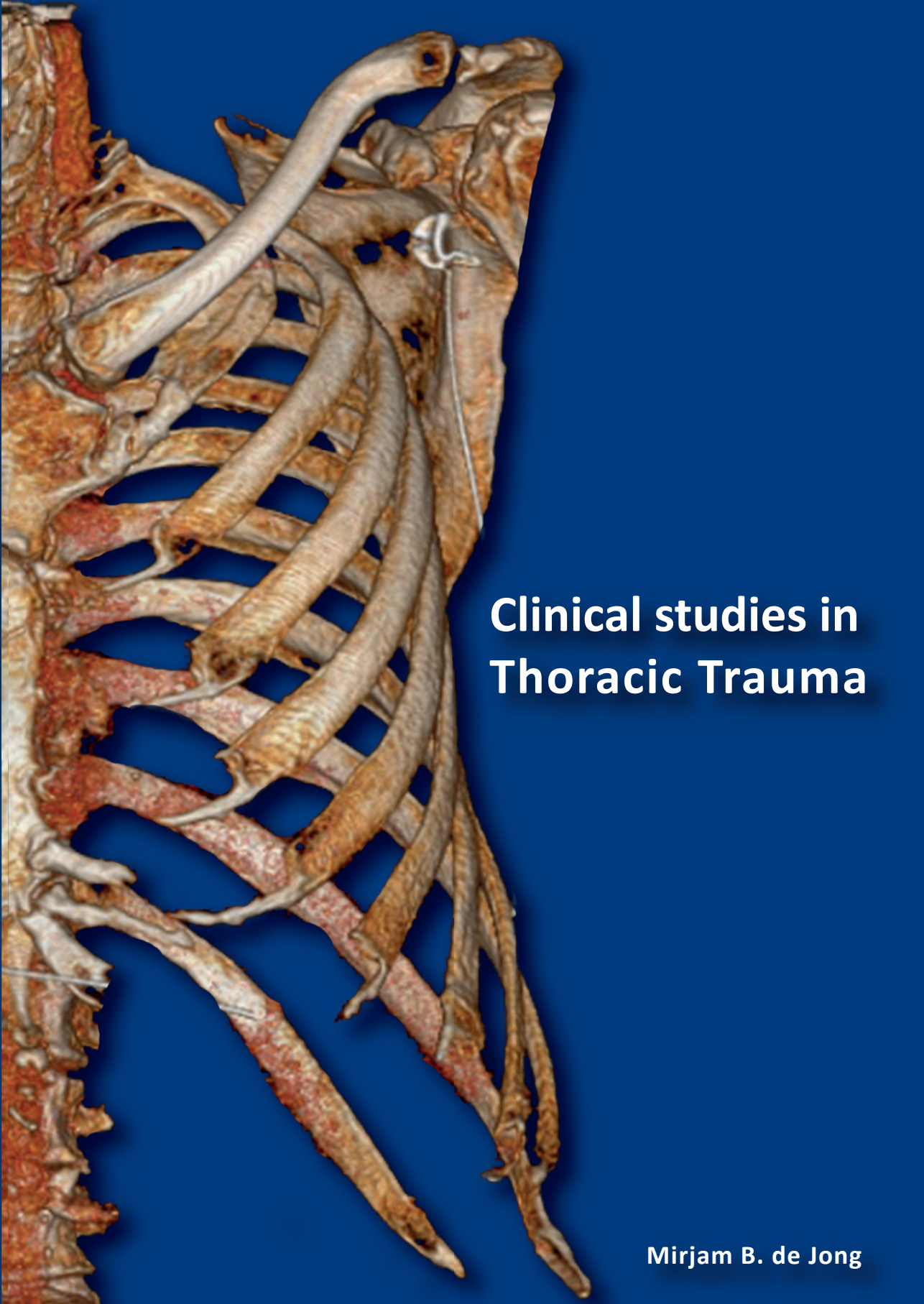

Clinical studies in Thoracic Trauma

Mirjam B. de Jong

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Clinical studies in thoracic trauma

Thesis, Utrecht University, the Netherlands, with summary in Dutch
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(met een samenvatting in het Nederlands)

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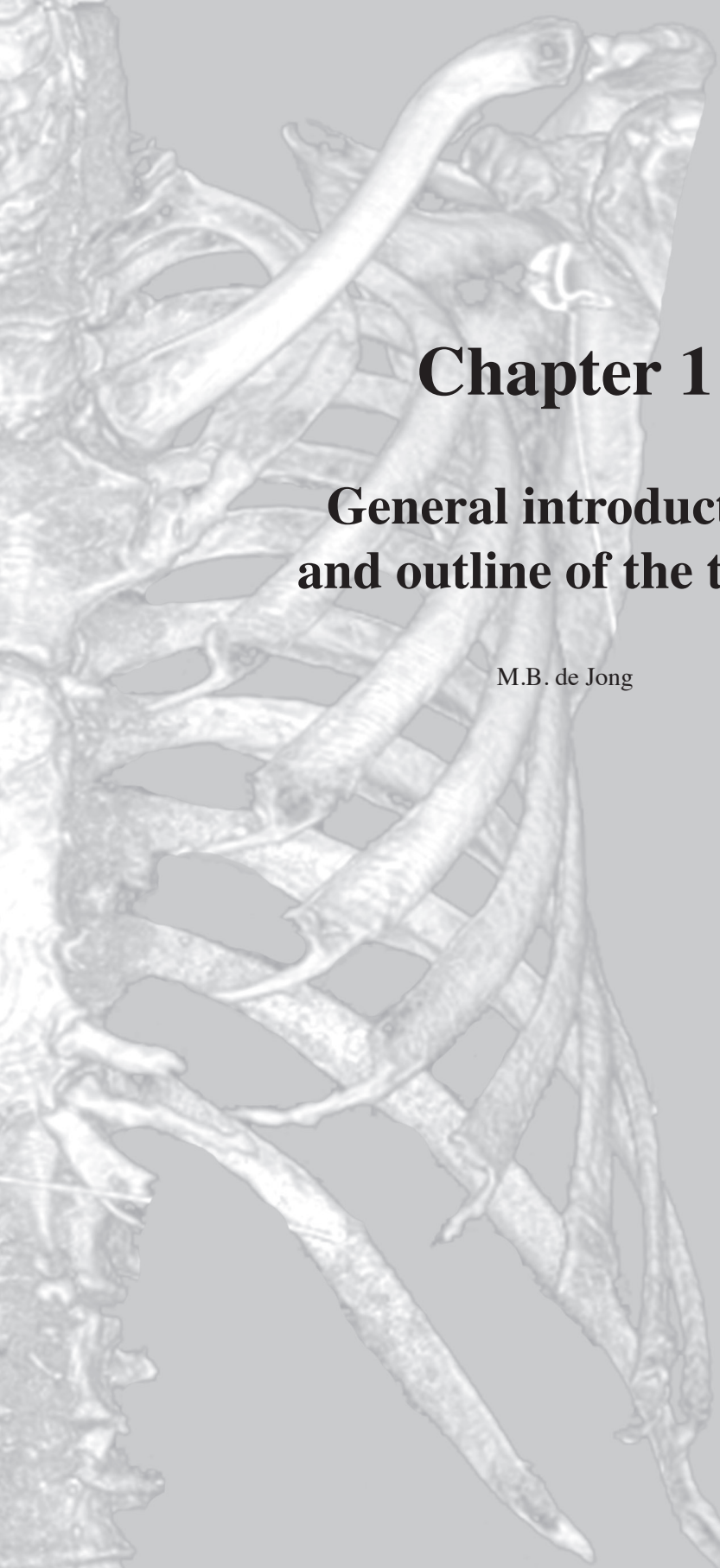

Chapter 1

General introduction and outline of the thesis

M.B. de Jong

General introduction

Trauma is a significant cause of morbidity and mortality worldwide. Chest trauma accounts for 25% of all deaths from traumatic injury (1). Blunt chest trauma is most common with 90% incidence and is most frequently caused by vehicular or pedestrian accidents. Penetrating injuries occur only in 10% of the chest trauma patients, usually caused by stab- or gunshot wounds. Most chest injuries can be managed non-operatively. Less than 10% of the blunt chest injuries and 15-30% of the penetrating chest injuries require surgery. Management of patients with traumatic chest injury is largely standardized according to Advanced Trauma Life Support (ATLS®) principles (2). In the majority of the patients with a haemopneumothorax due to blunt or penetrating chest trauma, tube thoracostomy is the primary treatment (3). Placement of a chest tube is a frequently used procedure in managing traumatic chest injuries, although contamination during drain insertion can be a major cause of infection such as a pneumonia and empyema (4, 5). The incidence of post-traumatic empyema has been reported to range from 2 to 25%. Contamination of the pleural space may occur from the injury, after tube thoracostomy, via transdiaphragmatic migration of intraabdominal infectious processes or from a parapneumonic process similar to patients without antecedent trauma (6). The primary causative organism in posttraumatic empyema is staphylococcus aureus, which suggests bacterial migration from the skin, either by the penetrating object or during the tube thoracostomy placement (7, 8). Several randomized clinical trials have evaluated the effectiveness of antibiotic prophylaxis in patients with traumatic thoracic injuries requiring tube thoracostomy as primary treatment. However, the use of prophylactic antibiotics for traumatic thoracic injuries requiring tube thoracostomy is still under debate and it would be of interest to investigate whether prophylactic antibiotics can improve care for these group of trauma patients (9-19).

Although 90% of the chest injuries can be treated non-operatively or by chest tube, the majority of the remaining 10% will need special attention. These patients are mostly triaged and treated in level 1 trauma centers due to their severity of injury. As a result, this concentration of care for patients with specific injuries, allows for the improvement of treatment algorithms and the development of new surgical techniques. The last decade there has been more interest in the bony parts of the thoracic cage, as both the sternum and the ribs prove to be important factors in breathing mechanics.

Sternal fractures

Sternal fractures are present in up to 8% of the patients admitted after blunt thoracic trauma and motor vehicle crashes (20). Since the mandatory use of seatbelts, an increased incidence

of the sternal fractures is observed (21). Isolated sternal fractures are relatively benign injuries (22-24). Morbidity and mortality are usually determined by concomitant injuries of internal thoracic organs. Mortality varies from 4% to 45% (22, 23, 25). More often a sternal fracture is one of the injuries diagnosed in a multiple injured patient. Frequently observed associated thoracic injuries are vertebral injuries, rib fractures, pulmonary or cardiac contusion, haemopneumothorax and mediastinal injuries (22, 25-27). The majority of sternal fractures are treated conservatively by optimizing pain management and treatment of the accompanying injuries such as cardiac contusion. However, in case of unstable fractures, thoracic wall instability, fracture displacement or persistent dislocation, sternal deformity, respiratory insufficiency, severe pain and fracture non-union, surgical fixation can be performed (22, 25, 28-32). Several fixation methods are available. When surgical fixation is considered, good results with low complication rates after plate fixation are suggested (22, 24, 28, 31-33). However, due to the limited available evidence, standardized treatment guidelines for traumatic sternal fractures are lacking.

Rib fractures

Rib fractures are the most common thoracic injuries and occur in 10% of all trauma patients and approximately in 30% of patients with significant chest trauma (34).

Conservative management

Rib fractures are clinically important injuries. Even isolated rib fractures are associated with significant consequences, such as prolonged pain and disabilities (35). An increased number of fractures, older age, and multiple injured patients with rib fractures are associated with increased rates of morbidity and mortality (36-38). The thoracic pain caused by rib fractures limits patients to cough and breath deeply, which can result in atelectasis and pneumonia. A combination of optimal pain control, pulmonary physical therapy, oxygen suppletion and positive pressure ventilation are considered to be pivotal in management of patients with fractured ribs (37, 39). Epidural analgesia, intercostal or paravertebral blocks and intravenous analgesia are the most frequently used analgesia modalities in patients with rib fractures. Although this concerns a frequently seen injury and multiple studies for the management of pain were performed, there is still room for improvement in pain management after blunt chest trauma. Currently, patients with non-operatively treated flail chest develop pneumonia in 27-70% and have a mortality rate of 25-51% (40). Despite optimal pain treatment as suggested in current literature, some patients still suffer from unbearable pain with impaired pulmonary functioning.

Surgical management

Providing external stability by surgical fixation, might offer an alternative treatment in the management of patients with multiple rib fractures. The aim of surgical treatment is to improve respiratory mechanics, reduce pain and prevent pulmonary complications. A meta-analysis concluded that surgical fixation of flail chest is associated with reduction in the duration of mechanical ventilation, reduction of complications associated with prolonged mechanical ventilation, reduction in hospital length of stay, as well as a reduction in mortality (41). Although these data were mainly based on retrospective studies and a few prospective trials, the current trend is to perform rib fixation in patients with flail chest and severe chest wall deformity, although the timing of fixation remains elusive. Nowadays, since surgeons have increased experience with operative treatment of rib fractures in flail chest, an expansion of indications is observed. Patients with multiple rib fractures and unbearable pain, despite optimal pain management, increasingly receive rib fixation as well. Indications however, are not very strict or well described.

Long-term follow up

Aside from the acute impact of rib fractures, long-term morbidity of pain, disability and deformity have been described (35, 42). In non-operatively treated patients a significant reduction in quality of life is seen (43). Only 71% of the patients returned to work (43).

Due to technical improvements there is a growing popularity of surgical rib fixation, which probably leads to better short-term outcome. However in the long-term follow up we encounter problems as implant related irritation, chronic implant related infection, persistent pain or implant failure, which occasionally lead to implant removal.

Patients undergoing surgery have a similar long-term recovery to those who are treated conservatively, except for a better range of motion in the chest wall (44). Quality of life improves the most between 6 weeks and 3 months after surgery. Between 6 weeks and 1 year after surgery there is a significant decrease in the proportion of patients experiencing problems with mobility, self-care, performance of usual activities and pain or discomfort. Although, approximately half of the patients still experience pain or discomfort after one year (45). Still a comparison between the follow up of operatively and non-operatively treated patients should be performed to discover the long term benefits of each treatment option.

A presumably small percentage of patients develop rib nonunion and an even smaller percentage develops symptomatic rib nonunion after non-operative treatment of rib fractures. Infrequently rib nonunion is also seen after operative treatment. Chronic, focal pain at the site of the nonunion is the dominant complaint of patients with fracture nonunion. Less common complaints are dyspnea, clicking sensation or jabbing with respiration and shortness of breath (35, 46). In patients with rib nonunion rib fixation can be a solution. However, studies describing long-term results after rib fixation and nonunion surgery are scarce.

OUTLINE OF THIS THESIS

The central theme of this thesis is the clinical treatment of thoracic trauma patients with a special focus on treatment of rib fractures. In **chapter 2** a general outline about the most common chest injuries and treatment is presented. In **chapter 3** the use of prophylactic antibiotics in trauma patients requiring tube thoracostomy is discussed. In **chapter 4** the different types of analgesic therapy in patients with traumatic rib fractures are described and compared. **Chapter 5** gives an overview of current treatment practice and outcome of traumatic sternal fractures. In **chapter 6** the outcome of surgical management of multiple rib fractures is reviewed. In **chapter 7** a retrospective multicenter cohort study about rib fixation versus non-operative treatment of flail chest and multiple rib fractures after thoracic trauma is presented. **Chapter 8** describes the long-term follow-up after rib fixation for flail chest and multiple rib fractures. One of the problems encountered in the long-term follow-up after chest trauma is rib-nonunion. This is a rare problem and results of surgical treatment are explained in **chapter 9**. Finally this thesis concludes with a general discussion and future perspectives (**chapter 10)**.

A summary of the research questions addressed in this thesis is presented in Table 1.

Table 1. Summary of research questions addressed in this thesis.

Chapter	
2	• What are the current diagnostic procedures and classification models necessary for an accurate assessment of patients with thoracic trauma?
	• What are the various thoracic injuries and their treatment options?
3	• What is the current evidence for antibiotic prophylaxis to prevent infections from chest drains in blunt and penetrating thoracic trauma?
4	• What is the best analgesic intervention for traumatic rib fractures?
6	• What is the current evidence for the treatment of multiple rib fractures?
7	• What is the best treatment of rib fractures, conservative versus operative treatment? A comparison of 2 treatment strategies?
8	• What is the long term follow-up of operative treatment of rib fractures?
9	• What is the current evidence of surgical treatment of nonunion rib fractures?

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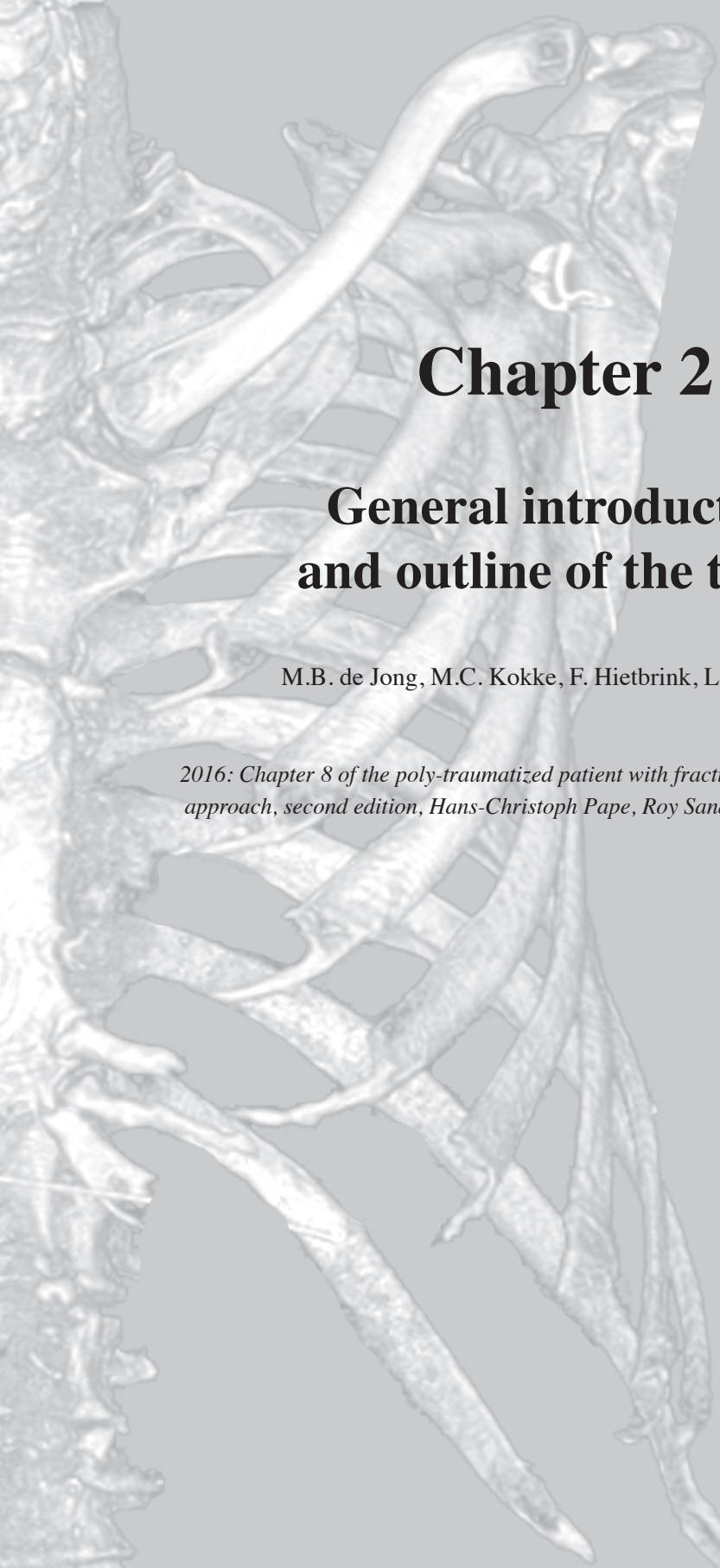

Chapter 2

General introduction and outline of the thesis

M.B. de Jong, M.C. Kokke, F. Hietbrink, L.P.H. Leenen

2016: Chapter 8 of the poly-traumatized patient with fractures, a multi-disciplinary approach, second edition, Hans-Christoph Pape, Roy Sanders, Joseph Borrelli, Jr.

Abstract

Thoracic trauma is a significant cause of morbidity and mortality. Some thoracic injuries are life-threatening and early diagnosis and prompt treatment is mandatory. A thorough evaluation of the patient and a systematic approach is necessary to manage the severity of different injuries. Knowledge of the trauma mechanisms and their specific injuries are required to improve patient care and decrease unfavorable outcomes and complications. This chapter gives an overview of the diagnostic procedures and classification model necessary for an accurate assessment of patients with thoracic trauma. Furthermore it describes the occurrence of the various thoracic injuries and their treatment options.

Introduction

Thoracic trauma is one of the major burdens in poly-traumatized patients. The mechanisms have changed throughout the years, as vehicles have become available that allow high speed traveling, along with changes in passive car safety.

Incidence

Thoracic trauma is a significant cause of morbidity. In persons younger than 40 years, traumatic injury is even the most common cause of death. Thoracic injuries are responsible for 25% of deaths in this population (1).

Trauma deaths due to chest injury occur in 76% in the first day, of which 38% takes place in the first hour (2). The majority of patients who dies from pulmonary complications will die more than 10 days after trauma. The so-called golden hour for thoracic trauma in which accurate treatment is required to prevent mortality is still very important. Less than 10% of the blunt chest injuries and 15-30% of the penetrating chest injuries require an operation. Most chest injuries can be managed non-operatively. A systematic approach like Advanced Trauma Life Support® provided by the American College of Surgeons is the most well known and most used system (3).

According to the principles of ATLS®, thoracic injuries are separated mainly in two main categories: acute life-threatening and potentially life-threatening injuries (Table 1). All injuries will be described in this chapter.

Table 1. Thoracic injuries (3).

Acute life threatening	Potentially life threatening thoracic injuries
• Tension pneumothorax	• Simple pneumothorax
• Open pneumothorax	• Hemothorax
• Flail chest and pulmonary contusion	• Pulmonary contusion
• Massive hemothorax	• Tracheobronchial tree rupture
• Cardiac tamponade	• Blunt cardiac injury
	• Traumatic aortic disruption
	• Traumatic diaphragmatic injury
	• Esophageal rupture

Trauma mechanism and pathophysiology

Chest trauma is mostly related to automobile for pedestrian accidents and commonly results in chest wall injuries like rib fractures. The pain associated with these injuries can make breathing difficult and this may compromise ventilation. This can be further aggravated by

pulmonary contusion, which leads to even more difficulty in breathing. Shunting and dead space ventilation produced by these injuries can also impair oxygenation. Space-occupying conditions include pneumothorax, hemothorax and hemopneumothorax. These interfere with oxygenation and ventilation by compressing otherwise healthy lung parenchyma. At a cellular level, lung contusion induces an inflammatory response signified by primed polymorph neutrophil granulocytes (PMNs) in blood and tissue (4).

Operative treatment is rarely necessary in blunt thoracic injuries although the advent of several plating systems for rib fixation increases intervention rates (see also rib fractures). Most blunt thoracic injuries can be treated with supportive measures and simple interventional procedures such as chest drainage. Traumatic asphyxia results from a severe blunt injury of the thorax. Patients present with cyanosis of the head and neck, subconjunctival hemorrhage, periorbital ecchymosis, petechiae of the head and neck and occasionally neurologic symptoms. Factors implicated in the development of these striking physical characteristics include thoraco-abdominal compression after deep inspiration against a closed glottis. This results in venous hypertension in the valveless cervicofacial venous system. Other injuries caused by blunt thoracic trauma are diaphragmatic injuries, pneumothorax, hemothorax, blunt tracheal injuries, bronchial injuries, esophageal injuries, cardiac injuries and injuries to the major thoracic veins or thoracic duct. These injuries and their management will be described in this chapter.

Classification

In the poly-traumatized patient chest trauma is only one part of all injuries. The evaluation of injury severity and the prediction of outcome is one of the most important functions of scoring systems. Several scoring systems for the classification of blunt thoracic trauma have been developed. The Abbreviated Injury Scale (AIS) is a prognostic scoring system allocating a severity score to every injury of the different body regions (head, face, neck, thorax, abdomen, spine, upper extremity, lower extremity, external and other trauma). High scores are associated with a lower probability of survival. The AIS is an anatomical scoring system for injury severity assessment of different body regions (5, 6).

Most of the thoracic trauma scores are based on pathological-anatomical changes. The Thoracic Trauma Severity Score (TTS score) seems to be the most suitable for severity assessment and prediction of outcome in poly-traumatized patients with blunt chest injuries (7). The TTS score is based on five anatomical and physiological parameters: pO2/FiO2, rib fractures, pulmonary contusion, pleural lesions and age. Each parameter is assigned a value of 0-5. The TTS score ranges from 0 to 25 and with increasing values, a more severe thoracic trauma can be assumed (Table 2) (8).

Table 2. Thoracic Trauma Severity Score according to Pape et al. (12).

Grade	PO_2/FiO_2	Rib fractures	Pulmonary contusion	Pleural lesion	Age (years)	Points
0	> 400	0	None	None	< 30	0
I	300-400	1-3 unilateral	1 lobe unilateral	Pneumothorax	30-40	1
II	200-300	4-6 Unilateral	1 lobe bilateral or 2 lobes unilateral	Hemothorax/ Hemopneumothorax unilateral	41-54	2
III	150-200	> 3 bilateral	< 2 lobes bilateral	Hemothorax/ Hemopneumothorax Bilateral	55-70	3
IV	< 150	Flail chest	≥ 2 lobes bilateral	Tension pneumothorax	>70	5

Diagnostics

Thoracic trauma may result in a variety of different injuries. A prompt assessment of correct diagnosis and severity assessment of thoracic trauma is crucial for the further treatment of thoracic lesions itself and concomitant injuries. There are several diagnostic tools for diagnosis and severity assessment of thoracic trauma.

Chest radiography

The supine anteroposterior (AP) chest radiography is the initial examination of choice in patients with thoracic trauma. Because of the supine position of the trauma patient in the emergency room there is no lateral view available and therefore limited information can be gained from chest radiography. The chest X-ray is used as a first screening method during the evaluation of the trauma patient at the emergency room. The availability of CT scan, even in the emergency room, leads to a reduction in the need for plain films (9). Although the CT scan is significantly more effective in detecting thoracic injuries, chest radiography still is recommended by Advanced Trauma Life Support protocol (3). Especially in unstable patients a chest radiograph is still useful as it is the quickest way to rule out (tension) pneumothorax and hemothorax. CT scan is still more time consuming and requires considerable radiation exposure. Transferring an unstable patient from the emergency room to the radiology suite provides unnecessary risk. Overuse of CT scans can lead to inappropriate delays in patient care (10). However, in the stable patient with suspicion of blunt thoracic injuries and an indication for chest CT scan, skipping the chest radiograph should be considered (11, 12).

In certain cases physicians even should not wait for a chest radiograph to confirm clinical suspicion. The classic example is hyper-resonant note on percussion and the absence of breath sounds over the affected hemi-thorax combined with signs of hemodynamic

compromise, which can be found in patients with tension pneumothorax. This should be immediately decompressed before obtaining a chest radiograph.

Computed tomography of the chest

The use of CT for thoracic trauma evaluation has increased dramatically in the past 15 years. Chest CT scan is superior in identifying and visualizing injuries like pulmonary contusions, pneumothorax, hemothorax, vascular injuries and fractures. In about 18-82% of the patients with a normal chest X-ray additional injuries are found on chest CT scan (11-13).

The marked increase in the number of occult injuries diagnosed on a chest CT scan in patients with blunt thoracic trauma was not, however, accompanied by a similar increase in therapeutic interventions (14). The disadvantages of a chest CT scan are exposure to radiation, costs and a CT scan being more time consuming than a plain chest X-ray. Therefore it is important not to make a chest CT scan routinely but only when significant injuries are suspected.

Using the Nexus (National Emergency X-radiography Utilization study) Chest decision instrument might be helpful in decision-making in patients suffering from blunt thoracic trauma. The sensitivity and negative predictive value for thoracic injury seen on chest imaging was 98.8% and 98.5% respectively (15). This Nexus chest decision instrument is meant for all blunt trauma patients over 14 years old who, by initial assessment, may need chest imaging to rule out intrathoracic injury. The criteria used are: age > 60 years, rapid deceleration mechanism defined as fall >20 ft. (>6 m) or motor vehicle crash > 40 mph (>64 km/hr.), chest pain, intoxication, abnormal alertness/mental status, distracting painful injury and tenderness to chest wall palpation. If all criteria are absent there is a very low risk for intrathoracic injury and chest imaging is not indicated. If one or more criteria are present intrathoracic injury can't be excluded and chest imaging should be done (Figure 1) (15).

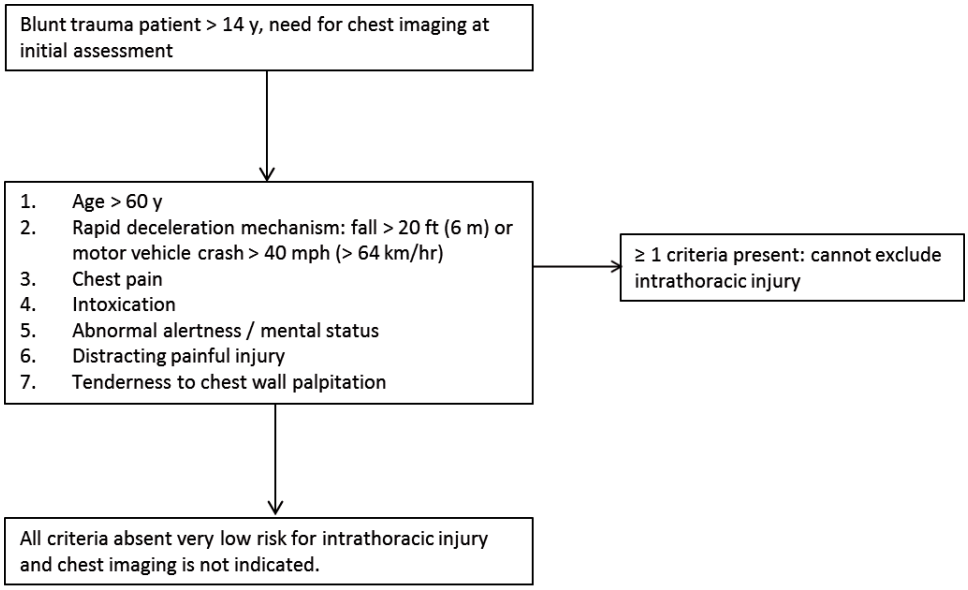

Figure 1. Nexus Chest Decision Instrument (15).

Ultrasonography

Transthoracic ultrasonography

The Focused Abdominal Sonography for Trauma (FAST) is a rapid ultrasound examination performed in the emergency room. Except for abdominal injuries also some thoracic injuries as hemothorax, pneumothorax and blood in the pericardium can reliable be diagnosed with a sensitivity of 93-96%. Most trauma patients are usually managed in the supine position with spinal immobilization, which underestimates the prevalence of thoracic lesion on chest X-ray. Especially in unstable high-risk patients thoracic ultrasonography as a bedside diagnostic modality is a better diagnostic test than clinical examination and chest X-ray together (16, 17). However in the evaluation of pneumothorax the accuracy is not sustained over time, probably as a result of the formation of intrapleural adhesions (18). As another disadvantage, subcutaneous emphysema precludes an accurate diagnosis by ultrasound.

Transesophageal echocardiography (TEE)

In the workup of possible blunt rupture of thoracic aorta, transesophageal echocardiography has sensitivity and specificity up to 93-96% in diagnosing a thoracic aorta rupture (19). TEE also may help define intracardiac anatomy, function and injuries like cardiac valve injury or traumatic rupture of the interatrial or interventricular septum. The TEE has a better

sensitivity and specificity than the transthoracic echocardiography (TTE) for depicting aortic injury, pericardial effusion, myocardial contusion, atrial laceration and cardiac valve injury (20). However, the use of the TEE may be limited in patients with severe trauma and hypotension or head, neck, and spine injuries (21).

Bronchoscopy

Fiber optic or rigid bronchoscopy is performed in thoracic trauma patients with suspicion for tracheobronchial injuries. Both techniques have high sensitivity for the diagnosis of these injuries. Bronchoscopy can be used in detecting tracheobronchial lesions, supraglottic injuries, bleeding and lung contusions. Bronchoscopy can also be therapeutic use for removing secretions and preventing the formation of atelectasis. Bronchoscopy is rarely used in the primary treatment of patient with thoracic trauma, but a few days after initial trauma it can be useful.

Acute life-threatening thoracic injuries

Tension pneumothorax

A tension pneumothorax occurs when a pneumothorax permits entry but no exit of air from the thoracic cavity (Figure 2). This results in increase of the air in the pleural cavity but leads to collapse of the ipsilateral lung and compression of the intrathoracic structures on the contralateral side.

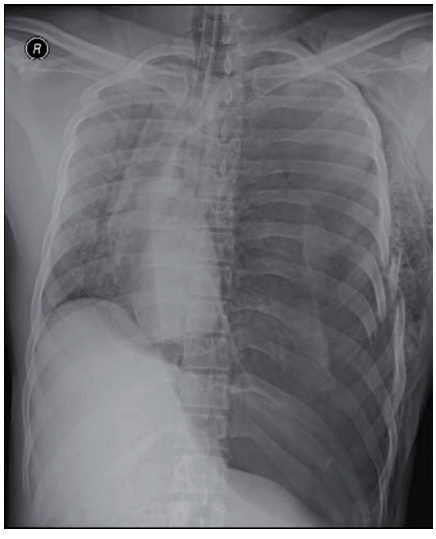

Figure 2. Tension pneumothorax.

Although needle decompression in the midclavicular line is the recommended method of initial treatment, the patency of this procedure has been subject of debate. In a porcine model of tension pneumothorax, 58-64% of the needle placement procedures failed in adequate decompression, compared to a 100% success rate in thoracostomy tube placement (22).

In the acute clinical setting, a success rate of 59% has been documented, while in the remaining 41% the needle did not reached the pleural cavity (23). Because of these flaws in needle thoracocentesis, blunt dissection and digital decompression should be the first step. When a chest tube cannot directly be placed, the incision is made in the midclavicular line in the second intercostal space, while in a later setting, a formal chest tube can be placed in the 4th intercostal space in the mid-axillary line (24). In most cases chest tube placement is performed according the ATLS® guidelines (3). An incision is made in the 4th or 5th intercostal space on the anterior axillary line, after which the pleura is bluntly opened. A large diameter (24-32 French) tube is inserted and placed dorso-cranially (25). A canister with water seal is connected to the tube and wall suction is initiated. Preferably, prophylactic antibiotics are given, however, this should not delay the placement of a chest tube in an emergency setting (26).

Open pneumothorax

An open pneumothorax occurs when a pneumothorax is associated with a chest wall defect (Figure 3). During inspiration, air is sucked into the pleural cavity due to the negative intra-thoracic pressure.

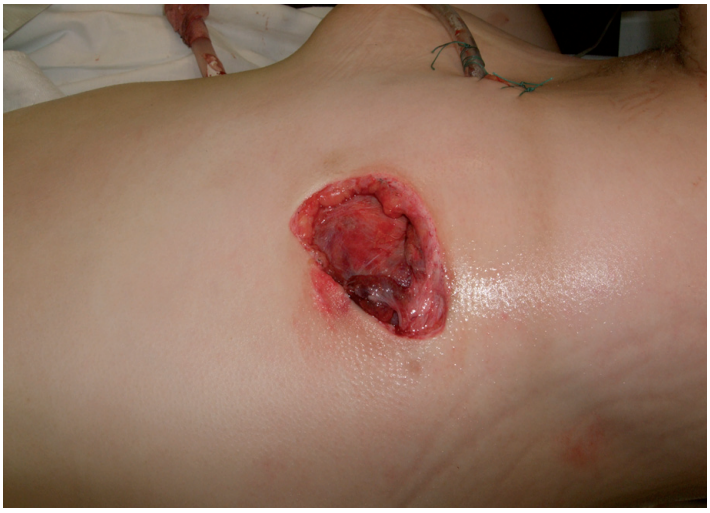

Figure 3. Open pneumothorax.

When the diameter of the external wound is over 2/3 of the diameter of the bronchial tree then the air prefers to go through the wound. The wound has to be treated by a venting bandage. This can be applied using commercially available seals (27), or by applying a bandage, which is taped on 3 sides, allowing air to be vented out, but seals the cavity during inspiration (28).

Massive hemothorax

A hemothorax is defined as blood in the interpleural space. This occurs in up to 40% of patients with blunt thoracic trauma. Bleeding is caused by parenchymal injuries, rib fractures, laceration of intercostal or internal mammary artery. Furthermore, hemothorax can be a life-threatening condition when caused by bleeding from the heart or hilar vessels.

All trauma patients with a hemothorax should undergo chest tube placement. In case of gross drain output, a second chest tube is placed promptly. Immediate surgery for massive hemothorax is mandatory when the patient's physiology is unstable (persistent blood transfusion required), regardless of the numbers of initial chest tube output. Furthermore, when >1500ml in the first 24 hours is evacuated, this should prompt surgical intervention (29). Injuries that are often found when massive hemothorax is present are bleeding from the azygos vein, the mammary artery, laceration of the hilar vessels, severe pulmonary tissue laceration or dissection of the aorta. When having a massive hemothorax it should not be forgotten to re-infuse the lost blood by using the cell-saver.

Pulmonary contusion

The most common injury after thoracic trauma is pulmonary contusion. It occurs in 30-75% of all patients (30). A severe lung contusion (Figure 4 and 5) can be life threatening because of the destruction of alveolar architecture of the lung and intramural bleeding, prohibiting diffusion over the alveolar membrane, leading to severe hypoxia. The lung contusion will further be dealt with later in this chapter.

Cardiac tamponade

A pericardial tamponade mostly occurs after penetrating trauma, but it also present in about 1% of blunt chest trauma patients. It develops because of bleeding into the pericardial sac, either from an injury to the heart or from coronary or aorta lesion (31). Immediate pericardiocentesis is indicated for restoration of normal cardiovascular function. Although successful outcome has been documented in pericardiocentesis as the sole procedure, in a patient with severe hemodynamic instability, the procedure is only to be used as a bridge to surgery or transfer to a definitive care facility (32). An alternative is the performance of a subxyphoidal window to evacuate the blood from the pericardium. The definitive treatment consists of thoracotomy, repair of the injury causing the bleeding and adequate evacuation of the blood from the pericardium.

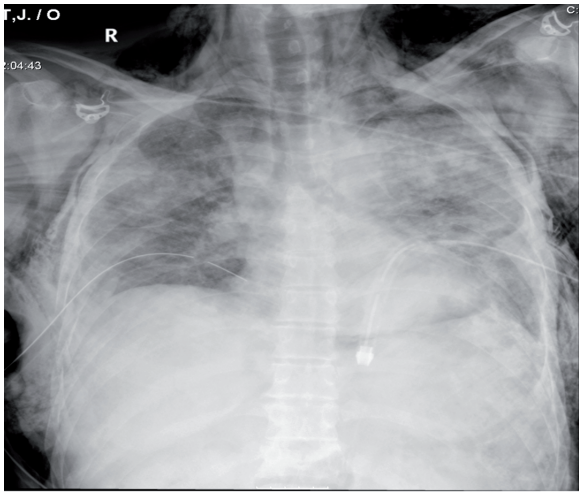

Figure 4. Pulmonary contusion.

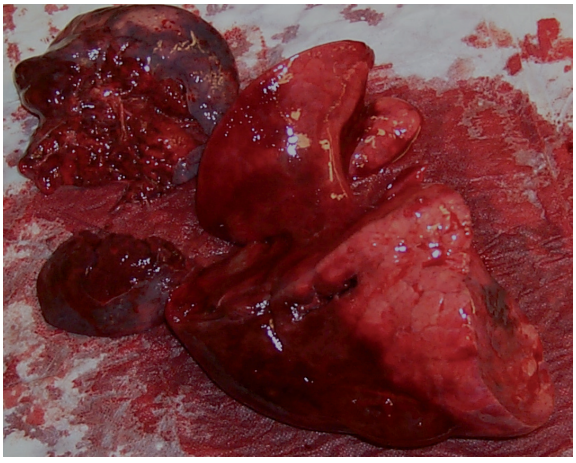

Figure 5. Lung tissue after pulmonary contusion.

Potentially life-threatening injuries

Besides the life-threatening injuries, which will lead immediately to death if left untreated, there are potentially life-threatening injuries in patients with thoracic trauma (Table 1). During the first minutes of trauma resuscitation these injuries can often be missed. So it is of great importance to have a high index of suspicion depending on the trauma mechanism and treat these injuries immediately to prevent further deterioration and eventually death. Additional imaging like a chest X-ray will help you in further diagnosis, however some of these injuries can easily be missed by conventional radiology alone (33).

Simple pneumothorax

A simple pneumothorax occurs as a result of air entrapment into the pleural cavity between the two pleural layers (visceral and parietal) and will cause a (partial) collapse of the lung and thereby compromising oxygenation and ventilation on the affected side. The air leakage is often caused by a lung laceration after blunt thoracic trauma, but damage to the lung by rib fractures or penetrating injury can account for this phenomenon.

Diminished breath sounds and hyper-resonance to percussion over the affected hemi-thorax indicates the presence of a pneumothorax. In stable patients an additional chest X-ray or even a CT scan in the case of an occult pneumothorax is necessary to demonstrate the diagnosis. An occult pneumothorax is a pneumothorax that was not suspected clinically, nor was evident on the plain radiograph, but rather identified on CT scan or ultrasound. When adequate follow-up is provided (by means of ultrasound or chest X-rays), occult pneumothorax does not require chest tube drainage (34). Even on positive pressure ventilation, conservative treatment of an occult pneumothorax can be successful and reduce the length of hospital stay, given an adequate follow-up by ultrasound or chest radiographs (35-37).

