Surgical Management of Rib Fractures Following Trauma

Eva-Corina Caragounis, M.D.

Department of Surgery, Institute of Clinical Sciences,
Sahlgrenska Academy, University of Gothenburg,
Gothenburg, Sweden.

UNIVERSITY OF GOTHENBURG

Gothenburg 2019

Cover illustration: “The sky is the limit” by Bertil Leidner.
Leidnerimaging.se

Surgical Management of Rib Fractures Following Trauma

eva-corina.caragounis@gu.se

ISBN 978-91-7833-314-1 (PRINT)
ISBN 978-91-7833-315-8 (PDF)
http://hdl.handle.net/2077/58504

Printed in Gothenburg, Sweden 2019
Printed by BrandFactory

In memory of Sophia Caragounis

"Jesus replied; Love the Lord your God with all your heart and with all your soul and with all your strength and with all your mind, and Love your neighbour as yourself".

Doctor Luke (New Testament, Luke 10:27)

Surgical Management of Rib Fractures Following Trauma

Eva-Corina Caragounis, M.D.
Department of Surgery, Institute of Clinical Sciences,
Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden.

ABSTRACT

Background: Surgical management of chest wall injuries has received increasing attention in recent years. The aim of this thesis was to study the mechanism of injury (MOI) in relation to chest wall injury patterns and short- and long-term outcome of surgery in patients with multiple rib fractures and unstable thoracic cage injuries.

Methods: Paper I is a retrospective study (n=211) of the association of MOI and injury patterns in patients operated for acute chest wall injuries. Paper II is a prospective longitudinal study (n=54) of the long-term outcome of surgery in patients with multiple rib fractures and flail chest. Paper III is a cross-sectional study (n=37) of the use of CT-lung volume estimation as a marker for lung function in patients operated for flail chest. Paper IV is a prospective controlled study (n=139) of the short- and long-term outcome of surgery in patients with unstable thoracic cage injuries.

Results: The MOI differs according to age and is associated with different chest wall injury patterns. Lateral and posterior flail segments are the most commonly seen. Symptoms of pain, lung function and Quality of Life (QoL), improve during the first post-operative year. CT-lung volume estimates increase significantly from pre-operative values to post-operative values and there is a high correlation between post-operative CT-lung volume and lung function. Surgery for unstable thoracic cage injuries does not decrease the need for mechanical ventilation. However, surgically managed patients have a decreased incidence of pneumonia (17% vs. 36%, p=0.013) and less pain (29% vs. 57%, p<0.05) the first months' post trauma. Patients operated without thoracotomy have a better residual lung function and lung volume. A gradual improvement in patient symptoms was seen and after one year there was no difference in symptoms, function or QoL between surgically and conservatively managed patients.

Conclusions: The MOI influences rib fracture pattern and associated injuries. Lung volume estimated by CT can be used as a marker for lung function. Surgery for unstable thoracic cage injuries decreases the incidence of pneumonia and reduces pain. Patients continue to improve gradually and no difference can be seen between the surgically and conservatively managed patients one year post trauma.

Keywords: Mechanism of Injury; Rib Fracture; Flail chest; Surgery; Mechanical Ventilator; Lung Function; Pain; Quality of Life

ISBN 978-91-7833-314-1 (PRINT)
ISBN 978-91-7833-315-8 (PDF)

Kirurgisk behandling av revbensfrakturer vid trauma

Eva-Corina Caragounis, M.D.

POPULÄRVETENSKAPLIG SAMMANFATTNING

Bakgrund: Revbensfrakturer är vanligt förekommande hos personer som drabbas av trubbigt våld mot bröstkorgen. Multipla revbensfrakturer med eller utan bröstbensskada, kan leda till instabil bröstkorg och andningssvikt. Kirurgisk behandling av revbensfrakturer har blivit allt vanligare på senare år med utvecklingen av plattor specifikt framtagna för revbensstabilisering. Syftet med denna avhandling var att studera skademekanism och dess relation till skademönster i bröstkorgen och associerade skador, samt korttids- och långtidsresultat av bröstkorgsstabiliserande kirurgi.

Delarbete I: Detta är en retrospektiv studie av 211 patienter som genomgått bröstkorgsstabiliserande kirurgi p.g.a. akuta bröstkorgsskador. Skademekanismen skilde sig beroende på ålder och det fanns ett samband mellan skademekanism och skademönster i bröstkorgen. Instabila revbenssegment var vanligast på sidan och baksidan av bröstkorgen. Skador i diafragma var vanligare än tidigare beskrivet, och sågs hos 18% av patienter som genomgick torakotomi.

Delarbete II: Detta är en prospektiv uppföljningsstudie av 54 patienter som genomgått bröstkorgsstabiliserande kirurgi p.g.a. multipla revbensfrakturer och instabil bröstkorg. Vi fann att patienternas besvär avseende smärta, rörelseförmåga, lungfunktion och livskvalitet förbättrades gradvis under ett år efter operationen.

Delarbete III: Detta är en tvärsnittsstudie av 37 patienter som genomgått bröstkorgsstabiliserande kirurgi p.g.a. instabil bröstkorg. Vi fann att lungvolym uppskattad genom datortomografi (CT) undersökning var större vid uppföljning jämfört med innan operation. Det fanns en stark korrelation mellan CT-lungvolym och lungfunktion.

Delarbete IV: Detta är en prospektiv studie av 64 patienter som opererats p.g.a. instabil bröstkorg och som jämförs med 75 patienter med liknande skador, som inte opererats. Det var ingen skillnad mellan behovet av respiratorvård. Lunginflammation var mindre vanligt hos patienter som opererades, 17%, jämfört med 36% hos patienter som inte opererats. Opererade patienter upplevde också mindre smärta första månaderna efter skadan. Efter ett år var det ingen större skillnad i symptom, funktion, aktivitet och livskvalitet mellan grupperna.

Slutsatser: Skademekanism påverkar skademönster i bröstkorgen och vilka associerade skador som ses. Lungvolym uppskattad med CT kan användas som markör för lungfunktion. Patienter som genomgår bröstkorgsstabiliserande kirurgi har lägre risk för lunginflammation och smärta första tiden efter skadan. Efter ett år ses ingen skillnad mellan opererade och icke-opererade patienter.

LIST OF PAPERS

This thesis is based on the following studies referred to in the text by their Roman numerals.

I. Mechanism of injury, injury patterns and associated injuries in patients operated for chest wall trauma. Caragounis E-C, Xiao Y and Granhed H.

Accepted in Eur J Trauma Emerg Surg. 2019.

II. Surgical treatment of multiple rib fractures and flail chest in trauma: a one-year follow-up study. Caragounis E-C, Fagevik Olsén M, Pazooki D and Granhed H.

World J Emerg Surg. 2016 Jun 14; 11:27.

III. CT lung volume estimates in trauma patients undergoing stabilizing surgery for flail chest. Caragounis E-C, Fagevik Olsén M, Granhed H and Rossi Norrlund R.

Injury. 2019 Jan; 50(1): 101-108. Epub 2018 Oct 16.

IV. Prospective controlled study of surgical management of unstable thoracic cage injuries and chest wall deformity in trauma. Caragounis E-C, Fagevik Olsén M, Sandström L, Rossi Norrlund R, Strömmer L and Granhed H.

Manuscript.

TABLE OF CONTENTS

ABSTRACT IV
POPULÄRVETENSKAPLIG SAMMANFATTNING V
LIST OF PAPERS VI
ABBREVIATIONS AND ACRONYMS 9
1 INTRODUCTION 11
1.1 Thoracic Trauma 11
1.1.1 Prevalence 11
1.1.2 Chest Wall Injury 11
1.1.3 Flail Chest 13
1.2 Diagnosing Thoracic Injuries 14
1.2.1 Chest X-Ray 14
1.2.2 Ultrasound 15
1.2.3 Computed Tomography 15
1.2.4 Injury patterns 15
1.3 Management of Chest Wall Injuries 16
1.3.1 History 16
1.3.2 Implants 18
1.3.3 Outcome of surgery 19
2 AIMS 21
3 PATIENTS AND METHODS 22
3.1 Thesis Overview 22
3.2 Methods 23
3.2.1 Patient and Trauma Demographics 23
3.2.2 Radiological Investigation 24
3.2.3 Surgical Technique 25
3.2.4 Subjective symptoms and Quality of Life 27
3.2.5 Movement of the Thorax, Spine and Shoulders 27

3.2.6 Lung Function and Volume 28
3.3 Paper I 29
3.4 Paper II 30
3.5 Paper III 31
3.6 Paper IV 32
3.7 Statistical Methods 34
4 ETHICAL CONSIDERATIONS 36
4.1 Patient inclusion 36
4.2 Ethical approval 37
4.3 Conflict of interest 37
5 RESULTS 38
5.1 Mechanism of Injury and Injury Patterns (Paper I) 38
5.2 Longitudinal Study- Outcome of Surgery (Paper II) 40
5.3 CT- Lung Volume (Paper III) 42
5.4 Prospective Controlled Study (Paper IV) 45
6 GENERAL DISCUSSION 49
7 CONCLUSIONS 60
8 FUTURE PERSPECTIVES 61
ACKNOWLEDGEMENTS 62
REFERENCES 64

ABBREVIATIONS AND ACRONYMS

AIS	Abbreviated Injury Scale
ARDS	Acute Respiratory Distress Syndrome
ATLS	Advanced Trauma Life Support
CI	Confidence Interval
CIS	Chest wall Injury Scale
COPD	Chronic Obstructive Pulmonary Disease
CPR	Cardiopulmonary resuscitation
CT	Computed Tomography
CXR	Chest X-Ray
DRI	Disability Rating Index
ECMO	Extra-Corporeal Membrane Oxygenation
FAST	Focused Assessment with Sonography in Trauma
*e*FAST	Extended Focused Assessment with Sonography in Trauma
FEV1	Forced Expiratory Volume in one second
FVC	Forced Vital Capacity
FC	Flail Chest
GCS	Glasgow Coma Scale
ICU	Intensive Care Unit
ISS	Injury Severity Score
KS	Karolinska University Hospital Solna
LIS	Lung Injury Scale
LOS	Length of Stay
MEP	Maximal Expiratory Pressure
MIP	Maximal Inspiratory Pressure

MOI	Mechanism of Injury
MODS	Multiple Organ Dysfunction Syndrome
MVC	Motor Vehicle Collision
NISS	New Injury Severity Score
NIV	Non-Invasive Ventilation
NSAID	Non-Steroidal Anti-Inflammatory Drugs
OR	Odds Ratio
ORIF	Open Reduction Internal Fixation
PEF	Peak Expiratory Flow
PVA	Pedestrian Vehicle Accident
RCT	Randomized Controlled Trial
RMMI	Respiratory Movement Measuring Instrument
SD	Standard Deviation
SU	Sahlgrenska University Hospital
TBI	Traumatic Brain Injury
TEDA	Thoracic Epidural Analgesia
3D	Three-dimensional
TLC	Total Lung Capacity
TTO	Time Trade-Off
VAS	Visual Analogue Scale
VATS	Video-Assisted Thoracoscopic Surgery
VCAR	Volume Computer Assisted Reading
WBCT	Whole Body Computed Tomography
QoL	Quality of Life

