname. Een verklaring hiervoor is dat een fladderthorax wordt veroorzaakt door een zeer hoge impact op de thoraxwand, waardoor de overgrote meerderheid van deze patiëntenpopulatie naast ernstig intra-thoracaal letsel ook vaak aan ernstig cerebraal, abdominaal of extremiteitsletsel lijdt.

Deel 2 – Pijnmanagement

Deel 2 van dit proefschrift richt zich op het vergelijken van de verschillende pijnbestrijdingsmodaliteiten. In **hoofdstuk 4** ondersteunen onze bevindingen het internationale standpunt dat epidurale analgesie mogelijk betere pijnverlichting geeft in vergelijking met een systemische intraveneuze benadering. Desalniettemin, met betrekking tot de secundaire uitkomsten (mortaliteit, pulmonale complicaties, totale verblijfsduur in het ziekenhuis en op de intensive care), liet onze meta-analyse geen enkel gunstig effect zien van thoracale epidurale analgesie in vergelijking met de andere modaliteiten. Echter, bij de interpretatie van deze data dient de heterogeniteit tussen alle studies, de grote variatie in technieken en de algemene lage methodologische kwaliteit van de studies in ogenschouw te worden genomen.

Hoewel op basis van de huidige internationale protocollen epidurale pijnstilling de voorkeur krijgt, is er weinig literatuur ten aanzien van de effectiviteit en complicaties van epidurale pijnstilling. In **hoofdstuk 5** is het succespercentage van epidurale analgesie en de incidentie van medicatie-gerelateerde bijwerkingen en katheter-gerelateerde complicaties onderzocht bij patiënten met ernstig thoraxtrauma. Deze retrospectieve cohortstudie toonde aan dat epidurale katheters succesvol waren bij 59% van de patiënten. Echter, bij 30% van de patiënten waren een of meerdere aanvullende interventies noodzakelijk om adequate pijnbeheersing te bereiken. Complicaties of bijwerkingen van de epidurale katheters werden gezien in ongeveer de helft van de patiënten.

Toekomstig onderzoek naar de optimale pijnbehandeling bij patiënten met ribfracturen blijft noodzakelijk. Aangezien epidurale katheters vaak gecontra-indiceerd zijn bij patiënten met multipele ribfracturen of een fladderthorax, is de toepasbaarheid ervan beperkt, voornamelijk in de polytrauma patiënt. Onderzoek naar andere (regionale) technieken die breder toepasbaar zijn bij ernstige gewonde patiënten en een hoger succespercentage hebben is derhalve wenselijk.

Deel 3 – Operatieve behandeling

In **hoofdstuk 6** worden de resultaten beschreven van een systematisch review en meta-analyse waarin het behandelingseffect van ribfixatie wordt vergeleken met conservatieve behandeling bij patiënten met multipele ribfracturen en fladderthorax. De resultaten van deze studie lieten zien dat ribfixatie bij patiënten met een fladderthorax resulteerde in een lagere mortaliteit, kortere opnameduur, afname van het aantal dagen op de intensive care en het aantal dagen aan de beademing en een lager risico op het ontwikkelen van pulmonale complicaties. Echter, de data van de huidige literatuur was onvoldoende toereikend om het behandelingseffect te bepalen voor patiënten met multipele ribfracturen zónder een fladdersegment. Derhalve is verder onderzoek noodzakelijk ten behoeve van de exacte indicatiestelling van ribfixatie.

Hoofdstuk 7 richt zich op het complicatierisico en de langetermijnresultaten van ribfixatie. Deze studie laat zien dat chirurgische fixatie kan worden beschouwd als een veilige procedure met een laag risico op complicaties. Chirurgische- en implantaat gerelateerde complicaties bleken voor te komen bij ongeveer 10% van de patiënten. Echter, de incidentie van de klinisch meest relevante complicaties, waaronder infecties, nonunion of falen van het osteosynthesemateriaal was laag. Tevens kwamen er weinig complicaties voor die een onmiddellijke (chirurgische) behandeling vereiste.

In **hoofdstuk 8** en **hoofdstuk 9** rapporteerden wij over respectievelijk de longfunctie en de kwaliteit van leven op lange termijn na ribfixatie. **Hoofdstuk 8** toonde aan dat ribfixatie bij meervoudige ribfracturen of fladderthorax resulteert in een adequaat herstel van de longfunctie binnen 3 maanden na de operatie. Op basis van de aanvullende systematische review bleek chirurgische fixatie van ribfracturen te resulteren in een betere longfunctie en een kortere hersteltijd in vergelijking met conservatieve behandeling, vermoedelijk doordat ribfixatie de integriteit van de borstwand herstelt, hetgeen leidt tot minder pijn, verbeterde ventilatie en een vermindering van het aantal pulmonale complicaties. In **hoofdstuk 9** wordt de kwaliteit van leven vastgesteld middels de EQ5D-5L vragenlijst. De resultaten van deze studie laten zien dat patiënten een goede kwaliteit van leven rapporteerden ten minste één jaar na de operatie. Echter, implantaat-gerelateerde irritatie bleek een veelvoorkomend langetermijneffect van deze procedure te zijn en trad op bij een derde van de patiënten.

LIST OF PUBLICATIONS

Peek J, Kremo V, Beks R, van Veelen N, Leiser A, Link BC, Houwert RM, Minervini F, Knobe M, Babst RH, Beeres FJP. Long-term quality of life and functional outcome after rib fracture fixation. *Eur J Trauma Emerg Surg.* 2020. Online ahead of print.

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CURRICULUM VITAE AUCTORIS

Jesse Peek was born on February 18th, 1994 in Gorinchem, the Netherlands. After he graduated from the Merewade College Wijdschildlaan in Gorinchem in 2012, he started Law School at Utrecht University. After finishing his first year of Law School, he started Medical School in 2013 at the University of Utrecht.

During his clinical internships he gained increasing interest in emergency medicine, critical care, and acute care surgery. During his first scientific internship in his third year of Medical School het met Dr. R.M. Houwert, who offered him a chance to join the trauma research group under guidance of Prof. dr. L.P.H. Leenen at the Department of Surgery of the University Medical Center in Utrecht. He became involved in studies evaluating the epidemiology and treatment of patients sustaining traumatic rib fractures after thoracic trauma.

In 2018, he worked as a non-graduate research assistant at the Orthopedic Trauma Department of the Massachusetts General Hospital in Boston, United States. Under guidance of Dr. M. Heng, he was involved in several projects on thoracic trauma and upper extremity fractures. After returning from his six-month internship in Boston, he moved to Switzerland to continue his research on traumatic rib fractures at the Department of Orthopedic and Trauma Surgery at the Lucerne Cantonal Hospital, supervised by Dr. F.J.P. Beeres.

Upon returning to the Netherlands in 2019, Jesse finished his clinical internships and continued working on his PhD thesis at the University Medical Center Utrecht. In 2020 he graduated from Medical School and finished his thesis. Currently, Jesse works as a surgical resident (not in training) at the Department of St. Antonius Hospital in Nieuwegein, under the supervision of Dr. D. Boerma.