The treatment of a pneumothorax will consist of a tube thoracostomy to release the air and thereby re-expand the collapsed lung. This tube should be placed according to the ATLS® recommendations (3). Although some authors have stated the drainage of a simple traumatic pneumothorax in patients without other injuries can be done with a pigtail, we strongly suggest that this procedure should be reserved for a very selected patient population (38). Since the majority of trauma patients with a pneumothorax (especially in blunt trauma) have concomitant injuries, which will often lead to persistent air leak and/or hemothorax, these patients require a formal chest tube. If left untreated a simple pneumothorax can convert into a tension pneumothorax and this certainly needs prompt intervention.

Hemothorax

A hemothorax occurs in up to 40% of patients with blunt thoracic trauma. As a result of lung laceration, which damages the lung parenchyma, blood can enter the pleural cavity thereby causing a hemothorax. Both bleeding from an intercostal vessel or internal mammary vessel can also contribute to a hemothorax. Depending on the bleeding source and severity, the hemodynamical status of the patient will be influenced and should be treated accordingly. A hemothorax should be treated with a tube thoracostomy to evacuate the accumulated blood. The chest tube production should be monitored closely to recognize a massive hemothorax directly. No further immediate surgical intervention is necessary as a hemothorax is often self-limiting unless there is ongoing bleeding or there consists a massive hemothorax. By draining the intrathoracic hemorrhage the lung can re-expand

and the formation of fibrous adhesions is prevented which reduces the risk of a pleural empyema and restrictive pulmonary disease (31, 39).

If a retained or persistent hemothorax is present a VATS is necessary to remove the clotted blood. The VATS procedure should be done within the first 3-7 days after trauma, in order to reduce the chance on conversion to thoracotomy and decrease the risk of infection (29). Intrapleural thrombolytic therapy only has limited use and should not be considered as standard of care (40).

Tracheobronchial tree rupture

Injuries to the tracheobronchial tree (trachea or major bronchus) are rare and most patients die before they reach the hospital. They are frequently caused by blunt trauma which causes compression of the trachea between the sternum and vertebrae, or by a rapid deceleration trauma. Patients are in severe respiratory distress with coughing, stridor or an altered voice and present with hemoptysis, massive subcutaneous emphysema, or associated pneumothorax.

A delay in diagnoses leads to a high mortality, even if the patient reaches the hospital alive. So if tracheobronchial injury is suspected immediate treatment is required. The first step is to establish a patent airway by endotracheal intubation. If the endotracheal tube can be managed distal to the tracheal injury, it can prevent a massive air leak (Figure 6).

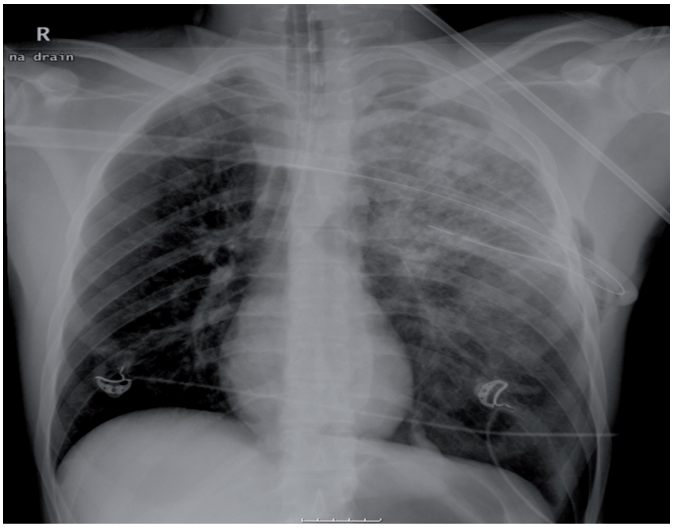

Figure 6. Tube passes right-sided bronchial rupture.

Advantage is that there is no positive pressure in the injured lung, usually healing will appear without surgical intervention. A fiber-optic bronchoscopy can be used as a diagnostic adjunct and if a bronchial injury is diagnosed the tube can be placed in the contralateral bronchus. As the trachea and main bronchus are in the proximity of the great vessels and esophagus, associated injuries must be suspected and treated accordingly. In both tracheal and bronchial disruption further surgical repair is mandatory. When performing a thoracotomy it is possible to intubate directly in the ruptured bronchus (Figure 7).

Tracheal lesions due to blunt trauma usually appear as transverse tears between cartilaginous tracheal rings or longitudinal tears in the posterior tracheal membrane. In tracheal injuries surgical repair is required in order to ensure airway continuity. This can be done by primary suturing with absorbable sutures or by the resection of several tracheal rings and re-anastomosis. Once this has been done, autogenous tissue is wrapped around the reconstructed trachea. In the neck, all strap muscles can be used for this procedure, while in the chest the intercostal muscles, serratus anterior, latissimus or pericard patches can be used.

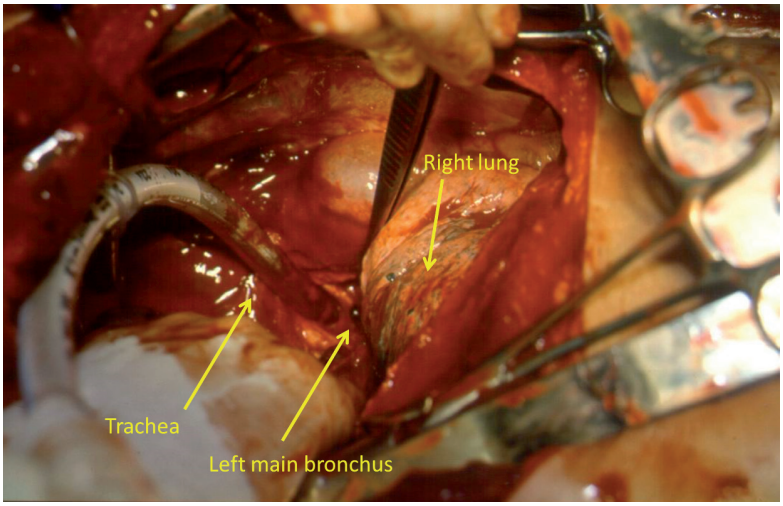

Figure 7. Intubation through left main bronchus.

Traumatic aortic disruption

Aortic injury caused by blunt trauma is mostly lethal at the scene; however those that have only an intimal tear reach the hospital alive so treatment can be established. In blunt trauma the shearing forces due to rapid deceleration will cause a partial laceration of the aortic wall near the ligamentum arteriosus. This will result in a contained rupture of the aorta (Figure 8). Diagnosis is difficult as specific clinical signs are absent. Together with

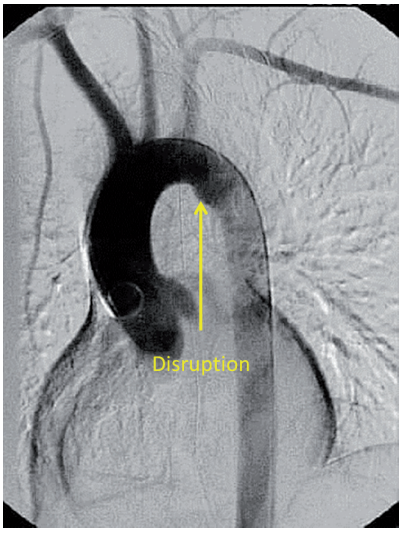

Figure 8. Traumatic aortic disruption.

the trauma mechanism and a high index of suspicion an additional chest X-ray may reveal abnormalities like deviation of the trachea, widened mediastinum or presence of an apical cap (3). A CT angiogram of the aorta is more accurate and will confirm the diagnosis and the extent of the injury. Therapy consists of maintaining the mean arterial blood pressure around 60 mmHg, which will reduces the risk of rupture. Thereby it is possible to delay the nowadays often-used endovascular repair of the aortic injury (Figure 9 and 10), while treating other severe associated injuries (41, 42).

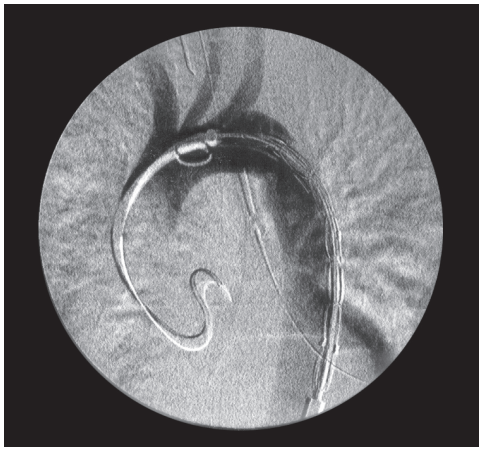

Figure 9. Stent positioning in aorta.

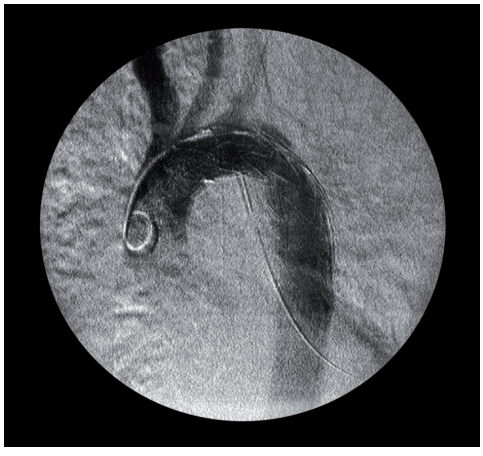

Figure 10. Stent in aorta after expansion.

Traumatic diaphragmatic injury

Blunt torso injury produces large tears and predominantly occurs at the left hemi-diaphragm. These tears can lead to herniation of intra-abdominal organs, which can be diagnosed, on chest X-ray (Figure 11). Diagnosis however is often hampered by the fact that the multiply injured patients are treated with positive pressure ventilation, which prevents dislocation of abdominal organs into the thorax. Nowadays early CT scanning can reveal the discrete changes that go with diaphragmatic injury.

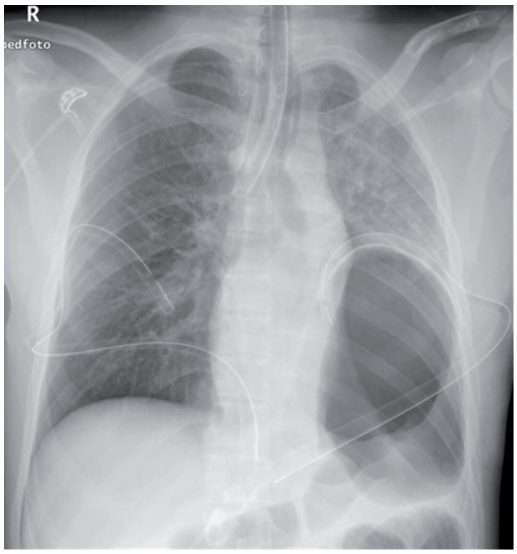

Figure 11. Ruptured diaphragm.

Many of the diaphragmatic injuries however are diagnosed during an emergency laparotomy or thoracotomy for associated intra-abdominal or intrathoracic injuries. The treatment exists of direct repair. Only in the minority of cases a mesh is necessary.

Esophageal rupture

Blunt esophageal injuries are very rare. They are caused by a sudden increase in the intra-abdominal pressure for example by a blow in the upper abdomen. Gastric contents will eject in the esophagus causing a rise in intraluminal pressure. Pressure rise can lead to a tear in the esophagus with leaking of content into the mediastinum.

Patients present with clinical signs like subcutaneous emphysema, pneumomediastinum, pneumothorax or intra-abdominal free air. Time between trauma and definitive treatment may influence the outcome by developing esophageal injury related complications (43).

If diagnosed early the majority of the patients can be treated with primary surgical

repair and additional drainage of the mediastinum is necessary. Nowadays an endoscopic esophageal stent is a possible alternative (44). If left undiagnosed patients often present with fever and signs of systemic sepsis caused by mediastinitis at a later stage.

Bone injuries

Rib fractures

Rib fractures are the most common thoracic injuries and occur in 10% of all trauma patients and approximately 30% of patients with significant chest trauma (45). Fractures of the first and second rib suggest severe thoracic trauma. These ribs provide a protection of vital structures like brachial plexus and vessels (subclavian artery and vein). Ribs 4-10 are most frequently involved. The mechanism is often due to direct forces on the chest wall. With fractures of ribs 8-12 the presence of intra- abdominal injuries should be considered.

Physical signs of rib fractures include local tenderness and sometimes crepitus over the site of the fracture. Rib fractures may also by an indicator for other significant intrathoracic injuries. Elderly patients and patients with osteoporosis or osteopenia have an increased risk of number and severity of fractures. This in contrast to children where higher forces are needed to cause fractures, because the chest wall is more pliable and compliant. The most common symptom of rib fractures is pain, which makes it difficult to breath adequately. Up to 30% of the patients with rib fractures develop a pneumonia; the older the patient the higher this percentage (46, 47). The greater the number of fractured ribs the higher the mortality and morbidity (45). Up to 10% mortality is reported in patients with more than 4 rib fractures, this increases to 34% in patients with 8 or more fractures (48). It is also known that patients with more than 4 rib fractures after the age of 45 have an increased risk of adverse outcomes (48-51).

A flail chest can be defined as fractures of four or more consecutive ribs in two or more places resulting in paradoxical movement of the chest wall during respiration. Paradoxical movement of the chest can increase the work and pain involved with breathing. In most patients the severity and extent of the lung injury determines the clinical course and the requirement of mechanical ventilation. Patients with flail chest have a significant higher need for mechanical ventilation. Although the recovery of mechanical ventilation ensured a better result in the treatment of flail chest, it is also responsible for several ventilation related complications.

Management of rib fractures involves pain control and adequate oxygenation and ventilation possibly using positive pressure ventilation when necessary. In patients with

a flail chest non-operative treatment leads to a mortality of 25-51% and 27-70% develop pneumonia (52). External stability by means of operative fixation is an alternative treatment of multiple rib fractures in order to avoid mechanical ventilation (Figure 12 and 13). The goal of operative therapy is to improve respiratory mechanics, reduce pain and prevent pulmonary restriction associated with significant chest wall deformities. Current indication for operative fixation is the presence of a flail chest which is associated with reduction in duration of mechanical ventilation, complications associated with prolonged mechanical ventilation, length of stay in the hospital and mortality (53, 54).

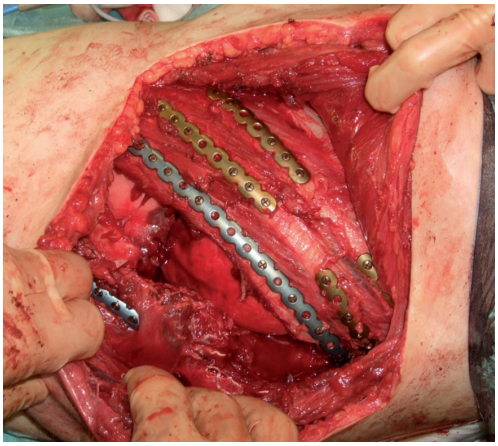

Figure 12. Rib fixation.

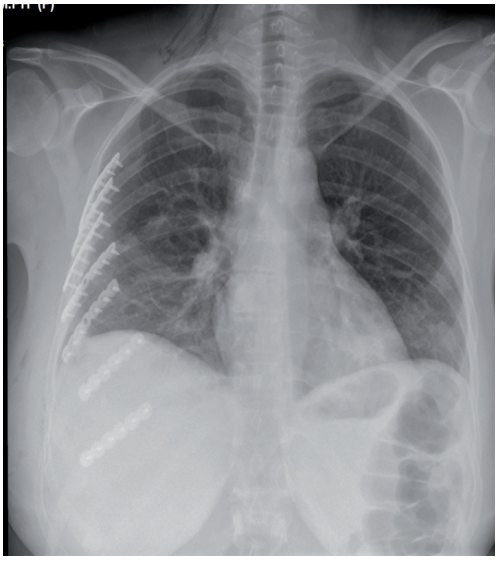

Figure 13. Rib fixation.

Other indications are patients with rib fractures who, notwithstanding good pain management, are still in pain, have chest wall deformity, or have one or more symptomatic non-union rib fractures. Age over 45 years and more than four rib fractures seems to be important factors in determining outcome of patients with multiple rib fractures. Therefore an operative approach of patients older than 45 years with four or more rib fractures should be considered.

Sternal fractures

Sternal fractures are present in up to 8% of the admissions after blunt thoracic trauma and motor vehicle crashes (55). Before the use of the seatbelt a sternal fracture was a marker of high-energy trauma. Since the mandatory use of a seatbelt, the survival after motor vehicle crashes increase together with a rise in the incidence of the sternal fracture, also called the typical "seat belt injury" (56).

The typical sternal fracture is a transverse fracture located in the upper and mid-portions of the sternal body. The symptoms consist of localized tenderness, swelling and deformity. A sternal fracture can be diagnosed by a lateral view because a sternal fracture is rarely apparent on the anteroposterior chest film. The highest sensitivity is reached by the chest CT scan.

As in all thoracic fractures, sternal fractures are often associated with more serious occult injuries. Underlying myocardial injury is not uncommon. Treatment of sternal fractures is similar to that for rib fractures. It consists primarily of pain control and appropriate pulmonary hygiene. Patients with isolated, stable sternal fractures that have normal radiographic findings and normal electrocardiograms can be treated as outpatients (57).

When the sternal fracture is severely displaced open reduction and internal fixation by a midline incision should be done. Various techniques are described, including wire suturing and the placement of plates and screws. Although there are several pre-contoured plates available for this aim, the less massive plates employed for rib fixation can also be used. In the presence of a flail chest a different approach can be followed to fixate both ribs and sternum.

Scapular fractures

Fractures of the scapula are uncommon and they are due to a high-energy dissipation. These patients usually have associated injuries (61%) with higher treatment priority. The associated injuries reported most frequently are rib fractures but also pneumothorax, hemothorax, pulmonary and spinal injuries are described.

A patient with a scapular fracture typically presents with the arm adducted along the body. In physical examination swelling, crepitus, ecchymosis and local tenderness may

be present. Active range of motion is restricted in all directions. With the presence of a scapular fracture, arterial injury and / or brachial plexopathy should also be considered. Most fractures occur in body (30%) and neck (25%) and can be treated non-operatively. In contrast displaced intraarticular fractures of glenoid mostly need operative fixation.

Lung injuries

Pulmonary lacerations

Pulmonary laceration can be the result of penetrating chest trauma. But also blunt injury, which causes penetration due to rib fractures or torn lung tissue as a result of shearing forces can lead to lacerations of the lung parenchyma. Lung lacerations are characterized by the disruption of the pulmonary architecture, which will cause air or blood leakage. If this ruptures through the visceral pleura it will lead to a pneumothorax, hemothorax, or both. When blood or air becomes entrapped in the lung parenchyma a traumatic cyst develops which will be called pulmonary hematoma or pneumatocele respectively (58).

The only classification system for pulmonary lacerations published until now is from Wagner et al. (Table 3). They describe 4 types of lacerations based on CT findings or mechanism of injury: compression rupture, compression shear, rib penetration and adhesion tears (59). Treatment is often non-operative; however depending on the grade and location, sometimes surgical treatment is necessary. A thoracotomy with preservation of the lung is the primary goal in combination with wedge resection and segmentectomy if required. In case of penetrating injury caused by rib fractures with a through and through tract a pulmonary tractotomy can be performed (Figure 14 and 15).

Table 3. Classification pulmonary lacerations according to Wagner et al. (60).

Type	Mechanism of injury	Appearance on CT
1	Compression rupture	• air filled or air-fluid level in intraparenchymal cavity • linear tear (when rupture through visceral pleura)
2	Compression shear	• paravertebral laceration
3	Rib penetration	• small peripheral cavity • small peripheral linear radiolucency
4	Adhesion tear	• only seen at surgery of autopsy

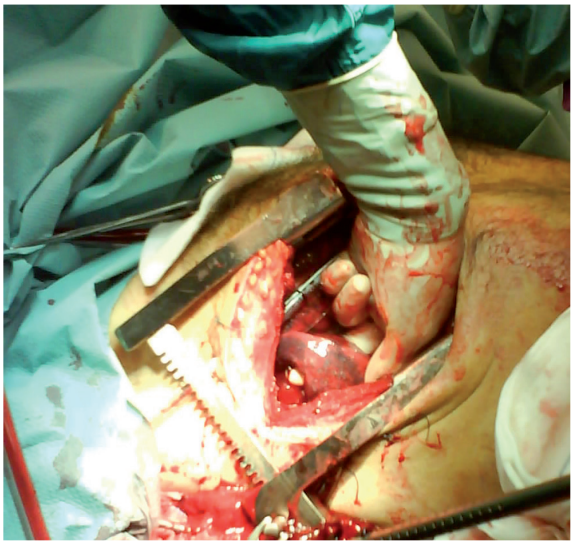

Figure 14. Tractotomy.

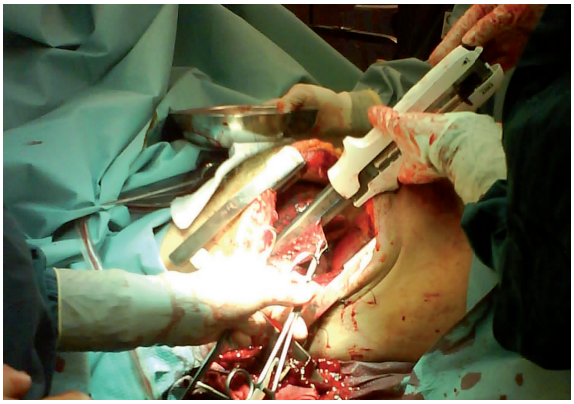

Figure 15. Tractotomy, stapling with stapling device.

Pulmonary contusion

The most common injury after thoracic trauma is pulmonary contusion. It occurs in 30-75% of all patients (30). It arises after severe blunt impact with chest wall injury, due to shearing forces in deceleration trauma or after penetrating injury, especially gunshot wound with high energy missiles. In adults pulmonary contusion is often associated with other injuries whereas in children, as their chest is pliable, it can be found in isolation. The lung is affected due to the direct trauma and damage to the parenchyma causing extravasation of blood and edema in the alveolar space (Figure 4 and 5). It occurs mostly on the peripheral lung parenchyma and in contrast to aspiration pneumonia it does not stick to the anatomic pulmonary segments. The

patient often present with respiratory distress or failure. On the initial chest X-ray, significant pulmonary contusion will be apparent; however, only approximately half of the abnormalities are detected at the time of admission (60). Additional CT scans will show the extent of the contusion. Depending on the severity of the pulmonary contusion, resulting in hypoxia and hypercarbia, optimization of oxygenation by ventilatory support may be necessary. After 5-7 days the pathophysiological changes of pulmonary contusion resolve but the recovery of the patient will depend on associated injuries or the appearance of complications.

Pulmonary herniation

Herniation of the lung through a traumatic event is rare (61). Patients who are involved in motor vehicle accidents can suffer multiple rib fractures by the compression forces of their seat belt. If those rib fractures originate at the costochondral-sternal junction and are dislocated they can cause a ventral chest wall defect. The protrusion of lung parenchyma and pleural membranes through the thoracic cage defect results in pulmonary herniation. As the anterior wall has minimal soft tissue support, this location is more prone to herniation although it may occur even in other areas. It can also be caused by costochondral or clavicle sternal dislocation. Patients can be asymptomatic or will have clinical signs like respiratory distress, thoracic ecchymosis caused by the safety belt or subcutaneous emphysema (62). Furthermore an obvious soft bulging mass, which changes in size with the respiratory cycle, may be present. A CT scan of the chest will reveal the diagnosis but even a standard chest X-ray can show some signs of herniation. The treatment is surgical and may vary from open reduction and internal fixation to using a mesh to close the defect.

Cardiac injuries

The exact incidence of cardiac injuries in varying degree of severity is unknown but is reported to be between 16-76% (63). Blunt cardiac injury (BCI) occurs when the heart is crushed between the sternum and thoracic vertebrae mostly in motor vehicle accidents; this injury can also occur after a fall from height, crush injuries or even in sports trauma with a direct blow to the chest. These type of injuries can result in myocardial contusion, cardiac rupture, coronary artery injury or valvular disruption (3).

To diagnose BCI after thoracic trauma is difficult, but to rule out BCI is important especially in patients without further associated injuries who do not require monitoring or even admission to the hospital. The Eastern Association recommends ECG and troponin evaluation and states that a normal ECG with the addition of a normal troponin I has a negative predictive value for BCI of 100% (64).

Myocardial contusion

Myocardial contusion is the most common of BCI with an incidence ranging from 3 to 56%

(65). The patients complain of chest pain; however, as this is a common symptom after chest trauma, the differentiation between a musculoskeletal origin and myocardial contusion or even infarction is challenging. Intramyocardial hemorrhage, edema and necrosis of muscle cells after myocardial contusion can cause a similar increase in serum troponin, due to loss of membrane integrity, as seen in acute myocardial infarction. ECG changes may show non-specific abnormalities, conduction disorders or arrhythmias but these changes may be the result of non-cardiac factors like hypoxia or anemia. The last decade the CT technology has developed and improved overall sensitivity and specificity. A Multidetector CT with ECG gated capabilities might be able to differ between traumatic or ischemic injury in selected patients (64). Echocardiographic evaluation, preferably esophageal, can reveal motility and contractility disorders in these cases.

Coronary artery injury

As a result of blunt chest trauma injury to the coronary vessels might appear. This can consist of dissection, intimal tear, thrombus, vessel spasm, vessel rupture or embolism. Due to its anterior position and the proximity of the chest wall, the coronary artery LAD, which is in the most a vulnerable anatomic position, is affected most after blunt cardiac trauma. Secondary to this injury myocardial infarction can develop. Therefore in patients complaining of acute chest pain without pre-existent angina pectoris clinical suspicion must arise. An ECG must be performed to rule out coronary artery injury in an early phase.

Late presentation will consist of single vessel coronary disease in young patients without atherosclerosis disease as cause for angina pectoris or myocardial infarction. Treatment should consist of acute PTCA and stenting as often intimal tears or dissections are present. Thrombolytic therapy is contraindicated as this will worsen the case (66).

Cardiac rupture

The incidence of cardiac rupture after blunt thoracic trauma is rare and is reported to be 0.16-2% (67). Most patients die at the scene in consequence of acute cardiac tamponade. There are several etiologic mechanisms described. Due to compression forces the atria or ventricle, at times of maximal filling status, may tear. Furthermore a rapid deceleration of the heart may cause a rupture at the junction between the atria and the vena cava or pulmonary veins (68). Patients present with signs of cardiac tamponade and if other causes of hypotension are ruled out (tension pneumothorax, abdominal bleeding) a high index of suspicion must exist. In case of an additional pericardium laceration, massive hemothorax and exsanguination - due to loss of tamponading effect - will result. In certain cases emergency thoracotomy can be lifesaving; however, even in emergency thoracotomy survival rates are limited.

Fracture treatment in patients with concomitant thoracic trauma

In severely injured patients, damage control surgery is the current standard. This treatment algorithm is primarily developed for patients with massive abdominal haemorrhage. The surgical procedure focuses on bleeding control and limitation of contamination. Only the most necessary procedures are performed and the patient is transported to the intensive care unit as soon as possible. Definitive surgical procedures are postponed until the lethal triad of acidosis, hypothermia and coagulopathy is corrected (69). In instable patients, interventions should be rapid and minimally traumatic to the patient. The primary focus is haemorrhage control and other life saving measures. Complex reconstructive work is delayed until the patient is better able to withstand the additional surgical trauma. This approach was readily adopted in patients with pelvic injuries (70).

Damage control surgery is developed to counter the homeostatic complications arising from hypovolemic shock. In addition, severely injured patients suffer immunological disturbances as well (71). Surgery functions as a second trauma and increases the alterations in the immunological response (71). This second hit is deemed the underlying mechanism for the development of organ failure, frequently affecting the pulmonary tissue. By minimizing the burden of surgery, an attempt is made to attenuate the inflammatory response and reduce the incidence of organ failure. Damage control orthopaedics is used as the current strategy to limit the surgical hit in severely injured patients, in contrast to the early total care principles, in which the patient is treated to the full extent in the first session (72-75).

Currently the two concepts are both used in the clinical setting for the fixation of fractures. “Early total care” (ETC) is used in patients who are deemed stable, while “damage control orthopaedics” (DCO) is the treatment of choice in patients who are unstable. Early total care consists of immediate repair by complex operative procedures. In contrast, based on the concept of damage control orthopaedics long bone fractures are stabilized by external fixation, which is later converted to intramedullary nailing or plate fixation. Early fracture fixation has been described to be essential to avoid pulmonary complications in multi-trauma patients, such as infection and pulmonary dysfunction (76, 77). However, ETC gives an increased incidence of pulmonary failure in severely injured patients (78, 79). In these cases, DCO might be a more suitable approach, keeping in mind the increased percentage of complications at the fracture site, such as delayed union and infectious complications (80). In conclusion, stable patients can undergo ETC, while unstable patients or patients in extremis undergo DCO. For so called “borderline” patients however a clear cut answer is still pending (Table 4) (81).

Table 4. Borderline patients according to Pape et al. (82).

Borderline patients
• ISS > 40
• Hypothermia < 35°C
• Multiple trauma with ISS > 20 and AIS_{chest} > 2
• Multiple trauma with abdominal / pelvic injury (AIS > 2) and shock (RR_{syst} < 90 mmHg)
• Bilateral lung contusion in chest radiography or CT
• Pulmonary artery pressure (PAP) > 24 mmHg
• Increase of PAP > 6 mmHg during femoral nailing

Patients with concomitant thoracic injuries are at increased risk for the development of pulmonary complications when long bone fractures are treated with intramedullary nailing. In post-mortem studies large amounts of neutrophils are found in the lungs of patients who died of organ failure. These patients did not have infectious problems in the lungs and thus it is thought that the damage to the pulmonary tissue is caused by the neutrophils (82, 83). This is supported by the increase in circulating levels of cytokines and activation of circulating neutrophils in patients undergoing intramedullary nailing of a femur fracture (81, 84, 85). On the contrary, this alteration in inflammatory response is not seen during intramedullary reaming of a tibia fracture.

Patients who are in extremis or are unstable undergo damage control, whether it is thoracic/abdominal surgery or orthopaedic surgery. When damage control is applied in the correct "borderline" patients, the incidence of acute lung injury (ALI), acute respiratory distress syndrome (ARDS), sepsis and multiple organ failure (MOF) is decreased. However, when damage control is applied in patients who would have been stable enough to undergo ETC, more adverse events are seen in the staged approach group (78). Which patients are at increased risk and who should undergo ETC / DCO is still subject of research. Several immunological parameters have been discovered to aid the treating physician, and new drugs to modify the inflammatory response are being tested. However, future prospective randomized studies are needed to increase the sensitivity and specificity of parameters to identify those patients who might benefit from DCO concept of fracture care.

Complications

Acute respiratory distress syndrome

Acute respiratory distress syndrome (ARDS) is a syndrome of inflammation and increased

permeability that is associated with clinical, radiological and physiological abnormalities, which usually develops over 4 to 48 hours and persists for days or weeks (Table 5) (86).

The most important risk factors for the development of ARDS are Injury Severity Score (ISS) and the presence of pulmonary contusion (87, 88). Other risk factors described are transfusion requirement and hypotension on admission. ARDS is associated with complex changes in the lung, manifested by an early exudative phase and followed by proliferative and fibrotic phases. The pathogenesis of ARDS is described in Table 6. The treatment of ARDS is supportive care, including optimized mechanical ventilation, nutritional support, manipulation of fluid balance and prevention of intervening medical complications. All patients with acute respiratory insufficiency require ventilatory support in order to minimize the risks of endobronchial mucus plugging, pneumonia and atelectasis. The main aim of mechanical ventilation is to maintain adequate oxygenation and ventilation while preventing ventilator-induced lung injury and maintaining adequate tissue perfusion.

With the use of mechanical ventilation we know that next to the pulmonary contusion also mechanical ventilation can also induce an inflammatory response (4). Positive end expiratory pressure (PEEP) ventilation maintains PaO2 above 60 mmHg and is considered to be effective in patients with ARDS. The use of PEEP can partially correct the ventilation-perfusion mismatching in the lung and improve oxygenation. Low tidal volume ventilation reduces mortality compared with high tidal volume ventilation, but can lead to respiratory acidosis. There is no evidence for the use of nitric oxide, corticosteroids or nursing in a prone position in ARDS (89). Alternative techniques like permissive hypercapnia, inverse ratio ventilation and high frequency ventilation are used to protect the lung and prevent more ventilator-induced lung injury. However, early use of mechanical ventilation cannot prevent from developing ARDS.

Chylothorax

Traumatic chylothorax is a rare complication following thoracic trauma and is usually due to penetrating trauma or iatrogenic, secondary to operative procedures. There is a disruption of the thoracic duct. After blunt thoracic trauma a chylothorax is a seldom seen complication. The most common form of blunt injury to the thoracic duct is produced by hyperextension of the spine with rupture of the duct just above the diaphragm in the right thorax. The thoracic duct enters the thorax through the aortic hiatus and travels up just at the right side of the spine. Approximately at the level of the fifth or sixth thoracic vertebra the thoracic duct crosses posterior to the aorta and the aortic arch into the left posterior mediastinum. Therefore a left sided chylothorax is found in case of ruptures of the upper part of the thoracic duct, whereas right-sided chylothorax is seen in injury of lower levels. The color of the pleural fluid seen is chylous and has a white and milky aspect. However the color of the pleural fluid is not always indicative of a chylothorax. Pleural fluid may

Table 5. Features of ARDS (87).

- Bilateral pulmonary infiltrates on chest X-ray
- PaO_2/FiO_2 ratio of 200 mmHg or less
- Absence of clinical evidence of left atrial hypertension

Table 6. Pathogenesis of acute respiratory distress syndrome (91).

Cellular mechanism:
• Macrophage activation
• Neutrophil recruitement and activation
• Endothelial injury
• Platelet aggregation and degranulation
• Plasma protein activation
• Alveolar epithelial injury
Tissue responses
• Increased pulmonary microvascular permeability
• Microvascular thrombosis
• Intraalveolar and interstitial edema
• Intraalveolar fibrin deposition
• Altered pulmonary vasomotor tone
Pathophysiology
• Hypoxemia
• Decreased pulmonary compliance
• Increased shunt fraction
• Decreased functional residual capacity
• Increased work of breathing

not appear chylous if the patient is fasting or the pleural fluid is mixed with blood. An easy test to perform is giving the patient fatty liquid as whipped cream, which induces the production of chylous fluids. The diagnosis chylothorax can be confirmed by the presence of chylomicrons in the pleural fluid. Other characteristics of the fluid are pH 7.4 to 7.8, lymphocyte predominance in cell count of a specific gravity of 1.012 or higher (90).

A chylothorax may also be suspected if the pleural fluid to serum triglyceride ratio is more than 1 and a pleural fluid to serum cholesterol ratio is less than 1 (91). The treatment for chylothorax usually starts with total peripheral nutrition or medium chain triglycerides instead of a normal diet combined with a chest tube. Conservative treatment had a success rate up to 88% (92). Surgical intervention gives better results than conservative management when the daily production exceeds 1 liter for a period more than 5 days (93).

This can be done by an open thoracotomy or video-assisted thoracoscopic surgery (VATS) in order to ligate or clip the thoracic duct. When the thoracic duct cannot be

found, pleurectomy can be done. Newer techniques described are percutaneous CT guided drainage, percutaneous embolization and robotic surgery (94, 95).

Pleural empyema

An empyema has been defined as a loculated collection of pus within the pleural cavity. Common etiologies are post-pneumonic, post-resection and post-traumatic. Untreated post-traumatic empyema results in a restrictive ventilator deficit and atelectasis. Several factors may contribute to a potentially higher risk for empyema in the trauma population. Potential causes for post-traumatic empyema include iatrogenic infection of the pleural space during chest tube placement, direct infection resulting from penetrating injuries of the thoracic cavity, secondary infection of the pleural cavity from associated intra-abdominal organ injuries with diaphragmatic disruption, secondary infection of undrained or inadequately drained hemothorax, hemotogenous or lymphatic spread of sub-diaphragmatic empyema resulting from post-traumatic pneumonia, pulmonary contusion or acute respiratory distress syndrome. Almost 27% of the patients with a retained hemothorax will develop an empyema (96). Management of thoracic empyema includes decortication by a thoracotomy. Thoracoscopy seems to be an effective method also in selected patients if performed early. Several studies are performed to prove the evidence of the use of prophylactic antibiotics in chest tube placement. Patients who require a chest tube after penetrating injury might benefit from prophylactic antibiotics. Further research is needed to prove the benefit of the use of antibiotics in blunt thoracic injury (26).

Persistent air leakage

If the air leakage is large or persistent without re-expansion of the lung a tracheobronchial injury or deep parenchymal injury should be suspected.

A persistent pneumothorax is arbitrarily defined as failure to seal an air leak and achieve full lung expansion within 72 hours of chest tube placement. We suggest performing a VATS (video assisted thoracic surgery) when a persistent pneumothorax is present after 72 hours, as the cause of this persistent air leak is often deep parenchymal injury (97). Another temporary solution in the acute setting is to ventilate both lungs separately or making the tube pass the defect by pushing is little deeper.

Operative techniques

For the hemodynamically unstable patient a left anterolateral thoracotomy in the 4th intercostal space is the first approach to be applied in supine position (Figure 16). With this approach you still can extend to the other side crossing the sternum and also the

abdomen is reachable without repositioning the patient. To make is easier you can shove a rolled sheet behind the scapula in order to lift and medially rotate the patient a little. In just three strokes with a knife; skin and subcutaneous tissue, pectoralis and serratus muscle, intercostal muscle, the thoracic cavity can be reached. The posterior mediastinum cannot be reached with this approach. A double-lumen endotracheal tube placed by an experienced anesthesiologist gives a advantage, however it can be time consuming with an inexperienced anesthesiologist. In that case a blocker can give the solution after a rapid single lumen intubation.

The anterolateral approach can easily be extended towards the other side by going through the sternum by using a Gigli saw or just big scissors. The bilateral anterolateral approach combined with a transverse sternotomy results in the "clamshell" incision, the largest incision commonly used in thoracic surgery (Figure 17). By crossing the sternum always look for and take care of the internal mammary artery, which can cause severe bleeding once the patients is not instable anymore.

Once you are inside the chest, first cut the inferior pulmonary ligament so the lung can be manipulated more easily. In case of a massive bleeding from a central lung injury try to stop the bleeding by manual pressure first. If this is not effective enough than clamp the pulmonary hilum (Figure 18). Realize that it might be tricky because you often cannot see what you are doing within the restricted workspace provided by an anterolateral thoracotomy.

It might be clear that there are more operative options in peripheral pulmonary lesions than in central injuries close to the hilum. The tractotomy is a very useful technique for fixing through-and-through lung injuries. You can either remove injured lung when it is peripherally located or you can do a tractotomy which is lung sparing. With a staple device the injured tract inside the lung can be opened and connected with the lung surface and bleeding vessels ligated (Figure 14 and 15).

An anatomic resection is seldom necessary. A median sternotomy is a good approach for pericardial penetrating wounds or wounds close to the sternum. The internal mammary artery, the heart and even both pulmonary hilar structures can be reached. The peripheral pulmonary structures and the posterior mediastinum cannot be accessed. It should be realized that this approach is of limited use in patients with a massive hemothorax where the bleeding structure still is not known. Choosing the wrong incision can give a lot of trouble.

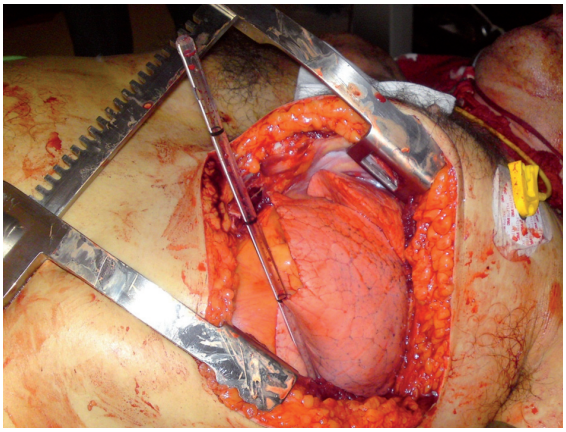

Figure 16. Anterolateral thoracotomy.

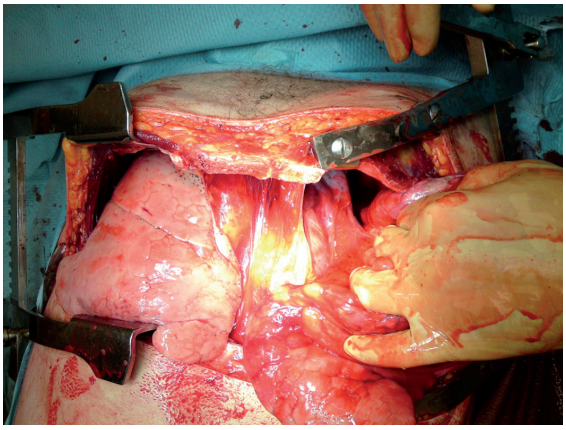

Figure 17. Clamshell thoracotomy.