1 INTRODUCTION

Trauma is a major global health issue and responsible for causing injury in tens of millions of people that result in long-term disability and over five million deaths annually.[1] In Sweden, despite having the second lowest incidence of deaths due to road traffic accidents in Europe,[2] trauma was responsible for hospitalizing over 109,000 injured people[3] and causing 4,984 deaths in 2017.[4] Trauma is the sixth leading cause of death in all age groups and the leading cause of death in people aged 10–44 years.[4] Although blunt trauma is the dominating mechanism of injury (MOI) in Sweden, occurring in approximately 90% of cases, the incidence of penetrating injuries is on the rise.[5]

1.1 Thoracic Trauma

1.1.1 Prevalence

Trauma to the thorax causing injuries to the chest wall, lungs and cardiovascular system, accounts for approximately 23–37% of trauma-associated mortality.[6-10] Although traumatic brain injury (TBI) and exsanguination are the most common causes of death,[6,11] respiratory failure is a contributing factor in 17% of patients with blunt trauma.[11,12]

1.1.2 Chest Wall Injury

Rib fractures are common and occur in approximately 9-12% of all trauma patients[12-17] and in 34–39% of patients with thoracic trauma[18,19] seeking medical attention. Isolated rib fractures are seen in 6–13% of cases with thoracic trauma.[12,15,18] Rib fractures are commonly associated with both intra- and extra-thoracic injuries. Common intra-thoracic injuries include pneumothorax in 29–37%,[12,13,18,19] haemothorax in 21–32%,[12,13,18,19] lung contusion in 17–31%,[12,13,16,18] lung laceration in 1.6–5.3%,[12,13,16] cardiac injury in 0.7–1.3%,[13,16,18] great vessel injury in 1.5–2%,[12,13,16,18] and diaphragmatic injury in 1.2–3% of cases.[12,13,16,19] The majority of patients with thoracic trauma, especially blunt trauma, can be treated conservatively.[20-22]

Multiple rib fractures can lead to chest wall instability and flail chest (FC).[23] Flail chest has been described in 2.5–9% of patients with rib fractures[12,16,18,24] and in 22% of patients with major chest trauma requiring intensive care.[25] Sternal fractures are present in 11% of patients with unilateral FC and 21% of patients with bilateral FC.[26] Injury to the chest wall is associated with injuries to the upper extremities, with fractures in the clavicles and scapula, and the thoracic spine.[18,19,26] Patients with FC have a significantly higher prevalence of pneumothorax, haemothorax and lung contusion.[13] In fact, pneumothorax and haemothorax are seen in approximately 46–53% of patients with FC[13] and lung contusion in 46–54%.[13,27] No significant difference in the prevalence of lung laceration, cardiac injury, great vessel injury and diaphragmatic injury has been described when comparing flail injury with non-flail injury.[13]

Multiple rib fractures and FC are generally associated with high-energy trauma, such a road traffic accidents.[12,15,18,19,26,28] In the elderly, however, multiple rib fractures can occur after low-energy impact, such as falls that cause multiple, comminute and displaced rib fractures.[17,29-31] An increase in the number of rib fractures is associated with an increase in morbidity, and there is a correlation between the number of ribs fractured, injury severity score (ISS)[32] and mortality.[12,14] A scoring system, RibScore, has been suggested for defining the risk of respiratory failure, pneumonia and tracheostomy in relation to chest wall injuries.[33] Mortality increases markedly with more than five fractured ribs[12,14] (Fig. 1).

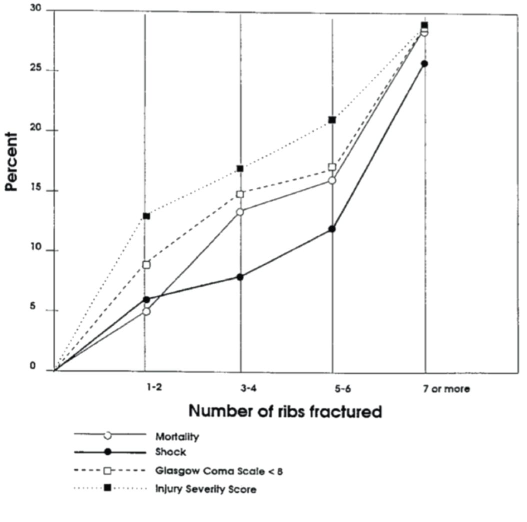

Figure 1

The association between the number of rib fractures and mortality, shock, GCS<8 and ISS. Reproduced with permission from Zeigler et al., 1994.[12]

Mortality rate in trauma patients with flail chest has historically been high and described as 33-44%.[12,13] However, with the development of trauma care, the mortality rate has decreased but is still described to be 16-19% in recent years.[18,27] The risk of mortality is associated not only with the number of fractured ribs[14] but also with the age of the patient,[16,17,29] with an increased risk already from the age of 45.[16] Elderly patients with rib fractures often present with a lower ISS but have a higher mortality, than younger patients.[17,29]

1.1.3 Flail Chest

Unstable thoracic cage injuries have been described using various terms. In 1945, Hagen described “stove in chest”, a term used for unstable thoracic cage injuries with chest wall deformity.[34] In 1949, Heroy used the term “steering wheel injuries” in patients admitted due to blunt thoracic trauma.[35] The MOI was head-on collision automobile accidents without restraints causing bilateral anterior rib fractures. Paradoxical respiration was described in 14% of the patients, and defined as “a movement of the thoracic cage in a direction opposite to that seen in the normal”.[35] The term flail chest (FC) was later coined by Cohen in 1955,[36] and has been used to describe both the paradoxical breathing associated with chest wall instability and the anatomical condition of multiple consecutive rib fractures. The currently widely used definition, according to the Abbreviated Injury Scale (AIS) 2008,[23] defines FC as an anatomical condition that requires three or more adjacent ribs, fractured in more than one location in order to produce a free-floating segment, and/or paradoxical chest movement. Paradoxical breathing is not, however, seen in all cases of anatomical FC,[37] but is classically described in “steering wheel injuries”[35] as these produce more anterior flail segments that are easier to visualize.

The pathophysiology in paradoxical breathing occurs when a free-floating segment of the chest wall and the underlying lung tissue moves inward during inspiration as the intra-pleural pressure becomes negative, thereby collapsing parts of the lung on the effected side and possibly causing the mediastinum to shift to the opposite side. During expiration, the intra-pleural pressure increases and the injured segment and the underlying lung tissue instead move outward, possibly causing the mediastinum to shift to the affected side. Parts of the lung, therefore, are not ventilated properly and the condition is associated with decreased lung compliance and increased lung resistance (Fig 2).[38]

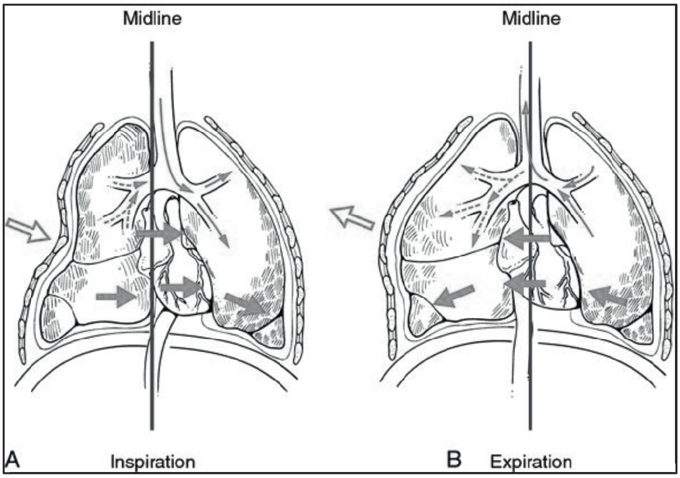

Figure 2

Movement of a flail segment (open arrows) and the underlying intra-thoracic structures (large arrows), during inspiration and expiration. Small arrows show normal air movement and dashed arrows show abnormal air movement. From Miller-Keane., 2003.[39]

The pain associated with rib fractures increases with every breath and movement of the chest wall, causing an inability to cough properly and increases the risk of pulmonary disease.[35] Flail chest is associated with pulmonary contusions, respiratory insufficiency, a need for ventilator support, development of Acute Respiratory Distress Syndrome (ARDS) and a high mortality, and can serve as a marker for significant injuries.[13] However, ARDS can be difficult to distinguish from pulmonary contusions. Quantification of pulmonary contusions on Computed Tomography (CT) has been used in order to predict both the development of ARDS and clinical outcome.[40-42] Acute Respiratory Distress Syndrome and Multiple Organ Dysfunction Syndrome (MODS) are responsible for mortality in 37% of patients with flail chest.[13]

1.2 Diagnosing Thoracic Injuries

Chest wall injuries are frequently underestimated and the sensitivity for their diagnosis depends on the radiological investigation used.

1.2.1 Chest X-Ray

Thoracic injuries can be diagnosed using a variety of modalities. Frontal Chest X-Ray (CXR) is often used in the initial assessment and resuscitation of the trauma patient, according to the Advanced Trauma Life Support® (ATLS®) protocol.[20] The CXR, however, has a low sensitivity for the diagnosis of anterior pneumothorax and lung contusions,[43] moreover, it fails to diagnose the majority of rib fractures, such that their occurrence is often underestimated.[44,45]

1.2.2 Ultrasound

Ultrasound of the trunk has been shown to be a valuable adjunct in the initial assessment and resuscitation of the trauma patient through the implementation of the Focused Assessment with Sonography in Trauma (FAST) or extended FAST (*e*FAST) protocols.[46,47] The ultrasound probe is placed in different positions to discern fluid in the pericardial sac, hepatorenal space, splenorenal space and pelvis in FAST,[46] with the addition of examining the thorax for the presence of pneumo- and haemothorax, in *e*FAST.[47] Although the examination has the advantage of being fast, non-invasive, radiation free, repeatable, and can be performed at the bedside with a high specificity, its disadvantage is a low sensitivity for diagnosing intra-abdominal injuries.[48] Ultrasound can also be used for diagnosing chest wall injuries and has a higher sensitivity for discovering rib fractures and chondral injuries than CXR.[49] It can, however, be time-consuming and difficult to perform in the awake patient due to pain. The presence of subcutaneous emphysema and the location of fractures behind the scapula make diagnosis difficult.[50]

1.2.3 Computed Tomography

Computed tomography (CT) is the diagnostic tool of choice in diagnosing chest wall and intra-thoracic injuries. The examination is often performed as part of a whole-body CT (WBCT) in a patient subjected to blunt poly-trauma. Computed tomography has a higher sensitivity for diagnosing rib fractures, discovering 75% more fractures than CXR.[45,49] Nevertheless, CT may also fail to diagnose rib fractures, especially if these are non-displaced, chondral[51] or anterior.[52] Whilst, three-dimensional (3D) images of the thorax provides an overview of the chest wall injury, it is often not possible to see chondral injuries clearly, although, these images can still aid the surgeon in planning an operative procedure.

1.2.4 Injury patterns

Rib fractures are typically described as anterior, lateral and posterior, and can be divided into upper and lower rib fractures, or rib fractures pertaining to different zones.[53] A formalized and generally accepted definition of these terms would be valuable. The location of a rib fracture may be associated with increased risk of concomitant injuries. Upper rib fractures, particularly fracture of the first rib, can be associated with subclavian vessel injuries, whereas, fractures of the lower ribs are associated with abdominal injuries.[54,55] There is a lack of knowledge in the association of MOI and different chest wall injury patterns.