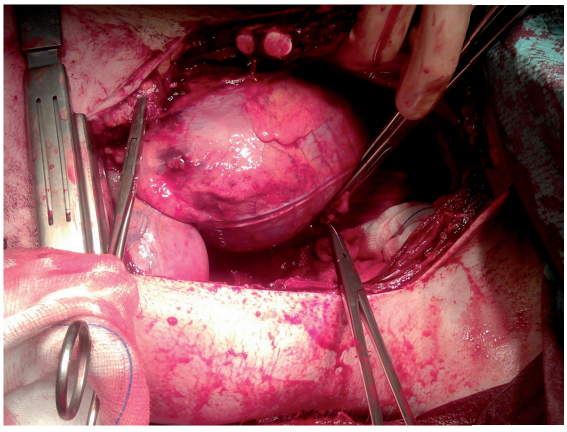

Figure 18. Hilar crossclamping.

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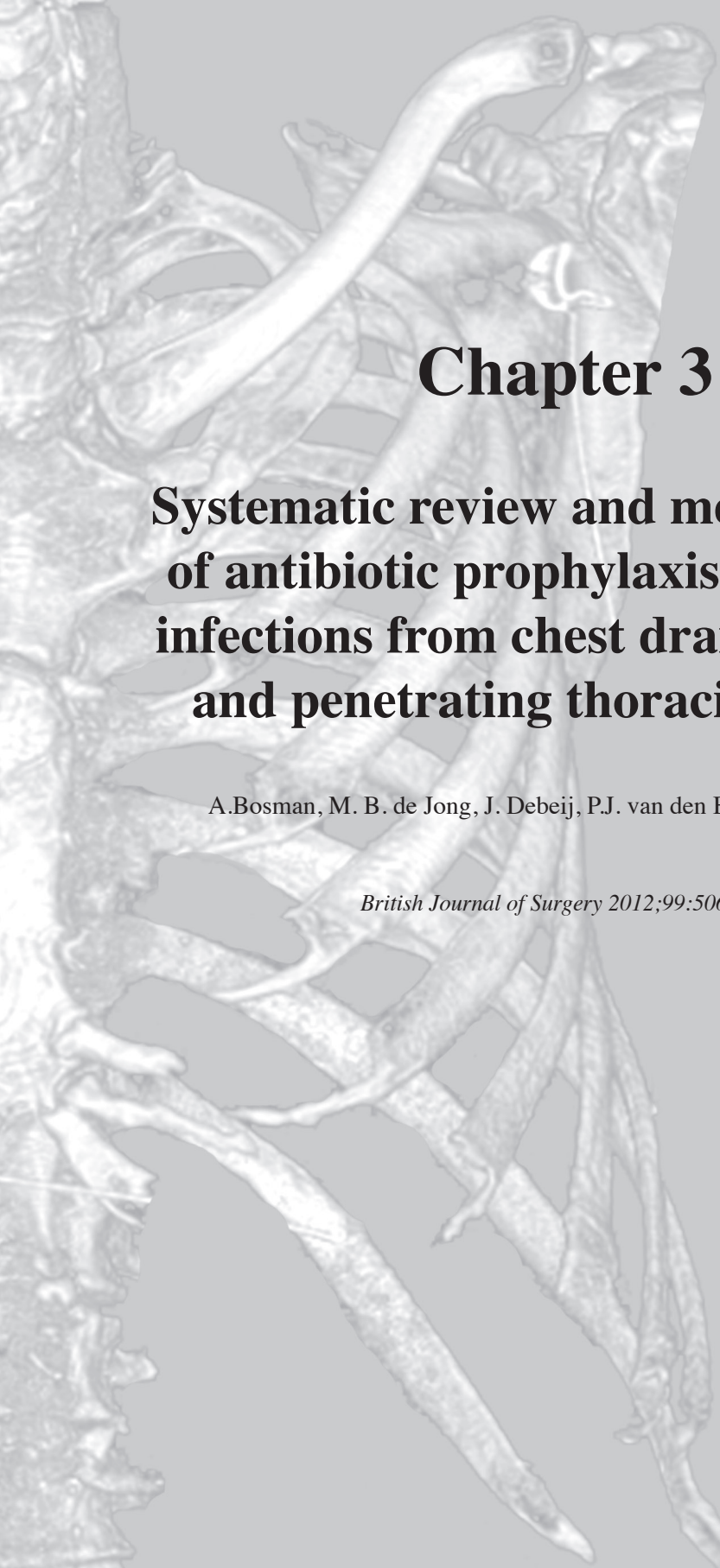

Chapter 3

Systematic review and meta-analysis of antibiotic prophylaxis to prevent infections from chest drains in blunt and penetrating thoracic injuries

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Abstract

Background: No consensus exists as to whether antibiotic prophylaxis in tube thoracostomy as primary treatment for traumatic chest injuries reduces the incidence of surgical-site and pleural cavity infections.

Methods: A systematic literature search was performed according to PRISMA guidelines to identify randomized clinical trials on antibiotic prophylaxis in tube thoracostomy for traumatic chest injuries. Data were extracted by two reviewers using piloted forms. Mantel–Haenszel pooled odds ratios (ORs) were calculated with 95% confidence intervals (c.i.).

Results: Eleven articles were included, encompassing 1241 chest drains in 1234 patients. Most patients (84.7%) were men, and a penetrating injury mechanism was most common (856, 69.4%). A favorable effect of antibiotic prophylaxis on the incidence of pulmonary infection was found, with an OR for the overall infectious complication rate of 0.24 (95% c.i. 0.12 to 0.49). Patients who received antibiotic prophylaxis had an almost three times lower risk of empyema than those who did not receive antibiotic treatment (OR 0.32, 0.17 to 0.61). A subgroup analysis in patients with penetrating chest injuries showed that antibiotic prophylaxis in these patients reduced the risk of infection after tube thoracostomy (OR 0.28, 0·14 to 0.57), whereas in a relatively small blunt trauma subgroup no effect of antibiotic prophylaxis after blunt thoracic injury was found.

Conclusion: Infectious complications are less likely to develop when antibiotic prophylaxis is administered to patients with thoracic injuries requiring chest drains after penetrating injury.

Introduction

Although the prophylactic use of antibiotics has been well established and proved beneficial for many trauma-related interventions, the value of prophylactic antibiotics in decreasing infectious complications after tube thoracostomy remains controversial (1-3). A previous meta-analysis concluded that prophylactic antibiotic treatment decreased the incidence of infectious complications, but this study included only five trials encompassing 315 patients (4). Maxwell and colleagues performed a large study and reported that antibiotic prophylaxis should not be used as standard in the care of injured patients in need of tube thoracostomy, as neither short- nor long-course antibiotic treatment reduced the incidence of empyema and pneumonia (5).

The management of patients with traumatic chest injury is largely standardized according to Advanced Trauma Life Support (ATLS®) principles (6). In 70–90% of patients with a haemopneumothorax due to blunt or penetrating trauma, tube thoracostomy is the primary treatment (7). Insertion of a chest drain is a frequent procedure in managing traumatic chest injuries, although contamination during drain insertion can be a major cause of development of infection, such as pneumonia and empyema (8, 9). The incidence of post-traumatic empyema has been reported to range from 2 to 25%, whereas that of Staphylococcus aureus-related complications is 35–75% (10, 11).

Several randomized clinical trials have evaluated the effectiveness of antibiotic prophylaxis in patients with traumatic thoracic injuries requiring tube thoracostomy as primary treatment. However, no consensus exists on the use of prophylactic antibiotics for traumatic thoracic injuries requiring tube thoracostomy (5, 12-21).

A systematic review and meta-analysis of prophylactic antibiotic treatment compared with no prophylactic antibiotics was carried out in patients requiring acute tube thoracostomy, in order to determine any potential beneficial effect of preventive antibiotics. The primary aim was to examine the effect of antibiotic prophylaxis on surgical-site and pulmonary infections. The effect of the trauma mechanism (blunt or penetrating thoracic injury) related to the need for prophylactic antibiotic treatment was also analyzed.

Methods

The systematic review and meta-analysis were performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (22).

Literature in the MEDLINE, Embase, Web of Knowledge and Cochrane Library databases (through October 2010) was queried. The main research question was whether administration of antibiotic prophylaxis is beneficial in reducing infectious complications

in patients undergoing tube thoracostomy for traumatic isolated thoracic injuries. The literature search was not restricted by date, language or publication status. Search terms were 'prophylactic antibiotic use', 'trauma', 'thoracic injuries' and 'tube thoracostomy'. A supplemental search of all references of the articles found by the initial search did not yield extra abstracts (Figure 1). All resulting abstracts were reviewed, using piloted forms, by two reviewers to determine whether the studies met the inclusion or exclusion criteria. Inclusion criteria were specified in advance: only randomized clinical trials comparing adult patients who underwent tube thoracostomy for isolated thoracic injuries treated with antibiotic prophylaxis and patients treated with placebo or no treatment at all. All other trials were excluded. Antibiotic prophylaxis was defined as antibiotic treatment in patients with no clinical or microbiological infection at the time of antibiotic administration. Inclusion

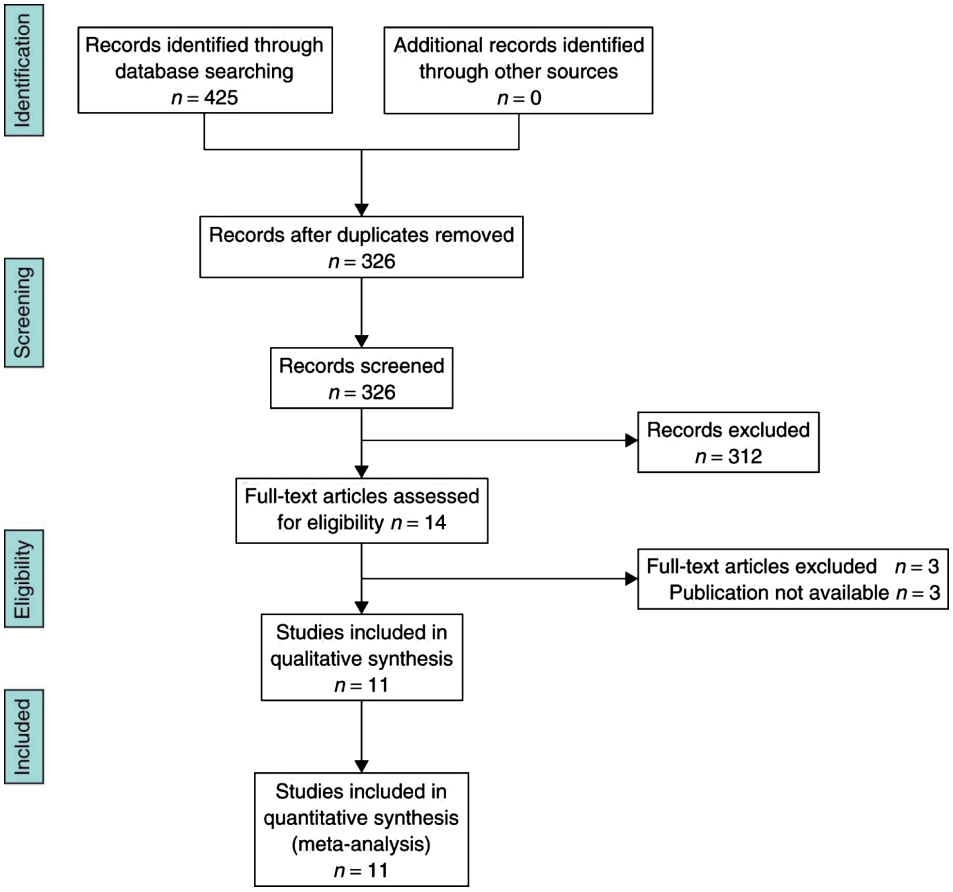

Figure 1. Prisma diagram for the literature review of the incidence of infectious complications and prophylactic antibiotic treatment.

was not restricted to any specific type of antibiotic. Unfortunately, not all studies had clear definitions of pneumonia, wound infection or empyema, and thus the standard definitions for these infections could not be used (23, 24). Of the outcome parameters, wound infection was defined as local erythema of the wound with or without purulent drainage. Empyema was defined as infection of the pleural cavity, diagnosed histopathologically or by pus outflow from the chest drain. Pneumonia was defined as infection of the lung shown as infiltration on chest X-ray with or without purulent sputum, with a positive blood or sputum culture.

The methodological quality of the articles was assessed by two reviewers. The Jadad score and the Chalmers system for assessing the quality of randomized controlled trials were used (25, 26). These scoring systems were used to review every potentially included study to determine whether or not they had been performed properly. They calculate an objective rating for the quality of each study. Differences in outcome can be weighted using these assessment scores.

Statistical analysis

For all included studies, the risks of any form of infection, of empyema, of a wound infection and of developing pneumonia were determined and compared in patients who received antibiotics and those who did not (placebo or no treatment). The occurrence of infection in different types of trauma (blunt or penetrating) and the use of different types of antibiotic were also examined. The numbers of patients receiving antibiotics and complications were extracted for all studies. Odds ratios (ORs) were calculated for all studies with sufficient data. To calculate the pooled ORs of the different studies, the Mantel-Haenszel method for effect measurement in meta-analysis was employed, in which the weight of an individual study is determined by the inverse of the variance. As there were a number of studies without infection in groups both with and without antibiotics, 0.25 was added to all zero values to enable valid ORs to be calculated. Both ORs and pooled ORs are given with 95 per cent confidence intervals (c.i.). All analyses were performed using SPSS® version 17.0 (SPSS, Chicago, Illinois, USA).

Results

A total of 326 studies were identified in the literature search, of which 14 were initially included for meta-analysis. Three studies were excluded because the publications could not be obtained (Figure 1). Eleven randomized clinical trials (5, 12-21), published between 1977 and 2009, and involving 1234 patients with 1241 chest drains, were used for data

extraction (Table 1). Of the documented data, 776 of the patients were men (84.7%) and 140 (15.3%) were women; penetrating chest injury was the most common injury (856 patients, 69.4%), followed by blunt injury (307, 24.9%) and spontaneous pneumothorax (70, 5.7%); the trauma mechanism was not documented in one patient. Patients with a spontaneous pneumothorax were not included in the analysis.

Quality of trials

Methodological quality assessment showed similar results for both scoring systems. The 11 randomized trials differed in quality. Randomization methods were inappropriate in four trials and three studies did not report the method of randomization (15-21). Most trials had comparable treatment groups at baseline and reported the number of patients lost to follow-up. Six trials were described as double-blind, one study reported the outcome assessors as blinded to treatment (5, 12-16, 19).

For seven of the included studies the authors concluded that antibiotic prophylaxis was effective in reducing infectious complications after tube thoracostomy for traumatic chest injuries and should therefore be administered routinely (12-16, 18, 21). Three studies did not report a positive effect in reducing infectious complications nor found a pattern of resistance in patients receiving prophylactic antibiotic therapy, arguing against its use (5, 17, 19, 20).

Infectious complications

An overall rate of infectious complications was determined (Figure 2); all infections documented as empyema, pneumonia and wound infection were combined. Ten of the 11 studies documented all of these outcomes, including 1112 chest tubes (5, 12-18, 20, 21). Analysis of the data showed a strong favorable effect of antibiotic prophylaxis on the incidence of infectious complications in general. The OR for the overall infectious complication rate was 0.24 (95% c.i. 0.12 to 0.49) (Figure 2).

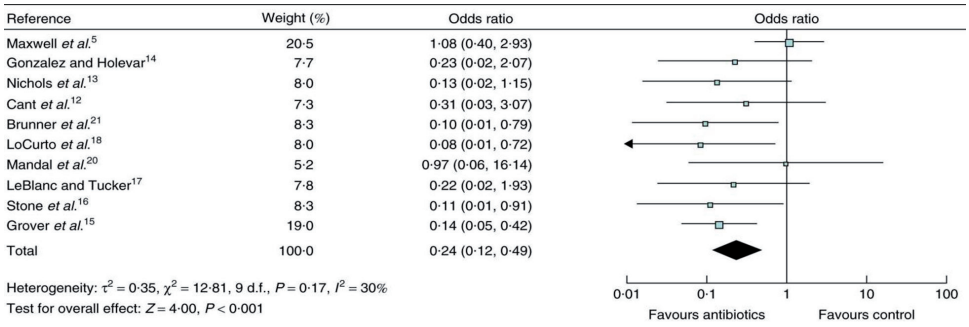

Figure 2. Meta-analysis of overall infectious complications after tube thoracostomy. A Mantel-Haenszel random-effects model was used. Odds ratio's are shown with 95% confidence intervals.

Table 1. Characteristics of the 11 included studies.

		No. of patients		Antibiotic used				
Reference	**Year of publication**	**Antibiotic arm**	**Control arm**	**Type**	**Dosage (mg)**	**Duration (h)**	**Mechanism of injury**	**Conclusion regarding routine prophylaxis**
Villegas-Carlos et al [19]	2009	63	63	Cefalotin	NA	NA	B,P	No
Maxwell et al[5]	2004	157	72	Cefazolin	1000	< 24 and > 24	B,P	No
Gonzalez and Holevar[14]	1998	71	68	Cefazolin	1000	> 24	B,P	Yes
Nichols et al.[13]	1994	63	56	Cefonicid	1000	> 24	B,P	Yes
Cant et al.	1993	57	56	Cefazolin	500	< 24	P	Yes
Brunner et al.[21]	1990	44	46	Cefazolin	Unknown	> 24	B,P	Yes
LoCurto et al.[18]	1986	30	28	Cefoxitin	1000	> 24	B,P	Yes
Mandal et al.[20]	1985	40	40	Doxycycline	200	> 24	P	No
LeBlanc and Tucker[17]	1985	39	46	Cephapirin	1000	> 24	B,P,S	No
Stone et al.[16]	1981	60	60	Cefamandol	1000	> 24	B,P,S	B and P: Yes: No
Grover et al.[15]	1977	38	37	Clindamycin	300	> 24	P	Yes

NA, data not available; B, blunt trauma mechanism; P, penetrating trauma mechanism; S, spontaneous pneumothorax.

All 11 studies, reported empyema as the primary outcome; of a total of 1241 chest drains, 669 patients received antibiotic prophylaxis and 572 did not (5, 12-21). Empyema was reported in 14 (2.1%) and 39 (6.8%) patients respectively, indicating that patients treated with antibiotic prophylaxis for tube thoracostomy after chest trauma had an approximately at threefold lower risk of developing empyema compared with patients not receiving antibiotics (OR 0.32, 0.17 to 0.61) (Figure 3).

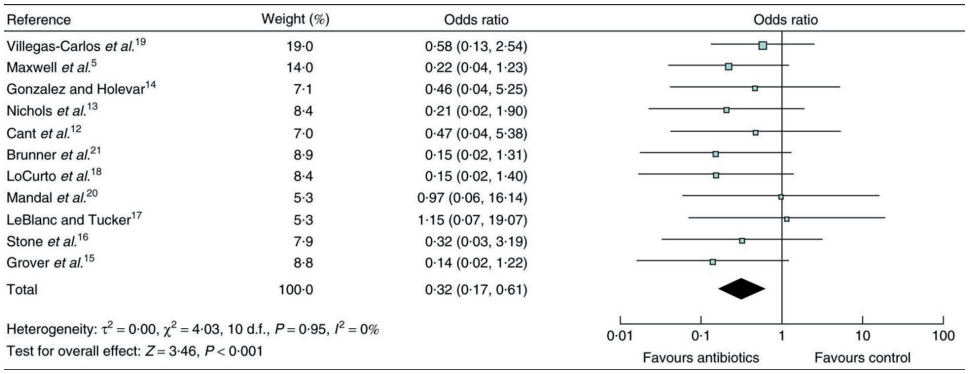

Figure 3. Meta-analysis of empyema after tube thoracostomy. A Mantel-Haenszel random-effects model was used. Odds ratios are shown with 95% confidence intervals.

Wound infections were reported by only two15, 17 of the included studies, encompassing 161 chest tubes (OR 0.41, 0.08 to 2.21) (Figure S1).

Pneumonia was reported in eight studies with 919 chest drains (OR 0.51, 0.24 to 1.07) (Figure S2) (5, 13-18, 21).

A subgroup analysis was performed to compare the incidence of all infectious complications in patients with blunt and penetrating chest injuries related to prophylactic antibiotic treatment. In patients with penetrating chest injuries, antibiotic prophylaxis resulted in a large reduction in the risk of developing an infection after tube thoracostomy (OR 0.28, 0.14 to 0.57) (Figure 4) (5, 12, 13, 15, 20, 21). The analysis for patients with blunt thoracic injuries included 171 patients from three studies and found an OR of 1.30 (0.46 to 3.67) (Figure 5) (5, 13, 21).

Discussion

The goal of prophylactic antibiotic therapy for acute tube thoracostomy in traumatic chest injury is to decrease the risk of infectious complications and its associated morbidities,

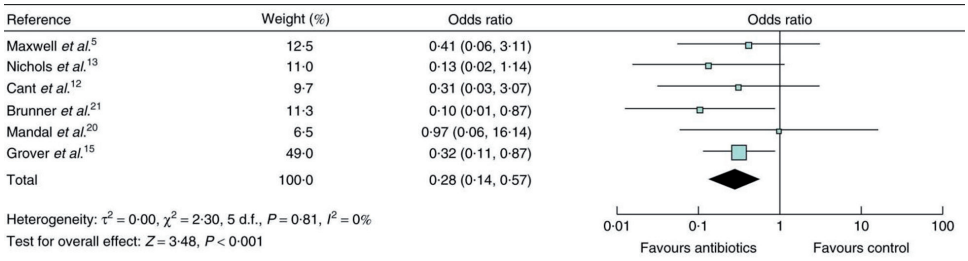

Figure 4. Meta-analysis of the incidence of infectious complications in penetrating traumatic chest injury. A Mantel-Haenszel random-effects model was used. Odds ratios are shown with 95% confidence intervals.

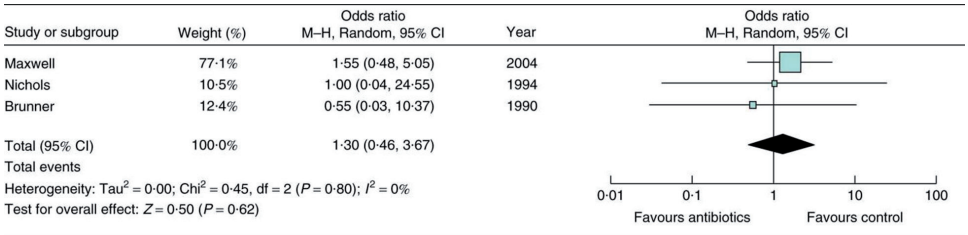

Figure 5. Meta-analysis of the incidence of infectious complications in blunt traumatic chest injury.

based on reasonable assumptions about the organisms most often cultured. Subsequently, the related morbidity, duration of chest drainage and duration of hospital stay are expected to decrease, and are thought to result in reduced treatment costs. On the other hand, avoiding unnecessary use of antibiotics is important to minimize the development of medication-related side-effects, bacterial resistance and treatment costs.

The meta-analysis shows that prophylactic antibiotic treatment reduces the risk of developing infectious complications after tube thoracostomy for traumatic injuries of the chest, with the effect best documented for penetrating injuries. In a subgroup analysis, a substantial beneficial effect was found in prevention of empyema after tube thoracostomy. The use of prophylactic antibiotics in the prevention of pneumonia and wound infections was beneficial, but owing to small patient numbers a significant result could not be demonstrated. In the relatively small group of patients with blunt injuries, no beneficial effect from antibiotic prophylaxis was determined.

The Eastern Association for the Surgery of Trauma (EAST) concluded in 2000 that the class 1 evidence for the use of prophylactic antibiotics was not sufficient for recommendation as routine use (3). This argument was based on analysis of four trials performed between 1977 and 1994 (12, 13, 15, 16). After presentation of the EAST guidelines, Sanabria and colleagues performed a meta-analysis, adding the study of

Maxwell et al. performed in 2004 (4, 5). The conclusion of the 2006 meta-analysis was that prophylactic antibiotic treatment reduced the incidence of infectious complications (4). The question arises whether the results were based on a sufficient number of patients, as there were only 351 included patients and the meta-analysis did not differentiate blunt from penetrating injuries. In addition, in a subgroup analysis one trial was excluded because of the types of antibiotic used, leaving the conclusion to be based on 313 patients (15). Three previous meta-analyses also reported a protective effect on the development of infectious complications after tube thoracostomy, but these studies appear to have some limitations (4, 27, 28). Two meta-analyses were conducted several years previously and the more recent studies were not included (27, 28). These meta-analyses did not report results for subcategories of lung infection such as empyema, pneumonia and wound infection.

Limitations of the present study include the fact that all relevant randomized trials were included, regardless of the types of antibiotic used, language or publication date, but it was not possible to include all trial data, despite contacting all authors. The results are therefore based on available data as documented in the articles retrieved. Although criteria for diagnosis of pneumonia, empyema and wound infections are clearly defined by high-quality centers, eight of the included trials used no or non-standard definitions, so it was not possible to use the standard definitions of infectious complications (5, 12, 15-17, 19-21, 23, 24). Grover and co-workers used radiographic changes as evidence of pneumonia, without culturing purulence or clinical signs of infection (15). They reported a high incidence of pneumonia in both control (13 of 37) and antibiotic (4 of 38) groups. Brunner and colleagues described two cases of culture-negative lung entrapment in the group treated with antibiotics (21). These entrapments could have been empyemas, despite the negative cultures for pathogens. Histopathological findings were not reported. The present authors believe the results of their meta-analysis were not likely to have been influenced by different diagnostic criteria used in the studies, because each study randomized the patients and all used similar definitions for outcomes. Only the true incidence of wound infection, empyema and pneumonia may have been lower than reported, owing to the use of non-standard definitions.

The literature supports the use of a first-generation cephalosporin, as these agents cover the most frequently isolated organisms in tube thoracostomy-related empyema (11). Trials in the present study using a non-cephalosporin antibiotic were also included. Amongst other organisms, S. aureus, Streptococcus pneumoniae and Haemophilus influenzae were cultured most often. Six of the included trials used a first-generation cephalosporin (5, 12, 14, 17, 19, 21); in the other studies various antibiotics, including a second-generation cephalosporin, clindamycin and doxycycline, were used (13, 15, 16, 18, 20). It is commonly known that clindamycin does not cover H. influenzae infections and that doxycycline is not the antibiotic of first choice, because microorganisms develop resistance against

doxycycline in about 10 per cent of patients receiving this antibiotic. The infection rates reported in the studies that used clindamycin and doxycycline were no different from those in the other included trials. Not all included studies reported the side-effects of antibiotic use. Maxwell et al. described a high incidence of antibiotic resistance in their patients and thus concluded that antibiotics should not be administered routinely in injured patients in need of tube thoracostomy (5).

The preferred or recommended duration of treatment cannot be given based on the results of this meta-analysis. Only two patient groups from two included trials received antibiotic prophylaxis for a maximum duration of 24 h (5, 12). Demetriades and co-workers found no significant differences between a short course or prolonged use of ampicillin, and concluded that single-dose antibiotic prophylaxis in penetrating chest injury was as effective as prolonged prophylaxis (29). Maxwell and colleagues also examined the role of short-course antibiotics, concluding that neither short-course nor continuous antibiotics reduced the incidence of empyema or pneumonia (5). The duration of thoracic tube placement may also influence the risk of infection; unfortunately, none of the included studies reported on this outcome.

Owing to the trauma mechanism, penetrating injuries are often much more contaminated than blunt injuries, and associated with higher rates of pneumonia (5). The present meta-analysis shows a significant benefit of antibiotic prophylaxis in reducing the incidence of infection after tube thoracostomy for penetrating chest injuries. The authors speculate that the infections are caused mainly by contamination of the wound and surgical site by pathogens present on the penetrating foreign body or the skin of the victim, such as S. aureus, which may play an important role in thoracic infections after penetrating trauma. In these patients, the infections are not solely attributable to insertion of the chest tube. By administering antibiotics, the risk of infection through the penetrating trauma itself will be reduced, resulting in decreased morbidity and mortality rates after tube thoracostomy for penetrating injuries. Based on available data, the effect of antibiotic prophylaxis for tube thoracostomy in patients with blunt traumatic chest injuries is still uncertain.

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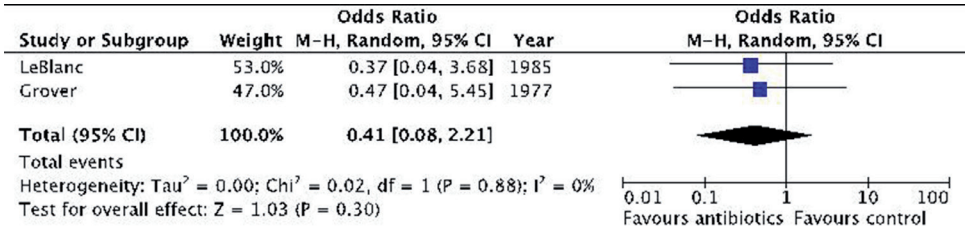


Figure S1. Meta-analysis of wound infection after tube thoracostomy. A Mantel–Haenszel random-effects model was used. Odds ratios are shown with 95% confidence intervals.

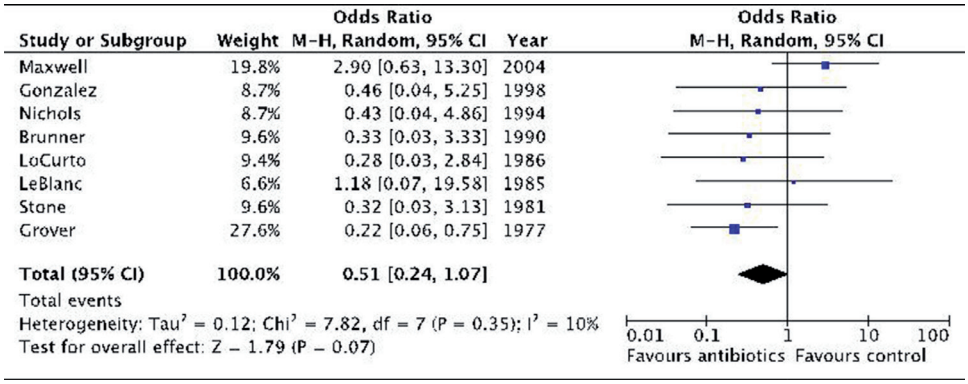
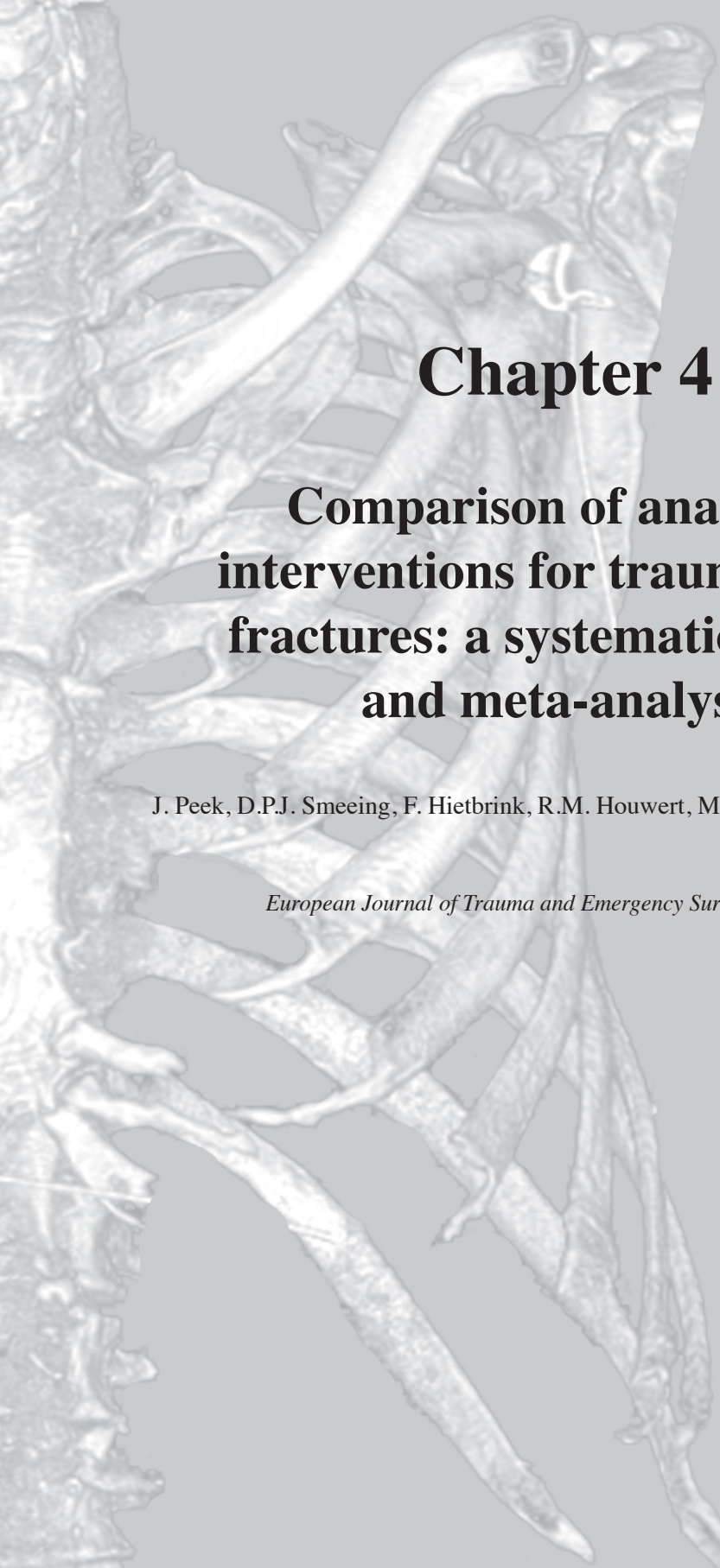


Figure S2. Meta-analysis of pneumonia after tube thoracostomy. A Mantel–Haenszel random-effects model was used. Odds ratios are shown with 95% confidence intervals.



Chapter 4

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

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Abstract

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

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

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

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

Introduction

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

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

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

The literature on the use of the different analgesic interventions is inconclusive. A clinical guideline supported by the Eastern Association for the Surgery of Trauma recommends epidural analgesia or a multimodal approach over opioids alone in patients with blunt chest trauma (9). On the other hand, two recently performed systematic reviews and meta-analyses of Duch et al. and Carrier et al. 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 (10, 11).

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

Methods

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

Literature search and eligibility criteria

This systematic review and meta-analysis was written in accordance to the PRISMA guidelines for reporting systematic reviews and meta-analyses (12). Two reviewers (JP, DS) independently performed a structured literature search, on September 16th 2017, to identify comparative studies investigating epidural, intravenous, paravertebral and intercostal 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 Table 2. 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.

Table 2. Search syntax representing the used search strings in the different databases.

Database	Search string	Hits
PubMed	(((((fracture[Title/Abstract] OR fractured[Title/Abstract] OR fractures[Title/Abstract]) AND ("Ribs"[Mesh] OR rib[Title/Abstract] OR ribs[Title/Abstract]))) OR "Rib Fractures"[Mesh]) AND ((((epidural[Title/Abstract] OR intercostal[Title/Abstract] OR interpleural[Title/Abstract] OR paravertebral[Title/Abstract] OR intrathecal[Title/Abstract] OR oral[Title/Abstract] OR parenteral[Title/Abstract]) 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)	238
CENTRAL	Rib fracture	183

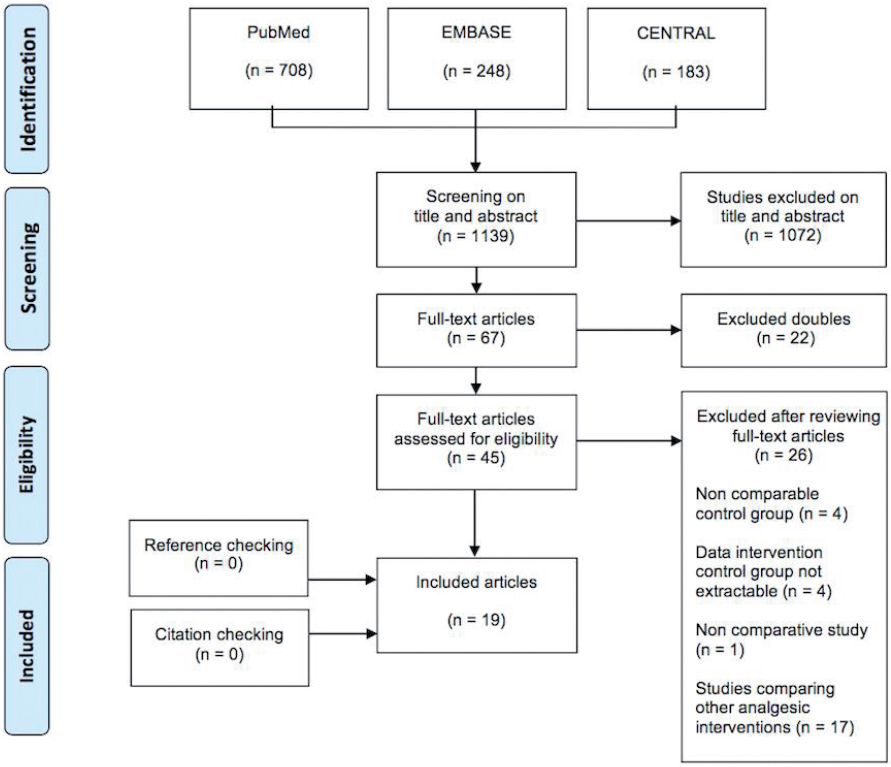

Figure 1. Prisma flow diagram representing the search and screen process of articles describinganalgesic interventions in patients with traumatic rib fractures.

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 5 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 Table 3, were defined in order to make further

Table 3. 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

distinction in quality between the included studies. The quality was determined by means of the total MINORS score. Studies were not excluded based on the quality assessment. Disagreement was resolved by discussion with a third independent reviewer (MJ), followed by consensus.

Data extraction

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

Outcome measures

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

Data analysis

Data were pooled according to the analgesic modalities that were compared. Meta-analyses were performed if the endpoints were reported by two or more studies. If the extracted data were initially noted as median with an interquartile range, the mean and standard deviation (SD) were estimated as follows: the reported median value was used as mean value, and de 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 2x2 Table of that study (14)**.** *P*-values < 0.05 were considered statistically significant.

After the primary statistical analyses, sensitivity and subgroup analyses were conducted. In the sensitivity analyses on study design, only RCTs were included. In the sensitivity analyses on time, only studies published after the year 2000 were included. In the sensitivity analyses on quality, arbitrarily all studies with more than 16 points were

included (15). A sensitivity analyses on outlier studies was conducted. For the subgroup analyses on etiology, only studies describing cohorts with solely traumatic rib fractures were included. Studies describing mixed cohorts of patients with blunt chest trauma were excluded. All statistical analyses were performed using Review Manager (RevMan, Version 5.3.5 Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014).

Results

Search

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

Quality assessment

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

Baseline characteristics

Of the 19 included studies, 8 were RCTs, 10 were retrospective cohort studies, and 1 study was a prospective cohort study using a historical control group. The included studies describe a total of 2801 patients. Eleven studies compared epidural analgesia with intravenous analgesia (8, 16-21, 27-29). Eight of these studies (4, 16-18, 20, 21, 27, 28) compared epidurals with local anesthetics with or without opioids as drugs, with intravenous analgesia. Three studies (19, 24, 29) compared epidurals, with only opioids as drugs, with intravenous analgesia. Three studies (22, 25, 26) compared epidural analgesia with intercostal blocks, 3 studies compared epidural analgesia with paravertebral blocks (6, 30, 31), 1 study compared paravertebral blocks with intravenous analgesia (32) and 1 study (23) compared intercostal blocks with intravenous analgesia. The characteristics of the included studies are shown in Table 4.

Epidural analgesia versus intravenous analgesia

The results of the studies comparing epidural with intravenous analgesia are summarized in Table 5. Meta-analyses are shown in Figure 2. Of the 11 included studies, 4 studies examined pain scores on different intervals after treatment with epidural or intravenous analgesia (16, 20, 21, 28). 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 hours 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 Table 6. Meta-analyses are shown in Figure 3. As a consequence of insufficient data and variability of outcome measurement, meta-analyses were only possible for the length of hospital and ICU stay.

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).

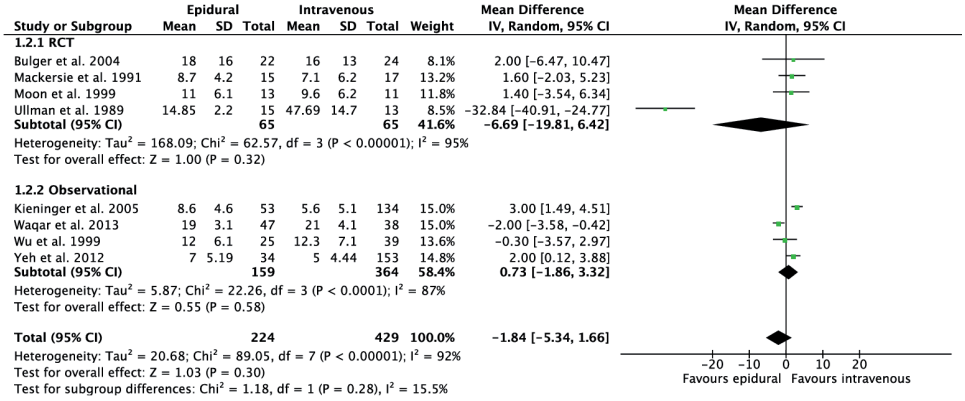

Figure 2a

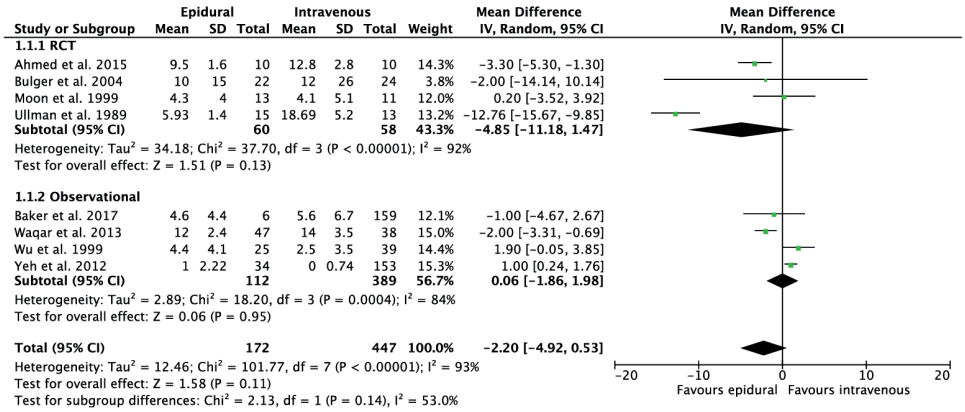

Figure 2b

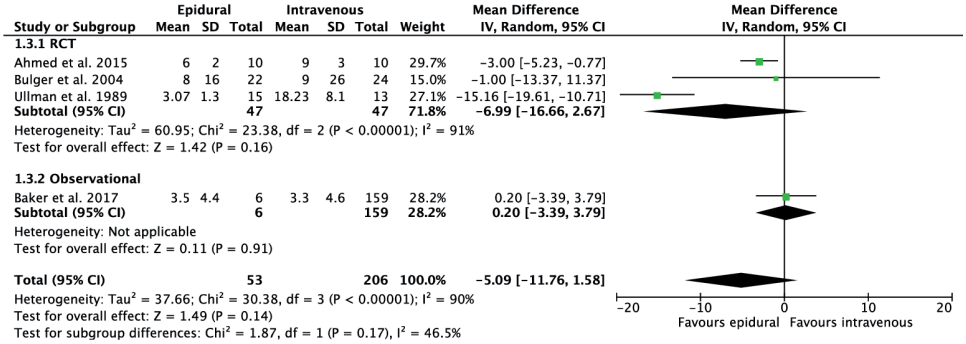

Figure 2c

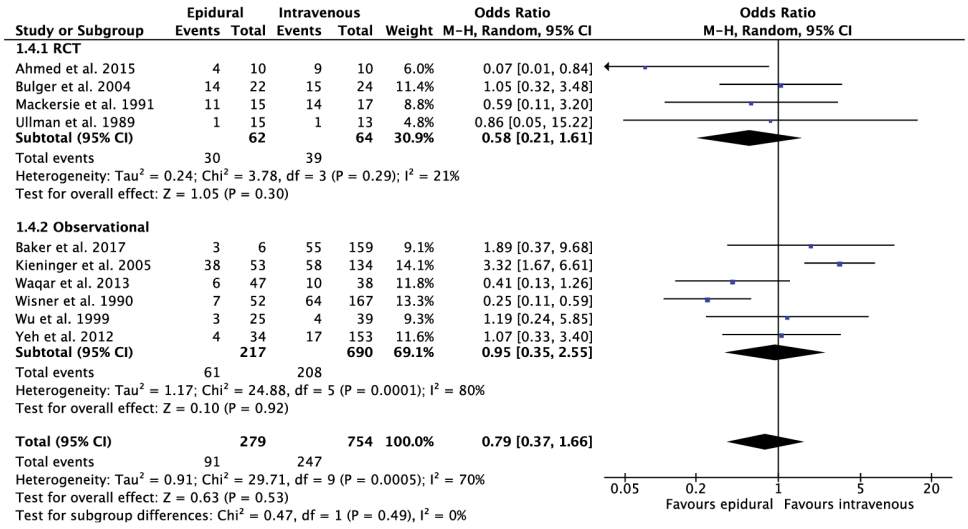

Figure 2d

Figure 3. Forest plot of the length of **a** hospital stay **b** intensive care unit stay (epidural vs intercostal).

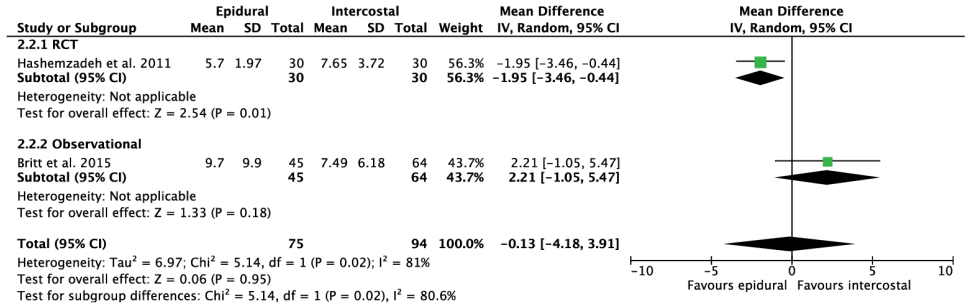

Figure 3a

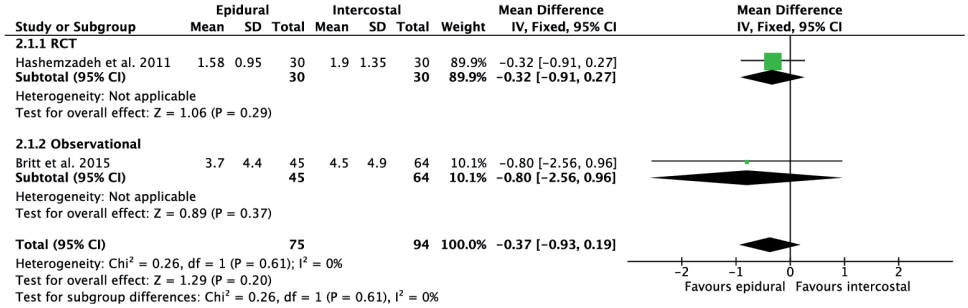

Figure 3b

Table 1. Results of 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 After 8h After 24h After 48h After 72h	*(4 (3,4) vs 4 (3.3,4), p < 0.82)* *(2 (2,1) vs 3 (2,4), p < 0.001)* *(1 (1,2) vs 3 (3,4), p < 0.001)* *(2 (1,2) vs 3 (2,3), p < 0.001)* *(1 (1,2) vs 3 (2,3), p < 0.001)*	
*Moon et al.	Verbal rating scale (0-10)[b]	First 24h After 48h After 72h	*(5.8 vs 7.5, p < 0.05)* *(6.0 vs 6.3)* *(3.8 vs 6.2, p < 0.05)*	
*Mackersie et al.	Visual analogue scale (0-100)[b]	Percentage change in VAS score:		
		At rest Coughing and deep breathing	*(-32 ± 24 vs -27 ± 27, p < 0.05)* *(-42 ± 25 vs -25 ± 26, p < 0.05)*	
			At rest:	Coughing:
		Pre-analgesia Post-analgesia After 48h After 72h	*(56 vs 62)* *(24 vs 37)* *(28 vs 38)* *(19 vs 26)*	*(88 vs 89)* *(45 vs 63)* *(51 vs 53)* *(42 vs 58*
Epidural analgesia versus intercostal block				
*Hashemzadeh et al.	Verbal rating scale (0-10)	Mean pain score during hospital admission:		
		At rest: Coughing:	*(2.2 ± 0.74 vs 3.3 ± 1.005)* *(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 Post-analgesia	*(7.5)* *(2.6)*	*(9.4)* *(3.6)*
		No comparison with epidural group		

Table 1. Continued.

First author	Pain assessment tool	Outcome (mean ± SD)		
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)	Baseline	At rest:	
		Post-analgesia	*(9.43 vs 8.16)*	
		After 24h	*(5.39 vs 7.42, p* = 0.007)	
		After 7 days	*(5.04 vs 6.16, p* = 0.024)	
			(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.

Table 4. Baseline characteristics.

First author, Year of publication	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	Pakistan	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*
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*

Comparator	Number of 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
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

Table 4. Continued.

First author, Year of publication	Country	Design, Setting	Patient characteristics		Intervention
			Inclusion criteria	Exclusion criteria	
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*
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 continuous intercostal

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	Number of patients		Male, n (%)		Age (mean ± SD)		ISS (mean ± SD)	
	INT	COM	INT	COM	INT	COM	INT	COM
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
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
and/or fentanyl patch) + nerve block (CINB)	23	31	44 81,4%)		48.5±NR		NR	NR

Table 5. Results of studies comparing epidural analgesia with intravenous analgesia.

First author	Number of patients		Mortality (during hospital admission)		Mechanical ventilation (days)		Hospital LOS (days)	
	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]	
Ahmed et al.	10	10	0 (0%)	1 (10%)	6±2	9±3	NR	NR
Waqar et al.	47	38	2 (4%)	1 (2,6%)	Reduction of days in epidural group		19±3.1	21±4.1
Yeh et al.	34	153	NR	NR	NR	NR	7 (5-12)[b]	5 (4-10)[b]
Kieninger et al.	53	134	5 (2,6%)		NR	NR	8.6±4.6	5.6±5.1
Bulger et al.	22	24	2 (9%)	1 (4,2%)	8±16	9±26	18±16	16±13
Wu et al.	25	39	0 (0%)	0 (0%)	NR	NR	12.0±6.1	12.3±7.1
Moon et al.	13	11	0 (0%)	0 (0%)	NR	NR	11±6.1	9.6±6.2
Mackersie et al.	15	17	0 (0%)	0 (0%)	NR	NR	8.7±4.2	7.1±6.2
Wisner et al.	52	167	2 (4%)	26 (16%)	4.4±0.7		NR	NR
Ullman et al.	15	13	NR	NR	3.1±1.3	18.2±8.1	14.9±2.2	47.7±14.7

Abbreviations: ARDS, acute respiratory distress syndrome; EPI, epidural group; 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)

Length of ICU stay (days)		Pulmonary complications		Other complications	
EPI	**IV**	**EPI**	**IV**	**EPI**	**IV**
4.6±4.4	5.6±6.7	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
9.5±1.6	12.8±2.8	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%)
12±2.4	14±3.5	Pneumonia n = 6 (13%)	Pneumonia n=10 (26%)	Cardiac n = 2 (4%)	Cardiac n = 1 (2,6%)
1 (0-3)[b]	0 (0-1)[b]	Overall n = 4 (11,8%)	Overall N = 17 (11%)	Overall n = 7 (20,6%)	Overall n = 25 (16,3%)
NR	NR	Overall n = 38 (72%)	Overall n = 58 (43%)	NR	NR
10±15	12±26	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%) Hypotension n = 1 (5%)	Pruritus n = 5 (21%) Nausea/vomiting n = 6 (25%) Depressed level of consciousness n = 1 (4%)
4.4±4.1	2.5±3.5	Pneumonia n = 3 (12%)	Pneumonia n = 4 (10%)	Cardiac n =1 (4%) Neurologic n=1 (4%)	Cardiac n = 5 (13%) Neurologic n = 7 (18%)
4.3±4.0	4.1±5.1	NR	NR	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%)
NR	NR	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
5.9±1.4	18.7±5.2	None	None	Urinary retention n = 2 (13,3%)	None

Two studies reported on pain scores (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 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 Table 7. Meta-analyses are shown in Figure 4. Two studies reported on pain scores. One study 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 described that there was no difference between both groups in the mean change of pain during hospital admission (Table 1) (6, 30).

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).

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 Table 8, respectively, Table 1. Significant differences in pain relief were described on different intervals, in favor of the intercostal blocks.

Figure 4. Forest plot of the length of **a** hospital stay **b** intensive care unit stay (epidural vs paravertebral).

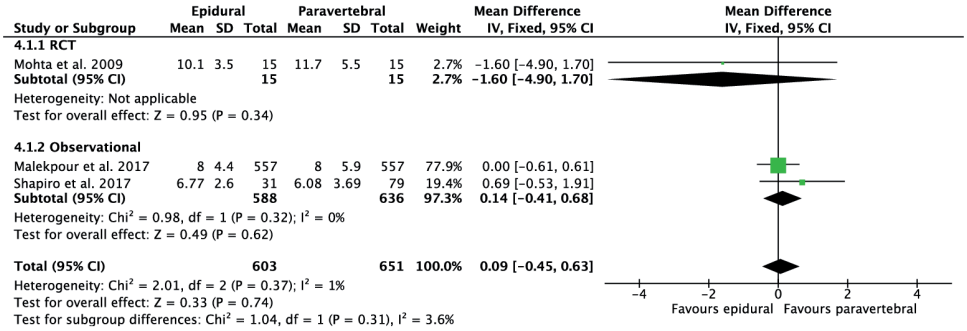

Figure 4a

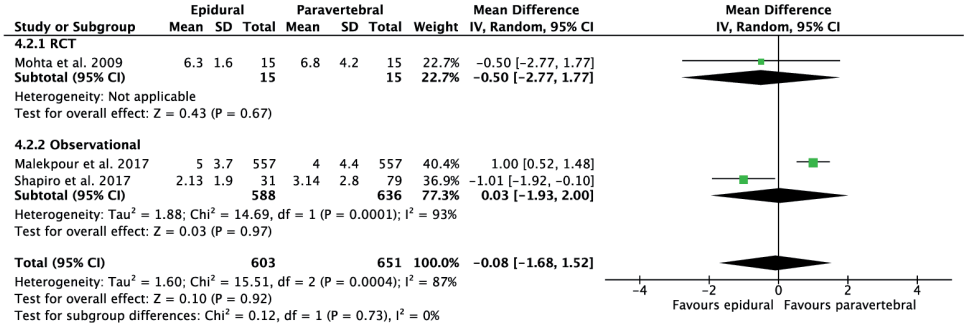

Figure 4b

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 Table 9, respectively Table 1. Significant differences in pain relief were described on different intervals, in favor of the paravertebral blocks.

Sensitivity and subgroup analyses

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

Table 6. Results of studies comparing epidural analgesia with intercostal block.

First author	Number of patients		Mortality		Mechanical ventilation (days)		Hospital LOS (days)		Length of ICU stay (days)		Pulmonary complications		Other complications	
	EPI	IB	EPI	IB	EPI	IB	EPI	IB	EPI	IB	EPI	IB	EPI	IB
Britt et al.	45	64	NR	NR	No significant intergroup difference in ventilator days (p = 0.61)		9.7±9.9	7.5±6.2[a]	3.7±4.4	4.5±4.9	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

Table 7. Results of studies comparing epidural analgesia with paravertebral block.

First author	Number of patients		Mortality		Mechanical ventilation (days)		Hospital LOS (days)		Length of ICU stay (days)		Pulmonary complications		Other complications	
	EPI	PVB	EPI	PVB	EPI	PVB	EPI	PVB	EPI	PVB	EPI	PVB	EPI	PVB
Shapiro et al.	31	79	0 (0%)	0 (0%)	NR	NR	6.77±2.6	6.08±3.69	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

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

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

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

Table 9. Results of studies comparing paravertebral block with intravenous analgesia

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

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

Table 10. Results of sensitivity and subgroup analysis.

Comparison	Outcome	Results	Sensitivity analyses on study design	Sensitivity analyses on study quality	Sensitivity analyses on time	Sensitivity analyses on outlier studies	Subgroup analyses on etiology
Epidural analgesia 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

Discussion

This systematic review and meta-analysis of both RCTs and cohort series focused on the analgesic therapy for patients with traumatic rib fractures. Results of this study show that overall epidural analgesia provides better pain relief than the other modalities. In three studies (16, 20, 28) significant differences ($p < 0.05$) were found in the improvement of pain in favour of epidural analgesia when compared with intravenous analgesia. 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 favour 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 (16-20, 23, 25-27, 29-32) resulting in a larger patient database.

The current guideline of the Eastern Association for the Surgery of Trauma (EAST) recommend epidural analgesia or a multimodal approach over opioids alone, for pain relief

in patients with blunt chest trauma (9). In comparison with this guideline of the EAST, our study differs in certain respects. Firstly, 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. Secondly, 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). Thirdly, 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 (15, 51, 52). 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 et al. (31). As we could only include 3 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 hours of ICU admission, in favour of epidural analgesia.

The type of medication is not reflected in our analysis. The different modalities were compared, as described in the baseline characteristics (Table 4). However, it could be relevant if only opioids were administered, or if local anaesthetics 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. In order to compare the results of pain reduction more homogeneously, future studies should use a universal pain assessment tool. Secondly, 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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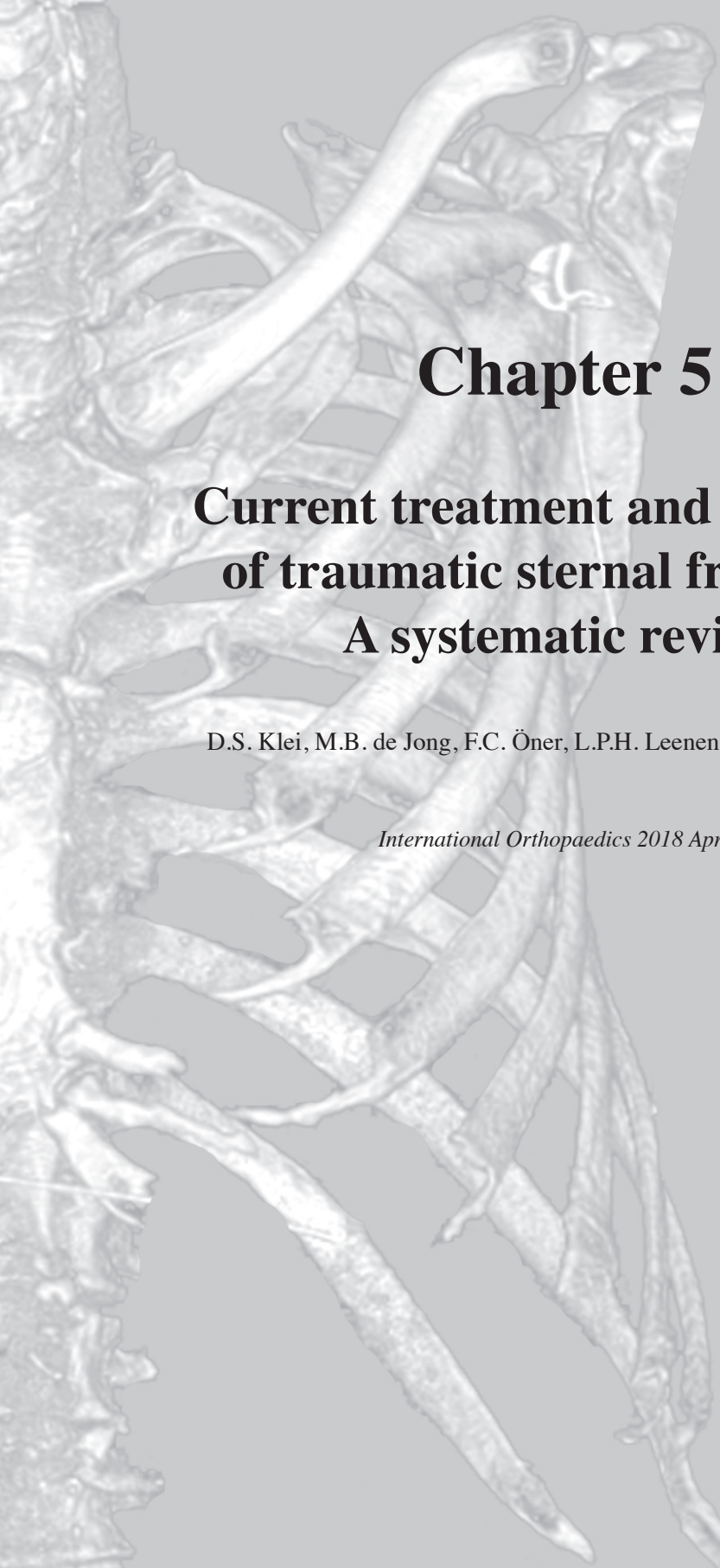

Chapter 5

Current treatment and outcomes of traumatic sternal fractures: A systematic review

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Abstract

Purpose: Traumatic sternal fractures are rare injuries. The most common mechanism of injury is direct blunt trauma to the anterior chest wall. Most (>95%) sternal fractures are treated conservatively. Surgical fixation is indicated in case of fracture instability, displacement or non-union. However, limited research has been performed on treatment outcomes. This study aimed to provide an overview of the current treatment practices and outcomes of traumatic sternal fractures and dislocations.

Methods: A systematic review of literature published from 1990 to June 2017 was conducted. Original studies on traumatic sternal fractures, reporting sternal healing or sternal stability were included. Studies on non-traumatic sternal fractures or not reporting sternal healing outcomes, as well as case reports (n=1) were excluded.

Results: Sixteen studies were included in this review, which reported treatment outcomes for 191 patients. Most included studies were case series of poor quality. All patients showed sternal healing and 98% reported pain relief. Treatment complications occurred in 2% of patients.

Conclusions: Treatment of traumatic sternal fractures and dislocations is an underexposed topic. Although all patients in this review displayed sternal healing, results should be interpreted with caution since most included studies were of poor quality.

Introduction

Sternal fractures are rare injuries, with an incidence of <0,5% of all fractures and an estimated 3-8% in blunt trauma patients (1-4). Traumatic sternal dislocations occur even less frequently (5). The most common mechanism of injury is direct blunt trauma to the anterior chest caused by motor vehicle accidents (1, 6-8). The incidence of sternal injury has increased since the introduction of seatbelt legislation (3, 9, 10). Additionally, sternal injuries are frequently caused by falls from height or indirect trauma due to spinal flexion-compression injury (1, 2, 5, 6, 11). Traumatic sternal fractures are mostly transverse sternal body fractures, while manubrial and xiphoid fractures occur less frequently (3, 8, 10). Two types of sternal dislocations are distinguished: the sternal body is dislocated either posteriorly (type 1) or anteriorly (type 2) to the manubrium (2, 5, 7, 12).

An isolated sternal fracture is seen as a relatively benign injury (2, 3, 6). Morbidity and mortality of sternal fractures are mostly determined by concomitant injuries of internal thoracic organs and mortality rates range from 4% to 45% (2, 3, 10). Frequently encountered associated thoracic injuries include vertebral fractures (particularly of the cervical and thoracic spine), rib fractures, clavicular fractures, scapular fractures, pulmonary contusion, haemopneumothorax, cardiac and mediastinal injury and aortic dissection (2, 9, 10, 13). Other common associated injuries include brain injury and abdominal injury (3, 9). Concomitant injuries and severe chest pain could lead to respiratory insufficiency, organ failure and ultimately mortality (1, 2).

The majority of sternal fractures (>95%) is treated conservatively (1, 3, 10, 14). Conservative treatment options consist of analgesia, corset fixation, rest, and passive reduction of displacement if necessary (1, 15). Adequate analgesia is of vital importance to prevent pulmonary complications caused by respiratory insufficiency as a consequence of painful respiration (15, 16). However, in case of unstable fractures, thoracic wall instability, fracture displacement or persistent dislocation, sternal deformity, respiratory insufficiency, severe pain, and fracture non-union, surgical fixation could be performed (1, 2, 4, 5, 7, 10, 17). Several fixation methods have been described in literature, of which wiring and plating are most regularly used (2, 5, 6, 11, 17). Biomechanically, surgical plating provides more stability and a better restoration of anterior chest wall function than wiring, and recent evidence suggests that plating results in improved bone healing and decreased complications and non-union (1, 2, 6, 7, 17, 18).

Few studies have been published about the (long-term) treatment outcomes of either conservative or surgical treatment of traumatic sternal fractures and dislocations (6, 7).

No randomized controlled trials (RCTs) have been conducted on this topic. To our knowledge, only one systematic review has been conducted by Harston and Roberts in 2011 which focussed on surgical fixation of sternal fractures (4). However, no systematic review has compared conservative and operative treatment of sternal fractures or dislocations. The aim of this study was to conduct a systematic literature review to provide an overview of the current treatment practice and outcomes of traumatic sternal fractures.

Materials and methods

PubMed and EMBASE/Medline were searched with the terms 'sternum', 'fracture', 'injury', 'treatment', and their respective synonyms. Both searches were performed with a combination of free text entry terms and MeSH terms (PubMed) or Emtree terms (EMBASE/Medline). No filters or language restrictions were applied to the searches.

Primary and secondary outcomes for sternal fracture and dislocation treatment were defined (Table 1). Articles were eligible for inclusion if they were original studies on the treatment of traumatic sternal fractures and dislocations; had a human study population >18 years of age; reported on >1 primary outcome parameters; and had been published after 1990. Articles were excluded if they involved the treatment of non-traumatic sternal fractures or dislocations, or fractures caused by cardiopulmonary resuscitation, or if they were review articles. Due to the limited research performed on sternal injury, all types of original studies were included except case reports (i.e. articles with a study population of n=1. All included articles were assessed for eligible cross-references. Finally, from all included articles, the parameters depicted in table 1 were extracted.

The review of search results and the quality assessment were performed by two authors (DK and KW) independently. In case of disagreement, final consensus was reached through a thorough re-assessment of the relevant article.

Quality of included studies was assessed using the methodological index for non-randomized studies (MINORS) assessment criteria, a validated instrument for the assessment of comparative and non-comparative surgical studies (19). In the current review, only the 8 criteria for non-comparative studies were used. For each criterion, a score of 0, 1 or 2 points was awarded: 0 points were assigned if an item was not reported, 1 point if an item was reported but inadequate and 2 points if an item was reported and adequate, leading to a maximum of 16 points per study. An appropriate study endpoint was defined as confirmation of fracture healing or sternal stability, reported for all included

Table 1. Parameters for the assessment of included articles.

Study characteristics
- Year of publication
- Journal of publication
- Country
- Study type
- Study period
- Number of included patients
- Length of follow-up

Patient characteristics
- Age (mean and range)
- Gender (male or female)
- Type of sternal injury (fracture or dislocation)
- Location of sternal injury (manubrium, sternomanubrial joint, sternal body, xiphoid process)
- Associated injuries (isolated or combined sternal injury)
- Acute (< 1 month) or non-healing sternal fracture (> 3 months) (if applicable)
- Comorbidities

Treatment methods
- Type of treatment (surgical or conservative)
- Conservative treatment method (if applicable) Surgical indication (if applicable)
- Type of fixation material (if applicable)

Treatment outcomes
- ***Primary outcome parameters***
  - (Fracture) healing
  - Sternal stability
- ***Secondary outcome parameters***
  - Pain relief
  - Treatment complications
  - Removal of fixation material (if applicable) Other re-operation (if applicable)
  - Hospital length of stay

patients. An appropriate follow-up period was defined as > 3 months follow-up.

Since many studies did not report outcome parameters for all patients, the number of evaluable patients varied for each outcome parameter. Hence, analyses were conducted with ratios and percentages. Treatment outcomes were evaluated in the general patient population and in subgroups of patients with different sternal injuries and treatment types. Due to the limited and incomplete data availability, no further subgroup analyses were conducted. Data were analysed using IBM SPSS Statistics, version 22.0 (Armonk, NY, USA).

Results

Search results

The literature search was conducted on June 8, 2017. The PubMed and EMBASE/Medline searches generated 598 and 846 hits respectively, yielding a total of 1444 hits. After removal of 390 duplicates, the resulting 1054 articles were assessed based on title and abstract. Subsequently, 967 articles were excluded based on title and/or abstract showing no relevant data for the current analysis. The remaining 87 articles were assessed based on full-text, and 14 of these articles were included. For 2 articles, a full-text version was not available and these articles were excluded. Additionally, through cross-referencing of the included articles, another 2 articles were obtained. A summary of the search process and search results is depicted in figure 1.

Study characteristics

All 16 included studies were published between 2006 and 2017. There were 12 case series, 2 cross-sectional studies, and 2 prospective cohort studies. Study periods ranged from 1 to 13 years, while follow-up length varied between 1 month and 7 years. Although all studies together comprised 354 individual patients, many studies did not report the primary outcome parameters for all patients. Therefore, only 191 patients were included in the analysis for this review (Table 2).

Patient characteristics and treatment methods

Mean age was 38 years (range 17-88 years). There were 101 males (70%), 44 females, and 45 patients for whom no gender was reported. Most patients (180/191, 94%) demonstrated a sternal fracture, most commonly located at the sternal body (30/64, 47%), followed by a fracture of the manubrium (16/64, 25%). Of these sternal fracture patients, 137 sternal fracture patients (77%) were treated for an acute fracture, while 42(23%) suffered from non-union. Eleven patients (11%) displayed a sternal dislocation, all located at the manubriosternal joint. The anatomy of sternal injuries is depicted in figure 2.

The majority of patients (105/143, 73%) suffered from associated injuries. Frequently occurring associated injuries were rib fractures, haemothorax or pneumothorax, pulmonary contusion, spinal fractures, clavicular fractures, extremity fractures and head injuries. However, associated injuries were not further analysed. Underlying comorbidities were not reported for any patient.

In total, 170 patients (89%) were surgically treated for their sternal injury. Of these patients, 141 (83%) underwent surgical fixation with plates, 28 (16%) with plates and bone graft, and one (1%) was treated with wires. The type of surgical plating varied per

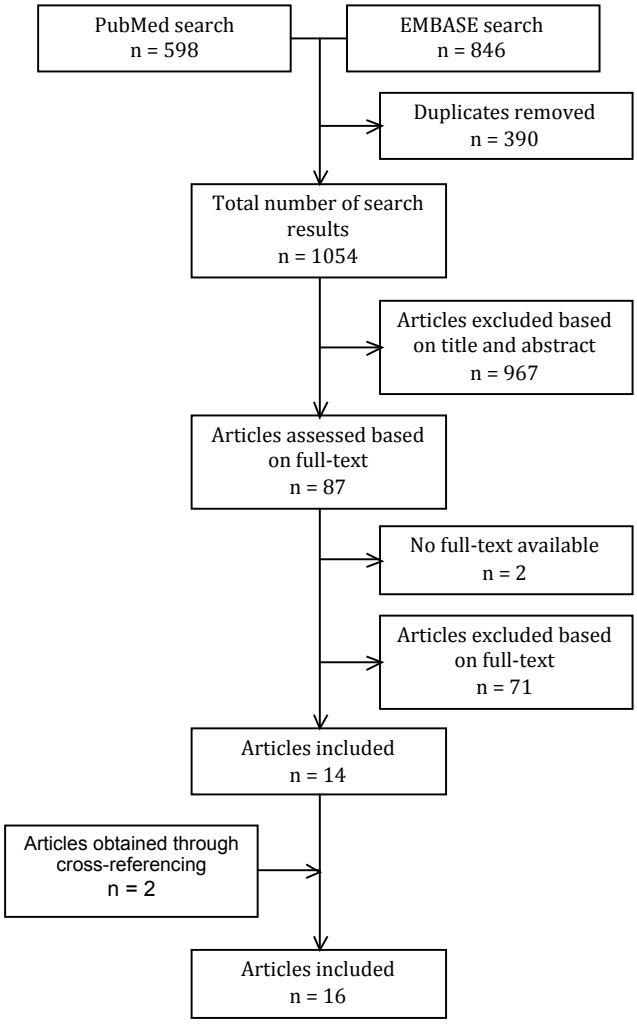

Figure 1. PRISMA diagram for the literature review.

study: for instance, some studies used locking plates, while others used non-locking plates. Indication for surgery were fracture displacement or sternal dislocation, pain, respiratory insufficiency, sternal instability, sternal deformity, and fracture non-union. Most studies did not provide detailed information on the surgical indications. Hence, further analysis of surgical indications was not performed.

Twenty-one patients (11%) received conservative treatment. Only one study reported their conservative treatment method: passive reduction of the sternal fracture or dislocation by surgical fixation of the associated spinal fracture (Table 3).

Table 2. Characteristics of included studies.

	Study type	Study period	N	Follow-up length
Abdul-Rahman et al. (2009)(23)	Case series	-	2 (primary outcome available for n = 1)	8 weeks
Al-Qudah (2006) (24)	Case series	7 years	4	-
Ciriaco et al. (2009) (14)	Case series	6 years	6	2 – 7 years
Divisi and Crisci (2011) (7)	Cross-sectional study	16 months	11 (primary outcomes available for n = 8)	Mean 2 (1-3 months)
Ergene et al. (2013) (25)	Case series	20 months	15 (primary outcomes available for n = 8)	-
Gloyer et al. (2011) (12)	Case series	-	3 (primary outcomes available for n = 2)	Mean 10 (6-12) months
Kälicke et al. (2006) (5)	Case series	-	2 (primary outcomes available for n = 1)	Mean 1.5 (1-2) years
Krinner et al. (2017) (2)	Case series	3 years	103 (primary outcomes available for n = 11)	2 years
Labbe et al. (2009) (13)	Case series	3 years and 5 months	11	-
Nazerali et al. (2014) (18)	Case series	7 years	57 (traumatic sternal fracture in n = 3)	3 months
Queitsch et al. (2011) (20)	Single arm prospective cohortstudy	5 years	12	-
Richardson et al. (2007) (26)	Case series	13 years	35	-
Schulz-Drost et al. (2014) (27)	Prospective cohort study	1 year	10	6 months
Schulz-Drost et al. (2016) (8)	Cross sectional study	22 months	13	12 weeks
Wu et al. (2005) (21)	Case series	1 year	6 (traumatic sternal fracture in n = 2)	6 – 18 months
Zhao et al. (2017) (1)	Case series	5 years	64 (primary outcomes available for n = 63)	6 months
	Total case series (n =12) Cross sectional study (n=2) Prospective cohort study (n=1) Single arm prospective Cohort study (n=1)	Mean 52 months (range 1-13 years)	Total n = 354 Including analysis: n=191	Range 1 month – 7 years

N Number of patinets, - not described

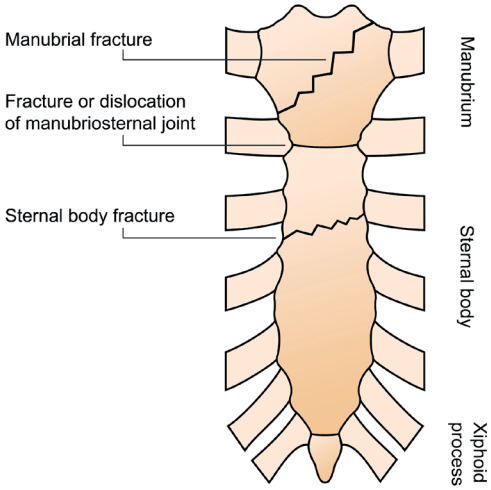

Figure 2. Regions of the sternal bone.

Treatment outcomes

All patients in this review demonstrated sternal healing (187/187, 100%) and/or sternal stability (35/35, 100%) after either conservative or surgical treatment. In virtually all patients (133/136, 98%), treatment resulted in pain relief. Three patients (3/174, 2%), all treated surgically for an acute sternal fracture, suffered from treatment complications: one patient showed post-operative wound seroma, one patient was re-operated due to loosening of fixation materials, and one patient suffered from an intra-operative bleeding due to injury to the mammary artery (without post-operative complications). In 15 cases (15/145, 10%), removal of fixation materials was reported: indications varied between patient discomfort and insurance reasons. However, several studies did not specify the indication for osteosynthesis removal. Mean length of hospital stay was 15 days (range 3 to 59 days), the length of stay was however often not reported (Table 4).

Quality assessment

The mean total quality score was 6.7 out of 16 (range 3 to 10). Most studies had appropriate endpoints to study aim (10/16) and a loss to follow-up below 5% (14/16). No study reported an unbiased assessment of study endpoints or prospective calculation of sample size. Two studies reported their data collection methods, of which one collected data prospectively. Patient inclusion criteria were described in three studies, all of which included patients consecutively. Six studies clearly stated their study aim and nine studies had an appropriate follow-up period (Table 5).

Table 3. Patient characteristics and treatment methods.

N	Mean age (range)	Gender	Type and location of sternal injury		Isolated or combined injury	Acute or non-healing fracture[a]	Surgical or conservative treatment	Fixation materials[b]
191	38 (17–88) years	Male	Fracture	Manubrium	Isolated injury	Acute fracture	Surgical treatment	Plates
		101/145 (70%)	180/191 (94%)	16/64 (25%)	(38/143, 27%)	(137/179, 77%)	170/191 (89%)	141/170 (83%)
		Female		Manubriosternal joint	Combined injury	Non-healing fracture	Conservative treatment	Wires
		44/145 (30%)		12/64 (19%)	(105/143, 73%)	(42/179, 23%)	21/191 (11%)	1/170 (1%)
				Manubriosternal joint and body				Plates with bone graft
				1/64 (2%)				28/170 (16%)
				Manubrium and body				
				5/64 (8%)				
				Sternal body				
				30/64 (47%)				
				Xiphoid process				
				0/64 (0%)				
			Dislocation	Manubriosternal joint				
			11/191 (6%)	11/11 (100%)				

All ratios and percentages were calculated with the data available. Therefore, the number of patients analysed per parameter might not equal the total population number
N number of patients, – not described
[a] Acute or non-healing fracture: only applicable to sternal fractures
[b] Fixation materials: only applicable to surgical treatment

Table 4. Treatment outcomes.

		N	Isolated injury	(Fracture) healing	Sternal stability	Pain relief	Treatment complications	Removal of fixation material[a]	Other re-operation[a]	Mean (range) hospital LOS in days
All patients		191	15/67	187/187	35/35	133/136	3/174	15/145	1/89	15 (3–59)
			(22%)	(100%)	(100%)	(98%)	(2%)	(10%)	(1%)	
Acute fracture	Surgical treatment	117	14/43	113/113	33/33	98/101	3/114	3/73	1/73	15 (3–59)
			(33%)	(100%)	(100%)	(97%)	(3%)	(4%)	(1%)	
	Conservative treatment	20	0/20	20/20	–	–	0/20	N/a	N/a	–
			(0%)	(100%)			(0%)			
Non-healing fracture	Surgical treatment	42	0/1	42/42	2/2	32/32	0/30	1/14	0/14	12
			(0%)	(100%)	(100%)	(100%)	(0%)	(7%)	(0%)	
	Conservative treatment	–	–	–	–	–	–	N/a	N/a	–
Sternal dislocation	Surgical treatment	10	1/2	10/10	–	2/2	0/8	2/10	0/1	5 (4–6)
			(50%)	(100%)		(100%)	(0%)	(20%)	(0%)	
	Conservative treatment	1	0/1	1/1	–	–	0/1	N/a	N/a	–
			(0%)	(100%)			(0%)			

All ratios and percentages were calculated with the data available. Therefore, the number of patients analysed per treatment group might not equal the total population number

N number of patients, *N/a* not applicable, – not described, *LOS* length of stay

[a] Removal of fixation material and other re-operation: only applicable to surgical treatment group

Table 5. MINORS quality assessment.

Study	Clearly stated aim	Inclusion of consecutive patients	Prospective collection of data	Endpoints appropriate to study aim	Unbiased assessment of study endpoint	Follow-up period appropriate to study aim	Loss to follow-up < 5%	Prospective calculation of study size	Total quality score
Abdul-Rahman et al. (2009) [23]	1	0	0	1	0	1	2	0	4
Al-Qudah (2006) [24]	1	2	0	2	0	0	2	0	7
Ciriaco et al. (2009) [14]	1	2	0	2	0	2	2	0	9
Divisi et al. (2011) [7]	2	0	0	1	0	1	0	0	4
Ergene et al. (2013) [25]	1	0	0	1	0	0	2	0	5
Gloyer et al. (2011) [12]	2	0	0	1	0	2	2	0	8
Kälicke et al. (2006) [5]	0	0	0	1	0	2	2	0	5
Krinner et al. (2017) [2]	1	0	0	1	0	2	2	0	7
Labbe et al. (2009) [13]	1	0	0	2	0	0	0	0	3
Nazerali et al. (2014) [18]	2	0	1	2	0	2	2	0	9
Queitsch et al. (2011) [20]	2	2	2	2	0	0	2	0	10
Richardson et al. (2007) [26]	1	0	0	2	0	1	2	0	6
Schulz-Drost et al. (2014) [27]	2	0	0	2	0	2	2	0	8
Schulz-Drost et al. (2016) [8]	1	0	0	2	0	2	2	0	7
Wu et al. (2004) [21]	1	0	0	2	0	2	2	0	7
Zhao et al. (2017) [1]	2	0	0	2	0	2	2	0	8
Mean quality score (range)	1.3 (0–2)	0.4 (0–2)	0.2 (0–2)	1.6 (1–2)	0 (0)	1.3 (0–2)	1.8 (0–2)	0 (0)	6.7 (3–10)

0 not reported, 1 reported but inadequate, 2 reported and adequate

Discussion

Few studies have been conducted on the treatment outcomes of traumatic sternal fractures and dislocations and to date, no randomised controlled trials have been published. Most studies included in this review were case studies, with only two cross-sectional studies and two cohort studies available. Case studies lack a randomised or consecutive methodological approach and are thus prone to selection and publication bias. Since case studies typically report on remarkable patients and treatment outcomes, their results do not reflect the findings in a general patient population. Notably, in the current review, most studies were of poor quality, with a mean total quality score of 6.7 out of 16. For this reason, results of the this review should be carefully interpreted. In total, 16 studies with 191 patients were included in this review. The majority of patients suffered from associated injuries (73%) and underwent surgery (89%). All patients displayed sternal healing and/or sternal stability, with a complication rate of only 3%.