1.3 Management of Chest Wall Injuries

1.3.1 History

The preferred treatment of multiple rib fractures and flail chest has alternated through time between conservative management and surgical stabilization, according to advances made within different disciplines of medicine. In the beginning of the last century, different types of external fixation were tried. Adhesive tape in conjunction with local nerve block was described in 1941 by Berry as a form of external fixation.[56] The Drinker respirator, also known as the "iron lung", was used as a form of external splinting.[34] Apart from adhesive tape, sandbags were used for external stabilization, although admittedly it was painful for the patient.[35] External stabilization of flail chest was attempted with the use of different types of traction[57 35] (Fig. 3 and 4).

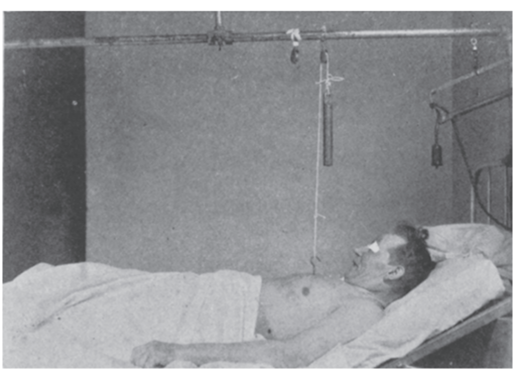

Figure 3
Skeletal traction of sternal flail chest by means of clothes´ hanger hook with a counter-weight. Reproduced with permission from Jaslow, 1946.[57]

The goal of the traction was to stabilize the chest to reduce chest pain, as well as to improve lung function by reducing resistance to lung expansion and reducing the risk of atelectasis, respiratory failure and pneumonia. With the development of artificial respiration using a mechanical ventilator, internal stabilization with continuous positive pressure ventilation became the treatment of choice.[58] The patient was treated with continuous ventilation until paradoxical breathing had subsided, and was slowly weaned with successively longer periods of spontaneous ventilation.[59]

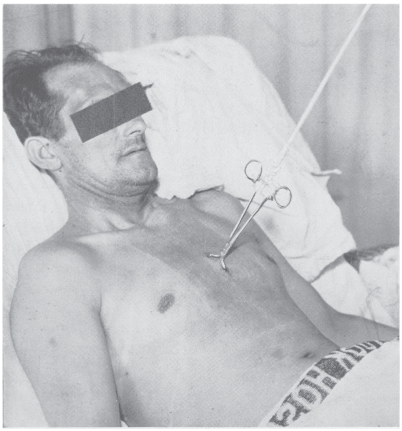

Figure 4
Step-wise skeletal traction of "steering wheel injury" applied under local anaesthesia. Initially, two small incisions were made in the midline of the sternum and the outer cortex was drilled. Vitallium wood screws were applied with traction, which lasted approximately 12 hours before the screws were pulled out. These were then replaced with reduction forceps and ten pounds of traction was applied and maintained for 17 days. Reproduced with permission from Heroy et al., 1951.[35]

The problem with the early external and percutaneous stabilization and traction methods, as well as the internal splinting with a mechanical ventilator, was the long period of hospitalization and immobilization.[27,60] Immobilization is associated with an increased risk of pulmonary infections[61] and thromboembolic events.[62] In addition, mechanical ventilation causes injury to the lungs through the administration of high pressure and high volume.[63] The ventilation induced lung injury does not only include barotrauma[64] but causes injury on a microscopic level with the release of inflammatory mediators.[65]

The conservative management of rib fractures and flail chest is associated with long-term disability and chronic pain. Although, there are only a few small follow-up studies including different variables and follow-up times, they show a marked level of problems with chronic chest wall pain, decreased lung function, and a need for the patient to change their level of activity and often their profession[60,66,67] (Table 1).

Acute pain can be a predictive factor for prolonged pain and disability. The severity of acute pain after thoracotomy, for example, has been shown to predict long-term pain.[68] Curbing the experience of pain in the acute phase in patients with multiple rib fractures may, therefore, decrease long-term morbidity. Thoracic epidural analgesia (TEDA) has been used to alleviate pain in hospitalized patients. Whilst TEDA has been shown to decrease mortality, it has no effect on the incidence of pneumonia in patients with rib fractures.[14,69] Patients receiving epidural analgesia also have a longer hospital length of stay (LOS).[69]

Table 1 *Chronic subjective and objective problems for patients with previous flail chest.*

Parameter	**Landerscaper et al., 1984 [60] n=32**	**Beal et al., 1985 [66] n=22**	**Fabricant et al., 2013 [67] n=203**
Follow-up time	0.5–12 years	50–732 days	2 months
Thoracic pain	49%	23%	59%
Chest tightness	25%	n/a	n/a
Dyspnoea	63%	18%	n/a
Limited chest expansion	46%	n/a	n/a
Visible deformity	28%	14%	n/a
Decreased CXR lung volume	27%	9%	n/a
Abnormal lung function	57%	n/a	n/a
Limited activity	37%	n/a	76%
Lifestyle changes	72%	n/a	n/a
Return to work	54%	n/a	n/a
Unable to work	39%	18%	6%
Chronic lung infection	n/a	18%	n/a

n/a= non-applicable

1.3.2 Implants

The different types of techniques for external and percutaneous stabilization of rib fractures have largely focused on anterior instability and placing the sternum under traction. Open surgery for rib fractures was first described by Dor in 1967, who used Kirschner wires (K wires) to stabilize rib fractures.[70] Open reduction and internal fixation (ORIF) was performed using different orthopaedic devices and techniques.[71] Sillar was the first to report the use of ORIF with plate fixation.[72] With the development of fixation materials dedicated to rib fracture stabilization and improved techniques, surgical management has gained increasing attention in recent years, challenging the role of mechanical ventilation as the preferred or only method for managing patients with multiple rib fractures and unstable thoracic cage injuries in respiratory failure.

Different types of implants are available (Fig. 5). These include the flexible Labitzke plate,[73] Judet plate or struts[74] and Sanchez-Lloret plate,[75] and are all fitted with clamps and require no drilling into the bone. The RibLoc® plate or U-plate (Acute Innovations™)[76] and the Stratos® system consist of short plates that are fixed with angular stable screws.[77] Different types of anatomical plates have also been developed, such as the MatrixRIB™

Fixation System (DePuy Synthes); where the plates and splints are fixed with locking screws.[71,78] The Inion OTPS™ Fixation System (Inion Oy, Tampere Finland) has the advantage of being biodegradable.[79,80]

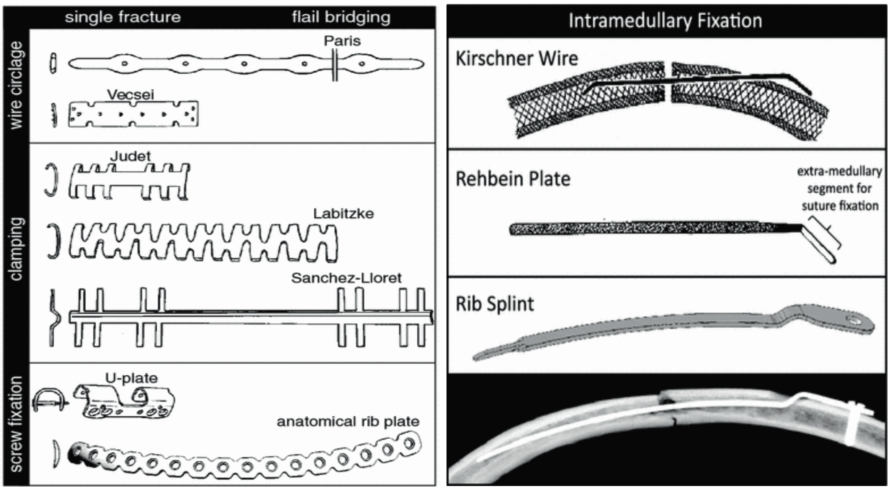

Figure 5 *Different implants for rib fracture fixation. Plates (left) and intramedullary splints (right). Reproduced with permission from Fitzpatrick et al., 2010* [81]

Several studies have been published describing surgical management with the different types of implants depicted above. Few reports, however, document the problems encountered and the differences in biomechanical stability achieved with different implants, making any comparison of study results difficult.

1.3.3 Outcome of surgery

Three small Randomized Controlled Trials (RCT´s) comparing surgical and conservative management of flail chest, using different forms of stabilization have been carried out.[79,82,83] Two of the studies found a decreased LOS on mechanical ventilator,[82,83] although a third study found no statistical difference between surgically and conservatively managed patients.[79] The studies found a decreased LOS in Intensive Care Unit (ICU)[79,82,83] and in one study LOS in hospital was decreased in the operated patients.[79,83] Similarly, several prospective and retrospective studies have found decreased LOS on mechanical ventilator[78,84-86] and in ICU in surgically managed patients.[25,87-89] However, in patients with pulmonary contusions the benefit of surgery has not been shown.[86,90] A decreased time of ventilator support in patients with chest wall injuries can potentially be more cost-effective than conservative management. [79,82,91] However, there is no evidence that surgery decreases the need for mechanical ventilation. As most studies only include patients already in respiratory failure, requiring ventilation, it is unknown if an early operation will prevent ICU care. One of the RCTs included patients not on mechanical ventilator at the time of inclusion, and found no difference in the need of mechanical ventilation between surgically and conservatively managed patients (35-45%).[83]

Several studies have found a decreased incidence of complications such as tracheostomy[25,79,82,88,92] and pneumonia,[25,82,83,88,89] in operated patients compared to controls. Two studies found a decreased mortality rate in surgically managed patients.[25,92] In contrast, other studies found no difference in the need for a tracheostomy,[89,90] in the incidence of pneumonia[79,84] or in the mortality rate between surgically and conservatively managed patients.[83] However, there are differences in the demographics, injury burden and timing and mode of surgical stabilization between the patients included in the studies, which may influence the results.

Two RCT studies comparing surgical and conservative management of flail chest have reported significantly better lung function in surgically managed patients two months after surgery[83] and consistently up to a year after surgery.[82] None of the studies have shown a significant improvement in Forced Expiratory Volume in one second (FEV1).[79,83] The only RCT to study quality of life (QoL) found no difference between the groups after 6 months.[79] A clinical follow of 23 patients managed surgically for flail chest found remaining chest pain in 35% of patients, reduced lung function and a decreased range of motion in the thorax on the operated side six months after surgery[93] However, there is still a lack of knowledge concerning the impact of surgery on the healing of the chest wall, the experience of pain, physical function and the ability to return to work, as well as the Quality of Life.

2 AIMS

The overall aim of this thesis was to study the role of surgery in the management of rib fractures and its impact on clinical outcome.

The specific aims were to:

I Study the mechanism of injury (MOI), injury patterns and associated injuries in patients with chest wall trauma undergoing surgery.

II Investigate the long-term patient outcomes associated with pain, physical function, lung function and quality of life (QoL) after surgical stabilization of chest wall injuries.

III Evaluate the use of pre- and post-operative computed tomography (CT) images of the thorax in order to estimate and compare pre- and post-operative lung volumes and the use of CT as a marker for lung function.

IV Compare short-term and long-term clinical outcomes in patients with unstable thoracic cage injuries treated surgically compared to those treated conservatively.