Due to the limited research available, standardised treatment guidelines for traumatic sternal fractures and dislocations are lacking. Most notably, information about conservative and surgical treatment indications and long-term treatment outcomes, both in terms of functional outcome and health-related quality of life, could significantly improve the treatment of these injuries.

In literature, one systematic review has been published, which reported on surgical treatment of sternal fractures (4). The current review evaluated both surgical and conservative treatment, as well as treatment of sternal dislocations. Also, more studies were included in this review (16 comparedto 12 studies in the review by Harston et al.) (4).

Sternal fractures and dislocations are rare injuries, which was confirmed by the current review (1-3, 5). The included studies comprised only 354 patients (of whom 191 patients could be analysed) in a total study period of 56 years and 3 months. Although only patients over 18 years of age were included in this review, one study reported an age range of 17-54 years (20). Since the mean age of the patients was 33 years, we decided not to exclude this study from our analysis.

In accordance with literature sternal injury mostly occurred in young male patients and most fractures were located at the sternal body (3, 4, 10). Since one of the included studies exclusively assessed manubrial fractures and did not report outcome data for patients with other sternal fractures, the incidence of manubrial fractures might be overestimated in our analysis (8).

In literature, the majority of sternal fractures occur as isolated injuries and are treated conservatively (1, 3, 10 14). However, in this review, the majority of patients (89% of all patients and 85% of patients with acute sternal fracture) received surgical treatment.

Many included studies reported that some of their patients received conservative treatment, but did not include this conservative treatment group in the follow-up. Moreover, only 22% of patients in the current analysis sustained an isolated sternal injury. This overrepresentation of surgically treated polytrauma patients could be explained by the lack of consecutive patient inclusion and complete follow-up in case series. Also, publication bias could have caused the underrepresentation of conservatively treated patients in literature.

Fracture non-union is a rare entity in sternal fractures, with an incidence of <1% in literature (20, 21). Nonetheless, 23% of our patient population was treated for fracture non-union. This difference could be explained by the fact that the majority of patients in this review was treated surgically, and sternal non-union is generally considered an indication for surgical treatment (4).

Not one study reported on underlying comorbidities in their patients. Hence, although this review focusssed on the treatment of traumatic sternal fractures and dislocations, it was impossible to assess whether patients suffered from osteoporosis or other underlying bone diseases.

Almost all surgically treated patients underwent sternal fixation with plates (83%) or a combination of plates with bone graft (16%). Former studies have shown that sternal plating provides more stability and better chest wall function, as well as a decreased chance of non-union and improved bone healing, compared to wires (1, 2, 4, 17). While Harston found that 32% of all patients underwent surgical fixation with wires, it seems that surgeons have increasingly embraced the biomechanical advantages of plating. Bone graft is often used for the treatment of fracture non-union, due to its osteoinductive properties (7, 22). Indeed, most patients receiving bone graft (70%) were treated for non- union, while in the other patients, bone graft was used for extra fusion between plate and bone after sternal dislocation.

In correspondence with the findings of Harston et al., operative treatment of sternal fractures and dislocations seems to be safe and effective (4). All patients in this review displayed (fracture) healing and/or sternal stability. Only 3% of patients suffered from treatment complications and 1% needed re-operation. Harston et al. found that 19% of surgically treated patients suffered from complications (4). This high percentage could be explained by the fact osteosynthesis removal was defined as a complication. In the current review, authors of the included studies did not seem to consider removal of osteosynthesis

as a complication, since removal was reported separately from complications and reasons for removal were often not specified.

Only 21 patients were included in the conservative treatment group of this review. Of these patients, 11 were treated by passive reduction of their sternal injury and 10 patients received unknown non-surgical treatment. Although all patients in the conservative treatment group reached fracture healing and none suffered from complications, treatment methods could not be compared. Furthermore, the group is too small to generalise the findings.

Although most studies provided information on the occurrence of complications in their patients, comprehensive definitions and numbers were often lacking. Similarly, pain relief was often not defined nor quantified. Only one study reported an average decrease in Pain Severity Score (PSS) for their patient population, although the authors did not report whether pain relief was experienced by all patients individually (1). Hence, for the analysis of both complications and pain relief in this review, data might be biased or incomplete. Notably, length of follow-up ranged from one month to 7 years. Some complications, such as sternal non-union, appear later than others; therefore, in some studies follow-up for complications might have been incomplete.

The mean length of hospital stay was 15 days, but ranged from 3 to 59 days. Only few studies reported the length of stay: most of them reported a mean hospital stay of 3 to 12 days, while one study demonstrated a prolonged mean stay of 31 days (2). This difference could be caused by the fact that in the latter study, all patients suffered from associated injuries, while in the other studies, the majority of patients presented with an isolated sternal fracture. This difference in hospital length of stay could be explained by the association between associated injuries and length of hospital stay found in literature (3).

This systematic review has several limitations. Firstly, many studies did not report all primary and secondary outcome parameters. Therefore, for each outcome parameter, analysis could be performed on only a limited number of patients; consequently, results could be highly skewed by the outcomes of an individual study. Secondly, most studies included in this review were low-quality case series, with potential selection and publication bias. Finally, the positive treatment results found in this review could not be extrapolated to the general population of sternal injury patients. Most notably, merely 191 patients were included in this review, with only 21 patients treated conservatively and 11 patients suffering fromsternal dislocation. Moreover, it was impossible to assess how many patients who initially received conservative treatment ultimately required surgery. Furthermore, indications for surgery could not be verified.

In conclusion, both surgical and conservative treatment of traumatic sternal fractures and dislocations seem to be safe and effective. All patients evaluated in this review displayed sternal healing, while reported complication rates were as low as 3%. However, very limited research has been performed on this topic and only 191 patients could be included in the current analysis. Available evidence mainly consists mainly of case series with low scores on quality assessment. Consecutive cohort studies and randomised controlled trials are lacking and study results should be interpreted with caution. Both additional high-quality research and comprehensive information from patient registries are essential to verify surgical indications and treatment outcomes in the relevant patient populations.

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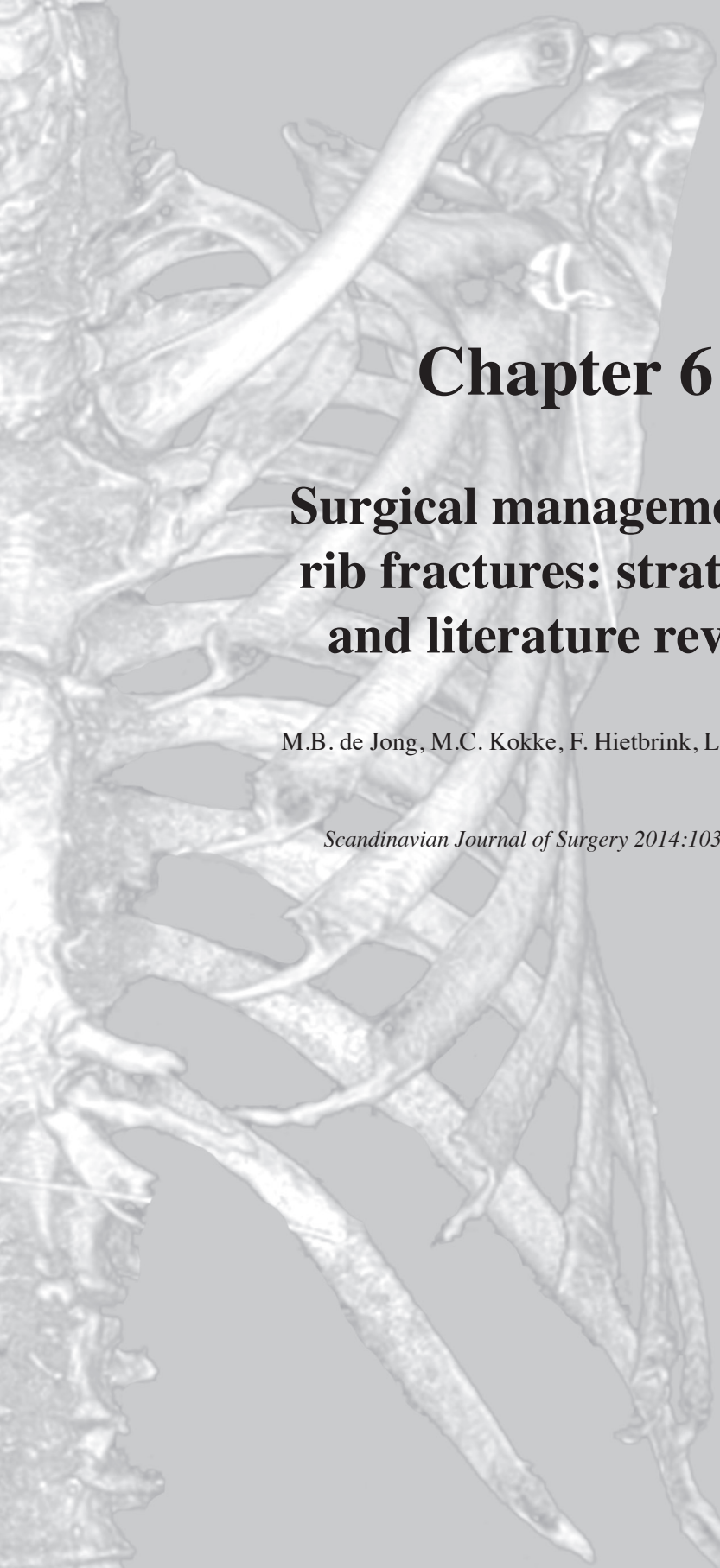

Chapter 6

Surgical management of rib fractures: strategies and literature review

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Abstract

Background and aims: Rib fractures can cause significant problems in trauma patients, often resulting in pain and difficulty with respiration. To prevent pulmonary complications and decrease the morbidity and mortality rates of patients with rib fractures, currently there is a trend to provide surgical management of patients with flail chest. However, the indications for rib fracture fixation require further specification.

Material and Methods: Past and current strategies are described according to a review of the medical literature. A systematic review was performed including current indications for rib fracture fixation. Medline (2000-2013) was searched, as well as Embase (2000-2013) and Cochrane databases using the keywords: rib, fracture, fixation, plate, repair, and surgery.

Results: Three retrospective studies were found that described different techniques for rib fracture fixation. The results demonstrated a reduced number of ventilation days, decreased long term morbidity and pain, and satisfactory rehabilitation after surgical treatment. In addition to flail chest, age, Injury Severity Score (ISS) and the number of rib fractures were important predictive factors for morbidity and mortality.

Conclusions: Surgical rib fracture fixation might be indicated in a broader range of cases than is currently performed. Prospective randomized trials are needed for further confirmation.

Introduction

Chest wall injury, after blunt thoracic trauma, is relatively common. This type of injury can vary in severity from isolated rib fractures to severe, bilateral crush injuries leading to respiratory problems. The mechanism associated with these injuries is often due to direct forces acting on the chest wall. Elderly patients and patients with osteoporosis or osteopenia have an increased risk for the number and severity of rib fractures. This is in contrast to children where higher forces are needed to cause rib fractures; they have a chest wall that is more pliable and compliant. The most common symptom associated with rib fractures is pain, which makes it difficult to take adequate breaths. Up to 30% of patients with rib fractures develop pneumonia; older patients are at risk for this complication (1, 2).

Rib fractures occur in 10% of all trauma patients and in approximately 30% of all patients with significant chest trauma (3). Rib fractures can be a sign of severe trauma. The greater the number of fractured ribs the higher the associated morbidity and mortality (3). Flagel et al. reported 10% mortality in patients with more than four rib fractures; this increases to 34% in patients with eight or more fractures (4). In addition, patients with more than four rib fractures, and that are 45 years of age or more, have an increased risk of adverse outcomes (4-7). In a retrospective study, from the National Trauma databank, Kent et al reported that 56% of the mortality rate, in patients with thoracic trauma that were older than 65, was due to rib fractures and no other injuries (7).

The management of rib fractures involves pain control as well as adequate oxygenation and ventilation; with the use of positive pressure ventilation when necessary. However, use of mechanical ventilation is associated with several ventilation related complications. It is known that patients with flail chest, not treated surgically, develop pneumonia in 27-70% cases and have a mortality rate of 25-51% (8).

Therefore, rib fractures can lead to significant morbidity and mortality, which increases with age and the number of rib fractures. An age of 45 years or greater and more than four rib fractures appear to be important risk factors associated with patient outcome.

Providing external stability by surgical fixation might offer an alternative treatment for the management of multiple rib fractures in older adults with the goal of avoiding mechanical ventilation. The aim of surgical treatment is to improve the respiratory mechanics, reduce pain and prevent pulmonary restriction that can be associated with significant chest wall deformity. Although the majority of patients with rib fractures heal spontaneously, without surgical therapy, there might be a select group of patients that can benefit from surgical repair.

A recently published meta-analysis concluded that surgical fixation of a flail chest is associated with reduction in the duration of mechanical ventilation, the complications associated with prolonged mechanical ventilation, the length of hospital stay, as well as mortality (9). Although these data are based mainly on retrospective studies and a few prospective trials, the trend currently is to provide surgical fixation of the ribs in patients with flail chest (9). This management has been reported in the recent guidelines published by Surgical Critical Care, which has recommended surgical fixation of rib fractures in patients with a flail chest segment, severe chest wall deformity, with or without pulmonary herniation, or symptomatic fractures of three or more consecutive ribs (10). However, surgical management of cases with non-flail chest remains controversial.

A protocol has been developed at this hospital, based on previous literature, for patients with multiple rib fractures. All patients with flail chest and/or more than four rib fractures and/or are 45 years of age or greater are treated surgically (Figure 1 to 3).

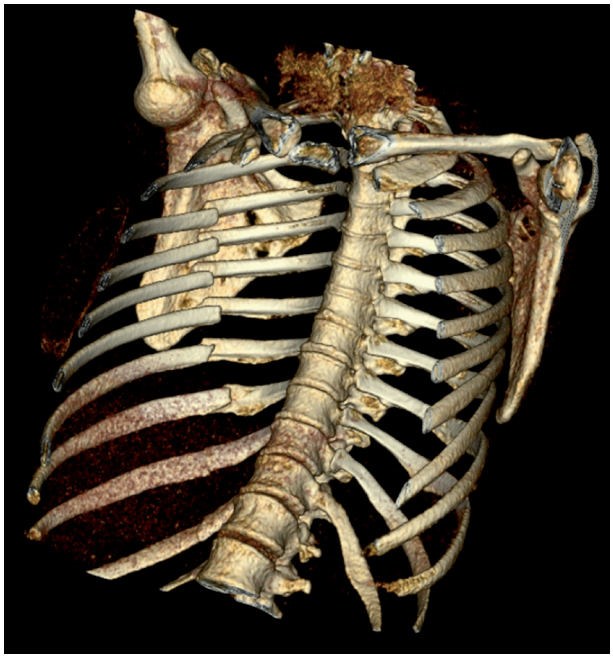

Figure 1. 3D CT reconstruction of multiple rib fractures.

3D: three dimensional; CT: computed tomography

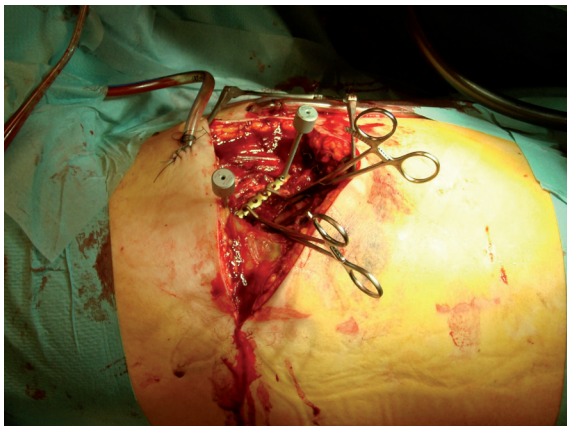

Figure 2. Rib fixation.

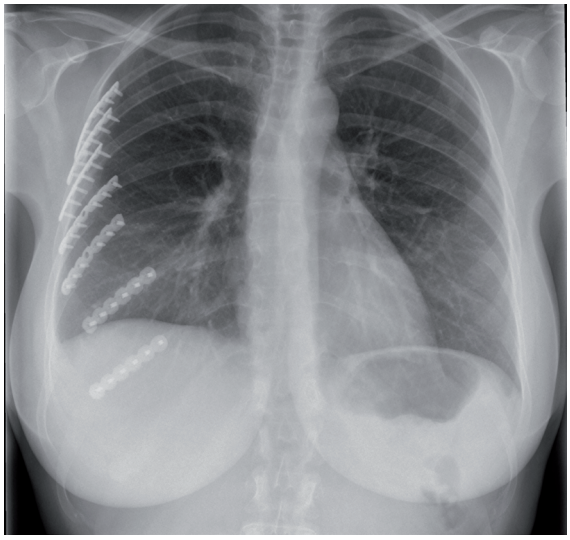

Figure 3. Chest X-ray after rib fixation.

History

The treatment of multiple rib fractures can be divided roughly into two main groups: internal support techniques and external support techniques (11). Jones reported the first case of external support for a flail chest 25 years before the introduction of mechanical ventilation. He described a percutaneous technique where traction was applied to the ribs (12). Many alternatives to this technique followed thereafter. A non-operative device used was the Cape Town limpet, described by Schrire; this sink plunger like device was used to give traction

to the flail segment (13). Significant complications from these external traction devices were associated with the prolonged bed rest required. After the introduction of mechanical ventilation, the external traction devices became more or less obsolete. Avery et al. first described continuous mechanical ventilation, which could provide internal stabilization for flail chest (14). Garzon et al. reported combined mechanical ventilation with tracheostomy to remove problematic pulmonary secretions (15).

Over time, after the introduction of mechanical ventilation the associated problems became apparent. Therefore, a few years after the introduction of mechanical ventilation the search for a safe and effective internal fixation technique to treat rib fractures, to provide stability to the chest wall and reconstruct the chest shape, continued. The use of K-wires, intramedullary repair and an arsenal of self-made plates have been described. Even drittel rohr plates were used, but they broke after 12 hours (16). In 2008, the Stratos system® (MedXpert, GmbH Heitersheim, Germany) was introduced, this plate is fixed to the ribs with hooks. In addition, the RibLoc® plate (Acute Innovations Hillsboro,OR, USA) used a U-shaped plate that slides over the rib combined with fixation using stable angular screws. In 2009, Ivancic et al. described a technique based on the use of K-wires with a Figure of eight wire to create stability (17). Most recently, Depuy Synthes® (Amersfoort, the Netherlands) introduced the MatrixRIB™ system, consisting of specifically contoured titanium plates, which are fixed to the ribs with locking screws.

Surgical technique

There are several options for hardware available for fixation of rib fractures; metal plates, absorbable plates and intramedullary fixation. One technique reported by Mayberry and co-workers includes plates fixed with a cerclage (18). Common disadvantages associated with this method are intercostal nerve impingement and wire breakage. The Judet plate is a metal plate with crimps on the side that clamp around the ribs (19). This technique can also damage nerves. The U-plate, which is fixed with locking screws, also uses crimps, but they only clamp onto the superior aspect of the ribs; this avoids damage to nerves, which can cause chronic pain. A cadaveric study reported by Sales et al. demonstrated that the U-plate is more durable than anterior plate fixation (20). These 3.5 mm reconstruction plates require intra-operative contouring, which results in increased operating time. Using pre-contoured locking plates can save time. Alternatives include absorbable plates; however, these plates have been associated with a greater risk of tissue reaction. Both Mayberry et al. and Marasco et al. described several complications associated with absorbable plates, when used alone; they advised that these plates be used in conjunction with metal plates for posterior chest wall stabilization (21, 22).

Intramedullary fixation provides less stability; however, it is suitable for fractures that are

difficult to reach, like fractures behind the scapula. In addition, there are pre-contoured rib splints that are fixed with one locking screw to prevent migration. The problem with these splints is that they can easily perforate a rib, especially in older patients. Therefore, at this center we prefer to use splints only in combination with plates, and do not rely on them alone.

Radiology evaluation

The standard chest x-ray commonly underestimates the number of rib fractures present but gives accurate information about the presence of a pneumothorax or hemothorax (23). A CT (Computed Tomography) scan is more reliable for the detection of rib fractures but is not a standard investigation for the detection of rib fractures; the additional information gained usually does not significantly change the management of rib fractures. However, as part of modern trauma screening, after high-energy accidents, a chest CT is usually performed. A CT scan gives more detailed information about the location and number of rib fractures present as well as the magnitude of dislocation, which can be useful in the preoperative planning of rib fixation (24, 25).

Indications for rib fixation

There is no hard evidence on the best method to use for the repair of rib fractures. However, there are some generally accepted indications for surgical rib fixation. The most common indication for rib fixation is the presence of a flail chest (26). Other accepted indications are patients with rib fractures who, notwithstanding good pain management, are still in pain, have a chest wall deformity, or have one or more symptomatic non-union rib fractures. Furthermore, rib fractures can be fixed while performing a thoracotomy for other indications (26).

A literature search was performed to determine suitable indications for rib fracture fixation, in addition to the current indication of flail chest, as described in in prior meta-analyses and guidelines (18, 26, 27).

Review

A systematic literature search was performed. Medline (2000-2013) was searched, as well as Embase (2000-2013) and Cochrane databases using the keywords: rib, fracture, fixation, plate, repair, and surgery. The last search was performed in December 2013. The literature search was restricted to articles published after 1999, as surgical techniques changed dramatically after this point in time. Two reviewers independently decided whether the studies met the inclusion and exclusion criteria and reviewed all titles and abstracts.

Study selection and data extraction

First a Medline search was performed and the two reviewers screened all titles. The abstracts of selected titles were further screened to ensure that the study included surgical treatment of non-flail chest. If adequate information was not present in the abstract or the abstract was absent, full text of the article was requested. After the abstracts were selected, the two reviewers analyzed the full text articles. Included in the review were all studies with at least 10 surgically treated human patients with non-flail chest rib fractures. The articles had to be written in English, Dutch or German. Excluded were case reports, biomechanical studies, animal studies, expert opinions, and studies with less than 10 surgically treated patients. Then, review of the Embase and Cochrane databases was performed in the same way. A supplemental search of all references included with the articles, found by the initial search, did not yield extra abstracts. All relevant outcome data, for each of the included studies, were extracted independently, by the two authors, using the Cochrane Collaboration tool (28).

Results

Flow chart 1 outlines the study flow and selection of the included articles. There were 673 titles reviewed, 10 full text articles were retrieved. Seven articles were excluded and three manuscripts remained for data extraction. Table 1 summarizes the included studies. All of the studies were retrospective; one study was a matched case control study (Table 2). For the comparison group treatment consisted of analgesia and mechanical ventilation when necessary. A variety of surgical techniques were used including: struts, intramedullary fixation and absorbable or non-absorbable plates. The indications used in the studies are described in Table 3.

Table 1. Description of included studies.

Author	Study period	Year of Publication	Study design	O, n	NO, n	Operative technique
Campbell et al. (27)	2004-2008	2009	Retrospective	32		ABsorbable plate (Inion OTPS)
Mayberry et al. (18)	1996-2005	2009	Retrospective	46 (15 non-flail)		Titanium plates with screws, stainless steel plates cerclaged with wire, absorbable plates fixed with absorbable screws.
Nirula et al. (26)	1996-2000	2006	Retrospective, matched case-control	30	30	Adkins struts

O: Operative patients; NO: Non-operative patients

Table 2. Matched case-control study.

Author	O, n	NO, n	Timing of operation (mean), days	Hospital admission days (mean)	Ventilator days (mean)		
				O	NO	O	NO
Campbell et al. (27)	32		5 (6-13)	13.5 (8.8-22)		NA	NA
Mayberry et al. (18)	46 (15 non-flail)		7 ± 5 (0-33)	NA	NA	NA	NA
Nirula et al. (26)	30	30	2.7 (0-20)	18.8 ± 1.8	21.1 ± 3.9	6.5 ± 1.3	11.2 ± 2.6

NA: not available; O: Operative patients; NO: Non-operative patients

Table 3. Summary of study characteristics.

	Indications	Follow-up (months)	Operative technique	Complications	ISS
Campbell et al. (27)	• Chest wall instability • Respiratory distress • Pain • Thoracotomy for other reason	NA	Absorbable plate (Inion OTPS)	5 wound infection 3 pneumonia 1 pulmonary embolus 1 delirium 1 cardiac arrest 1 nonunion 1 chest wall numbness	26
Mayberry et al. (18)	• Flail chest • intractable pain associated with displaced rib fractures • chest wall deformity/ defect • pulmonary herniation • thoracotomy for other indication	26.3 ± 27.6	Titanium plates with screws, stainless steel plates cerclaged with wire, absorbable plates fixed with absorbable screws.	3 fixation failure 1 bilateral chest wall rigidity 1 osteomyelitis	NA
Nirula et al. (26)	• flail chest • pain • bleeding • inability to wean from ventilator	NA	Adkins struts	NA	25.7

NA: not available; ISS: Injury Severity Score

Conclusions

Pneumonia and ventilator associated complications pose a major threat to patients with rib fractures. With the development of specifically designed rib fixation devices, the materials used for surgical treatment of rib fractures has undergone a revival. Although there is accumulating evidence to support surgical treatment of flail chest, the evidence for surgical treatment of non-flail chest rib fractures is limited. In our experience, there is a benefit from early stabilization of rib fractures in selected patients, which increases the likelihood of preventing ventilator support and pneumonia. We searched the literature to determine whether

there is support of our own experience. However, there were only a limited number of articles on rib fracture fixation fulfilling the selection criteria, when flail chest was excluded. None of the included articles reviewed, were prospective randomized trials and they all consisted of only a small number of patients. Moreover, the three manuscripts finally selected on rib fixation were difficult to compare because of the significant variation in study design. Only Nirula et al. concluded that rib fracture fixation showed a trend toward fewer total ventilator days. Mayberry et al. investigated the quality of life after rib fixation and they concluded that there was low long-term morbidity and pain. Campbell at al. demonstrated low levels of pain and satisfactory rehabilitation (18, 26, 27). There was significant variability in the timing of surgery and the indications for surgery were not standardized. Brasel et al. demonstrated that age and ISS were the only important predictors of mortality in patients with rib fractures, which might suggest that every older patient with a high ISS might benefit from surgical treatment of their rib fracture(s) (29). Flagel et al. reviewed the National Trauma Data Bank (4). He concluded that an increase in the number of rib fractures correlated directly with an increase in pulmonary morbidity and mortality.

A recently published meta-analysis showed that surgical treatment of flail chest was associated with a significant reduction in morbidity, mortality and resource expenditures. The comparison of studies, in this meta-analysis, showed a tendency toward reduction of ventilator days as well as hospital admission days (30). This reduction was more evident when the interval to surgery was short.

These findings are consistent with our own experience in patients with both flail chest and non-flail chest rib fractures. We have observed a reduction in ventilator time and the need for ICU admission as well as hospital admission days (unpublished data). For the non-flail chest rib fractures this includes: patients with continued pain despite adequate analgesia, inability to wean from the ventilator and the presence of a chest wall deformity.

The presence of multiple rib fractures is associated with a significant mortality rate and pulmonary morbidity. Age, ISS and the number of rib fractures are important risk factors. The level of evidence for rib fixation for flail chest is limited because of the lack of randomized controlled trials. Although it is more common currently to operate on patients with a flail chest, a prospective randomized trial is needed with standardized indications for surgical management of rib fractures, not only as part of a flail chest but also in patients with non-flail chest rib fractures. Age, the number of rib fractures, timing of surgery, and ISS must be taken into account when starting such a trial. As it was previously suggested, any attempt to reduce pneumonia may also reduce mortality, and as such, rib fracture fixation might have much broader indications than is currently accepted in routine practice.

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Chapter 7

Rib fixation versus non-operative treatment for flail chest and multiple rib fractures after blunt thoracic trauma. A multicenter cohort study

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Submitted

Abstract

Background: Over the years a trend has evolved towards operative treatment of flail chest although evidence is limited. Furthermore, little is known about operative treatment for patients with multiple rib fractures without a flail chest. The aim of this study was to compare rib fixation based on a clinical treatment algorithm with nonoperative treatment for both patients with a flail chest or multiple rib fractures.

Methods: All patients with ≥3 rib fractures admitted to one of the two contributing hospitals between January 2014 and January 2017 were retrospectively included in this multicenter cohort study. Primary outcome measures were intensive care length of stay and hospital length of stay for patients with a flail chest and patients with multiple rib fractures, respectively. To control for potential confounding, propensity score matching was applied.

Results: A total of 332 patients were treated according to protocol and available for analysis. The mean age was 56 (SD 17) years old and 257 (77%) patients were male. The overall mean Injury Severity Score was 23 (SD 11) and the average number of rib fractures was 8 (SD 4). There were 92 patients with a flail chest, 37 (40%) had rib fixation and 55 (60%) had non-operative treatment. There were 240 patients with multiple rib fractures, 28 (12%) had rib fixation and 212 (88%) had non-operative treatment. For both patient groups, after propensity score matching, rib fixation was not associated with intensive care unit length of stay (for flail chest patients) nor with hospital length of stay (for multiple rib fracture patients), nor with the secondary outcome measures.

Conclusion: No advantage could be demonstrated for operative fixation of rib fractures. Future studies are needed before rib fixation is embedded or abandoned in clinical practice.

Background

Multiple rib fractures are the most common type of thoracic injury, with mortality rates around 10% with even higher rates observed with elderly trauma patients (1-4). An increased number of rib fractures corresponds to a worse outcome in part due to respiratory complications resulting from pain and an impaired ventilation capacity (5-7). Consequently, superinfection leading to pneumonia and prolonged mechanical ventilation are common in patients with chest wall injuries (2). It is important to distinguish between multiple rib fractures with and without a flail chest, as the latter is associated with an increased mortality rate and significant morbidity due to the effects of paradoxical chest movement and higher incidence of concomitant injuries like pulmonary contusion (8, 9).

Nonoperative treatment has been the gold standard for the past few decades and is focused on the underlying pulmonary contusion- and rib fracture- associated complications, including pain, atelectasis, and compromised pulmonary hygiene (4). Over the years, a trend has evolved towards operative treatment of flail chest as physicians aim to improve mortality rates and reduce the prolonged length of stay for these patients. In a recent systematic review, rib fixation in patients with a flail chest was associated with a reduced: intensive care unit length of stay, days on mechanical ventilation, mortality rate, pneumonia rate, and treatment costs, although evidence remains limited (10). Studies investigating the effect of rib fixation in patients with multiple rib fractures are even more scarce, although two retrospective cohort studies showed promising results (11, 12).

For both flail chest and multiple rib fractures, the indication for surgery is heterogeneously described in the aforementioned studies (10-12). Therefore, no clear consensus on indication is available based on the current literature. It can be hypothesized that for patients with multiple rib fractures, early fixation might be beneficial. Therefore, the aim of this study was to compare rib fixation based on a clinical treatment algorithm with nonoperative treatment for both patients with a flail chest and patients with multiple rib fractures.

Methods

Study design and participants

All patients with three or more rib fractures admitted to one of the two contributing hospitals between January 2014 and January 2017 were retrospectively included in this multicenter cohort study. Both hospitals are academic tertiary referral centers with a level one trauma facility of similar size. Patients were included if they fulfilled the following criteria: age 18

years and older, blunt thoracic trauma resulting in multiple rib fractures (defined as three or more rib fractures) or a flail chest (defined as three or more consecutive ribs fractured in at least two places and clinical signs of paradoxical chest wall movement), and being alive two days after hospital admission (mean time till surgery). Exclusion criteria were: transfer to another hospital, initial admission in another hospital, no availability of a computed tomography (CT) scan, and rib fixation more than four days after trauma. Patients were followed from admission until discharge or death.

Eligible patients were identified using procedural codes and the Dutch National Trauma Registry. The non-operative group was formed by all patients with rib fractures admitted to the Radboud University Medical Center where treatment consisted of adequate pain management, supportive mechanical ventilation when indicated, and physiotherapy for breathing exercises according to standard national guidelines. The surgical group consisted of all patients who had rib fixation performed in the University Medical Center Utrecht where the same non-operative treatment guidelines were followed, but in addition, rib fixation was considered according to a clinical based algorithm (Figure 1). Pain was arbitrarily defined as a numerical rating scale of 5 or higher during coughing or deep inspiration and if pain was suspected not to decrease over the subsequent days with adequate pain management. It was the decision of the surgeon on call to perform rib fixation. This study was approved by the institutional review board of the participating centers (METC 17-544/C & 2016-2861).

Surgical procedure rib fixation

All procedures were performed by a senior trauma surgeon experienced in surgical treatment of rib fractures. Preoperative planning of the procedure was done using chest computed tomography (CT) with 3D reconstructions. Preoperative antibiotic prophylaxis (2 grams of Cefazolin) was administered intravenously in all patients. Depending on the site of the fractures, patients were positioned in the supine, lateral or prone position and the surgical approach was performed as described by Taylor (13). In the case of intercostal muscle interposition, debridement was performed. After reduction, internal fixation using the MatrixRIB™ system (Depuy Synthes®, Amersfoort, the Netherlands) was performed. Fixation was preferably done with 3 bicortical screws on each side of the fracture. The number of fixed ribs was at the discretion of the surgeon, and depended upon the possibility to regain stability of the chest wall during respirations. Tube thoracostomy was only performed in the case of clinical suspicion of pneumothorax during surgery. Postoperative chest radiography was performed in all patients to document surgical result and to rule out complications. Patients were allowed to perform their daily activities as soon as possible.

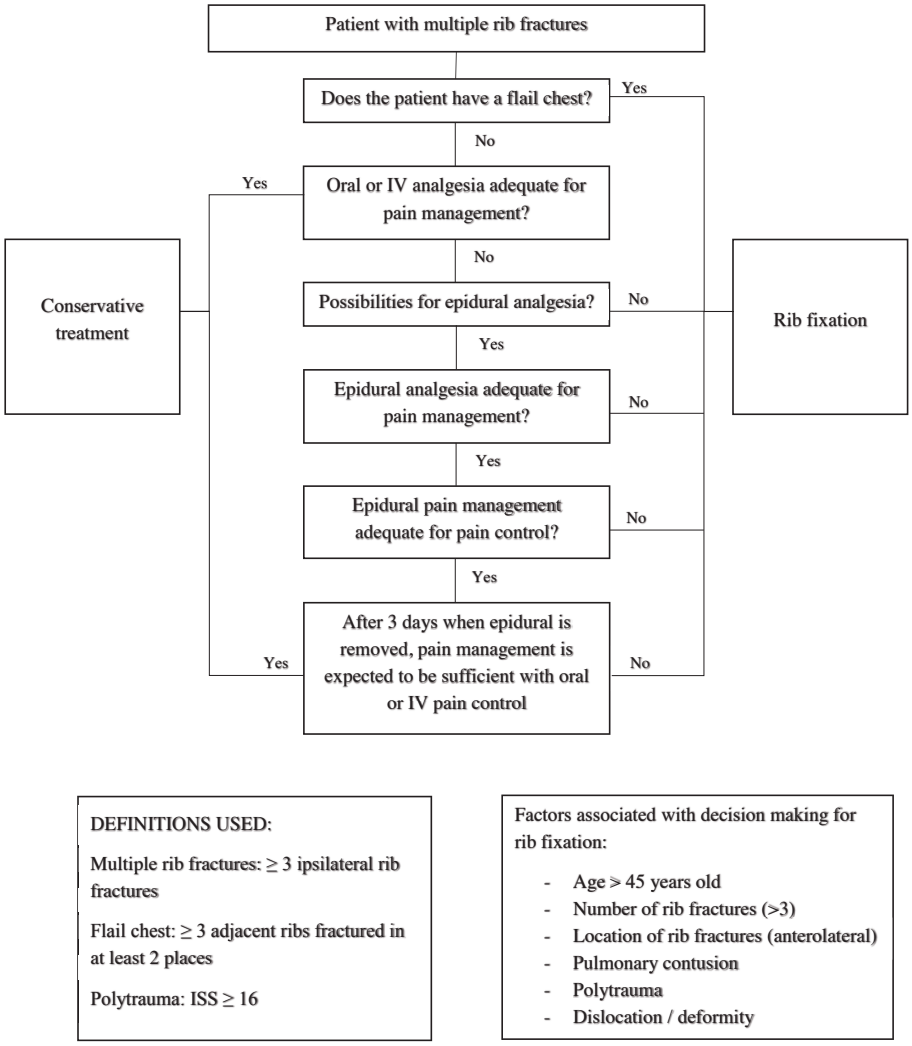

Figure 1. Clinical-based algorithm for the treatment of multiple rib fractures.

Baseline characteristics

Data for the following baseline characteristics were extracted from medical records: age, sex, American Society of Anesthesiologists (ASA) score, trauma mechanism, Injury Severity Score (ISS), thoracic trauma severity score (TTSS), abbreviated injury scale (AIS) head, AIS face, AIS thorax, AIS abdomen, AIS extremities, number of rib fractures, bilateral rib fractures, concomitant injuries (pulmonary contusion, pneumothorax, hemothorax,

sternum fracture) as recorded on the admission CT scan, and first available blood pH and base excess. Additionally, for the surgical group: duration until surgery in days, duration of surgery in minutes, and number of surgically fixated rib fractures. The ISS is a measure (range 0 - 75) of the severity of traumatic injury and is calculated by adding the square of the three highest AIS scores. The AIS is a standardized anatomical-based coding system ranging from zero to five to classify the severity of traumatic injury per body region. The AIS is registered in the Dutch National Trauma Registry by trained data managers based on radiology reports from admission CT scans and medical records. The TTSS is a score (range 0 - 25) based on number of rib fractures, pulmonary contusion, PaO_2/FiO_2 ratio, age, and pleural involvement and helps to predict outcome after thoracic trauma (14-16). Rib fractures, pulmonary contusion, pneumothorax, and hemothorax were assessed on the admission CT scan.

Outcome measures

In line with previous trial reports, the primary outcome measure for patients with a flail chest was intensive care unit length of stay (ILOS) and for patients with multiple rib fractures, hospital length of stay (HLOS). For both patient groups, secondary outcome measures were duration of invasive mechanical ventilation (IMV), duration of epidural analgesia, pneumonia, need for tracheostomy and in hospital mortality. Pneumonia was defined as having clinical signs (fever, coughing, desaturation) requiring antibiotic treatment, with or without positive cultures. Additionally, we assessed in hospital complications after rib fixation.

Statistical analysis

All analyses were stratified by patient group, i.e., performed separately for patients with a flail chest and patients with multiple rib fractures. Baseline characteristics were presented as proportions for categorical variables, mean and standard deviation (SD) for normally distributed continuous variables, and median and interquartile range (IQR) for non-normally distributed continuous variables. Differences in distributions of baseline characteristics between the study groups were quantified by means of standardized differences and statistical tests (t-test for normally distributed continuous data, Mann-Whitney test for non-normally distributed data, and Chi square test for categorical data) (17).

We applied multiple imputation (25 times) to impute missing values for ASA (2.1% [7/332]), TTSS (20% [67/332]), AIS head (0.6% [2/332]), pulmonary contusion (0.6% [2/332]), pH (9.0% [30/332]), and base excess (9.0% [(30/332]). Multiple imputation was performed using the mice() algorithm in R (18).

To control for potential confounding, propensity score (PS) matching was applied. First, a PS model was fitted using logistic regression analysis, with rib fracture fixation as the dependent variable, and age, sex, ASA-score, trauma mechanism, ISS, TTSS, AIS head, AIS face, AIS thorax, AIS abdomen, AIS extremities, number of rib fractures, bilateral rib fractures, concomitant injuries, blood pH, and base excess were included as covariates in the model. We performed 2:1 nearest neighbor matching, with a maximum caliper of 0.2 of the standard deviation of the logit of the PS using the Matchit() algorithm in R (19). After matching, the balance in the distributions of baseline characteristics between the study groups were quantified using standardized differences, where a standardized difference < 0.1 is generally accepted as indicating fair balance of confounders between the matched treatment groups (i.e. successful matching) (17).
In the primary analysis, for patients with a flail chest, we estimated the relation between rib fracture fixation and ILOS by means of linear regression analysis. For patients with multiple rib fractures, we estimated the relation between rib fracture fixation and HLOS by means of linear regression analysis. Secondary analyses focused on the relation of rib fracture fixation with duration of IMV and duration of epidural analgesia using linear regression analysis. The relation between rib fixation, pneumonia, tracheostomy, and in hospital mortality was assessed by means of a logistic regression analysis. A two-tailed p-value less than 0.05 was considered significant. All analyses were performed using R v3.4.1 (20).

Results

A total of 332 patients were available for analysis (Figure 2). The overall mean age was 56 (SD 17) years old and 257 (77%) patients were male (Table 1). Most patients were injured in a motor vehicle accident or after a fall from height resulting on average in 8 (SD 4) rib fractures and an overall mean ISS of 23 (SD 11).

Among the 92 patients with a flail chest, 37 (40%) had rib fixation and 55 (60%) had non-operative treatment (Figure 2). For the flail chest population, surgically treated patients had a lower AIS head and a higher blood pH. Among the 240 patients with multiple rib fractures, 28 (12%) had rib fixation and 212 (88%) had non-operative treatment. In this group, surgical patients had a significantly lower AIS head, higher AIS thorax, higher AIS abdomen, and higher number of rib fractures (Table 1).