3 PATIENTS AND METHODS

3.1 Thesis Overview

Patients included in the studies (Table 2) were recruited from Sahlgrenska University Hospital (SU) (papers I–IV) and Karolinska University Hospital (KS) (Paper IV). Patients from SU were managed surgically, whereas patients from KS were managed conservatively.

Table 2 *Main research questions, study design and outcome measures in papers I-IV.*

Paper	Main Research Question	Study Design	Patients	Outcome Measures
I	Mechanism of injury and injury patterns in patients undergoing chest wall surgery	Retrospective	n=211	Mechanism of Injury Chest Wall Injury Patterns Associated Injuries
II	Long-term effects of chest wall surgery	Prospective, Longitudinal	n=54	Complication Mortality Pain Lung Function Breathing Movement Range of Motion Disability QoL
III	CT-lung volume estimation as a marker of lung function in patients with flail chest	Cross-sectional	n=37	CT-Lung Volume Lung Function Pain Range of Motion Breathing Movement
IV	Need of mechanical ventilator in surgically vs. conservatively managed patients with unstable thoracic cage injuries	Prospective, Controlled	n=139 Clinical follow-up n=92	LOS on ventilator, ICU and hospital Complication Mortality Pain Range of Motion Shoulder Function Breathing Movement Lung Function CT-Lung Volume Disability Physical activity Return to Work QoL

QoL=Quality of Life, CT=Computed Tomography, LOS=Length of Stay, ICU=Intensive Care Unit

Data from 211 trauma patients treated at SU during the period September 2010 to September 2017 and from 75 patients treated at KS during the period June 2014 to June 2017 were included in this thesis. All patients from SU in papers II–IV were included in Paper I. Some patients were included in three of the papers, twenty patients in papers I–III and nine patients in papers I, III and IV. Patients in papers II and IV did not overlap (Fig. 6).

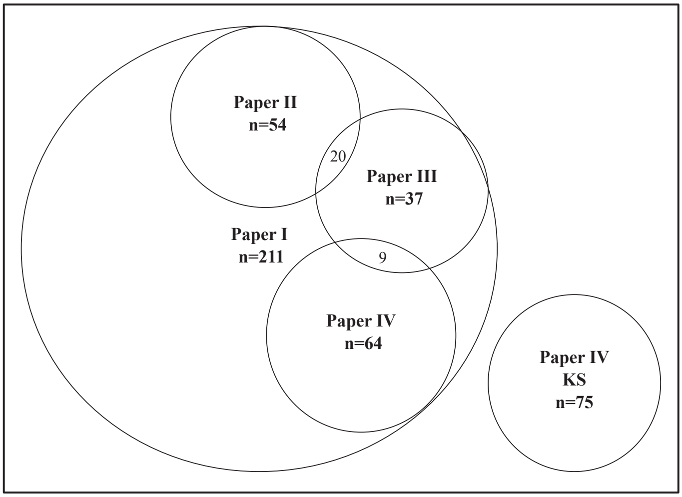

Figure 6 *Distribution of patients in the studies in papers I–IV.*
KS=Karolinska University Hospital Solna.

3.2 Methods

3.2.1 Patient and Trauma Demographics

Patient and trauma demographics were collected from studied patients. Injury severity scores were used to assess trauma burden and the severity of injury. Abbreviated Injury Scales (AIS) for the different injuries were estimated (1–6)[23] and ISS (1–75)[32] and New Injury Severity Score (NISS) (1–75)[94] were calculated (Table 3).

Included patients were offered routine analgesia with paracetamol, Non-Steroidal Anti-Inflammatory Drugs (NSAID), opioids and TEDA. Some surgically managed patients received an inter-pleural catheter per-operatively for administration of local analgesia. Low-molecular weight heparin was given subcutaneously as thrombotic prophylaxis in all trauma patients, as routine.

Table 3 *Criteria for inclusion and patient characteristics in papers I-IV.*

Patient characteristics	Paper I	Paper II	Paper III	Paper IV	
	Operated (n=211)	Operated (n=54)	Operated (n=37)	Operated (n=64)	Controls (n=74)
Inclusion	≥ 15 years Acute chest wall injuries	≥ 18 years FC or >4 rib fractures and respiratory insufficiency	≥ 18 years FC	≥ 18 years Unstable thoracic cage injury and/or chest wall deformity	
Exclusion	Non-union fractures Post-CPR fractures	Severe TBI Spinal cord injury	Severe TBI Spinal cord injury Decreased lung function Decreased wall chest movement	Severe TBI (AIS>3) Spinal cord injury Decreased lung function Decreased chest wall movement	
Sex					
Male	155(73.5%)	40 (74%)	26 (70%)	47 (73.4%)	67 (89.3%)*
Female	56 (26.5%)	14 (26%)	11 (30%)	17 (26.6%)*	8 (10.7%)
Age	58.2±15.6	56.2±14.9	62.6±13.7	58.6±15.0	54.9±16.0
ISS	21 (9–66)	20 (9–66)	20 (9–54)	21 (9–50)	21 (9–66)
NISS	34 (14–66)	34 (16–66)	27 (17–66)	34 (17–59)	29 (14–66)

FC=Flail Chest,[23] CPR=Cardiopulmonary Resuscitation, TBI=Traumatic Brain Injury, AIS=Abbreviated Injury Scale,[23] ISS=Injury Severity Score, NISS=New Injury Severity Score. *Pearson's Chi-square Test $p<0.05$.

3.2.2 Radiological Investigation

Patients for whom a trauma team activation had been triggered were assessed and resuscitated according to ATLS® principles.[20] Frontal CXRs and FAST[46,47] were performed in selected patients. Upon admission, patients underwent a CT of the thorax with intravenous contrast medium, often as part of a WBCT. In patients undergoing surgery, 3D reconstructions based on images with 0,625 mm slice thickness were produced using the program AW Volume Share™ 5 (Advantage Workstation 2.0, GE Healthcare, Waukesha, USA) to plan the surgical procedure (Fig. 7).

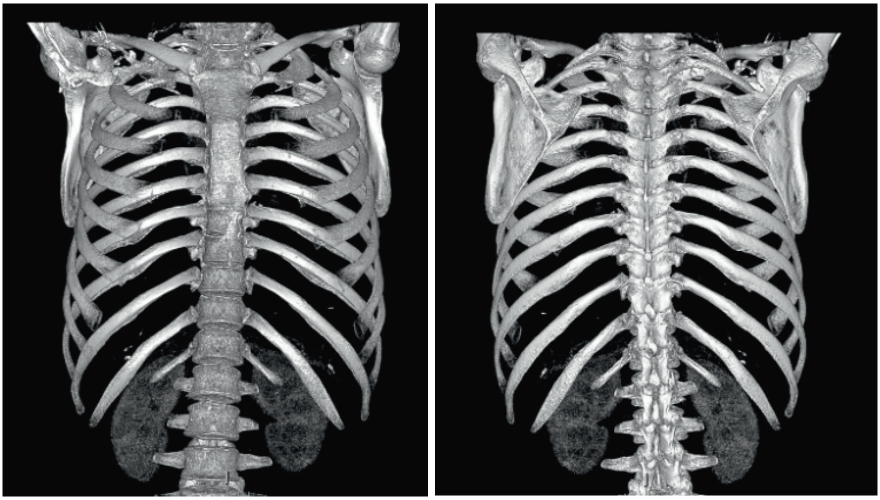

Figure *7 Anterior (left) and posterior (right) 3D images of CT Thorax.*

3.2.3 Surgical Technique

Patients undergoing chest wall surgery received broad-spectrum intravenous antibiotic therapy prophylactically, which was discontinued as soon as the chest drains had been removed. Patients were intubated with either a double-lumen endotracheal tube (Paper II and selected patients in papers I, III and IV) or with a single lumen endotracheal tube. General anaesthesia was administered. Patients were placed in either a supine, abdominal or lateral (left vs. right) position, depending on the location of the fractures to be stabilized. In patients, in Paper II, large skin incisions were made and a non-muscle sparing thoracotomy was performed to gain good access to the chest wall and the intra-thoracic structures (Fig. 8). In papers I, III and IV, the operative technique varied with the development of a more minimally invasive approach, typically using one or more incisions, with or without a thoracotomy (Fig. 9). Open reduction internal fixation (ORIF) of rib fractures was performed using the MatrixRIB™ Fixation System (DePuy Synthes, West Chester, USA), consisting of pre-shaped angular locked plates with bi-cortical screws in titanium and intra-medullary splints to stabilize rib fractures. In case of a short intermediate segment, a long plate was placed above both fractures with bridging technique.[95] Intramedullary splints were preferred for subscapular fractures in order to retain the normal configuration of the thoraco-scapular space. Likewise, the plates were used for stabilizing sternal fractures. The aim was not to stabilize all fractures, but to convert a flail segment into a non-flail segment.

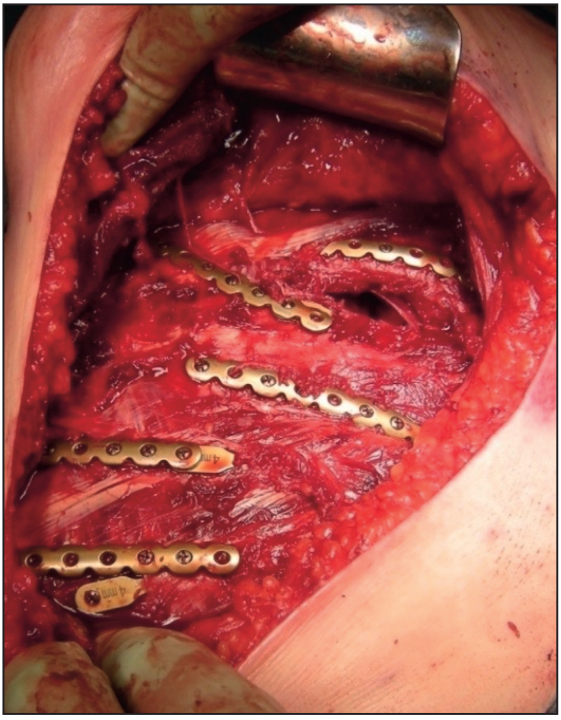

Figure 8

Rib fracture surgery with a non-muscle sparing approach, where the retractor lifts up the scapula. A thoracotomy has been performed to clean out haematoma, and identify and manage intra-thoracic injuries. Multiple plates and an intra-medullary splint, from the MatrixRIB™ Fixation System (DePuySynthes) has been placed above and below the thoracotomy.

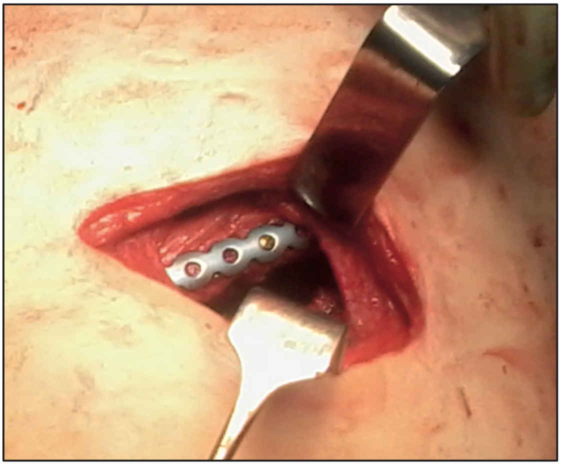

Figure 9

Rib fracture surgery with a minimally invasive muscle sparing approach. The muscles are split along the length of the fibers instead of being divided. A mini thoracotomy incision has been performed for pleural toilet and to inspect the diaphragm. A plate from the MatrixRIB™ Fixation System (DePuySynthes) has been placed below the thoracotomy. Deep Langenbeck retractors show the size of the incision.

3.2.4 Subjective symptoms and Quality of Life

A standardized questionnaire was developed, where patients answered yes/no to pain at rest, pain when breathing normally, breathlessness, local discomfort, and the use, type and dose of analgesia.

Physical activity was assessed by using the Grimby activity scale, where patients graded their activity according to; physically inactive (1), light physical activity (2), regular physical activity and training (3), hard physical training for competitive sports (4).[96,97]

Physical function was estimated by using the Disability Rating Index (DRI) questionnaire.[98] Patients marked their answers to the questions on a Visual Analogue Scale (VAS). The distance from 0 (i.e., no difficulties) to 100 (i.e., maximal difficulty) was measured as 0 – 100 mm using a ruler. The mean of all results in each individual patient was calculated, where 100 was the worst possible outcome and 0 was the best.

Quality of Life (QoL) was assessed using the three-graded EQ-5D-3L instrument[99] in Paper II, and the five-graded EQ-5D-5L instrument[100] in Paper IV from EuroQoL (Rotterdam, Netherlands). The EQ-5D instrument poses questions concerning mobility, self-care, usual activities, pain or discomfort and anxiety or depression. Patients answered whether they had no difficulty (1), some difficulty (2) or severe problems (3) with the aforementioned tasks for 3L or no problems (1), slight problems (2), moderate problems (3), severe problems (4), unable (5) for 5L. The results from EQ-5D-3L were converted into a single summary index using the Time Trade-Off (TTO) technique with a Swedish reference value set.[101] As no Swedish reference value set was available for the conversion of EQ-5D-5L to a single summary index, the most appropriate, from Denmark, was used.[102] In addition, patients assessed their QoL on a VAS from worst imaginable health (0%) to best imaginable health (100%).

3.2.5 Movement of the Thorax, Spine and Shoulders

The range of motion in the thorax was assessed by measuring thoracic excursion in a standardized manner. The difference in thoracic circumference between maximal inspiration and maximal expiration was measured in an upright patient, using a tape measure. Upper thoracic excursion was measured at the level of the fourth costae and lower thoracic excursion at the level of the xiphoid process.[103]

Flexion and extension in the thoracic spine were assessed by identifying the C7 spinal process and a point 30 cm below; the levels were marked with a pen. The patient was asked to bend forwards and backwards with straightened legs, and the difference from the original measurement was recorded.[104]

Lateral flexion was measured by the patient standing upright against a wall while measuring the movement of the tip of the index finger on each hand as the patient flexed laterally.[104]

Range of motion in the shoulders was assessed with the patient sitting. The degree of movement (0–180º) during flexion and abduction of straight arms was measured with a Goniometer. Shoulder function was assessed by a five-step test whereby each result was graded 1–6, depending on degree of movement, using the Boström summary score.[105]

Breathing movement was measured at rest and during maximal breathing with the patient lying in a supine position using a Respiratory Movement Measuring Instrument, RMMI® (ReMo Inc. Keldnaholt, Reykjavik, Iceland).[106] Laser sensors were placed along a sagittal line, approximately 1/3 the length of the clavicle from the sternal notch, at the level of the fourth rib (upper thorax), xiphoid process (lower thorax) and umbilicus (abdomen) bilaterally. Changes in distance between the sensors and the skin surface were registered during one minute and the average movement for each site was calculated. Comparison of movement between the operated and non-operated side was done. Patients with bilateral unstable thoracic cage injuries or bilateral surgical fixations were excluded from analyses.

3.2.6 Lung Function and Volume

Lung function tests were performed in a standardized manner using an EasyOne® Spirometer (ndd Medical Technologies Inc., MA, US).[107] Forced Vital Capacity (FVC), FEV1 and Peak Expiratory Flow (PEF) were recorded. Total Lung Capacity (TLC) with body plethysmograph was measured in a subgroup of 17 patients in Paper III who had not been intubated at initial CT using the TLC Sensormedics Vmax Encore system

(Yorba Linda CA, USA) and SentrySuite™ v.2.21 software (Intramedic AB, Sweden). Maximal Inspiratory Pressure (MIP) and Maximal Expiratory Pressure (MEP) were measured by MicroRPM™ (Respiratory Pressure Meter; Care Fusion, Sollentuna, Sweden) in patients in Paper IV.

3.3 Paper I

The study included 211 trauma patients treated surgically for acute chest wall injuries at Sahlgrenska University Hospital during the period September 2010 to September 2017. Patients were identified through the surgical registry.

The MOI was divided into ten subgroups: 1) motor vehicle collision with other vehicle(s) (MVC other); 2) motor vehicle collision without other vehicle(s) (MVC single); 3) bicycle accident; 4) motorcycle accident; 5) pedestrian vehicle accident (PVA); 6) miscellaneous transport accidents (including gliding, skiing, jet-skiing, sledging, equine activities); 7) fall from the same level; 8) fall from height; 9) crush injury; and 10) assault by bodily force.

Computed tomography with intravenous contrast medium was performed on admission. Injuries to the chest wall, intra-thoracic and associated injuries were recorded. ISS[32] and NISS[94] were assessed. The CT findings of intra-thoracic injuries were compared to operative findings in 161 patients undergoing thoracotomy.

The rib cage was divided into sections by identifying the anterior axillary line (lateral border of the pectoralis major muscle) and the posterior axillary line (anterior border of the latissimus dorsi muscle) on cross-sectional CT images of the thorax at the level of the fourth rib. Anterior rib fractures were located anterior to the anterior axillary line. Lateral rib fractures were located between the anterior and posterior axillary lines. Posterior rib fractures were located posterior to the posterior axillary line. The location of rib fractures was divided into three zones: Zone 1 (ribs 1–4), Zone 2 (ribs 5–8) and Zone 3 (ribs 9–12) (Fig. 10).

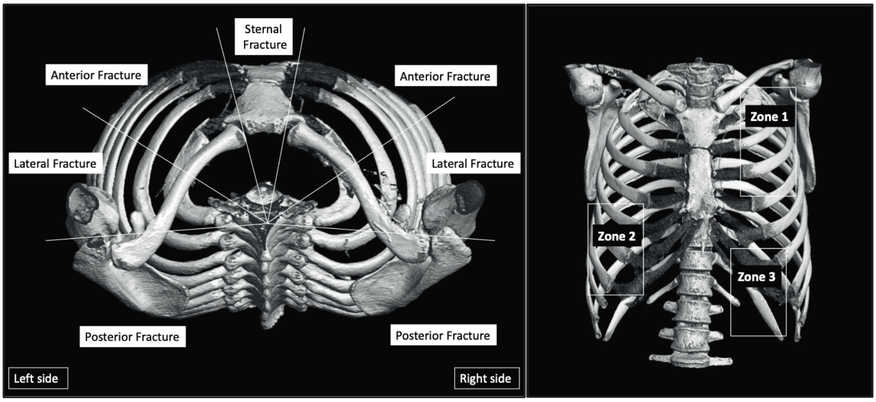

Figure 10 *The location of sternal fractures and anterior, lateral and posterior rib fractures (left) and Zone 1 (ribs 1–4), Zone 2 (ribs 5–8) and Zone 3 (ribs 9–12) rib fractures (right).*

Flail segments were defined as anterior, lateral and posterior flail. Sternal flail was added to the AIS definition[23] and defined as a segment consisting of at least two chondral or costal fractures bilaterally in conjunction with two horizontal sternal fractures or a vertical and horizontal fracture combined with two rib fractures on one side. Anterior flail was defined as a flail segment stretching between sternum and the anterior axillary line. Lateral flail was defined as a flail segment stretching from anterior ribs to posterior axillary line or anterior axillary line to posterior ribs. Posterior flail was defined as a segment stretching from posterior axillary line to the thoracic spine. The patient could have more than one flail segment,[23] although each individual rib fracture was not included in more than one flail segment.

3.4 Paper II

The study included 54 patients treated surgically for acute chest wall injuries at Sahlgrenska University Hospital during the period 2010 to 2013.

Patients were seen six weeks, three months, six months and one year post surgery. Patients answered a standardized questionnaire concerning subjective symptoms of pain, physical function with DRI,[98] and QoL assessment with EQ-5D-3L.[99] A subgroup of patients (n=16) with flail chest and no comorbidities also underwent lung function tests three months, six months and one year post surgery.[107] The subgroup was also assessed concerning the range of motion in the thorax and in the thoracic spine.[103,104]

Breathing movements were measured with RMMI® (ReMo Inc. Keldnaholt, Reykjavik, Iceland).[106]

3.5 Paper III

The study included 37 patients who had undergone stabilizing surgery for flail chest[23] at least six months previously, median time passed was 3.9 (0.5–5.6) years post trauma. The patients were included during the period October 2015 to January 2018.

Computed tomography was performed pre-operatively with intravenous contrast medium. Fractures in the thoracic cage and concomitant injuries to the clavicles, scapulae and thoracic spine were assessed. Injuries to the lungs were evaluated by using the Lung Injury Scale (LIS),[108] whereby injuries are graded 1–6, according to the presence and extent of contusions, lacerations and vascular injury. In cases of no lung injury, the patient was graded LIS 0. Injuries to the chest wall were assessed by using the Chest Wall Injury Scale (CIS),[109] and graded 1–5 according to the presence and extent of contusions and lacerations of soft tissues and fractures of the sternum and ribs. An unenhanced CT Thorax was obtained, at the earliest, six months post operatively. Pre- and post-operative CT images were analyzed and compared in the program AW Volume Share™ 5 software (Advantage Workstation 2.0, GE Healthcare, Waukesha, USA). The presence of lung changes, non-united fractures, implant dysfunction and healing patterns were assessed.

Lung volume on CT was estimated by calculating air-filled lung parenchyma distal to the lung hili, and excluding atelactasis, pneumothorax and pleural fluid. However, volumes of pneumothoraces ≥1cm were estimated. Automatic CT-lung volume was measured by using the program Thoracic VCAR (Volume Computer Assisted Reading) Parenchyma Analysis imaging software (GE Healthcare, Waukesha, USA), in patients where 0.6mm thick CT images were available pre- and post-operatively (n=18) (Fig 11 left). Lung volume was calculated manually by outlining air-filled lung tissue in each CT image, where only 5 mm slice thickness was available pre-and post-operatively (n=21 vs. n=19) (Fig. 11 right). All manual estimations were done twice and nine patients were assessed with both automatic and manual methods. Pre- and post-operative CT-lung volume estimates were compared. Lung function tests with FVC were performed at the time of CT, and 17 patients also underwent TLC measurement with body plethysmography using the TLC Sensormedics Vmax Encore system (Yorba Linda CA, USA) and SentrySuite™ v.2.21 software (Intramedic AB, Sweden). At follow-up, patients answered a standardized questionnaire concerning pain and the range of motion in the thorax and the breathing movements were measured.