The median time until surgery was one day (IQR 1-2)(Table 2). The median number of surgically fixated rib fractures for patients with a flail chest was 5 (4-6) and for patients

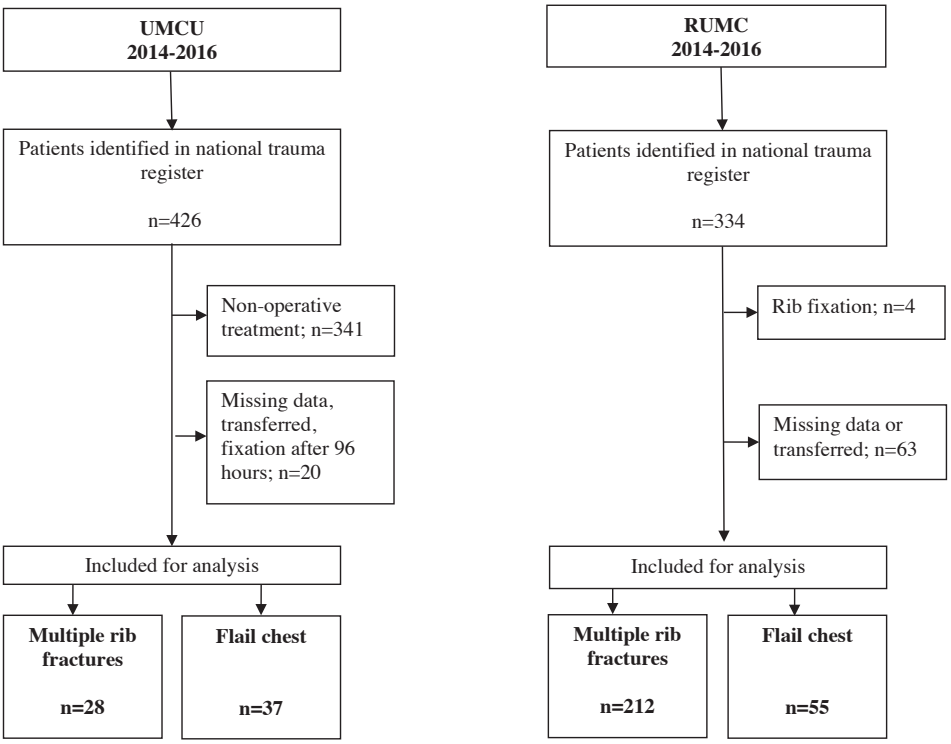

Figure 2. Flowchart showing inclusion of patients for analysis.

with multiple rib fractures was 4 (IQR 3-5). Four (6%) patients were treated with both plate osteosynthesis and intramedullary splints; two patients with flail chest and two with multiple rib fractures. Nine (14%) patients had a postoperative complication. Two patients had a persistent postoperative pneumothorax and were treated with a chest tube. Two patients developed pleural empyema requiring video assisted thoracoscopic surgery to evacuate the empyema. One patient had a postoperative tension pneumothorax and was treated with a chest tube. One patient had a hemothorax and required a thoracotomy to evacuate the hematoma. One patient had excess pleural fluid and was treated with a chest tube. One patient had a hematoma near the surgical incision and needed surgical debridement of the old hematoma. And one patient had a deep infection near the osteosynthesis material and was successfully treated with antibiotics.

After propensity score matching, for patients with a flail chest there was no association of rib fixation and ILOS (CI -13.9 – 8.5, p = 0.638) and the secondary outcome measures (Table 3).

Table 1. Baseline characteristics.

Variable	Multiple Rib Fractures					Flail Chest				
	Surgery (n=28)	Non-operative (n=212)	*P* value	SMD unmatched cohort	SMD matched cohort	Surgery (n=37)	Non-operative (n=55)	*P* value	SMD unmatched cohort	SMD matched cohort
Age (mean ± SD)	57 (13)	55 (18)	0.587	0.122	0.037	59 (13)	57 (17)	0.630	0.106	0.075
Male (n,%)	24 (86)	162 (76)	0.386	0.239	0.051	29 (78)	42 (76)	1.000	0.048	0.110
ASA-score (n,%)			0.363	0.270	0.040			0.195	0.452	0.029
1-2	26 (93)	179 (84)				37 (100)	50 (91)			
> 2	2 (7)	33 (16)				0 (0)	5 (9)			
Trauma mechanism (n,%)			0.661	0.181	0.081			0.439	0.273	0.175
Motor vehicle accident	8 (29)	74 (35)				14 (38)	14 (26)			
Fall from height / stairs	11 (39)	66 (31)				10 (27)	19 (35)			
Other	9 (32)	72 (34)				13 (35)	22 (40)			
ISS (mean ± SD)	21 (9.4)	21 (9.6)	0.933	0.017	0.077	25 (12)	30 (13)	0.054	0.418	0.050
TTSS (mean ± SD)	10 (3.6)	9.3 (2.9)	0.237	0.242	0.101	13.1 (3.1)	13 (2.9)	0.951	0.014	0.087
AIS (median, IQR)										
Head	0 (0 - 1)	1 (0 - 3)	**0.008**	0.576	0.088	0 (0 - 3)	3 (0.3 - 4)	**0.001**	0.722	0.050
Face	0 (0 - 0)	0 (0 - 0)	0.138	0.269	0.053	0 (0 - 1)	0 (0 - 0.5)	0.796	0.077	0.069
Thorax	3 (3 - 4)	3 (3 - 3)	**0.010**	0.567	0.017	3 (3 - 4)	4 (3 - 4)	0.149	0.301	0.102
Abdomen	2 (0 - 2)	0 (0 - 0)	**<0.001**	0.585	0.016	0 (0 - 2)	0 (0 - 0.5)	0.238	0.244	0.118
Extremities	1 (0 - 2.3)	2 (0 - 2)	0.770	0.079	0.040	2 (0 - 3)	2 (0 - 3)	0.442	0.164	0.097
No. of rib fractures (median, IQR)	7 (6 - 10.3)	6 (4 - 8)	**0.001**	0.643	0.096	10 (8 - 12)	9 (7 - 13)	0.405	0.049	0.059
Bilateral rib fractures (n,%)	10 (36)	69 (33)	0.904	0.067	0.041	14 (38)	25 (46)	0.610	0.155	0.037
Concomitant injuries (n,%)										
Pulmonary contusion	11 (39)	99 (47)	0.561	0.159	0.017	22 (60)	38 (69)	0.467	0.202	0.094
Pneumothorax	19 (68)	117 (55)	0.285	0.263	0.058	27 (73)	47 (86)	0.226	0.311	0.071
Hemothorax	3 (11)	37 (18)	0.529	0.195	0.059	9 (24)	22 (40)	0.182	0.340	0.041
Sternum fracture	5 (18)	24 (11)	0.491	0.186	0.071	5 (14)	9 (16)	0.938	0.080	0.053
Blood pH (mean ± SD)	7.34 (0.12)	7.32 (0.08)	0.308	0.173	0.046	7.33 (0.1)	7.27 (0.13)	0.034	0.475	0.036
Base excess (mean ± SD)	-2.4 (5.6)	-3.1 (3.5)	0.367	0.154	0.052	-2.6 (3.5)	-4.7 (6.2)	0.063	0.426	0.068

SMD standardized mean difference; ASA American Society of Anesthesiologists; ISS injury severity score; TTSS thoracic trauma severity score; AIS abbreviated injury score; SD standard deviation; IQR interquartile range

For patients with multiple rib fractures there was no association between rib fixation and HLOS (confidence interval [CI] -0.6 – 13.6, p = 0.074) and the secondary outcome measures (Table 4).

Table 2. Surgery-related characteristics and in-hospital complications.

Variable	Multiple rib fracture n=28	Flail chest n=37
Duration until rib fixation in days (median, IQR)	1 (1-2)	1 (1-2)
Duration of surgery in minutes (mean ± SD)	130 (83)	148 (64)
Number of surgically-fixated rib fractures (median, IQR)	4 (3-5)	5 (4-6)
Ratio surgically-fixated ribs and total number of rib fractures	0.54	0.50
In-hospital complications after surgical rib fixation (n,%)		
Pneumothorax	0 (0)	2 (5.4)
Tension pneumothorax	1 (3.6)	0 (0)
Pleural empyema	0 (0)	2 (5.4)
Excess pleural fluid	1 (3.6)	0 (0)
Infection of osteosynthesis material	1 (3.6)	0 (0)
Hematoma	0 (0)	1 (2.7)
Hemothorax	0 (0)	1 (2.7)

Table 3. Regression analysis assessing the influence of rib fixation for a flail chest after propensity score matching.

Continuous variables	Rib fixation for flail chest							
	Median (IQR)		δ	95% CI			SE	*P* value
	Surgery	Non-operative						
Duration of ICU stay in days	6 (0-13)	2 (0-8)	-2.7	-13.9	-	8.5	5.721	0.638
Duration of IMV in days	3 (0-9)	0 (0-7)	-2.3	-11.6	-	7.0	4.750	0.624
Duration of epidural analgesia in days	0 (0-3)	2 (0-7)	-1.2	-3.4	-	1.0	1.116	0.290
Duration of hospital stay in days	21 (11-31)	11 (8-18)	1.9	-14.3	-	18.0	8.240	0.820
	n (%)		OR	95% CI			SE	*P* value
Pneumonia	4.8 (23)	5.6 (20)	1.1	0.2	-	5.8	0.826	0.871
Tracheostomy	2.6 (12)	3.5 (13)	NA	NA	-	NA	NA	NA
In hospital mortality	2.2 (10)	3.3 (12)	NA	NA	-	NA	NA	NA

δ indicates the difference in mean outcome value between rib fixation and non-operative treatment; SE standard error; OR odds ratio
ICU intensive care unit; IMV invasive mechanical ventilation; CI confidence interval; IQR interquartile range; NA no answer

Table 4. Regression analysis assessing the influence of rib fixation for multiple rib fractures after propensity score matching.

Outcome variable	Rib fixation for multiple rib fractures							
	Median (IQR)		δ	95% CI			SE	*P* value
	Surgery	Non-operative						
Duration of ICU stay in days	0 (0-11)	1 (0-2)	1.6	-3.5	-	6.7	2.600	0.530
Duration of IMV in days	0 (0-9)	0 (0-1)	2.4	-2.8	-	7.6	2.637	0.365
Duration of epidural analgesia in days	0 (0-4)	0 (0-3)	-0.1	-1.9	-	1.7	0.917	0.939
Duration of hospital stay in days	12 (9-23)	10 (6-16)	6.5	-0.6	-	13.6	3.636	0.074
	n (%)		OR	95% CI			SE	*P* value
Pneumonia	7.4 (34)	5 (14)	3.2	0.8	-	13.9	0.743	0.114
Tracheostomy	1.7 (7.8)	0.7 (2)	NA	NA	-	NA	NA	NA
In-hospital mortality	0 (0)	3.3 (9.1)	NA	NA	-	NA	NA	NA

δ indicates the difference in mean outcome value between rib fixation and nonoperative treatment; SE standard error; OR odds ratio
ICU intensive care unit; IMV invasive mechanical ventilation; CI confidence interval; IQR interquartile range; NA no answer

Discussion

We compared rib fixation with nonoperative treatment for both flail chest and multiple rib fractures. This is the first study with a clearly defined indication for surgery, based on a clinical treatment algorithm. After propensity score matching, adjusting for all anticipated confounding variables, rib fixation for a flail chest was not associated with differences in ILOS or the other outcome measures. Neither did we find a difference in HLOS for rib fixation in patients with multiple rib fractures, nor for the other outcome measures.

In our study there was no association between rib fixation and the primary and secondary outcome measures as compared to nonoperative treatment for patients with a flail chest. Three RCTs have been published on this subject. The first was from Tanaka et al. who studied 37 patients (18 surgical, 19 non-operative) with a flail chest unable to wean from mechanical ventilation and performed surgery on average seven days after admission; they excluded patients with severe head trauma, spinal injury, and no development of respiratory failure (21). Granetzny et al. compared 40 patients (20 surgical, 20 non-operative) with a flail chest and performed surgery 24 to 36 hours after intensive care admission; they excluded patients with disturbed consciousness after head trauma, fractures of the upper three ribs, and severe associated trauma to other systems (22). Marasco et al. studied 46 patients (23 surgical, 23 non-operative) with a flail chest who were ventilator dependent

without prospect of successful weaning within 48 hours and performed surgery on average 4.6 days after admission; they excluded patients of 80 years old and older, spinal injury, open fractures, and a Glasgow Coma Scale of <10 at the scene or on admission (23). All three studies reported a significant decrease in DMV and ILOS. One possible explanation for these contrasting results as compared to our study might be the more restrictive inclusion criteria used in the aforementioned studies. In our study, all patients with multiple rib fractures or a flail chest were studied, including patients with head trauma or other severe injuries. Less strict inclusion criteria will result in a more diverse patient selection and will increase the generalizability of the results; however, it could also have diminished the effect of rib fixation in an already heterogeneous patient group.

Interestingly, the ILOS of both the surgical (median 6 days; mean 8.9 days) and non-operative group (median 3 days; mean 10.5 days) in our cohort were lower as compared to Tanaka et al. (surgical:16.5; non-operative: 26.8 days), Granetzny et al. (surgical: 9.6 and non-operative: 14.6 days), and Marasco et al. (surgical: 13.5 and non-operative: 18.7 days) (21-23). Also the DMV in our entire cohort was lower as compared to the published RCTs.

In the current literature, only one study compared rib fixation with non-operative treatment for patients with multiple rib fractures without a flail chest. In a retrospective study with 124 patients, Qiu et al. reported a significantly shorter HLOS after rib fixation for multiple rib fractures as compared to non-operative treatment (11.1 days vs 15.9 days; p=0.013) and also found lower pneumonia rates (4.6% vs 17%; p = 0.025) (11). Fitzgerald et al. performed a cohort study of patients 65 years old and older with more than one rib fracture, but did not report the number of patients with a flail chest (12). In that study, rib fixation resulted in a decrease in mortality and respiratory complications compared to non-operative treatment. Khandelwal et al. presented a study with 67 patients (38 surgical, 29 non-operative) with only two patients with a flail chest in the surgical group (24). They found a significant reduction in pain intensity and early return to work after rib fixation.

Few studies have reported on complication rates after rib fixation. Of the published trials only Granetzny et al. reported a complication rate of 35% including pneumonia and mortality (22). Other complications were empyema (5%), mediastinitis (10%), wound infection (10%), and chest wall deformity (5%). In another prospective study, Pieracci et al. reported an infection rate of 3% after rib fixation but did not report on other complications (25). In our study, nine (14%) of the surgically treated patients had a postoperative complication.

The results of this study should be interpreted considering several limitations. The retrospective design of the study might have affected the outcome measures due to the

effects of data loss and under reporting. Pain is the most important indication for rib fixation in our clinical based treatment algorithm. However, due to the retrospective design of this study, we were unable to compare pain scores and interventions for pain treatment. Therefore, we might have missed this potential beneficial effect of rib fixation. Instead, we used HLOS as a surrogate marker for treatment success, but this outcome measure might have been influenced by other factors such as intensive care treatment, ventilation modalities and logistic issues with patient transfer and could therefore have diminished differences in treatment effect. Additionally, there is still no good fracture classification to distinguish between fracture type and location. It is speculated that lateral and lower rib fractures are more painful due to increased mobility of the fracture parts. Fracture classification could influence success of rib fixation and this should be investigated in future studies.

Even though this study is one of the largest studies reporting on this subject, the number of included patients is still relatively small and was possibly too small to detect relatively small yet clinically meaningful differences. Furthermore, as part of the between-hospital comparison and due to clinical practice, there were differences in the baseline criteria between the surgical group and the non-operatively treated group. However, using a propensity score model, we were able to successfully match on all measured baseline characteristics eliminating possible confounding due to measured patient characteristics. As with any observational study, our results are potentially biased by unmeasured confounding (e.g. pain scores and fracture classification), be it that we believe we have included most confounders in our analysis and the potential impact of unmeasured confounding therefore seems limited.

The University Medical Center Utrecht was the first hospital in the Netherlands to perform rib fixation for patients with flail chest and multiple rib fractures. With more than seven years of experience, rib fixation has become an established procedure with a univocal clinical-based treatment algorithm, with its main focus on clinical signs of flail chest and pain. Nevertheless, no benefit could be demonstrated in this population with rib fractures who received early operative fixation in their clinical course. Therefore results of this study, combined with the limited existing evidence and the substantial costs of surgical treatment, emphasize the need for future studies before rib fixation is embedded or abandoned in clinical practice, but also to identify specific patient groups who would benefit from rib fixation. These studies should focus on optimization of the indication and describe long-term outcome after rib fixation.

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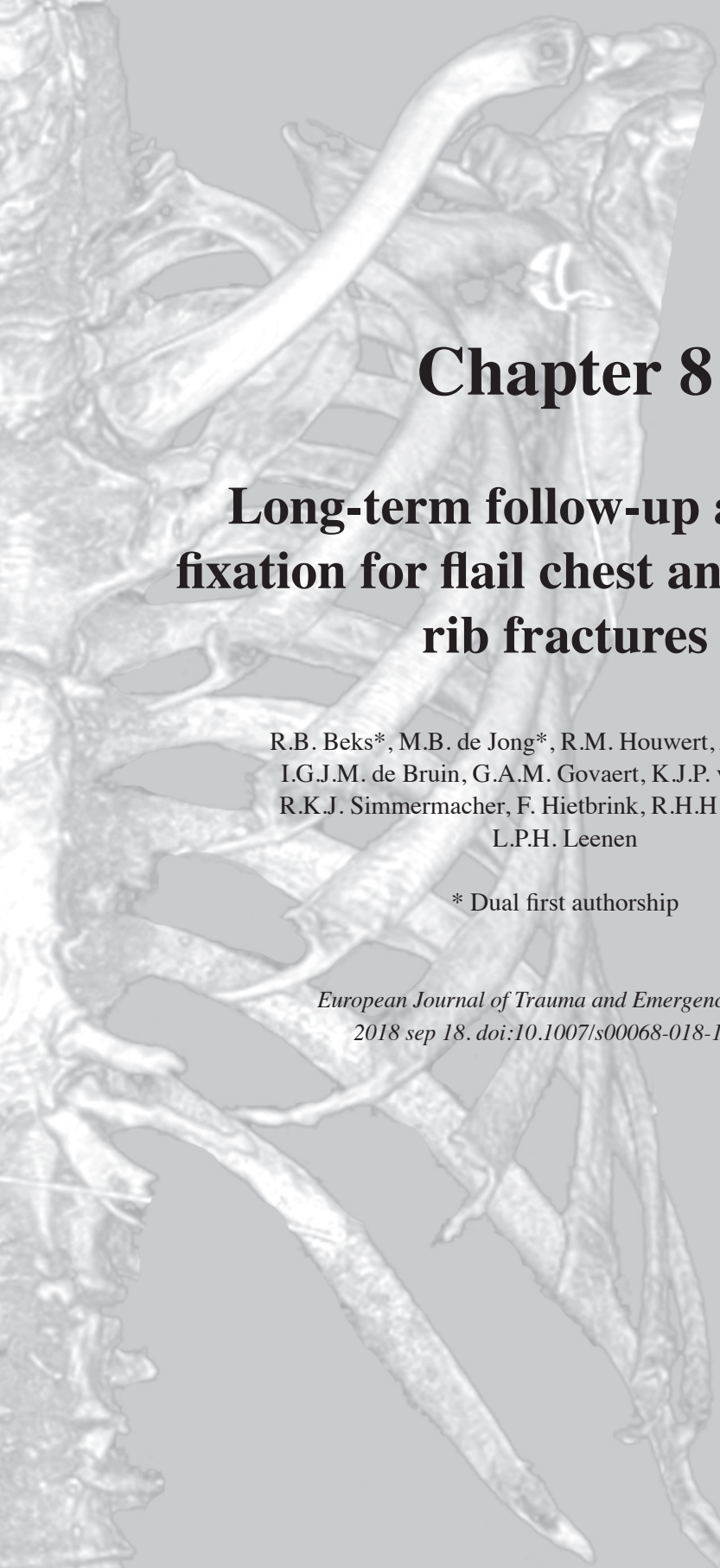

Chapter 8

Long-term follow-up after rib fixation for flail chest and multiple rib fractures

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Background

Chest trauma is currently the second leading cause of trauma-related death and multiple rib fractures are the most common injury in these patients (1). Due to the impact of pulmonary complications, flail chest and multiple rib fractures are still associated with a 10-22% mortality rate with increasing rates for every additional rib involved (2).

Conservative treatment for rib fractures is considered the gold standard and consists of mechanical ventilation (if indicated), pulmonary hygiene, and adequate pain management. In the last century, many different surgical techniques concerning rib fixation were described in literature without becoming common clinical practice. However, due to technical improvements there is a growing popularity of surgical rib fixation which aims to increase stability of the chest, lessen chest wall deformity, and improve pulmonary function (3).

In a recent meta-analysis the authors recommend rib fixation over conservative treatment for adult patients with flail chest in order to decrease mortality, shorten days on mechanical ventilation, hospital and intensive care length of stay, and decrease incidence of pneumonia and need for tracheostomy (3). Although rib fixation of patients with flail chest showed promising results, little is known about rib fixation for patients with multiple rib fractures without a flail chest. Furthermore, only few small studies have described the long-term outcome and quality of life after rib fixation (4-7). Therefore, the aim of this study was to describe the safety, long-term quality of life, and implant related irritation after rib fixation for flail chest or multiple rib fractures.

Methods

Study design and participants

All medical records of patients admitted with rib fractures following blunt thoracic trauma between January 2010 and December 2016 in the University Medical Center Utrecht, a level-1 trauma facility, were retrospectively reviewed. Eligible patients were identified using procedural codes and the Dutch National Trauma Registry. For this study, we included all adult patients with blunt thoracic trauma who underwent rib fixation for flail chest (defined as three or more consecutive ribs fractured in at least two places and clinical signs of paradoxical chest wall movement) or multiple rib fractures (defined as three or more unilateral rib fractures). We did not further distinguish between multiple rib fractures with or without chest deformity due to the retrospective nature of this study. Exclusion criteria were age below 18 years, fewer than three fractured ribs, no availability of an

admission CT scan of the chest, and transfer from or to another hospital. Our institutional review board approved a waiver of consent under protocol number 17-914/C.

Indication for surgery

The indication for surgical rib fixation followed from a clinical based algorithm considering several injury and patient specific characteristics as shown in Figure 1. There was a strict indication for patients with a clinical flail chest (paradoxical breathing). Failure of pain management with tachypnea and dyspnea was considered an indication for surgical rib fixation in patients with multiple rib fractures.

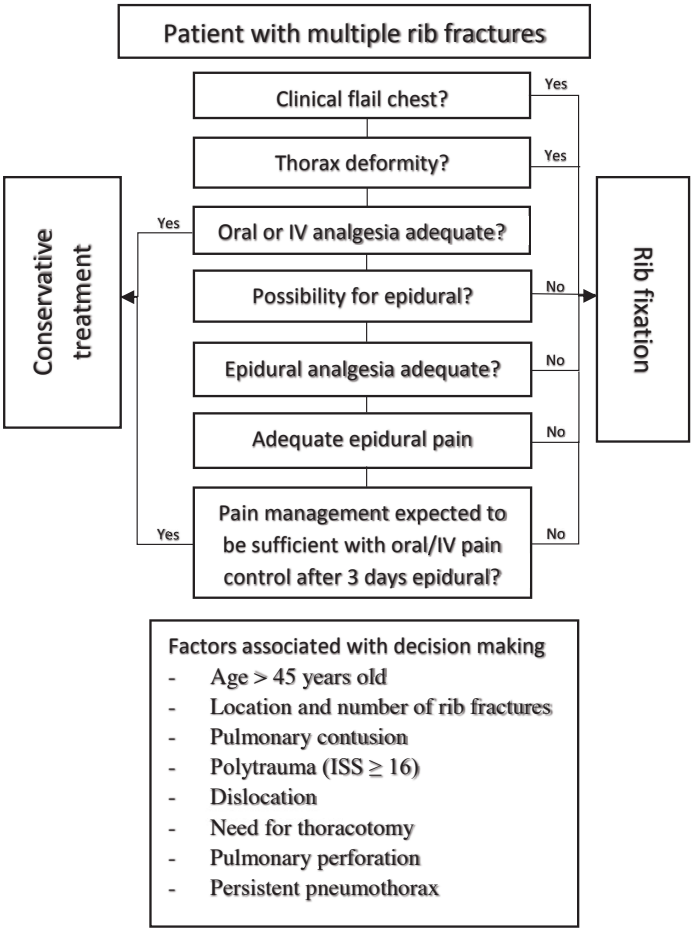

Figure 1. Clinical treatment algorithm for patients with rib fractures.

Patient characteristics at hospital admission

The following characteristics were obtained from medical records based on the recording at admission: age, sex, American Society of Anaesthesiologists (ASA) score, trauma mechanism, Abbreviated Injury Scale (AIS), ISS, Thoracic Trauma Severity Score (TTSS), number of rib fractures, bilateral rib fractures, involvement of the first rib as these are associated with higher impact trauma, rib fractures in the upper/middle/lower third or dorsal side of the thorax, displacement, concomitant injuries as described on the admission CT scan, and blood pH and base excess. The TTSS (range 0-25) is a scoring system that helps to predict thorax related complications after thoracic trauma and is based on number of rib fractures, pulmonary contusion, PaO2/FIO2 ratio, pleural involvement, and age (8). Displacement was defined as a shaft width displacement of the fracture parts in the transversal plane on CT. Dorsal fractures were defined as rib fractures behind the dorsal axillary line.

Surgical procedure and characteristics

All procedures were performed or supervised by senior trauma surgeons experienced with surgical treatment of rib fractures. Preoperative planning of the procedure was done using chest computed tomography (CT) with 3D reconstructions. Preoperative antibiotic prophylaxis (2 grams of Cefazolin) was administered intravenously in all patients. Depending on the site of the fractures, patients were positioned in the supine, lateral or prone position. The surgical approach was performed as described by Taylor (9). After reduction, internal fixation using the MatrixRIB™ system (Depuy Synthes®, Amersfoort, The Netherlands) was performed. Fixation was preferably done with 3 bicortical screws on each side of the fracture. If plate fixation was not possible due to anatomical boundaries and rib fixation was deemed necessary, splints were used. The number of fixed ribs was at the discretion of the surgeon, and depended on anatomical boundaries and the possibility to regain stability of the chest wall during respiration. Tube thoracostomy was performed in case of pneumothorax or hemothorax at initial presentation or clinical suspicion of pneumothorax during surgery. Postoperative chest radiography was performed in all patients to document surgical result and to rule out early complications. Patients were encouraged to mobilize as soon as possible with the help of physiotherapy and aggressive pain management. All patients had an outpatient department visit six weeks after discharge and were counselled to visit if they experienced any thorax related problems like pain, dyspnoe or irritation.

The following surgery related characteristics regarding rib fixation were extracted from the medical record: time until surgery, duration of surgery, surgical approach, number of ribs fixated, the ratio of fixated ribs to fractured ribs, side of rib fixation, and fixation of dorsal rib fractures.

Short and long-term outcome measures

Short-term outcome measures were hospital length of stay (HLOS), ICU-LOS, duration of invasive mechanical ventilation (IMV), need for tracheostomy, and incidence of surgical complications after rib fixation (e.g. pneumonia, implant related infection, wound infection, and acute respiratory distress syndrome [ARDS]). Pneumonia was defined as having clinical signs (fever, coughing, desaturation) requiring antibiotic treatment, with or without positive cultures. Implant related infection was defined as clinical symptoms (e.g., redness, drainage from surgical wound, fever, pain, elevated CRP, or leukocytes) requiring incision and drainage and intravenous antibiotics following a previously published protocol (10). ARDS was defined by severe hypoxemia with a PaO2/FIO2 smaller than 100mm Hg.

Long-term outcome measures were quality of life, number of implant removals due to complications of patient complaints, and level of dyspnea. To assess the long-term outcome measures after rib fixation, patients were contacted by phone after a minimum of 12 months of follow-up. The patient's contact person and general practitioner were approached for additional contact details if patients could not be reached after a minimum of five phone call attempts.

Quality of life was assessed with the EQ-5D-5L, which is a standardized instrument for generic health status measurement (11). The EQ-5D-index ranges from -0.33 to 1.00 where higher scores indicate better quality of life. 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 Scale (mMRC) which is a five-category scale that characterizes the level of dyspnea with physical activity where higher scores corresponds with more dyspnea (12). Patients who had implant removal were asked for the reason of removal following the algorithm and definitions as described by Hulsmans et al. (13). Implant removal due to irritation was considered a minimum of six months after rib fixation and after discussing the possible harms and benefits with the patient. Apart from the well-known pitfalls after implant removal in general, the most important pitfall of rib implant removal is the risk of a pneumothorax. Therefore standard chest tube placement should be considered after this procedure. Implant related irritation at the time of the interview was defined as physical complaints which could be attributed to the implant.

Statistical analysis

All analyses were performed separately for the groups of patients with flail chest and the group of patients with multiple rib fractures. Baseline characteristics were presented as median and interquartile range (IQR) for continuous variables, and absolute numbers

with percentage for categorical variables. The non-parametric outcome measures were normalized with a cubic transformation for left skewed data and a log transformation for HLOS and ICU-LOS. In bivariate analysis, the association of the HLOS, ICU-LOS, and EQ-5D-index with the baseline characteristics was assessed using linear regression. Variables with a p value of below .05 in this analysis were entered into a multivariable linear regression model to assess their ability to explain the variation in in HLOS, ICU-LOS, and quality of life. Given the small dataset with the high number of potential variables a robustness check of the primary multivariable regression model was performed by means of the least shrinkage and selection operator (LASSO) technique (14). LASSO performs automatic variable selection by shrinking coefficients and giving a penalty for the number of variables in the model. LASSO is considered a robust and objective alternative for the more regularly performed step wise variable selection for multivariable regression. The two statistical models were compared in terms of the variables that showed a relation with the outcome of interest. All analyses were performed with Stata 13 (StataCorp LP, College Station, TX, USA); a p value of less than .05 was considered significant.

Results

Between 2010 and 2016, in our hospital, a total of 864 patients were admitted with chest trauma resulting in three or more rib fractures. Ultimately, 166 patients (19%) who underwent rib fixation were included for analysis; 67 with flail chest and 99 with multiple rib fractures (Figure 2). Of these, 137 (83%) were treated with plate osteosynthesis, 29 (17%) with a combination of plate osteosynthesis and intramedullary splints, and one only with intramedullary splints. Outcome information, at a minimum of twelve months after rib fixation, was obtained from 103 patients (62%); 40 with flail chest and 63 with multiple rib fractures.

Flail chest

The median age of patients with flail chest was 57 (IQR 48-69) years and the majority were male (n=52, 78%) (Table 1). The median ISS was 24 (IQR 18-34) and the median number of fractured ribs was 10 (IQR 8-12). Rib fixation was performed after a median of two (IQR 1-3) days and the ratio of fixated ribs to fractured ribs was 0.49 (Table 2).

Among patients with flail chest, the most common complication was pneumonia (n=26, 39%) followed by excess pleural fluid (n=3, 5%) and implant related infection (n=2, 3%) (Table 3). One patient had a tension pneumothorax perioperatively and required a chest tube. Six (9%) patients died during hospital admission; all were because of concomitant

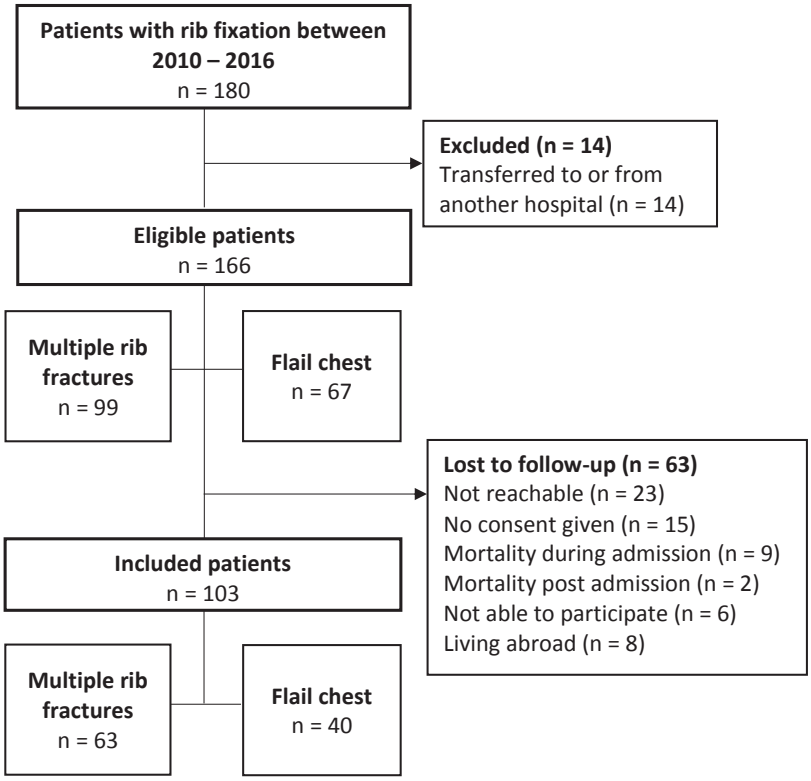

Figure 2. Flowchart of patient inclusion.

injuries that were not related to the rib fractures. Two patients had an infaust neurological prognosis, one patients died of cardiac failure, one patient developed secondary bacterial meningitis, and one patient with metastasized carcinoma and IC acquired weakness wished no further treatment.

The median HLOS was 19 (11-26) days and 44 (66%) patients required ICU admission with a median ICU-LOS 8 (6-14) days (Table 4). The median follow-up duration was 3.1 years (IQR 2.4-5.1; range 1-7.5) and 40 (60%) patients were available for follow-up. The median quality of life as measured with the EQ-5D index at follow-up was 0.85 (IQR 0.62-1) with an EQ-VAS of 75 (IQR 63-85). Figure 3 shows the proportion of patients reporting problems specified per EQ-5D domain. Twenty-one (53%) patients reported implant related irritation. Five (13%) patients had their implant removed due to irritation on average 1.1 (range 0.64-1.6) years after rib fixation.

Table 1. Baseline characteristics of patient with rib fixation for flail chest or multiple rib fractures.

Variable	Flail chest n = 67	Multiple rib fractures n = 99
Age (median, IQR)	57 (48 - 69)	56 (47 - 64)
Male (n,%)	52 (78)	81 (82)
ASA-score (n,%)		
1-2	57 (92)	82 (84)
> 2	5 (8)	16 (16)
Trauma mechanism (n,%)		
Motor vehicle accident	25 (37)	33 (33)
Fall from height / stairs	17 (25)	29 (29)
Other	25 (37)	37 (37)
AIS (median, IQR)		
Head	0 (0 - 3)	0 (0 - 2)
Face	0 (0 - 0)	0 (0 - 0)
Thorax	4 (3 - 4)	4 (3 - 4)
Abdomen	0 (0 - 2)	0 (0 - 2)
Extremities	2 (0 - 3)	2 (0 - 2)
ISS (median, IQR)	24 (18 - 34)	21 (16 - 29)
TTSS (median, IQR)	13 (11 - 15)	10 (8 - 12)
No. of rib fractures (median, IQR)	10 (8 - 12)	7 (6 - 10)
Bilateral rib fractures (n,%)	26 (39)	34 (34)
First rib fracture (n,%)		
Unilateral	18 (27)	16 (16)
Bilateral	7 (10)	11 (11)
Location rib fracture (n,%)		
Costae 1 - 4	62 (93)	84 (85)
Costae 5 - 8	67 (100)	99 (100)
Costae 9 - 12	46 (69)	60 (61)
Displacement (n,%)	47 (70)	58 (59)
Dorsal fracture (n,%)	59 (88)	67 (68)
Concomitant injuries (n,%)		
Pulmonary contusion	44 (66)	43 (43)
Pneumothorax	50 (75)	66 (67)
Hemothorax	16 (24)	21 (21)
Sternum fracture	7 (10)	16 (16.2)
Blood pH (median, IQR)	7.3 (7.28 - 7.4)	7.4 (7.3 - 7.4)
Base Excess (median, IQR)	-2 (-5 - -1)	-1 (-3.5 - 0.7)

ASA American Society of Anesthesiologists; ISS injury severity score; TTSS Thoracic trauma severity score; AIS abbreviated injury score; IQR interquartile range

Table 2. Surgery related characteristics.

Variable	Flail chest n = 67	Multiple rib fractures n = 99
Time until surgery (days, median, IQR)	2 (1 - 3)	2 (1 - 4)
Duration of surgery (minutes, median, IQR)	130 (91 - 155)	98 (71 - 122)
Surgical approach (n,%)		
Anterior	9 (13)	12 (12)
Anterolateral	9 (13)	17 (17)
Posterior	10 (15)	19 (19)
Posterolateral	32 (48)	39 (39)
Combination	7 (10)	12 (12)
No. of ribs fixated (median, IQR)	4 (4 - 6)	4 (3 - 5)
No. of ribs fixated / total ribs fractured (median, IQR)	0.5 (0.36 - 0.6)	0.5 (0.38 - 0.67)
Side of rib fixation (n,%)		
Left	34 (51)	45 (46)
Right	26 (39)	46 (47)
Bilateral	7 (10)	8 (8)
Fixation of dorsal fractures (n,%)	35 (52)	36 (36)

IQR interquartile range; ICU Intensive care unit; IMV invasive mechanical ventilation

Table 3. In hospital complications after rib fixation.

In hospital complications	Flail chest (n,%) n = 46	Multiple rib fractures (n,%) n = 50
Pneumonia	26 (39)	32 (32)
Excess pleural fluid	3 (4.5)	3 (3)
Implant related infection	2 (3)	3 (3)
Hemothorax	2 (3)	2 (2)
Pneumothorax	2 (3)	2 (2)
Tension pneumothorax	1 (1)	2 (2)
ARDS	1 (1.5)	0 (0)
Postoperative bleeding	1 (1.5)	1 (1)
Wound infection	1 (1.5)	0 (0)
Pleural empyema	1 (1.5)	0 (0)
Hematoma	0 (0)	1 (1)
Revision of dislocated splints	0 (0)	1 (1)
In hospital mortality	6 (9)	3 (3)

ARDS acute respiratory distress syndrome

Table 4. Outcome measures after rib fixation for flail chest or multiple rib fractures.

	Flail chest	Multiple rib fractures
Short-term outcome measures	**n = 67**	**n = 99**
HLOS (days, median, IQR)	19 (11 - 26)	14 (10 - 28)
ICU admission (n,%)	44 (66)	44 (44)
ICU-LOS among those admitted to ICU (days, median, IQR)	8 (6 - 14)	9 (2 - 16)
Number of patient with IMV (n,%)	40 (60)	35 (35)
Duration of IMV among those ventilated (days, median, IQR)	6 (4 - 12)	9 (4 - 16)
Tracheostomy (n,%)	7 (10)	9 (9)
Long-term outcome measures	**n = 40**	**n = 63**
EQ-5D index (median, IQR)	0.85 (0.62 - 1)	0.79 (0.62 - 0.91)
EQ VAS (median, IQR)	75 (63 - 85)	73 (65 - 80)
Implant related irritation (n,%)	21 (53)	28 (44)
Implant removed (n,%)	5 (13)	4 (6)
Reason removed (n,%)		
Attributable to implant-related irritation	5 (13)	4 (6)
Patient's wish or surgeon's preference	0 (0)	0 (0)
Status not removed (n,%)		
No irritation	19 (47)	35 (56)
Experiencing irritation, but implant removal not necessary	12 (30)	11 (18)
Experiencing irritation, but no request for removal owing to fear of reoperation	1 (3)	2 (3)
Experiencing irritation, considering removal	3 (8)	10 (16)
Revision implant (n,%)	1 (3)	1 (2)
mMRC (n,%)		
0	17 (43)	31 (49)
1	12 (30)	23 (37)
2	6 (15)	5 (8)
3	4 (10)	3 (5)
4	1 (3)	1 (2)
Follow-up duration in years (median, IQR)	3.1 (2.4 - 5.1)	4.4 (3.4 - 5.9)
Follow-up range duration in years (min, max)	1 - 7.5	1 - 7.6

HLOS hospital length of stay; ICU-LOS intensive care unit length of stay; IQR interquartile range; IMV invasive mechanical ventilation; mMRC modified Medical Research Council

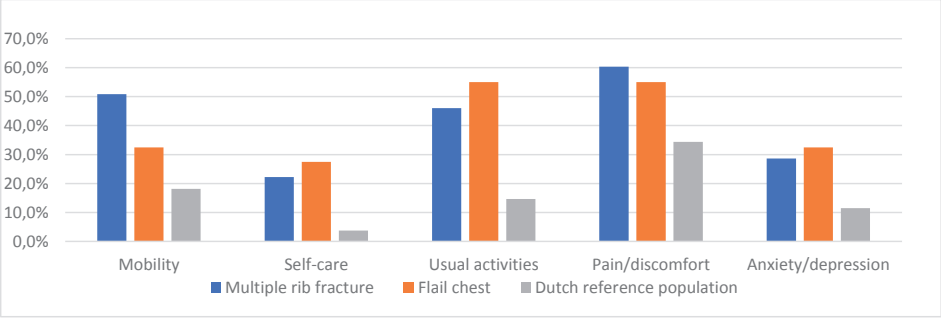

Figure 3. EQ-5D-5L reported problems per domain.

Patients reporting implant related irritation at the time of the interview had a significant lower median EQ-5D index compared to patients without implant related irritation (z = 2.97; p = 0.003). Eleven patients (28%) reported mild to severe complaints of dyspnea.

The association between each patient characteristic and the outcomes are presented in Appendix 1. In multivariable linear regression, male sex and sternum fracture appeared to be independently associated with the EQ-5D index (Appendix 2). We did not observe an association with HLOS. A higher AIS-head appeared to be associated with ICU-LOS. The associations found in the three multivariable models were also found when applying LASSO, indicating robustness of the models.