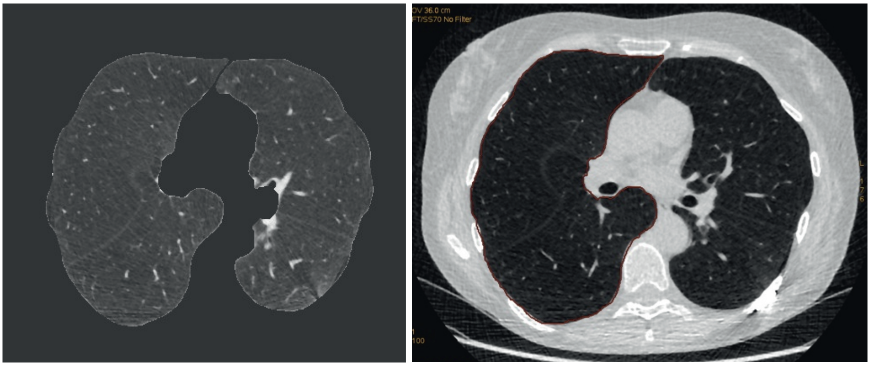

__Figure 11__ Automatic CT-lung volume estimation (left) and manual CT-lung volume estimation (right). Reproduced with permission from Caragounis et al., 2019. [110]

3.6 Paper IV

This study included adult trauma patients with unstable thoracic cage injuries and/or chest wall deformity treated surgically at SU or conservatively at KS during the period June 2014 to June 2017. Patients were included in a one-year follow-up. During the study period, KS began treating selective patients surgically, therefore inclusion was terminated before statistical power was reached. The study was expanded to include hospital data on all eligible patients (n=139) during the study period (Fig. 12).

Data on the need for and LOS on mechanical ventilator, using Non-Invasive Ventilation (NIV), in ICU and in hospital were collected. Complications, such as pneumonia, tracheostomy and re-operation, were studied. Mortality within 30 days and one year was documented.

Patients included in the follow-up were seen six weeks, six months and one-year post-trauma.

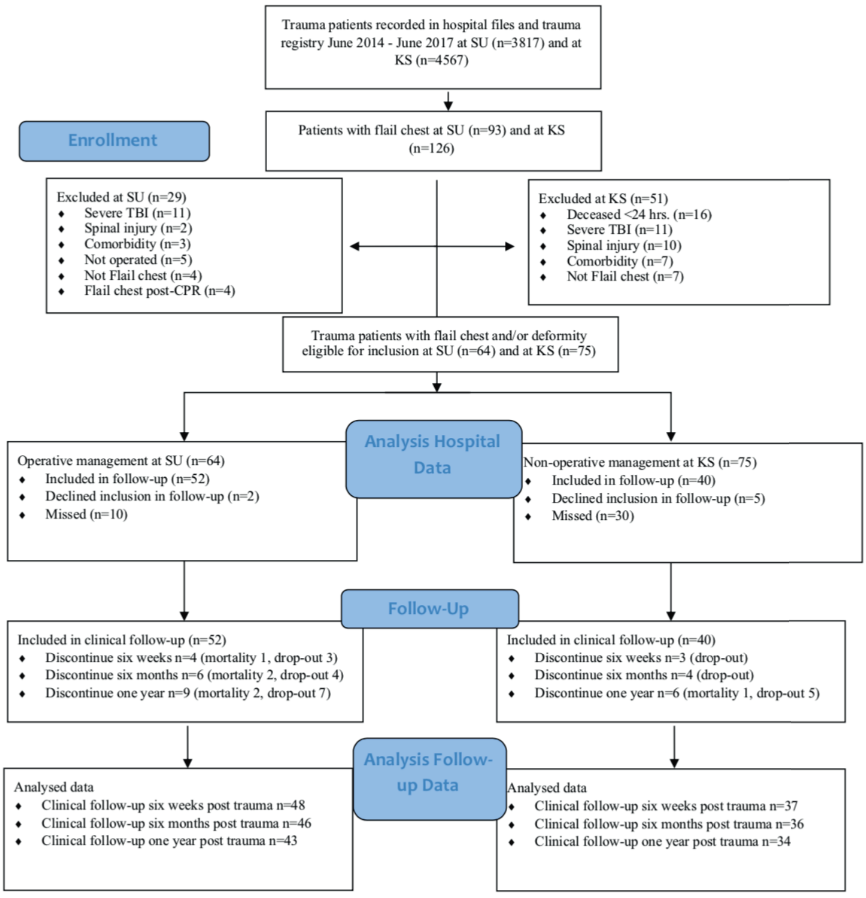

Figure 12 *Flow chart of patients studied in Paper IV.*
SU=Sahlgrenska University Hospital, KS=Karolinska University Hospital Solna, TBI=Traumatic Brain Injury, CPR=Cardiopulmonary Resuscitation.

At the time of follow-up, patients answered standardized questionnaires concerning subjective symptoms and pain, physical activity according to the Grimby activity scale,[96,97] physical function according to DRI[98] and QoL with EQ-5D-5L.[100] Patients were asked which type of work they did (non-physical, physical and heavy physical), or if they were unemployed or retired at the time of the trauma. Work activity was documented. Range of motion was assessed by measuring thoracic excursion,[103] flexion, including lateral, and extension of the thoracic spine.[104] Shoulder movement was assessed by measuring degree of movement (0–180º) with a Goniometer and shoulder function by using the Boström summary score.[105] Breathing movements were measured at rest and during maximal breathing using a Respiratory Movement Measuring Instrument, RMMI® (ReMo Inc. Keldnaholt, Reykjavik, Iceland).[106] Lung volume was estimated on pre- and post-operative CT, as described in Paper III. Lung function tests were performed with the measurement of FVC, FEV1, PEF, MIP and MEP.

3.7 Statistical Methods

The statistical software and methods used in this thesis are shown in table 4.

Table 4 *Overview of statistical methods used in papers I-IV.*

Paper	**I**	**II**	**III**	**IV**
Software Package	SPSS v.21 (IBM® 2012)	SAS® (NC, USA)	SPSS v.21 (IBM® 2012)	SPSS v.25 (IBM®2017)
Descriptive Statistics				
Continuous variables				
▪ Mean ± SD	X	X		X
▪ Median with Range		X	X	X
▪ Median with Q_1 and Q_3			X	
▪ Median with P_5 and P_{95}				X
Categorical variables (n and %)	X	X	X	X
Comparative Statistics				
Continuous variables - paired				
▪ Wilcoxon signed rank test		X	X	
Continuous variables - 2 groups				
▪ T-test (2-tailed)	X			X
▪ Mann-Whitney test			X	X
Categorical variables - 2 groups				
▪ Pearson's Chi-square test	X			X
▪ Fisher's exact test	X			X
Categorical variables - paired				
▪ Sign test		X		
Categorical variables >2 groups				
▪ Cochran's Q-test	X			
▪ Z-test	X			
Validation Statistics				
Correlation				
▪ Spearman's rank correlation coefficient with 95% CI using Fisher's Z			X	
Agreement				
▪ Bland-Altman diagram			X	
Predictive Statistics				
▪ Sensitivity	X			
▪ Logistic Regression				X

SD=Standard Deviation, Q_1=25th quartile, Q_3=75th quartile, P_5=5th percentile, P_{95}=95th percentile, n=number and CI=Confidence Interval.

For Paper IV a power analysis was performed before the study began, based on data from a previous study[78] using a proportions test[111] with equal inclusion giving 59 patients needing to be included in each group to give a power of 80% with a 95% significance level.

Significance was considered to be $p<0.05$ in all analyses.

4 ETHICAL CONSIDERATIONS

4.1 Patient inclusion

Prospective research on trauma patients remains a challenge, as many patients are unable to give informed consent due to physiological derangement causing impaired cognitive function. It is, therefore, the clinician's responsibility that the patient, who is in a vulnerable position, receives appropriate care and that any research performed is in accordance with ethical standards.

Whilst a randomized controlled trial would have been preferable to address the questions posed in this thesis, surgery for flail chest had already been established as the preferred treatment at Sahlgrenska University Hospital making it an ethical dilemma for the responsible surgeon not to operate patients who fulfilled the criteria for surgery. An expected low rate of inclusion would have added to the difficulty in carrying out a single-center RCT. Therefore, a control group was obtained from Karolinska University Hospital for the study described in Paper IV. Patients gave their informed consent to participate in the studies described in papers II–IV after receiving verbal and written information, and could withdraw at any time without explanation. In the study described in Paper IV, patients were treated according to local clinical practice and asked if they wanted to participate in a follow-up study. Clinical data from patients who fulfilled the criteria for inclusion in the study of Paper IV, but did not participate in the follow-up, were retrieved without the patients' consent in accordance with the ethical approval.

The study described in Paper I was a retrospective study on clinical data where consent was not requested. Although the patients included in the studies in papers II–IV benefitted from a more comprehensive follow-up, they did not personally reap the benefits from all of the results. Patients included in studies of papers III–IV also underwent additional CT scans with ionising radiation, although the dosages were kept to a minimum.

4.2 Ethical approval

The studies were performed in accordance with the World Medical Association Declaration of Helsinki (2013). Study protocols underwent vetting according to the Ethical Review Act by the Regional Ethical Review Board at Gothenburg University, Gothenburg, Sweden. Ethical approval was obtained for Paper I (Dnr 829-17), Paper II (Dnr 053-12) and papers III and IV (Dnr 887-13, with a later addition in 2017). Since the studies in papers III and IV involved ionising radiation of research subjects, approval was also obtained from the local radiation protection committee at Sahlgrenska University Hospital (Dnr 13-53). The study in Paper IV was registered at clinicaltrials.gov (NCT02132416).

4.3 Conflict of interest

The authors of papers I-IV included in this thesis declare that they and their respective institutions have no competing interests.

5 RESULTS

5.1 Mechanism of Injury and Injury Patterns (Paper I)

Flail chest was the most common indication for surgery in the 211 patients included in the study (Table 5).

Table 5 *Main indication for surgery of acute chest wall injuries in 211 trauma patients.*

Main indication for Surgery	Patients (n, %)
Flail chest	184 (87.2%)
Multiple rib fractures and pain	11 (5.2%)
Severely dislocated rib fractures affecting internal organs	9 (4.3%)
Rib fractures and lung herniation	3 (1.4%)
Rib fractures with chest wall deformity	2 (0.9%)
Rib fractures with massive haemothorax and diaphragmatic injury	1 (0.5%)
Rib fractures with continuous air leakage	1 (0.5%)

The most common MOIs were falls and traffic accidents (Table 6). All but one patient suffered blunt trauma. The MOI differed according to age, with traffic accidents being the most common MOI (62%) in patients aged 15–44 years, and falls being the most common MOI (59%) in patients aged >64 years. ISS and NISS varied according to MOI, rather than age group, where the highest values were seen in traffic accidents, especially MVC other and PVA. Crush injuries also generated high ISS and NISS values.

Table 6 *Mechanism of Injury distribution in 211 trauma patients.*

Main MOI	n (%)	Specific MOI	n (%)
Falls	93 (44.1%)	Fall from same level	51 (24.2%)
		Fall from height	42 (19.9%)
Traffic accidents	93 (44.1%)	MVC other	20 (9.5%)
		MVC single	19 (9.0%)
		PVA	17 (8.1%)
		Motorcycle accident	21 (10.0%)
		Bicycle accident	16 (7.6%)
Other accidents	25 (11.8%)	Crush injury	3 (1.4%)
		Miscellaneous accidents	13 (6.2%)
		Assault	9 (4.3%)

MOI=Mechanism of injury, MVC=Motor vehicle collision, PVA=Pedestrian vehicle accident

The most common MOI in patients with unilateral injuries was falls and the most common MOI in patients with bilateral injuries was traffic accidents. Isolated thoracic injury was found in 12% of the patients and was more prevalent after falls and other accidents than traffic accidents. The mean number of fractured ribs and rib fractures was 9.0±4.0 and 14.9±6.8, respectively. The mean percentage of fractured ribs and rib fractures operated was 57% and 40%, respectively. Posterior rib fractures were the most common, followed by lateral and lastly anterior, in unilateral injuries. In contrast, anterior, lateral and posterior rib fractures were equally common in bilateral injuries. Rib fractures were most commonly located in Zone 2 (99.5%), followed by Zone 1 (81.5%) and lastly Zone 3 (76.8%).

Paradoxical breathing was reported in 25% of patients with radiological flail chest and was predominantly seen in patients with bilateral injuries (43%), and was associated with sternal and anterior flail chest (Fig. 13). Lateral and posterior flail segments were the most common. Posterior flail chest was associated with Zone 3 rib fractures and was predominantly seen in falls and side collision MVC in patients with unilateral injuries. In contrast, sternal, anterior and lateral flail segments were more common with bilateral injuries, and associated with traffic accidents, especially frontal collision MVC. Rib fractures in Zone 1 were more common in traffic accidents and associated with anterior and lateral flail chest.

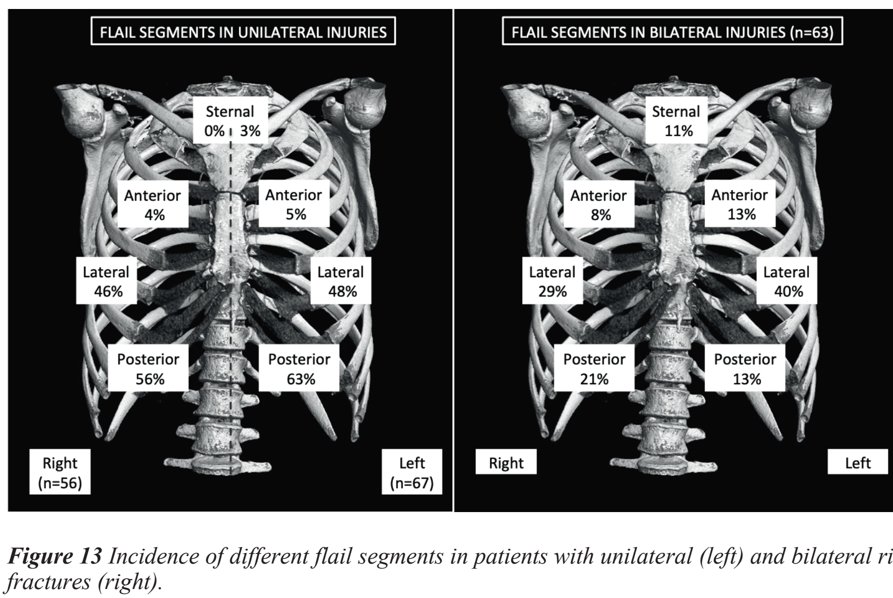

Figure 13 *Incidence of different flail segments in patients with unilateral (left) and bilateral rib fractures (right).*

Traffic accidents were associated with injuries to abdominal solid organs, pelvic fractures, extremity fractures, and spinal fractures. Frontal collision

MVC was especially associated with injuries to multiple body regions, compared to side collision MVC.

Sternal fractures were present in 43% of patients with bilateral injuries compared to 9.7% of patients with unilateral injuries. Fractures to clavicles (21%) and scapula (24%) were equally distributed between patients with unilateral and bilateral injuries. Per-operative assessment of intra-thoracic injuries in patients undergoing thoracotomy in conjunction with ORIF showed that CT underdiagnosed injuries, with a calculated sensitivity of 68% for pulmonary contusion, 29% for lung laceration and 14% for diaphragmatic injury. In fact, per-operatively 81% of patients were found to have pulmonary contusion, 62% lung laceration and 18% diaphragmatic injury.

5.2 Longitudinal Study- Outcome of Surgery (Paper II)

Of the 54 patients included in this study, forty-nine patients participated and five were lost to follow-up. Twenty-two patients attended all follow-up dates. A subgroup of patients with flail chest (n=16) were seen by a physiotherapist (Fig. 14).

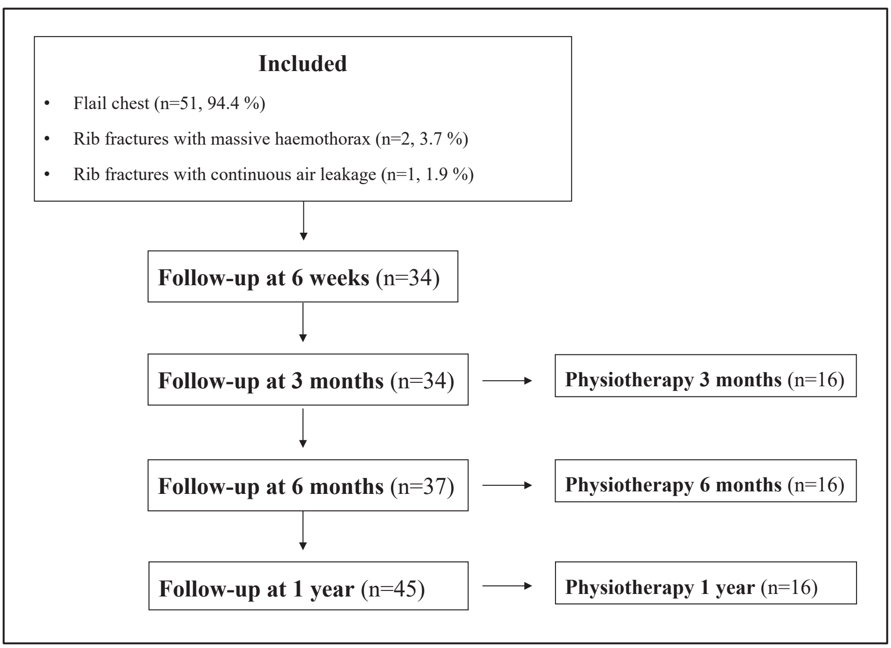

Figure 14 *Flow-chart of patients included in the study and attending follow-up. Reproduced and adapted with permission from Caragounis et al., 2016.* [112]

Two patients were re-operated within the year for extraction of rib plates, one due to chronic infection and another due to localized pain. Problems with pain at rest, pain when breathing, breathlessness and the use of analgesia decreased progressively, during the first post-operative year. After one year, 13% of patients had pain at rest, 9% had pain when breathing, 16% experienced breathlessness and 9% were on pain medication. Local discomfort did not decrease with time, but remained constant at 47%.

Patients' QoL measured by EQ-5D-3L showed median index values increasing progressively over time, with the greatest improvement occurring between 6 weeks and 3 months (Fig. 15). There was a significant decrease in the proportion of patients suffering problems with mobility (-27%, p=0.022), self-care (-36%, p=0.0005), usual activities (-55%, p=0.0001) and pain or discomfort (-27%, p=0.035) after one year, compared to 6 weeks post-operatively. There was no significant improvement in symptoms of anxiety or depression over time. Median VAS, measuring QoL, improved from 60% (20–96) at 6 weeks to 76% (40–97) at 3 months to 80% (20–100) at 6 months to 90% (30–100) after one year (p<0.0001).

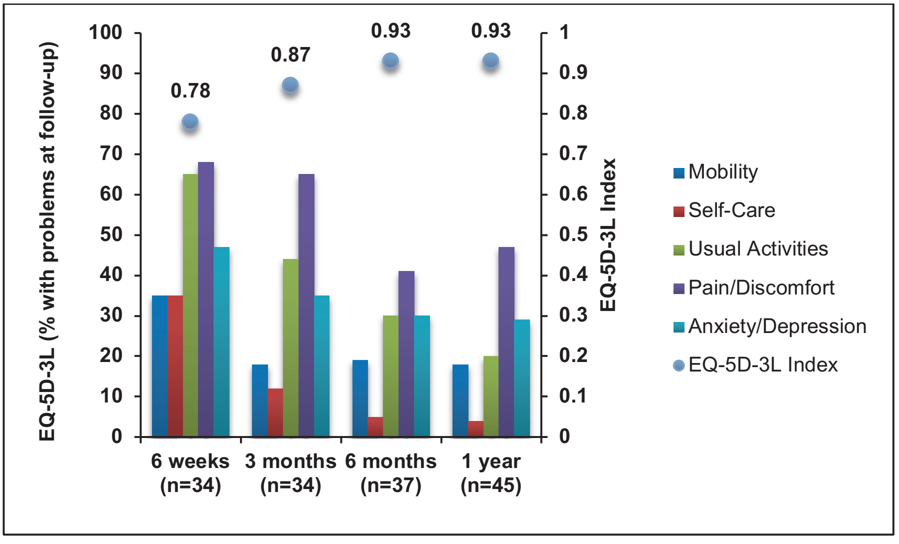

Figure 15 *Quality of Life measured by EQ-5D-3L showing the percentage of patients with some or extreme difficulties and median EQ-5D-3L index values at follow-up. Reproduced with permission from Caragounis et al., 2016.*[112]

Lung function tests were performed in a subgroup of patients with flail chest (n=16). Mean percent predicted FVC and PEF improved significantly with time and showed normal values one year post operatively (Table 7).

***Table** 7 Lung function of patients with flail chest (n=16) at follow-up. Reproduced and adapted with permission from Caragounis et al., 2016.* [112]

Lung Function	**3 months** % Predicted	**6 months** % Predicted	**12 months** % Predicted	**Δ 3–6 months** *p*-value	**Δ 3–12 months** *p*-value
FVC (L)	86.2 ± 19.4	93.1 ± 20.7	105.9 ± 17.5	**p=0.0002**	**p=0.0002**
FEV1 (L)	79.4 ± 22.7	81.8 ± 25.3	80.4 ± 29.6	p=0.100	p=0.74
PEF (L/min)	81.4 ± 19.5	83.7 ± 24.3	109.9 ± 24.8	p=0.50	**p<0.0001**

Evaluation of movement in the chest wall was performed in a subgroup of patients with flail chest (n=16). Breathing movements were initially decreased on the operated side but improved with time and showed greater movement on the operated side compared to the non-operated side, in the upper thorax at rest, after one year. Range of motion, thoracic excursion and thoracic flexion and extension showed a gradual improvement with time. The patients' ability to flex laterally towards and away from the injured side did not change significantly with time. Physical function improved and median DRI decreased from 23 (0–78) at three months, to 13 (0–65) at six months and to 0 (0–67) at one year post operatively.

5.3 CT- Lung Volume (Paper III)

Pre-operative CT findings were compared to CT at follow-up in 37 patients who had undergone stabilizing surgery for flail chest. Median CIS was 4.0 (3–4) and LIS was 2.0 (0–4). None of the included patients had undergone resection of lung tissue in conjunction with ORIF. The post-operative CT was performed at the earliest six months post-operatively and the median time for follow-up was 3.9 (0.5–5.6) years post trauma.