Multiple rib fractures

The median age of the 99 patients with multiple rib fractures was 56 (IQR 47-64) years and the majority were male (n=82, 82%) (Table 1). The median ISS was 21 (IQR 16-29) and the median number of fractured ribs was 7 (IQR 6-10). Surgery was performed after a median of two (IQR 1-4) days and the ratio of fixated ribs to fractured ribs was 0.52 (Table 2).

Among patients operated on multiple rib fractures, pneumonia was the most common complication (n=32, 32%) followed by excess pleural fluid (n=3, 3%) and implant related infection (n=3, 3%) (Table 3). Two (2%) patients suffered a tension pneumothorax postoperatively and were successfully treated with a chest tube. One (1%) patient needed revision surgery due to two dislocated intramedullary splints resulting in a hemothorax. Three (3%) patients died during hospital admission; one because of respiratory failure possibly associated with the suffered rib fractures and the other two as a result of concomitant injuries not related to the thorax. One had unmanageable infectious episodes from unknown origin and did not want further treatment. One patient had a systemic inflammatory response with decompensated liver cirrhosis, kidney failure, and developed

acute respiratory distress syndrome (ARDS).

The median HLOS was 14 (IQR 10-28) days and 44 patients (44%) required ICU admission with a median ICU-LOS of 9 (IQR 2-16) days (Table 4). The median follow-up was 4.4 years (IQR 3.4-5.9; range 1-7.6) and 63 patients (63%) were available for follow-up. The median quality of life as measured with the EQ-5D index at follow-up was 0.79 (IQR 0.62-0.91) with an EQ-VAS of 73 (IQR 65-80). Figure 3 shows the proportion of patients reporting problems specified per EQ-5D domain. After rib fixation for multiple rib fractures, 28 (44%) of the patients experienced implant related irritation. Four patients (6.3%) had their implant removed due to irritation on average 1.8 (range 0.91-4.2) years after rib fixation. Patients reporting implant related irritation at the time of the interview had a significant lower median EQ-5D index compared to patients without implant related irritation ($z = 3.30$; $p = 0.001$). Nine patients (14%) reported mild to serious complaints of dyspnea.

The association between each patient characteristic and the outcomes are presented in Appendix 3. In multivariable regression, we did not observe an association of the EQ-5D index and the baseline characteristics (Appendix 4). A higher AIS-head, AIS-extremities, and AIS-abdomen appeared to be associated with HLOS. A higher AIS-face, AIS-extremities, and base excess appeared to be associated with ICU-LOS. The associations found in the three multivariable models were also found when applying LASSO.

Discussion

In this cohort study of 166 patients admitted to a Dutch level-1 trauma facility the reported quality of life was relatively good after rib fixation for flail chest or multiple rib fractures at a median follow-up of 3.1 and 4.4 years, respectively. A mortality rate of 5% was demonstrated in this cohort. Approximately half of the patients experienced implant related irritation after rib fixation and about 10 percent had the implant material, or part of it, removed due to this irritation. At follow up 15-18% of the patients reported mild tot serious complaints of dyspnea as measured with the mMRC.

In our cohort, the mortality rate for patients with flail chest was 9% and for multiple rib fractures 3%; only one death could be directly ascribed as the consequence of the suffered rib fractures. There were three important surgery related complications resulting in a tension pneumothorax; all were successfully treated with a chest tube. The low mortality rate as well as the low number of surgical complications indicate the relative safety of this

procedure in this patient cohort. The most frequent complication was pneumonia in 39% of the patients with flail chest and 32% of the patients with multiple rib fractures and is comparable with the existing literature. However, definitions used for pneumonia differ in literature making this outcome measure difficult to compare across studies. The incidence of ARDS was 3% in both groups and was low compared to an ARDS incidence of 13% in a previously published cohort of poly trauma patients, predominantly chest trauma, from our hospital (15). This low rate of ARDS in our cohort could be attributed to the effects of rib fixation. The rate of implant related infection was 3% in our cohort and was similar to the infection rate reported by Pieracci et al in a similar but smaller cohort (16).

The duration of mechanical ventilation and ICU-LOS among patients admitted to the ICU in our cohort were comparable or shorter than the three RCTs available on this subject (17-19). Another interesting finding in our study was that injury severity, as defined by the abbreviated injury scale, in other body regions such as head, face, abdomen, and extremities were associated with a longer HLOS and / or ICU-LOS, while no association was seen with injury severity of the thorax. One explanation could be that rib fixation successfully minimized the impact of chest injury on the outcome measures. ICU-LOS and HLOS are frequently used to measure the success of rib fixation and it should be kept in mind that a small but potential beneficial effect could be masked by associated injury when comparing different treatment strategies for rib fractures. This emphasizes the necessity of sufficient group sizes when comparing treatment strategies in these often heterogeneous group of patients; nonetheless, there is a lack of large patient series in the current literature.

The quality of life in our study, a EQ-5D index of 0.85 for patients with flail chest and 0.79 for patients with multiple rib fractures, is comparable to the Dutch reference population index of 0.87 (20) and compared to studies describing different polytrauma cohorts these results were good (21-24). There was no difference in quality of life between patients with flail chest and patients with multiple rib fractures as both indices were within the range of the minimal clinically important difference for the EQ-5D (the minimal score difference detectable by the patient(25, 26) Although, one might expect a worse outcome for flail chest patients compared to patients with multiple rib fractures, in this cohort patients with multiple rib fractures had similar injury severity scores which might explain comparability. Caragounis et al presented comparable results after one year follow-up of 45 patients with rib fixation for flail chest and multiple rib fractures with an EQ-5D index of 0.93 (27). Similar results were reported by Mayberry et al in a cohort of fifteen patients after rib fixation (4). In another study, Campbell et al. reported on quality of life of 20 patients more than one year after rib fixation and showed a lower quality of life as compared to

the reference population possibly due to the higher ISS scores in this patients cohort (6). There was a high number of reported problems per domain ranging from 22 - 60%, with the most substantial limitation experienced in the domain of pain and discomfort. It cannot be extracted from the EQ-5D-5L if the pain is situated in the chest area. Farquhar et al. reported the EQ-5D-5L of 11 patients with rib fixation for flail chest at an unspecified long-term follow-up, and reported a slightly higher number of problems per domain as compared to our results, but also found the highest rate of problems in the domain of pain and discomfort (28). Although residual pain and chest stiffness are commonly reported in the literature, patient satisfaction is high after rib fixation at long-term follow-up (5,6,29).

Implant removal after rib fixation is a challenging and time consuming procedure. Due to the angular stable system and soft Titanium, we encountered several technical problems during implant removal. In one case a grinding machine was used to remove plate and screwheads leaving the body of the screws in place. In other cases a diamond drill was used to remove the screwhead from the plate also leaving the screw body behind. Because implant removal is challenging, perforation of the pleura happens easily. Therefore a chest tube should be considered after implant removal.

Two of the three clinical trials in this field performed rib fixation on patients with flail chest who were ventilator dependent without prospect of successful weaning. All three studies had different strict exclusion criteria such as severe injuries to other body systems, head trauma, or patients who did not development acute respiratory failure (17-19). Because of the heterogeneity in the aforementioned clinical trials, no clear indication for rib fixation has been defined. Also, very few studies have enrolled any substantial number of patients with multiple rib fractures without flail chest making the indication for these patients unknown. We made use of a clinical treatment algorithm (Figure 1) based on previous literature and experience in our hospital, which provides guidance in decision making for both patients with flail chest and patients with multiple rib fractures.

In addition to the right indication, timing of the procedure is of major importance. The main reason for rib fixation is to stabilize the thorax to increase pulmonary mechanics and reduce pain. In a recent published study, Pieracci et al. concluded that early surgical stabilization was indeed associated with favorable outcome (30). Additionally, they found that late surgical stabilization resulted in a significantly longer operating time for the same type of rib fracture. They hypothesized that this could be ascribed to tissue inflammation resulting in obscured planes and increased bleeding. Therefore, in our hospital, rib fixation is performed according to the treatment algorithm but preferably as early as possible after hospital admission.

The results should be interpreted in the light of several limitations. First, the EQ-5D-5L and mMRC are subjective questionnaires and assess general health and not specifically thorax-related problems. The vast majority of the patients described in this cohort were polytrauma patients, therefore, concomitant injuries but also comorbidities could have influenced the outcome. Second, due to the retrospective nature, this study could be subject to data loss and underreporting of complications. Consequently, no data was available on quality of life of patients before implant removal to objectify any improvement, although no differences were observed after implant removal compared with the rest of the patients. Third, follow-up differed per patient and ranged from 1-7.5 years. We assumed that for the majority of patients quality of life will improve most significantly in the first year after trauma and to a lesser extent thereafter, which is supported by our finding that there was no association between follow-up duration and quality of life (Spearman's rho 0.14; $p = 0.164$). Fourth, rib fixation was performed following the incision of a thoracotomy in the earlier years which gradually changed to a more minimal invasive approach in the following years. Nonetheless, there was no correlation between year of surgery and the outcome measures. Finally, the Dutch reference values for the EQ-5D were obtained from the three category EQ-5D version whereas our results were measured using the newer five category version. The additional answer categories provide the possibility for the patient to report milder problems which could have resulted in a higher percentage of reported problems as compared to the available Dutch reference population.

This is the largest study to present the long-term follow-up of patients after rib fixation following a clear clinical treatment algorithm. We show that rib fixation is a save treatment option for both patients with flail chest and patients with multiple rib fractures and that patients report a relatively good quality of life at long-term follow-up as compared to the Dutch reference population. Patients should be counseled that after rib fixation approximately half of the patients will experience implant related irritation and about 1 in 10 patients requires implant material removal due to this irritation. Future studies should focus on further development of the indication for rib fixation and should aim to identify the patient who will benefit most from rib fixation.

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Appendix 1. Bivariate analysis of the baseline characteristics and the outcome measures of patients with flail chest.

Variable	EQ-5D index			HLOS			ICU length of stay		
	coefficient	se	p	coefficient	se	p	coefficient	se	p
Age	0.000	0.001	0.837	0.002	0.006	0.705	0.018	0.010	0.085
Male	0.080	0.033	***0.019***	-0.130	0.206	0.530	0.200	0.366	0.586
ASA-score	0.044	0.090	0.625	0.716	0.312	***0.025***	1.400	0.557	***0.015***
Trauma mechanism	-0.017	0.017	0.332	-0.141	0.098	0.156	-0.102	0.177	0.566
AIS									
Head	-0.007	0.012	0.542	0.088	0.056	0.121	0.275	0.096	***0.005***
Face	0.020	0.017	0.257	0.080	0.109	0.465	0.055	0.195	0.780
Thorax	-0.010	0.021	0.640	0.070	0.115	0.544	0.319	0.200	0.116
Abdomen	0.000	0.011	0.987	0.084	0.065	0.200	0.209	0.114	0.072
Extremities	-0.013	0.011	0.227	0.187	0.061	***0.003***	0.493	0.099	***0.000***
ISS	-0.002	0.001	0.232	0.019	0.007	***0.013***	0.057	0.012	***0.000***
TTSS	-0.005	0.007	0.504	0.022	0.033	0.498	0.193	0.051	***0.000***
No. of rib fractures	-0.002	0.004	0.610	0.059	0.021	***0.007***	0.089	0.038	***0.024***
Bilateral rib fractures	-0.047	0.030	0.121	0.509	0.165	***0.003***	0.678	0.302	***0.028***
First rib fracture	0.005	0.021	0.807	0.260	0.126	***0.043***	0.232	0.227	0.312
Location rib fracture									
Costae 1 - 4	-0.023	0.058	0.693	0.669	0.323	***0.042***	-0.136	0.585	0.817
Costae 5 - 8	NA	NA	NA	NA	NA	NA	NA	NA	NA
Costae 9 - 12	0.011	0.031	0.718	-0.025	0.190	0.897	0.501	0.328	0.132
Displacement	-0.056	0.030	0.071	0.091	0.192	0.636	0.173	0.337	0.610
Dorsal fracture	0.005	0.046	0.920	-0.287	0.268	0.288	-0.374	0.473	0.431
Concomitant injuries									
Lung contusion	-0.009	0.032	0.769	0.329	0.177	0.067	0.487	0.317	0.129
Pneumothorax	-0.030	0.036	0.414	0.068	0.198	0.732	-0.010	0.352	0.977
Hemothorax	0.018	0.034	0.593	-0.149	0.201	0.461	-0.228	0.358	0.526
Sternum fracture	-0.103	0.048	***0.038***	0.472	0.276	0.091	1.255	0.475	***0.010***
Blood pH	0.025	0.142	0.863	-2.167	0.836	***0.012***	-4.863	1.412	***0.001***
Base Excess	0.001	0.004	0.904	-0.083	0.024	***0.001***	-0.174	0.041	***0.000***

Appendix 2. Bivariate analysis of the baseline characteristics and the outcome measures of patients with multiple rib fractures.

Variable	EQ-5D index			HLOS			ICU length of stay		
	coefficient	se	p	coefficient	se	p	coefficient	se	p
Age	0.000	0.001	0.767	0.004	0.005	0.414	0.005	0.009	0.600
Male	-0.016	0.044	0.713	-0.301	0.181	0.100	-0.288	0.322	0.373
ASA-score	-0.016	0.049	0.736	0.078	0.191	0.683	0.127	0.334	0.705
Trauma mechanism	0.012	0.018	0.513	-0.094	0.084	0.265	-0.070	0.148	0.639
AIS									
Head	0.008	0.013	0.545	0.220	0.043	***0.000***	0.340	0.077	***0.000***
Face	0.015	0.024	0.516	0.232	0.090	***0.012***	0.522	0.155	***0.001***
Thorax	0.020	0.021	0.362	0.091	0.104	0.382	0.014	0.183	0.941
Abdomen	-0.008	0.011	0.492	0.187	0.048	***0.000***	0.315	0.085	***0.000***
Extremities	0.007	0.013	0.602	0.259	0.049	***0.000***	0.368	0.091	***0.000***
ISS	0.001	0.002	0.488	0.037	0.006	***0.000***	0.056	0.010	***0.000***
TTSS	0.006	0.006	0.308	0.059	0.025	***0.019***	0.122	0.042	***0.005***
No. of rib fractures	-0.001	0.005	0.847	0.047	0.023	***0.042***	0.088	0.040	***0.028***
Bilateral rib fractures	-0.025	0.031	0.424	0.376	0.144	***0.011***	0.627	0.254	***0.015***
First rib fracture	0.005	0.021	0.809	0.111	0.106	0.297	0.252	0.185	0.177
Location rib fracture									
Costae 1 - 4	-0.038	0.042	0.370	0.065	0.205	0.752	-0.273	0.359	0.449
Costae 5 - 8	NA	NA	NA	NA	NA	NA	NA	NA	NA
Costae 9 - 12	-0.026	0.032	0.421	0.171	0.151	0.260	0.164	0.266	0.540
Displacement	-0.007	0.031	0.812	0.119	0.147	0.421	0.397	0.256	0.124
Dorsal fracture	-0.008	0.032	0.802	0.082	0.156	0.603	0.083	0.275	0.765
Concomitant injuries									
Lung contusion	0.009	0.032	0.786	0.255	0.141	0.073	0.547	0.245	***0.028***
Pneumothorax	0.016	0.032	0.619	0.233	0.148	0.121	0.197	0.263	0.456
Hemothorax	0.006	0.038	0.868	0.095	0.173	0.586	0.150	0.304	0.623
Sternum fracture	-0.043	0.040	0.289	-0.054	0.192	0.779	-0.139	0.338	0.682
Blood pH	-0.212	0.208	0.314	-2.102	0.700	***0.003***	-5.739	1.138	***0.000***
Base Excess	-0.003	0.005	0.508	-0.055	0.016	***0.001***	-0.139	0.026	***0.000***

Chapter 9

Surgical treatment of rib fracture nonunion: A single center experience

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Abstract

Introduction: In contrast to the emerging evidence on the operative treatment of flail chest, there is a paucity of literature on the surgical treatment of rib fracture nonunion. The purpose of this study was to describe our standardized approach and report the outcome (e.g. patient satisfaction, pain and complications) after surgical treatment of a rib fracture nonunion.

Methods: A single centre retrospective cohort study was performed at a level 1 trauma center. Symptomatic rib nonunion was defined as a severe persistent localized pain associated with the nonunion of one or more rib fractures on a chest CT scan at least 3 months after the initial trauma. Patients after initial operative treatment of rib fractures were excluded.

Results: Nineteen patients (11 men, 8 women), with symptomatic nonunions were included. Fourteen patients were referred from other hospitals and 8 patients received treatment from a pain medicine specialist. The mean follow-up was 36 months. No in-hospital complications were observed. In 2 patients, new fractures next to the implant, without new trauma were observed. Furthermore 3 patients requested implant removal with a persistent nonunion in one patient. There was a mean follow-up of 36 months, the majority of patients (n=13) were satisfied with the results of their surgical treatment and all patients experienced a reduction in the number of complaints. Persistent pain was a common complaint. Three patients reporting severe pain used opioid analgesics on a daily or weekly basis. Only 1 patient needed ongoing treatment by a pain medicine specialist.

Conclusion: Surgical fixation of symptomatic rib nonunion is a safe and feasible procedure, with a low perioperative complication rate, and might be beneficial in selected symptomatic patients in the future. In our study, although the majority of patients were satisfied and the pain level subjectively decreases, complaints of persistent pain were common.

Introduction

Rib fractures are common injuries, present in 10% of all trauma patients and in over 35% of patients after thoracic trauma (1). The incidence of rib fractures is underestimated because up to 54% of rib fractures are missed on routine chest radiographs (2). Although disabling and painful, the vast majority of fractured ribs will heal spontaneously without intervention. An unknown and presumably small percentage of patients develops rib nonunion and an even smaller percentage develops symptomatic rib nonunion with common complaints including chronic pain, dyspnea, clicking sensation or jabbing with respiration and shortness of breath (3, 4).

Chronic, focal pain at the site of the nonunion is the dominant complaint of patients with rib fracture nonunion. Pain is present at rest and exacerbates through increasing physical effort. The first report of operative fixation for rib fracture nonunion, using bone graft splints, was by Leavitt in 1942 (5). Due to a failure of the graft, two operations were needed before the result was satisfactory. The literature was subsequently silent on surgical intervention for rib fracture nonunion until 1996 when a single case of successful iliac crest bone grafting for rib fracture nonunion was reported by Morgan (6). Since that time different techniques with or without bone grafting have been described.

In contrast to the emerging evidence on the operative treatment of flail chest, there is a paucity of literature on surgical treatment of rib fracture nonunion. Only 11 publications, representing 47 patients, about surgical fixation of rib fracture nonunion have been described (7). The outcomes of operative treatment of rib nonunion have been described in several different manuscripts but most are case reports (5, 6, 8-15). As various operative techniques are used, it is difficult to draw conclusions about treatment results.

The purpose of this study was to describe our standardized approach and report the outcome (e.g. patient satisfaction, pain and complications) after surgical treatment of rib fracture nonunion.

Methods

The study was part of a registry for the surgical fixation of multiple rib fractures and flail chest. The institutional review board of the University Medical Center Utrecht (UMCU) approved a waiver of consent under protocol number 17-544/C.

A retrospective cohort study was performed. All consecutive adult (age ≥ 18 years) patients who underwent surgical treatment of rib fracture nonunion at the UMCU from July 2010 to May 2015 were included. The UMCU is a large tertiary referral center for trauma care and a level 1 trauma center. Symptomatic rib nonunion was defined as severe persisting localized pain associated with nonunion of one or more rib fractures on a chest CT scan at least 3 months after initial trauma (3). Patients after initial operative treatment of rib fractures were excluded.

Data were derived from a database, including all consecutive patients undergoing surgical treatment for rib fractures. Demographic data such as age, gender, smoking status, date of injury, trauma mechanism, date of surgery, number of rib nonunions, surgical implants used, number of ribs fixed, length of procedure, length of hospital stay and complications were collected from the database. All patients underwent a chest spiral computed tomography (CT) scan with 3 dimensional (3D) reconstructions to identify rib fracture nonunion and to optimize pre-operative planning.

Surgical procedure

All procedures were performed or supervised by one of the authors (MJ, LL), both trauma surgeons with extensive experience with surgical stabilization of rib fractures in an acute setting. Preoperative planning of the procedure was conducted using a chest CT with 3D reconstructions. All patients were asked to localize the painful areas. These areas were pre-operatively marked by the operating trauma surgeon.

Preoperative antibiotic prophylaxis (2 g of Cefazolin) was administered intravenously in all the patients. Depending on the site of the nonunion, patients were positioned in the supine, lateral or prone position and the surgical approach was performed as described by Taylor (16). In the case of intercostal muscle interposition, debridement was performed followed by internal fixation using the MatrixRIB™ system (Depuy Synthes®, Amersfoort, The Netherlands) was performed. In case of hypertrophic rib nonunion without interposition, the fixation was done without debridement in order to provide stability.

To obtain a rigid fixation with maximum stability, locking plates were used. Reposition forceps were used to keep the plate in position. Fixation was preferably done with 3 bicortical screws on each side of the nonunion. After measuring the rib, a drill bit with a stop was used to prevent the parietal pleura from being penetrated. The use of bone graft (Tutoplast, Taureon®, The Netherlands) in case of a large gap after debridement was left to the discretion of the operating trauma surgeon.

Tube thoracostomy was only performed in the case of suspected pleural perforation during surgery. Postoperative chest radiography was performed in all patients to assess the surgical results and to rule out any complications. Patients were allowed to perform their daily activities as soon as possible.

Follow-up

The follow-up included at least one outpatient department visit 2 weeks after surgery with a chest radiography to rule out any delayed pleural effusion or hemothorax. Additional visits to the outpatient department were planned on individual basis because the majority of the patients had been referred to the University Medical Center Utrecht from more local ones. In these cases, a follow-up telephone consultation was conducted. This was at the request of the patient. For study purpose a telephonic interview was performed to assess outcome.

Outcome

The primary goal of this study was to evaluate and assess the satisfaction and pain levels after surgery. This was conducted via a telephonic interview. Satisfaction was assessed by asking a single question with a multiple choice answer (yes, yes after additional surgery, no). Pain was assessed through a series of questions. Patients were asked to record the level of pain on a numeric pain rating scale (NRS) from 0 to 10. On this scale 0 corresponds with no pain and 10 corresponds with the worst imaginable pain (17). The use of analgesics and treatment by a pain medicine specialist were also recorded. These questions were based on extensive clinical experience and designed for easy use in a telephonic questionnaire.

Complications were evaluated by using electronic medical records. Non-union was defined as severe persisting localized pain associated with nonunion on a chest CT scan at least 3 months after initial surgery. Implant failure and implant removal were recorded. Implant removal was only performed at patients' request.

Statistical analysis

Variables are presented as a mean value with range for parametric continuous outcomes, as median with range for nonparametric continuous outcomes and as frequencies and percentages for categorical variables. Statistical analyses were performed using SPSS 21.0 software (SPSS Inc, Chicago, IL, USA).

Results

In the study period, operative stabilization of rib fractures was performed in 161 patients. Nineteen patients (11 men, 8 women), with symptomatic nonunions were included. Fourteen patients were referred from other hospitals and 8 patients received treatment from a pain medicine specialist. The mean follow-up assessment time was 36 months (8-65). Baseline characteristics are shown in Table 1.

Table 1. Patient demographics and treatment characteristics.

Number of patients†	19 (100%)
Age* (years)	49 (22 - 77)
Male / Female†	11 (58%) / 8 (42%)
Smoking†	11 (58%)
ASA†	
1	11 (58%)
2	7 (37%)
3	1 (5%)
Number of rib fractures	56
Number of nonunions on CT	42
Number of SRFN fixated	40
Location†	
Ventral	5 (26%)
Lateral	3 (16%)
Dorsolateral	5 (26%)
Dorsal	6 (32%)
Duration of surgery§ (min)	43 (14-178)
Tube thoracostomy†	
Peroperative	2 (11%)
Postoperative	0 (0%)
Duration of thoracostomy	1 day (n=2)

†Number (percentage of total) *Mean value (range). §Median value (range).

Seven patients sustained their rib fractures in a motor vehicle accident, five from a fall, four sustained cough induced rib fractures, two during sports and one during thoracic surgery (esophageal resection). Only 3 patients had an Injury Severity Score (ISS) above 16 (range 22-34).The median time from injury to nonunion surgery was 19 months (range 5-398). The mean follow up was 36 months (range 8-65). One patient refused to participate in the telephonic interview.

The median length of surgery (skin-to-skin) was 43 minutes (14-91). Out of 42, a total of 40 rib fracture nonunions were fixated. In all cases locking plates were used. Table 1 shows the location of the rib nonunions. In 8 ribs we were unable to place 3 screws on each side of the nonunion because the fractures were located dorsally near the spine or scapula. Allograft bone was used in two cases because of a large bone defect. In two patients a chest tube was placed during the operation due to the opening of the pleural cavity. In both cases the tube was removed the next day. There were no perioperative complications and no indications for blood transfusion. Postoperative chest radiographs were performed in all the patients. No pneumo- or hemothorax was identified.

During admission two patients received epidural analgesia. All other patients were treated with short course intravenous morphine followed by oral oxycodone. The mean length of hospital stay was 3 days (range 1-7). No in-hospital complications were recorded. Follow-up chest radiographs ruled out delayed pleural effusion in all patients.
A total of 6 (32%) patients needed additional surgery. The median time between initial surgery and additional surgery was 12 months (range 6-36). In 2 patients, implants were removed at the patients' request due to irritation. After having them removed, those patients were satisfied. One other patient requested an implant removal but during the removal procedure a persisting nonunion was observed and fixated. This patient recovered without any complications. In two patients, implant failure occurred due to loosening of the plate with a new fracture ventral to the plate. Fixation with longer plates was later performed. In the sixth patient, an intercostal neurinoma was excised with good clinical recovery. The mean hospital length of stay for the additional surgery was 3 days (range 1-8).

At a mean follow-up of 36 months, the majority of patients (n=13) are satisfied with the results of their surgical treatment and all patients experienced a reduction in the number of complaints (Table 2). Persistent pain was a common complaint. Three patients reporting severe pain used opioid analgesics on a daily or weekly basis. The mean reported NRS was 4 (range 0-10). Only 1 patient needed ongoing treatment by a pain medicine specialist.

Discussion

Surgical fixation of symptomatic rib nonunion is a safe and feasible procedure, with a low perioperative complication rate. Furthermore, it might be beneficial in selected symptomatic patients. Although the majority of patients were satisfied and the level of pain subjectively decreased, complaints of persisting pain were common. In two patients, new fractures next to the implant without new trauma were observed. Furthermore 3 patients

Table 2. Patient satisfaction at follow-up.

	No (%)
Satisfied after surgery	
Yes	11 (61%)
Yes after additional surgery	
No	
Pain (NRS)	
None (0)	6 (33%)
Mild (1-3)	2 (11%)
Moderate (4-6)	5 (28%)
Severe (7-10)	5 (28%)
Use of analgesics	**6**
Paracetamol	3 (17%)
Morphine	3 (17%)
Treatment by pain medicine specialist	
Pre-operative	8 (44%)
Post-operative	1 (6%)

requested implant removal a persistent nonunion in one patient.

Contrary to the increasing evidence of rib fixation for flail chest, there is limited data on the operative treatment of rib nonunion (18). The available studies are summarized in Table 3. Two larger series have been published: one prospective case series with 24 patients and one retrospective case series with 10 patients (3, 4). There have been 10 case reports of surgically treated rib nonunion (5, 6, 8-14). Regardless of the many different fixation techniques in the literature, it could be stated that the vast majority of the described patients in our study had no, or decreased level of pain after treatment and returned to work. Wound infections or other perioperative complications seldom occurred. In line with our results, implant removal due to irritation has been described. Remarkably, in 4 cases non-locking plates were used (9-12) and in two cases only a bone graft splint without plate fixation was performed (5, 6). Most of these patients fully recovered or only a minimal level of pain remained. In the retrospective series of Gauger, locking plate osteosynthesis was performed combined with an autograft (4). Complications were limited to 1 wound infection and 1 implant removal.

The operative technique used in our study is most comparable to the prospective case series of Fabricant who stabilized 24 patients with (absorbable) locking plates without conducting

Table 3. Literature overview.

Author	Study design	No.	Intervention (No.)	Bonegraft (No.)	Chest tube (No.)	Time from injury to intervention	Follow up	Results	Complications (No.)
Fabricant	Prospective	24	Locking (absorbable) plate (with cerclage) Intercostal release (9)	None	Not reported	4-197 months (mean 16)	60, 120, 180 days	Morphine dosage decreased Activity levels improved	Screw back-out (2) Wound infection (1) Pulmonary hernia (1)
Gauger	Retrospective	10	Locking plate	Autograft (local or iliac crest)	Yes (4)	8-60 months (mean 24)	3-46 months (mean 18.6)	8 of 10 returned to work without limitations	Wound infection (1) Hardware removal (1)
Gardenbroek	Case report	3	Locking plate	None	Yes (1)	6-8 months	18-26 months	Full recovery	Hardware removal (1)
Leavitt	Case report	1	Bonegraft splint without plating	Autograft (tibia)	Not reported	1 year	27 months	Improvement in pain	Iatrogenic intercostal artery lesion Persistent nonunion
Morgan-Jones	Case report	1	Bonegraft splint without plating	Autograft (iliac crest)	Not reported	2 years	12 months	Full recovery	None
Cacchione	Case report	1	Non locking plate	None	Yes	2 years	6 months	Full recovery minimal pain	None
Slater	Case report	1	Non locking plate with cerclage after resection of 1 cm of two ribs	None	Yes	6 years	18 months	Full recovery dyspnea improved	None
Ng	Case report	1	Non locking plate	None	Yes	11 months	1 week	Returned to daily activities	Wound infection
Beelen	Case report	1	Locking plate	None	Not reported	1 year	2 months	Full recovery	None
Cho	Case report	1	Non locking plate	Autograft (iliac crest)	Yes	3 years	12 months	Full recovery	None
Anavian	Case report	1	Locking plate	Autograft (local)	No	11 months	12 months	Full recovery	None
Dean	Case report	1	Locking plate	Autograft (iliac crest)	No	4 months	12 months	Full recovery	None

a bone graft (3). Seventy-two percent (n=13) of our patients were satisfied after surgery even though the pain level was scored mild to severe (NRS 2-7). The number of patients treated by pain medicine specialists decreased after surgery and over 80% had no need for the use of opioid analgesia. Despite this, 5 patients were not satisfied. The type of pain in those patients was mostly neuropathic, which is difficult to treat. Fabricant et al reported intercostal nerve entrapment in 9 out of 24 patients (3). This finding could indicate that persistent pain in rib nonunion should be recognized as multifactorial. Fracture instability, entrapment of the intercostal nerve and periost and long-term bruising of the neurovascular bundle might contribute to pain in these patients. The treatment of our 5 patients with persistent pain probably should be focused on the intercostal nerve damage.

In our population we can roughly distinguish between two groups considering the etiology of nonunion. The first group consisted of 9 patients who had some interposition of soft tissue which prevented the bone from healing. The second group consisted of 10 patients with hypertrophic nonunion due to lack of stability and excess movement in the fracture ends. For this reason we agree with Fabricant that stabilizing the ribs by locking plates without conducting a bone graft should be sufficient (3).

Another interesting finding is the occurrence of new fractures directly next to the implant in 2 patients without a new trauma. There is no literature regarding this complication. The locking plates might provide too much rigidity thereby acting as a stress riser. A second possibility could be that partial damage to the rib, a fissure, could have been missed on a CT scan. A solution might be to use longer plates in non-union surgery.

When we started operating rib fracture nonunion, we used bone graft to allow for better fracture healing. Later, after gaining more experience, we chose not to use bone grafting anymore because of the lack of supporting evidence. This corresponds with our observation and professional experience that providing stability and removing interposition, is sufficient for bone healing in most patients. Despite fixation, we found persistent rib nonunion during implant removal surgery in 1 patient. This patient continued smoking during the treatment which might have influenced fracture healing. It is still debatable whether routine bone grafting would lead to an improved union rate.

This study is subject to several limitations. First of all, the retrospective analysis has led to limited preoperative data and potential bias. Whereas pain is a major factor in the indication for surgery, validated preoperative data on pain are lacking and therefore evidence for improvement is merely circumstantial. Secondly, no follow-up CT scan was conducted to check for fracture consolidation. Although symptoms regarding rib nonunion seem multi

factorial, ruling out persistent nonunion might be warranted in the future. Furthermore this study describes a small case series of only 19 patients. Although the conclusions that could be drawn from a small population are limited, this study describes the second largest cohort in literature.

Conclusion

Our study shows that surgical fixation of symptomatic rib nonunion is a safe and feasible procedure, with a low perioperative complication rate. This might be beneficial procedure in selected symptomatic patients in the future. In our study, although the majority of patients were satisfied and the pain level subjectively decreased, complaints of persistent pain were common. Further investigation with a larger number of symptomatic patients is warranted. The use of bone graft in the surgical treatment of rib nonunion requires further investigation.

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Chapter 10

General discussion and future perspectives

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Based on an editorial by article from Thomas White – "Rib fracture repair" published in the Shanghai chest;2:16.

Thoracic trauma can cause a wide range of clinical presentations and injuries, making early diagnosis and timely management extremely challenging. Management of chest trauma patients is based on the Advanced Trauma Life Support (ATLS) protocol (1). Treatment already starts pre-hospitally and is continued in the emergency department and when necessary in the operation theatre. Mortality due to thoracic injuries goes up to 25% (2). Many of these deaths can be prevented by prompt diagnosis and treatment. In this thesis many aspects of clinical treatment strategies in thoracic trauma patients are described.

Thoracic trauma and tube thoracostomy

Thoracic trauma includes many acute (and potentially) life-threatening injuries (**Chapter 2**). The most simple and often life-saving minimal invasive treatment in thoracic trauma is the insertion of a chest tube. This procedure is frequently performed in the emergency department under less sterile circumstances. Contamination can easily occur. The incidence of post-traumatic empyema varies between 2 to 25% (3-6). However, other infection patterns including direct infection from penetrating injuries of the thoracic cage, secondary infection of the pleural cavity due to intra-abdominal organ injuries, undrained or incompletely drained hemothoraces or parapneumonic empyema can play a role as well. These other causes might not have a similar benefit from prophylactic antibiotic therapy. Also, the organisms responsible for the infection vary according to the mechanism of contamination.

Staphylococcus aureus or Streptococcus species are typically related to chest tube insertion. Secondary contamination usually involves gram-negative or mixed bacterial pathogens. The goal of prophylactic antibiotic therapy for acute tube thoracostomy in traumatic chest injury is to decrease the risk of infectious complications. On the other hand, avoiding unnecessary use of antibiotics is important to minimize the development of bacterial resistance, medication-related side-effects and treatment costs. According to trauma mechanism, penetrating injuries more often cause contamination compared to blunt thoracic trauma and are associated with higher rates of pneumonia (7). In this thesis we found a significant benefit of antibiotic prophylaxis in reducing the incidence of infection in patients with penetrating thoracic injuries requiring a tube thoracostomy **(chapter 3**). In blunt thoracic trauma the role of prophylactic antibiotics is still uncertain. We therefore concluded that infection occurring after penetrating injury most likely is caused by contamination of the wound and surgical site by pathogens present on the penetrating foreign body or the skin of the patient. In these patients, the infections are not solely related to chest tube insertion but also to the penetrating trauma itself. As stated above, a tube thoracostomy frequently is performed in an emergency setting. This means that a protocol concerning prophylactic antibiotics should be simple and clear. When the majority of the

population in a hospital suffers from penetrating thoracic injuries, prophylactic antibiotics for all trauma patients requiring a chest tube should be contemplated, thereby accepting that the minority of patients is over treated.

Pain management

The thoracic pain caused by rib fractures or chest wall contusion limits patients to adequately cough and breathe deeply, which can result in atelectasis and pneumonia. A combination of adequate pain control, respiratory assistance, and physiotherapy are considered to be key in management of patients with fractured ribs (8, 9). Nowadays 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 (10, 11). Comparing all modalities epidural analgesia is suggested to provide better pain relief compared to other modalities **(chapter 4).** However, the included studies are of low methodological quality and difficult to compare, due to the heterogeneity in study methods and investigated endpoints. To compare the results of pain reduction more homogeneously, future studies should use a universal pain assessment tool like NRS pain score. 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 and probably intensified (**chapter 4**).

Chest wall injuries

Sternal fractures

Sternal fractures are predominantly related with deceleration injuries and blunt anterior chest trauma and are present up to 8% of the victims of motor vehicle crashes (12). The number of sternal fractures is even higher in multi-trauma patients in combination with rib fractures (8 - 11%) and especially in flail chest injuries (11 - 21%)(13). This rise in incidence in the presence of other thoracic injuries means that the sternum might contribute to stability of the thoracic cage. Traumatic sternal fractures are mostly transversal corpus sterni fractures and are mainly caused by direct forces. Less frequently manubrial and xiphoidal fractures are seen (14-16). Fractures of the manubrium are often accompanied by concomitant injuries (17). However, the prognosis of isolated sternal fractures is excellent, which probably means that the sternum alone doesn't play a key role in the stability of the thoracic cage. Most patients recover within several weeks. For instance, a floating sternum, as a result of cardiopulmonary resuscitation, only rarely needs surgical intervention. However, two-thirds of the sternal fractures have concomitant injuries and associated morbidity and mortality ranging from 4 to 45% (14, 16, 18). These injuries can be divided

into three categories: soft tissue injuries, injuries to the chest wall and injuries to the spine. Soft tissue injuries include also myocardial contusion, pneumothoraces, hemothoraces and tamponade. Especially myocardial contusion is an injury that is frequently suspected in patients with sternal fractures. However the incidence of myocardial contusion after blunt thoracic trauma varies between 8% and 71% depending on the criteria used for establishing the diagnosis (19). Only a selected population will have complaints of myocardial contusion and need hospital admission (20). Most sternal fractures can be treated non-operatively (>95%) (14, 16, 21). Indications for surgical treatment are; severe or intractable pain, respiratory insufficiency, displacement, overlapping, or impaction of the fracture, sternal deformity or instability and delayed union associated with chronic pain (22). Due to limited research available, standardised treatment guidelines for traumatic sternal fractures are lacking. Based on case studies sternal fixation is a safe procedure, although these studies report only on selected patients or case series. Several different techniques are described like sternal plating, sternal plating with bonegraft or wiring. Sternal plating provides more stability and better chest wall function compared to wires (18, 21-23). Bonegraft is mostly used for the treatment of fracture non-union (24, 25). However, comparative studies are needed to reveal a more pinpointed indication for operation (**Chapter 5**).

Indication for rib fracture fixation

In regard to surgical fixation of rib fractures, there is still a paucity of prospective studies. However, there is increasing enthusiasm in many trauma centres to perform rib fixation. As the level of evidence is still limited, caution should be taken in order to prevent overtreatment. The available evidence of rib fixation mainly focuses on patients with clinically evidence of a flail chest. For patients with flail chest, 3 small randomized controlled trials are available, representing on only 60 patients who underwent rib fixation altogether. These three studies in patients with flail chest, despite all their shortcomings, all demonstrated a clear reduced need for mechanical ventilation, reduced ICU stay, less pain and less pneumonia in patients after rib fixation. Therefore, rib fixation in flail chest is more and more accepted, supported by these very positive results.

However, these results should be interpreted in the correct context. For one, selective inclusion criteria were used. Two of the above-mentioned studies performed rib fixation on patients with a flail chest who were ventilator dependent without prospect of successful weaning. Furthermore, all three studies had different strict exclusion criteria such as severe injuries to other body systems, head trauma, or the absence of respiratory failure (26-28). With regard to flail chest, different definitions are used in literature. Definitions vary from clinical flail chest to radiological flail chest defined as at least three consecutive ribs fractured in two or more places per rib (27-32). However, guidelines from surgical critical

care suggest four or more consecutive rib fractures on two places (33). Following the majority of studies, flail chest should be defined as at least three consecutive rib fractures in more than one place (26). Although this heterogeneity in the definition of flail chest makes studies difficult to compare and strictly selected patients were enrolled, a specified group of patients with flail chest might benefit from rib fixation. Therefore, the more widely accepted policy of rib fixation in this very specific population is probably justified.

The second and far larger group of patients are those with multiple (three or more) rib fractures without flail component. This group is even more interesting from an economic point of view, because of their need for health care resources. The majority of these patients heal uneventfully. However, primary severe dislocation or secondary dislocation of multiple rib fractures can lead to chest wall deformity which can result in restrictive pulmonary function, or chronic intercostal pain in the future. Rib fractures are initially frequently associated with a decreased vital capacity which results in an increase in pulmonary complications (34). Also one year after chest trauma pulmonary function remains decreased in patients suffering from chest trauma (35). Several factors can play a role in this decreased pulmonary function. Causes can be found in unbearable pain, severe pulmonary contusion or chest wall deformity which all leads to impaired breathing. In patients with multiple rib fractures, age and number of fractures are important outcome predictors (36, 37). Many of the complications of rib fractures are thought to be related to pain, which might result in impaired breathing. Optimal pain management improves breathing, but cannot always be achieved by anaesthetics. In patients with insufficient pain control, rib fixation might be a suitable option (38-40). However, evidence is once again scarce. In a retrospective study, Qiu et al. found that patients with multiple rib fractures without flail segment showed good short-term results and an earlier return to 'normal activity' after rib fixation (41). Another study on multiple rib fractures from Khandelwal et al. reported a significant reduction of pain and earlier return to work after rib fixation (42). No other studies reported results of rib fixation compared to non-operative treatment in patients with multiple rib fractures.

In **chapter 7** a retrospective multicenter cohort compared operative and non-operative treatment of rib fractures. After propensity score matching rib fixation in flail chest was not associated with differences in ICU length of stay or other outcome measures. Neither did we find a difference in hospital length of stay for rib fixation in patients with multiple rib fractures, nor for the other outcome measures. One possible explanation for these contrasting results might be the more restrictive inclusion criteria used in the aforementioned studies, compared to our study that applied a more liberal approach. Less strict inclusion criteria will result in more heterogeneity, which will increase the generalizability of the results and

mimic current practice; however, it could also have diminished the effect of rib fixation in an already heterogeneous group of mostly severely injured patients. Interestingly, the ICU hospital length of stay in both groups of our cohort, were lower as compared to Tanaka et al. (26). Also the duration of mechanical ventilation in our entire cohort was lower as compared to the published randomized controlled trials. Complication rates in literature go up to 35% (27), however is not always reported or specified in the available studies. In our study 14% of the surgically treated patients had a postoperative complication, but apparently did not result in an improvement for the primary endpoint. Also, on secondary outcome parameters, such as pain, this study is likely hampered by its retrospective design, as data loss and underreporting affect outcome measures. In our daily practice pain is the most important indication for rib fixation, however, we were unable to compare pain scores and interventions for pain treatment due to the limited availability of structured data.

Because the included patients came from two hospitals, there were differences in the baseline criteria between the surgical and non-operatively treated group. However, using a propensity score model, we were able to successfully match on all measured baseline characteristics eliminating possible confounding due to measured patient characteristics. Still there are unmeasured confounders (e.g. pain), but we have included most known and previously reported confounders in our analysis and the impact of unmeasured confounding therefore seems limited. Nevertheless, no benefit from rib fixation could be demonstrated in our population for either of the two stratified patient groups (i.e. flail chest and multiple rib fractures without flail chest). These results and the limited available evidence on this subject emphasize the need for future studies before rib fixation is embedded or abandoned in clinical practice and should temper the current rush to a broad implementation of this surgical procedure. Still there is a need to identify the right patient who would benefit from rib fixation and this should be done in a research setting.

Another very seldom indication is rib fracture nonunion. There is very limited data on the operative treatment of rib nonunion (43). The main complaint of rib fracture nonunion is pain. After rib fixation for nonunion the majority (72%) of the patients were satisfied with no remaining pain or only a little discomfort. Several operative techniques are used, but in our experience, in line with the findings of Fabricant, it is not necessary to use bone graft (**chapter 9**) (40). A possible cause for the atrophic nonunion is entrapment of intercostal muscle or periosteum, which is frequently encountered during surgery. Another cause is the lack of stability and excess movement in the fracture ends which causes hypertrophic nonunion. Removing this entrapment of intercostal muscle and offering stability to the bone by plating is enough to make the ribs heal properly. After surgery 28% of the patients were not satisfied and still were dependent on analgesics. The type of pain remaining was

mostly neuropathic. Fabricant reported intercostal nerve entrapment in several cases. In our opinion persistent pain in rib nonunion should be recognized as multifactorial. Fracture instability, entrapment of intercostal nerve and periosteum and long-term bruising of the neurovascular bundle might contribute to pain in these patients. When approaching rib nonunion it can be necessary to explore the intercostal bundle to prevent (persistent) neuropathic pain afterwards.

Possible or relative contraindications

Voggenreiter 1998 et al. (44) stated that the presence of pulmonary contusion associated with flail chest is a contraindication for rib fixation. However, the power of this study is limited with only very small groups of patients. Therefore, the contribution of pulmonary contusion to success or failure of rib fixation still remains questionable. Pulmonary contusion causes long-term respiratory dysfunction with decreased functional capacity (45). Early repair of the chest wall might be helpful in restoration of pulmonary function. Also Voggenreiter et al diagnosed pulmonary contusion by evidence of an acute infiltrate on the admission chest radiograph and by fibre-endoscopic bronchoscopy within 4 hours after admission. However, a pulmonary contusion can deteriorate considerably within 24 hours, so a diagnosis within 4 hours after trauma may underestimate the incidence of pulmonary contusion. In addition there are several studies that observed actual benefit from rib fixation despite pulmonary contusion. Althausen et al. described a possible benefit of rib fixation in patients with pulmonary contusion, compared to non-operatively treated patients (46). Tanaka et al., described no difference in pulmonary contusion between the operatively and non-operatively treated patients, suggesting that pulmonary contusion does not play a significant role in the indication for rib fracture fixation, however rib fixation was performed only after 5 days after the initial trauma (26). Earlier fixation therefore might show more benefit. During the current screening of poly-traumatized patients, the whole-body CT scan is increasingly used in emergency departments. With the use of a three -dimensional computed tomography the volume of the pulmonary contusion can be measured which might be helpful to identify patients at high-risk for respiratory failure (47). Taking all the aforementioned studies into account, there are currently no strict contraindications for rib fixation.

Surgical technique

Several approaches have been described. Anterior fractures can be accessed using an inframammary crease incision. The pectoralis major muscle can either be mobilised or split along the length of its muscle fibers. Access to lateral fractures can be achieved in several ways. The most common is the standard posterolateral thoracotomy incision at the level of the 7th intercostal space. The latissimus dorsi muscle can be divided as in the muscle

sparing approach. Another approach, which can be used for lateral fractures, is the smaller transverse incision. For dorsal fractures the dorsal approach, a longitudinal incision, between the medial border of the scapula and the spine can be used (48). These invasive surgical approaches might cause pain. Especially in obese patients, the surgical approach is often more extensive and fractured ribs are harder to find. Preoperative ultrasound can be useful in localizing rib fractures. Together with the use of the Alexisâ retractor or a Thompson retractor, approaches can be limited to 4 – 10 centimetres. When necessary, separate stab incisions can be made. Several tools for minimal invasive rib fixation, including angular drilling systems, have been developed recently. The development of these minimal invasive techniques may result in less pain due to a more restricted surgical approach (49).

Evidence based medicine

The last decade there has been growing experience with rib fixation, which resulted in an increased number of publications on this subject. Most studies concluded that more randomized controlled trials should be performed. However, the number of RCTs on this subject didn't increase at all in the last decade and that might be for a reason. RCTs in trauma surgery are difficult to conduct. One of the most common challenges of RCTs is the timely and efficient recruitment of patients. Several studies have shown that RCTs in surgery have low patient participation rate (50). Patients are often hesitant to participate in trials as they do not want their (surgical) treatment to be decided by chance. If patient recruitment is not carried out properly, an extended trial period and increased costs are to be expected, or the RCT might fail altogether.

Physicians in surgical trials also influence the low participation rate as they often prefer one of both treatment arms. Treatment preference results in less participating centers or selective inclusion of patients. This holds especially true for new surgical techniques like rib fixation. Introduction of a new technique might result in confounding due to the complexity of the procedure. The technical difficulty of a surgical procedure cannot be compared to, for example, administering drugs. A surgical procedure can be influenced by many other factors, such as the expertise and experience of the surgical team.

Last but not least, RCTs must be performed according to strict rules and require budget for approval by medical ethical committees and monitoring of the trial. In a field with limited financial resources, such as trauma surgery, these regulations might lead to a decrease in the quantity of RCTs.

More research is needed to further identify the right type of injury pattern 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. Observational studies might be an achievable first step in gathering high quality evidence, despite the fact that observational studies have a greater risk of bias because of the nonrandom allocation of treatment. Several studies compared RCTs and observational studies and showed similar results (51-53). Lonjon compared the outcome of RCTs and non-randomized studies involving use of propensity score and concluded that prospective non-randomized studies with suitable and careful propensity score analysis are reliable (54). Remarkable is that low-quality observational studies do have enough effect to possibly influence the outcome. Therefore, not only de study design is important but also the quality (using the MINORS score) of the study (53). So, a well-executed cohort series might be as valuable as a RCT. The advantage of performing an observational study is that a sufficient number of participants is more easily gained and specific physician preferences regarding possible treatments do not play a role. In observational studies the patient population tends to be more heterogeneous, which improves generalizability and subgroups can be identified more easily. Last but not least performing an observational studies is less expensive compared to RCTs.

Follow up

All available evidence is focused on the short-term follow up. In the University Medical Center Utrecht we performed rib fixation since 8 years. In this period, we encountered new problems. Short-term follow-up provides information on complications such as pneumonia (39%), excess pleural fluid (5%) and implant related infection (3%) (chapter 8). Pneumonia is the most frequent complication and our percentages are comparable with the existing literature. However, definitions of pneumonia differ in literature making this outcome measure difficult to compare across studies. Implant related infection (3%) was comparable to a study done by Pieracci (55). In long-term follow-up almost half of the patients experience implant related irritation after rib fixation. Twenty five percent of the patients who had complaint had their implants removed, or at least part of it, after a median follow-up duration of 3.1 years, half of the patients who underwent rib fixation complain about implant irritation (53%). In the majority of patients quality of life improved most significantly in the first year after trauma. Due to the retrospective design pulmonary function was not part this study. From **chapter 8** it can be concluded that rib fixation is a safe procedure with a relatively good quality of life after long-term follow up, despite 10% of the operated patients underwent implant removal.

Now how to proceed? The most important question remains: To fix or not to fix? And if so, who should we fix and when. Age and number of fractures are important in predicting outcome, but cannot solely be used as indication for surgery. The most important symptom in patients with rib fractures is pain, as pain might result in impaired breathing possibly leading to a cascade of complications. The relationship between dislocation of fractures and pain has not yet been established and thus dislocation might be considered as a separate criterion (56). In our search for the right indication for rib fixation, pain seems to be underestimated as an important factor. If pain management is optimized but still inadequate, patients might benefit from rib fixation. Combined with the indications, like flail chest and chest deformity, which are less debatable a flow chart was designed for patients with rib fractures based on clinical parameters (Figure 1).
For the future an algorithm, based on clinical and diagnostic parameters, for the treatment of rib fractures might help us in our search for the right indication, but for the present it is recommend to be very critical in determining the operation indication.

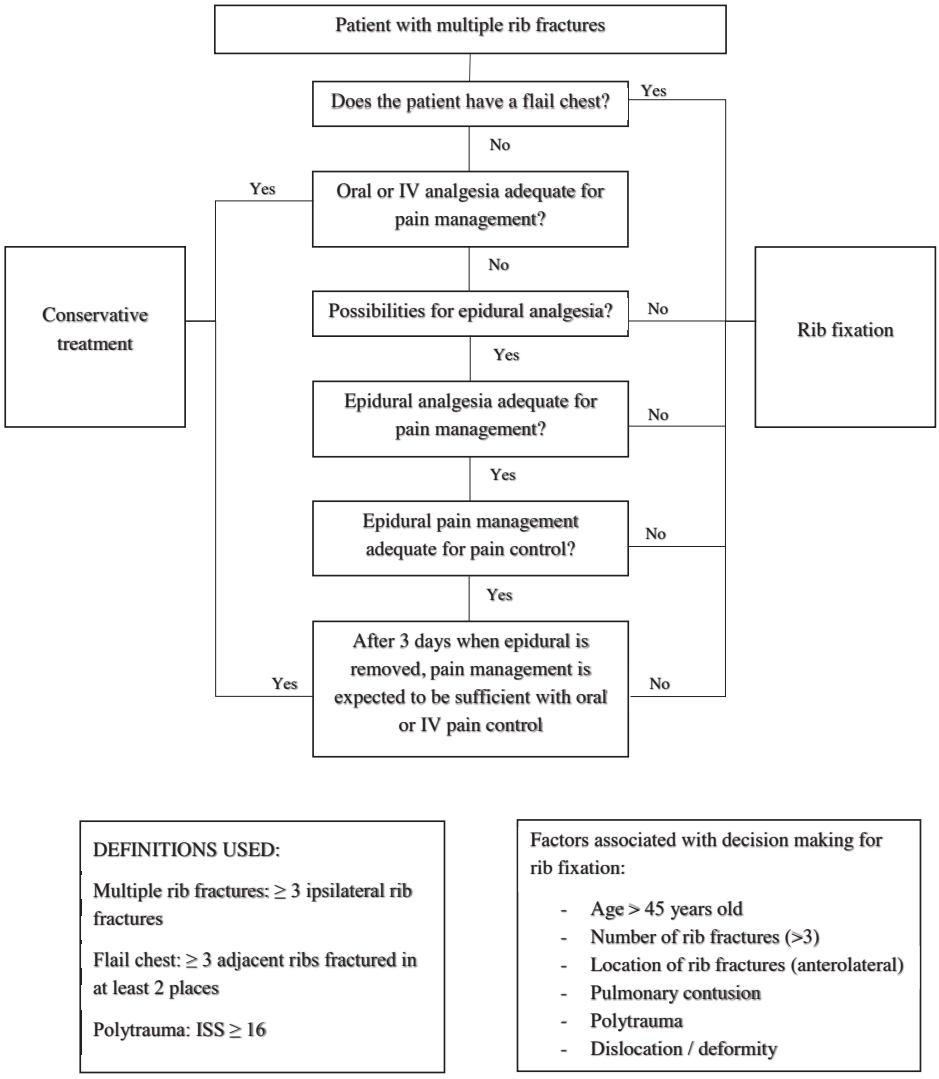

Figure 1. Clinical-based algorithm for the treatment of multiple rib fractures.

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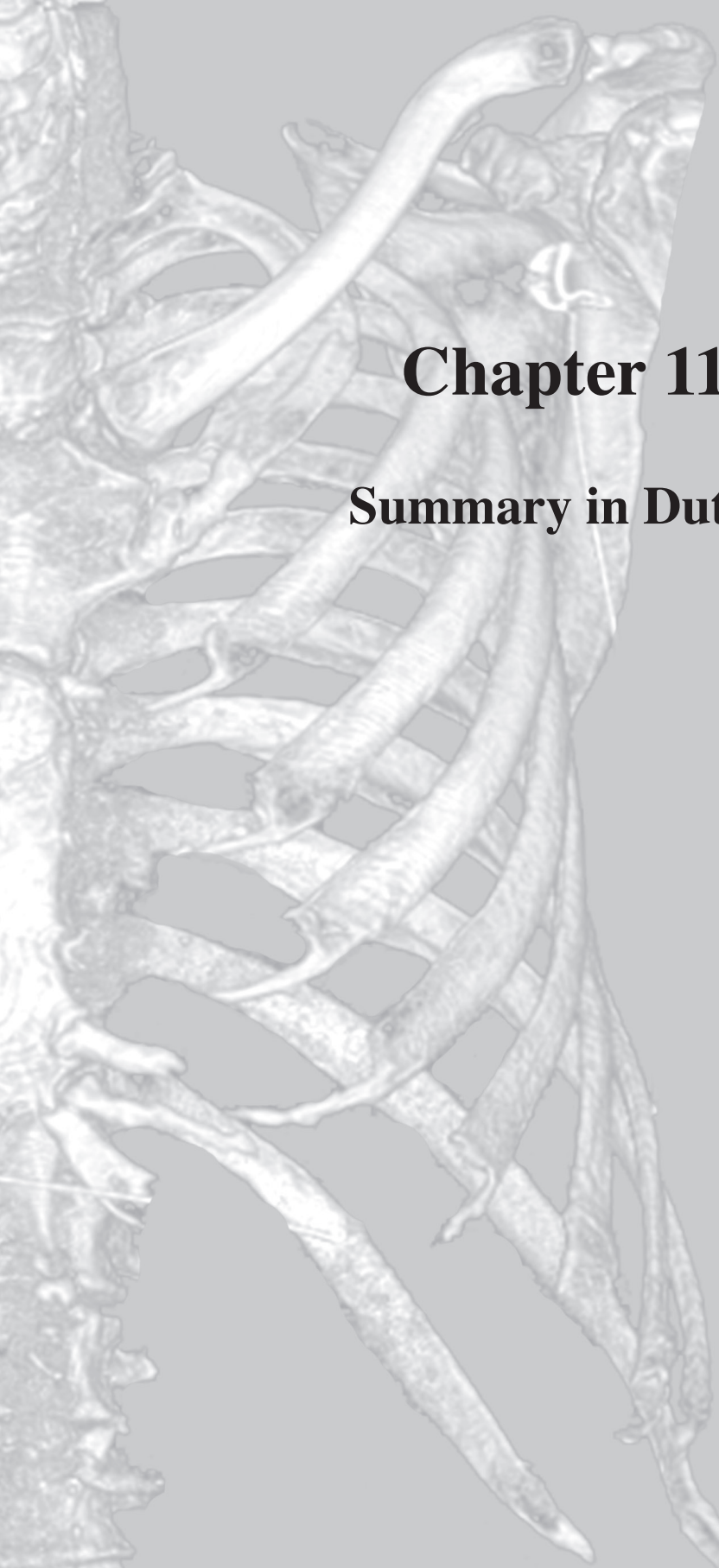


Chapter 11

Summary in Dutch

Wereldwijd is trauma de belangrijkste oorzaak van morbiditeit en mortaliteit. Vijfentwintig procent van alle doden door trauma worden veroorzaakt door thoraxtrauma. Thoraxtrauma betreft in 90% van de gevallen een stomp thoraxtrauma meestal veroorzaakt door verkeersongevallen. Slechts in 10% is er sprake van penetrerend letsel van de thorax, meestal veroorzaakt door schot- en steekwonden. De meeste thoraxletsels kunnen conservatief behandeld worden, slechts minder dan 10% van de stompe en 15-30% van de penetrerende thoraxletsels vereisen operatief ingrijpen. De behandelprincipes van thoraxtrauma zijn gebaseerd op de Advanced Trauma Life Support (ATLS®) principes. De centrale thema's van dit proefschrift zijn de diagnostiek en klinische behandeling van de patiënt met thorax letsel.

Hoofdstuk 2 geeft een overzicht van alles letsels die kunnen voorkomen in de thorax als gevolg van thorax trauma. Een deel van de thoraxletsels is levensbedreigend- of potentieel levensbedreigend, waarbij een vroege diagnose met directe interventie nodig is. Volledig onderzoek van de patiënt middels een systematische aanpak is nodig om verschillende letsels met de juiste prioriteit te kunnen behandelen. Kennis van het traumamechanisme met bijbehorend specifiek letsel is vereist om de patiëntenzorg van trauma patiënten te verbeteren zodat morbiditeit en mortaliteit verlaagd kunnen worden. Dit hoofdstuk beschrijft de diagnostiek en classificatiemodellen welke nodig zijn om de patiënt met thoraxtrauma te onderzoeken. Tevens worden de meest voorkomende thoraxletsels door trauma beschreven, gevolgd door de behandelingsstrategieën.

In de meerderheid van de patiënten is een eenvoudige handeling als het plaatsen van een thoraxdrain de primaire en vaak ook enige behandeling. Het plaatsen van een thoraxdrain gebeurt vaak op een spoedeisende hulp onder suboptimale steriele omstandigheden en is niet altijd zonder (infectieuze) complicaties. In **hoofdstuk 3** wordt de waarde van profylactische antibiotica bij thoraxdrains besproken. De incidentie van posttraumatisch empyeem varieert tussen de 2 en 25% na drainplaatsing. Contaminatie van de thoraxholte kan optreden na plaatsing van een thoraxdrain maar kan ook als gevolg van penetrerend letsel van de thorax, secundaire infectie van de thoraxholte door intra-abdominaal orgaan letsel of onvoldoende gedraineerde hematothorax of door parapneumonische effusie. Het meest voorkomende organisme verantwoordelijk voor een posttraumatisch empyeem is een staphylococcus aureus. Dit suggereert contaminatie vanuit de huid door bijvoorbeeld de drain plaatsing of door het trauma zelf. Afhankelijk van de oorzaak zal profylactische antibiotica bij plaatsing van een thoraxdrain vermindering van infectieuze complicaties geven. Het doel van profylactische antibiotica is om infectieuze complicaties te voorkomen echter, onnodig gebruik van antibiotica werkt resistentie in de hand en gaat gepaard met kosten en medicatie gerelateerde bijwerkingen. Uit de beschikbare literatuur blijkt dat profylactische antibiotica, bij trauma patiënten welke thoraxdrainage behoeven, een voordelig effect kunnen hebben bij

patiënten met penetrerend thoraxletsel. Er is geen evidence voor het gebruik van profylactisch antibiotica bij patiënten met stomp thoraxletsel. In de praktijk is het wenselijk om voor een spoedsituatie een eenduidig en simpel protocol te hebben. Wanneer de meerderheid van de patiëntenpopulatie in een ziekenhuis bestaat uit penetrerend thorax letsel is het te overwegen om profylactisch antibiotica te geven bij het plaatsen van een thoraxdrain bij trauma patiënten. Een deel van de populatie zal dan echter over-behandeld worden.

Pijn behandeling

In het volgende deel van dit proefschrift wordt ingegaan op de ossale letsels van de thoraxwand. Hiervan is bekend dat optimale pijnbehandeling van belang is om ophoesten en diepe inspiratie mogelijk te maken. Een combinatie van pijnstilling, (ademhalings-) fysiotherapie en zuurstof suppletie waar nodig is de eerste belangrijke stap in de behandeling van ossaal thoraxletsel. Tegenwoordig zijn er verschillende manieren van pijnstilling beschikbaar zoals een epiduraal catheter, intraveneuze (patiënt gecontroleerde) analgetica, intercostaal-, paravertebraal- of interpleurale blokkade, orale opioïden of een combinatie van bovenstaande opties. In **hoofdstuk 4** worden al deze verschillende technieken met elkaar vergeleken. De epidurale anesthesie lijkt de beste pijnbestrijding te geven vergeleken met de andere technieken. Echter, de heterogeniteit van alle studies en de grote variatie in technieken zorgen ervoor dat de studies lastig met elkaar te vergelijken zijn. Echter, de grote hoeveelheid contra-indicaties voor epidurale anesthesie en de hoge kans op falen maakt dat de andere technieken nog beter vergeleken moeten worden.

Sternum fracturen

Na de invoering van de verplichte drie-punts gordel en het gebruik van de air bag is er een toename in de incidentie van sternum fracturen. Sternum fracturen worden vooral gezien na deceleratie letsel en stomp thorax trauma met een incidentie van 8%. Geïsoleerde sternum fracturen genezen meestal zonder problemen. Morbiditeit en mortaliteit worden bepaald door de begeleidende letsels van de thoracale organen. Mortaliteit varieert derhalve van 4-45%. Sternum fracturen worden vaak gezien bij de meervoudige gewonde patiënt. Letsels die vaak voorkomen bij sternum fracturen zijn; rib fracturen, wervel fracturen, cor contusie, hemopneumothorax en mediastinale letsels. De meerderheid van de sternum fracturen kan behandeld worden met goede pijnstilling en behandeling van eventuele begeleidende letsels. Operatieve behandeling van sternum fracturen kan overwogen worden bij instabiele fracturen, thoraxwand instabiliteit, een gedisloceerde fractuur of persisterende dislocatie, sternum deformiteit, respiratoire insufficiëntie, ernstige pijn en non-union van het sternum. In **hoofdstuk 5** worden de ervaringen met de operatieve behandeling van sternum fracturen besproken. Verschillende operatietechnieken worden beschreven, van cerclages tot plaat fixatie met eventueel een bot spaan bij non-union. Plaat fixatie geeft de meest stabiele

fixatie en de beste thoraxwand functie vergeleken met cerclages. Uit de studies die hier vergeleken zijn, blijkt nog steeds dat er geen eenduidige behandelingsstrategie is voor sternum fracturen.

Rib fracturen

Rib fracturen zijn de meest voorkomende thoracale letsels en komen in 10% van alle trauma patiënten voor en in ongeveer 30% van alle patiënten met significant thoraxtrauma. De aanwezigheid van rib fracturen is van groot klinisch belang. Zelfs geïsoleerde rib fracturen kunnen gepaard gaan met aanzienlijke gevolgen zoals persisterende pijnklachten en handicaps.

Een verhoogd aantal fracturen, oudere leeftijd en meervoudig gewonde patiënten met ribfracturen gaan gepaard met verhoogde morbiditeit en mortaliteit. De thoracale pijn veroorzaakt door ribfracturen, zorgt voor problemen bij hoesten en diep ademen, wat kan resulteren in atelectase en pneumonie. Een combinatie van optimale pijnstilling, longfysiotherapie, zuurstofsuppletie en positieve druk beademing wordt beschouwd als cruciaal bij het behandelen van patiënten met gebroken ribben. Epidurale analgesie, intercostale of paravertebrale blokkades en intraveneuze analgesie zijn de meest gebruikte technieken bij patiënten met ribfracturen. Op dit moment ontwikkelen patiënten met niet-operatief behandelde fladderthorax een pneumonie in 27-70% en hebben ze een mortaliteit van 25-51%. Ondanks optimale pijnstilling, lijden sommige patiënten nog steeds aan ondraaglijke pijn met respiratoire problemen. Er is dus ruimte voor verbetering.

Operatieve behandeling van rib fracturen

In **hoofdstuk 6** wordt de operatieve behandeling van multipele rib fracturen besproken.
Met betrekking tot chirurgische fixatie van ribfracturen is er nog steeds een gebrek aan prospectieve studies. Er is echter een toenemend enthousiasme in veel traumacentra om ribfixatie uit te voeren. Aangezien het bewijsniveau nog steeds beperkt is, is voorzichtigheid geboden om overbehandeling te voorkomen. De beschikbare literatuur over ribfixatie richt zich voornamelijk op patiënten met een fladderthorax. Er zijn slechts 3 kleine gerandomiseerde studies beschikbaar waarbij totaal 60 patiënten operatieve behandeling hebben gekregen. Deze drie onderzoeken bij patiënten met fladderthorax, ondanks al hun tekortkomingen, vertoonden allemaal een duidelijk verminderde behoefte aan mechanische beademing, verkorte duur van intensive care opname, minder pijn en minder pneumonie bij patiënten na ribfixatie. Daarom wordt ribfixatie als behandeling voor fladderthorax toenemend geaccepteerd.

Deze resultaten moeten echter in de juiste context worden gezien. Ten eerste werden er selectieve inclusiecriteria gebruikt. Twee van de bovengenoemde studies hebben ribfixatie uitgevoerd bij patiënten met een fladderthorax die afhankelijk waren van beademing, zonder uitzicht op afbouwen van de beademing. Bovendien hadden alle drie de studies verschillende exclusiecriteria, zoals ernstige letsels elders in het lichaam, neurotrauma of de afwezigheid van respiratoire insufficiëntie. Met betrekking tot de fladderthorax worden in de literatuur verschillende definities gebruikt. Definities variëren van klinische fladderthorax of radiologische fladderthorax waarbij er ten minste drie opeenvolgende ribben op twee of meer plaatsen per rib zijn gebroken. Echter, een Amerikaanse richtlijn definieert fladderthorax als 4 opeenvolgende ribben die op 2 of meer plaatsen zijn gebroken. De meeste studies spreken echter over tenminste 3 opeenvolgende ribfracturen welke op meer dan één plaats per rib zijn gebroken. Deze heterogeniteit in de definitie van fladderthorax gecombineerd met de wisselende in- en exclusie criteria maakt het moeilijk om studies te vergelijken.

De tweede groep, een veel grotere groep patiënten, zijn patiënten met meerdere (drie of meer) ribfracturen zonder fladder component. Deze groep is vanuit economisch oogpunt nog interessanter aangezien patiënten met multipele rib fracturen frequent voorkomen en veel vragen van de zorgcapaciteit.

De meerderheid van deze patiënten geneest zonder problemen. Primaire ernstige dislocatie of secundaire dislocatie van meervoudige ribfracturen kan echter leiden tot vervorming van de thoraxwand wat in de toekomst kan leiden tot een beperkte longcapaciteit of chronische intercostale pijn. Ribfracturen worden aanvankelijk vaak geassocieerd met een verminderde vitale capaciteit, wat resulteert in een toename van pulmonale complicaties. Een jaar na het thorax trauma blijkt de longfunctie nog steeds verminderd. Verschillende factoren kunnen een rol spelen in deze verminderde longfunctie. Oorzaken kunnen worden gevonden in ondraaglijke pijn, ernstige longcontusie of thoraxwand deformiteit die allemaal leiden tot ademhalingsproblemen.

Bij patiënten met multiple ribfracturen zijn de leeftijd en het aantal fracturen belangrijke uitkomstvoorspellers. Van veel van de complicaties van ribfracturen wordt gedacht dat ze verband houden met pijn waardoor patiënten minder goed kunnen doorademen. Optimale pijn controle verbetert de ademhaling, maar kan helaas niet altijd worden bereikt door de anesthesist. Bij patiënten met persisterende pijnklachten, ondanks pijnstilling, kan ribfixatie een goede optie zijn. Het bewijs is echter schaars. In een retrospectieve studie, vond men dat patiënten met multipele ribfracturen, zonder fladder component, goede korte termijn resultaten lieten zien en er werd ook een eerdere terugkeer naar 'normale activiteiten' gezien

bij patiënten na ribfixatie. Een andere studie over multipele meervoudige ribfracturen rapporteerde een significante vermindering van pijn en ook eerder terugkeren naar werk na ribfixatie. Er zijn nog geen andere vergelijkende studies over de operatieve versus de niet-operatieve behandeling van multipele rib fracturen.

In **hoofdstuk 7** wordt retrospectief de operatieve en niet-operatieve behandeling van rib fracturen vergeleken tussen twee level 1 traumacentra. Na matching van beide groepen werd er geen significant verschil in opname duur gevonden tussen de operatieve en niet-operatieve behandeling van rib fracturen bij zowel de patiënten met fladderthorax als ook de patiënten met multipele rib fracturen. Een mogelijke verklaring voor deze contrasterende resultaten kan zijn dat er in de eerdere onderzoeken striktere exclusie criteria zijn gebruikt, in vergelijking met dit onderzoek. Minder strikte inclusiecriteria resulteren waarschijnlijk in meer heterogeniteit, waardoor de generaliseerbaarheid van de resultaten toeneemt en de huidige praktijk beter wordt nagebootst. Dit kan echter ook het effect van ribfixatie in een heterogene groep van voornamelijk ernstig gewonde patiënten verminderen. Interessant is dat de duur van de intensive care opname en eventuele mechanische ventilatie in beide groepen van ons cohort lager was in vergelijking met andere studies. Ook op secundaire uitkomstparameters, zoals pijn, wordt dit onderzoek beperkt door het retrospectieve ontwerp, omdat gegevensverlies en onderrapportage de uitkomstmaten beïnvloeden. In onze dagelijkse praktijk is pijn de belangrijkste indicatie voor ribfixatie, maar we konden pijnscores en interventies voor pijnbehandeling niet vergelijken vanwege de beperkte beschikbaarheid van gestructureerde gegevens.

Omdat de geïncludeerde patiënten uit twee verschillende ziekenhuizen kwamen, waren er soms verschillen in patiënt karakteristieken tussen de operatieve en de niet-operatief behandelde groep. Met behulp van een propensity-score model konden we echter met succes matchen op alle gemeten basiskenmerken, waardoor mogelijke verstoringen als gevolg van eventuele verschillen in patiënt populatie werden geëlimineerd. Er zijn nog steeds ongemeten confounders (bijvoorbeeld pijn), maar we hebben de meeste bekende en eerder gerapporteerde confounders in onze analyse opgenomen en de impact van ongemeten confounding lijkt daarom beperkt. Desalniettemin kon in onze populatie geen voordeel van ribfixatie worden aangetoond voor één van de twee groepen (d.w.z. fladderthorax en multipele rib fracturen). Deze resultaten en het beperkte beschikbare bewijsmateriaal over dit onderwerp benadrukken de noodzaak van toekomstige studies voordat ribfixatie ingebed of verlaten wordt in de klinische praktijk. Er blijft nog steeds behoefte bestaan om de juiste patiënt te identificeren die baat zou kunnen hebben bij ribfixatie.

Rib fractuur non-union

Hoofdstuk 9 beschrijft een andere zeer zelden voorkomende indicatie, rib fractuur non-union. Er zijn zeer beperkte gegevens over de operatieve behandeling van rib- non-union. De belangrijkste klacht van non-union voor ribfracturen is pijn. Na ribfixatie voor non-union was de meerderheid (72%) van de patiënten tevreden zonder resterende pijn of slechts een beetje ongemak. Verschillende operatietechnieken worden gebruikt, maar overeenkomstig de literatuur, lijkt het niet nodig om een bot-transplantaat te gebruiken. Een mogelijke oorzaak voor een atrofische non-union is interpositie van intercostale spieren of periost, wat vaak wordt aangetroffen tijdens de operatie. Een andere oorzaak is het gebrek aan stabiliteit en overmatige beweging in de uiteinden van de breuk, wat hypertrofische non-union veroorzaakt. Het verwijderen van deze beknelling van de intercostale spier en het bieden van stabiliteit aan het bot door een plaat is voldoende om de ribben op de juiste manier te laten genezen. Na de operatie was 28% van de patiënten echter nog steeds niet tevreden en waren ze afhankelijk van pijnstillers. De pijn die resteerde was vaak neuropathische van aard. Dit komt mogelijk door interpositie van de intercostaal zenuw. Persisterende pijnklachten bij rib non-union zijn multifactorieel. Enerzijds kan er sprake zijn van mobiliteit ter plaatse van de non-union en anderzijds kan er sprake zijn van beklemming of beschadiging van de intercostaal zenuw. Bij het benaderen van rib- non-union kan het dan ook nodig zijn om de intercostale bundel te onderzoeken om nadien (persistente) neuropathische pijn te voorkomen.

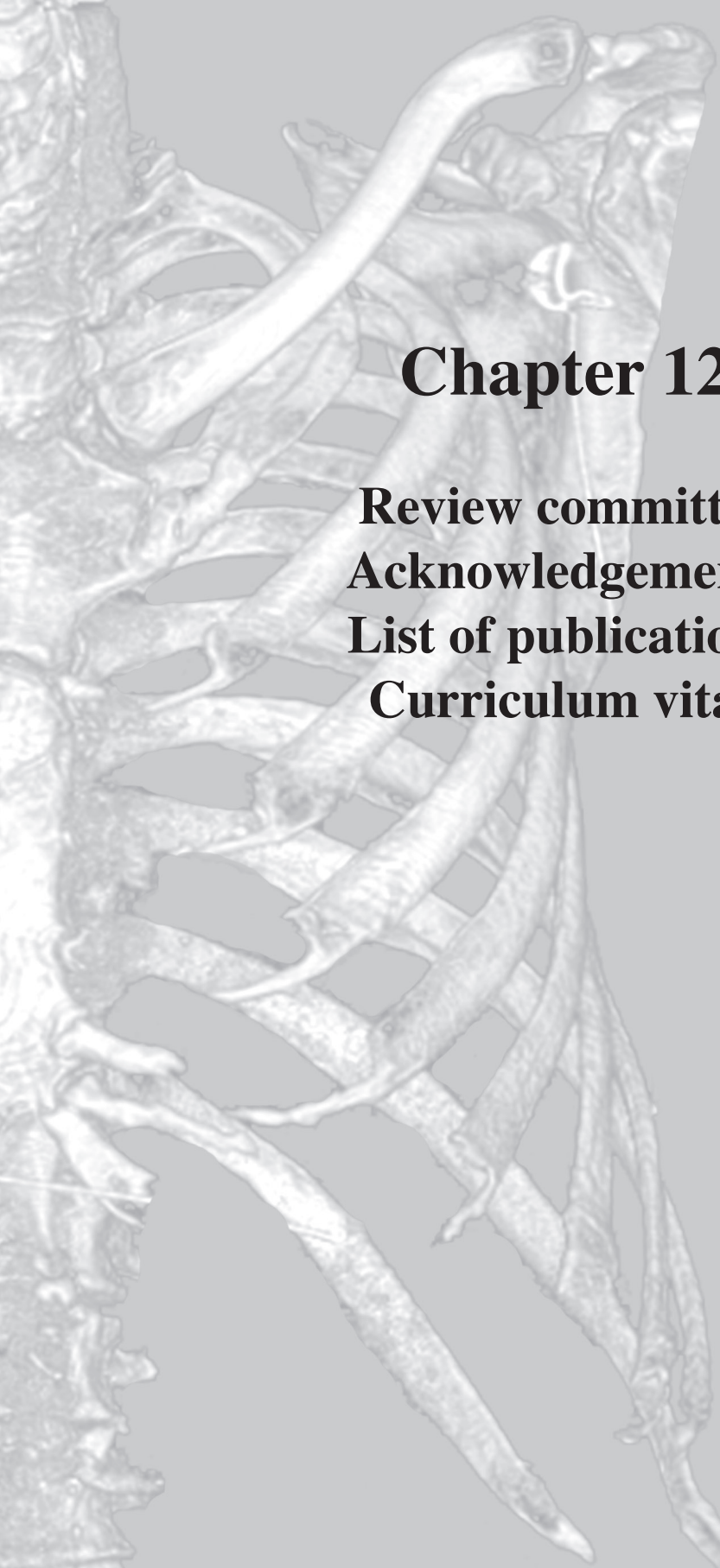
Lange termijn follow-up

Alle beschikbare gegevens zijn gericht op de follow-up op korte termijn. In het Universitair Medisch Centrum Utrecht hebben we sinds 8 jaar ribfixatie uitgevoerd. In deze periode hebben we nieuwe problemen ondervonden. Korte-termijn follow-up geeft informatie over complicaties zoals pneumonie (39%), overmatige pleuravocht (5%) en implantaat-gerelateerde infectie (3%) (**hoofdstuk 8**). Longontsteking is de meest voorkomende complicatie en onze percentages zijn vergelijkbaar met de bestaande literatuur. Infectie bij osteosynthese materiaal trad op in 3% van de operatief behandelde patiënten. Bij langdurige follow-up ervaart bijna de helft van de patiënten implantaat-gerelateerde klachten na ribfixatie. Bij vijfentwintig procent van de patiënten die klachten hadden, werden uiteindelijk alle, of een deel van de platen verwijderd na een mediane follow-up van 3,1 jaar. Drieënvijftig procent van de patiënten heeft klachten van de platen. Bij de meerderheid van de patiënten verbeterde de kwaliteit van leven het meest in het eerste jaar na het trauma. Vanwege het retrospectieve ontwerp was de longfunctie geen deel van deze studie. Uit **hoofdstuk 8** kan worden geconcludeerd dat ribfixatie een veilige procedure is

met een relatief goede kwaliteit van leven na langdurige follow-up, ondanks dat bij 10% van de geopereerde patiënten het implantaat is verwijderd.

Nu hoe verder te gaan? De belangrijkste vraag blijft: fixeren of niet fixeren? En zo ja, wie moeten we opereren en wanneer? Leeftijd en aantal fracturen zijn belangrijk bij het voorspellen van de uitkomst, maar kunnen niet alleen als indicatie voor een operatie worden gebruikt. Het belangrijkste symptoom bij patiënten met ribfracturen is pijn, omdat pijn kan leiden tot verminderde ademhaling, wat weer kan leiden tot een scala van complicaties.
In onze zoektocht naar de juiste indicatie voor ribfixatie lijkt pijn als een belangrijke factor te worden onderschat. Als de pijnbehandeling is geoptimaliseerd maar nog steeds onvoldoende is, kunnen patiënten baat hebben bij ribfixatie. Gecombineerd met de indicaties, zoals fladderthorax en thoraxdeformiteit, werd een stroomdiagram ontworpen voor patiënten met ribfracturen op basis van klinische parameters.

Voor de toekomst kan een algoritme, gebaseerd op klinische en diagnostische parameters, voor de behandeling van ribfracturen ons helpen bij het zoeken naar de juiste indicatie, maar voor het heden is het aan te bevelen zeer kritisch te zijn bij het bepalen van de operatie-indicatie.



Chapter 12

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Curriculum vitae

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Curriculum vitae

Mirjam Brenda de Jong was born in Utrecht on the 22nd of may 1973. After graduating from College Blaucapel (Atheneum) in Utrecht in 1991 she entered medical school at the university of Utrecht. In 1997 she went to the Groote Schuur Hospital in Cape town, South Africa, for her internship Gynaecology. In the same year she went to Boston, USA, for her internship neurology at the New England Medical Center followed by an internship Ear Nose Throat at the Harvard Eye and Ear infirmary also in Boston. In het last year of medical school she did experimental research in plastic surgery at the University Medical Center Utrecht (Prof. dr. M. Kon). After graduating from medical school in 1998, she started working as a resident at the department of general surgery of St. Franciscus Gasthuis in Rotterdam. In 1999 she started with a 2 and a half year period of research to sentinel nodes in esophageal cancer and breast cancer in Erasmus Medical Center Rotterdam (Prof. dr.H.W. Tilanus and Prof. dr. C.H.J. van Eijck).

In 2002 she started her training in general surgery in the Twenteborg Hospital in Almelo (Dr. J.G. van Baal). In 2006 she continued her last two years of training in the University Medical Center Utrecht (Prof.dr. I.H.M. Borel Rinkes) with focus on gastrointestinal surgery and oncology.

In 2008 she started as a fellow in pulmonary surgery in the Hagaziekenhuis in The Hague (Dr. P.V.M. Pahlplatz, Dr. W.H. Steup). In 2010 she worked as a locum surgeon at Maasziekenhuis Pantein in Boxmeer. After 6 months she started as a trauma fellow in the Leiden University Medical Center (Prof. dr. I.B. Schipper) where the research for the first part of this thesis started. Since 2013 she is a staff specialist at the department of Trauma Surgery of the University Medical Center Utrecht (Prof. dr. L.P.H. Leenen). She is married to Laurent-Jan van der Westen and they have 2 wonderful sons: Thom and Daniël.