Median CT-lung volume increased significantly from 3.51 l (1.50 – 6.05) on pre-operative CT to 5.59 l (2.18 – 7.78) on post-operative CT (p<0.0001). This improvement was seen regardless of whether or not patients had pneumothorax, lung contusions or were intubated at initial CT. Manual measurements were performed twice per patient (n=21 pre-operatively and n=19 post-operatively) and showed a median difference of 0.03 l (0–0.29) between measurements, which was not statistically significant (p=0.303).

There was a strong agreement between the first and second manual measurements of CT-lung volume (Fig. 16). When comparing manual and automatic CT-lung volume measurements (n=9), a median difference of 0.04 l (0–0.21) was found, which was not significant (p=0.066) (Fig. 17).

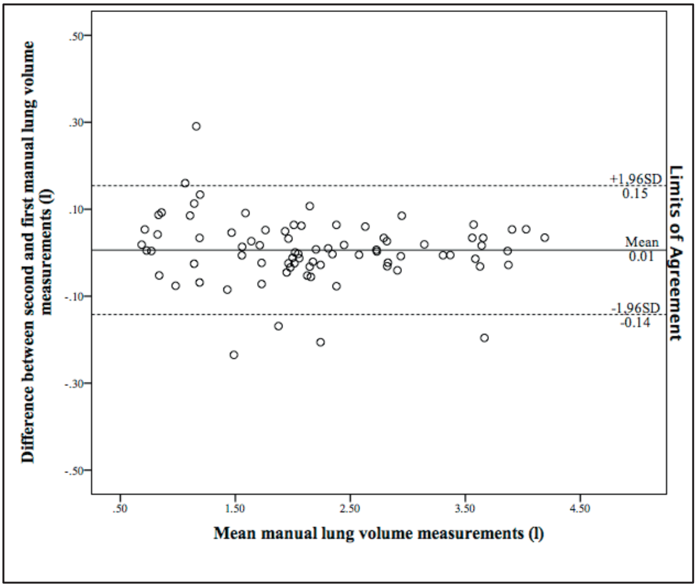

Figure 16

A Bland-Altman diagram of the first and second manual CT-lung volume measurements (n=40). Reproduced with permission from Caragounis et al., 2019. [110]

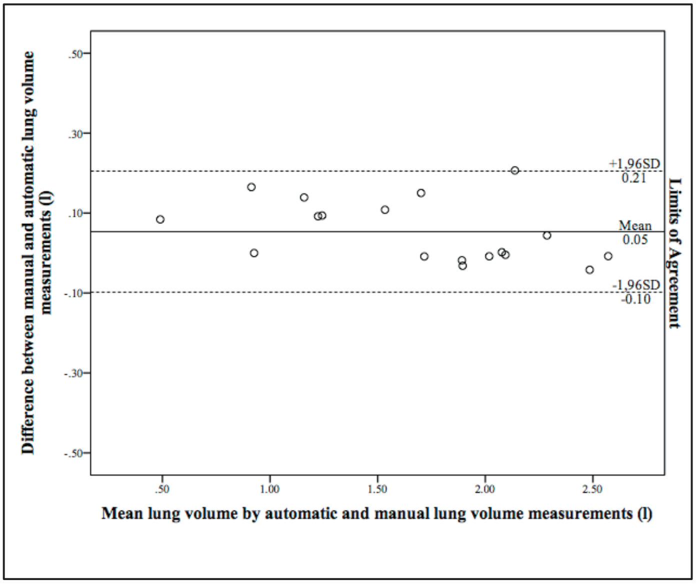

Figure 17

A Bland-Altman diagram of manual and automatic CT-lung volume measurements (n=9). Reproduced with permission from Caragounis et al., 2019. [110]

Median FVC at follow-up was 3.76 l (1.48–5.84), with a correlation to CT-lung volume [r_s=0.75 (95% CI 0.57–0.87, p<0.0001)] (Fig. 18). Total Lung Volume (TLC) (n=17) was 6.93 l (4.21–8.42), with a correlation to CT-lung volume [r_s=0.90 (95% CI 0.73–0.96, p<0.0001)] (Fig. 19). The CT-lung volumes obtained were higher than FVC but lower than TLC.

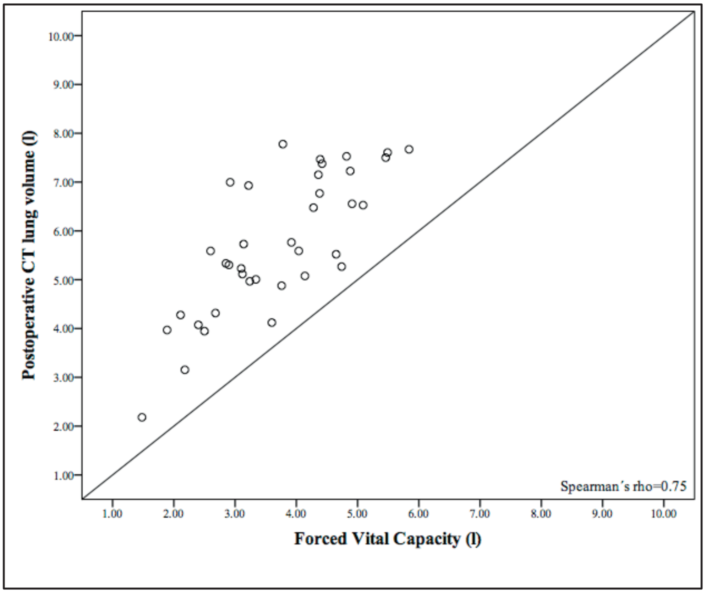

Figure 18

Correlation between post-operative CT-lung volume measurements and FVC in 37 patients. Reproduced with permission from Caragounis et al., 2019.[110]

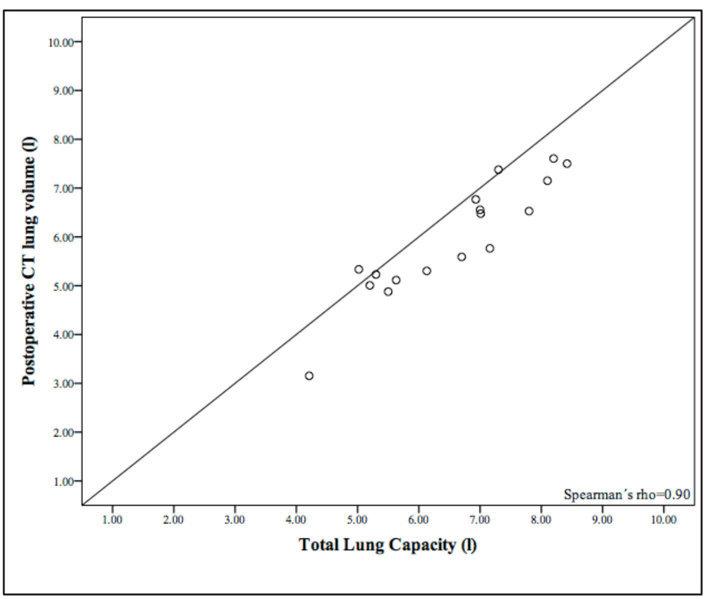

Figure 19

Correlation between post-operative CT-lung volume measurements and TLC in 17 patients. Reproduced with permission from Caragounis et al., 2019. [110]

Breathing movements were decreased on the operated side in the lower thorax and upper thorax at maximal breathing in patients with unilateral injuries. Patients with bilateral injuries had decreased breathing movement in the abdomen at rest. Patients complained of pain at rest and when breathing (n=2), breathlessness (n=6), local discomfort (n=14) and decreased local sensation (n=10). Three patients had non-united fractures in ribs that were not operated. One patient had implant dysfunction. Heterotopic ossification with rib synostosis was seen in eleven patients.

5.4 Prospective Controlled Study (Paper IV)

Unstable thoracic cage injuries were documented in 2.6% of all trauma patients seen at Sahlgrenska University Hospital and Karolinska University Hospital Solna June 2014–June 2017. Patients eligible for inclusion were compared concerning hospital clinical outcome measures (Table 8). There were more men in the conservatively managed group, otherwise the groups were comparable concerning age, ISS and NISS (Table 3). Patients included in the clinical follow-up differed in their demographics. Surgically managed patients were significantly older (58 vs. 52 years, p=0.036), had more severe thoracic injuries and a higher NISS (34 vs. 27, p=0.009) compared to conservatively managed patients.

Surgically managed patients were operated median day 4 post-trauma (2–14). Sixty-nine per cent of operated patients underwent a thoracotomy in conjunction with chest wall stabilization with 20% undergoing minor resection of leaking lung tissue. Eleven per cent were operated with a minimally invasive technique. Five patients underwent bilateral chest wall stabilization.

Twenty-eight per cent of patients required mechanical ventilator regardless of whether or not they underwent surgical stabilization for unstable thoracic cage injuries. For the patients requiring mechanical ventilation, median LOS was 8 days (1-42), and there was no significant difference between the two groups. In addition, no difference in need of and LOS of ICU care and NIV was found. However, the surgical group had significantly longer hospital LOS (14 vs. 11 days, p=0.001). No difference was found in the incidence of tracheostomy and mortality. Surgically managed patients had a significantly reduced incidence of pneumonia (17% vs. 36%, p=0.013). There was incomplete data in two patients in the conservatively managed group, as these had initially been treated abroad.

Table 8 *Hospital outcome.*

Variable		Surgical Management (n=64)	Conservative Management (n=75)	*p*-value
NIV	Need (n,%)	13 (20.3)	23 (31.5)*	0.137
	Days (P_5, P_{95})	0 (0, 6.5)	0 (0, 5.3)*	0.160
Mechanical ventilator	Need (n,%)	18 (28.1)	21 (28.4)*	0.974
	Days (P_5, P_{95})	0 (0, 21.3)	0 (0, 24.3)*	0.951
ICU care	Need (n,%)	31 (48.4)	40 (53.3)*	0.565
	Days (P_5, P_{95})	0 (0, 28.5)	1.0 (0, 28.0)*	0.830
Hospital LOS	Days (P_5, P_{95})	14.0 (7.3, 44.8)	11.0 (2.8, 41.4)	**0.001**
Pneumonia	(n, %)	11 (17.2)**	27 (36.0)	**0.013**
Empyema	(n, %)	0	3 (4.0)	
Tracheostomy	(n, %)	8 (12.5)	6 (8.0)	0.380
Re-operation	(n, %)	2 (3.1)	n/a	
Mortality	30-days (n, %)	2 (3.1)	2 (2.7)	1.000
	1 year (n, %)	5 (7.8)	5 (6.7)	1.000

Continuous variables are shown as median with P_5 and P_{95} and compared with Mann-Whitney U test. Categorical variables are shown as number and per cent and compared with Pearson's chi-square Test or Fisher's Exact Test. NIV=Non-Invasive ventilation, ICU=Intensive Care Unit, LOS=Length of Stay, P_5=5th percentile, P_{95}=95th percentile, n/a=not applicable.
*Incomplete data (n=2).
**Present pre-operatively (n=5).

A logistic regression with need of mechanical ventilation as outcome variable and age, sex, NISS and operation as covariates was performed. Odds Ratio (OR) for age was 1.011 (95% CI 0.978–1.045, p=0.519), sex 0.953 (95% CI 0.249–3.642, p=3.642), NISS 1.177 (1.114–1.244, p=0.000) and operation 0.675 (95% CI 0.245–1.857, p=0.446).

Lung function at follow-up was better in the conservatively managed patients compared to the surgical group, although per cent predictive values were decreased in both groups (Table 9). As the majority of patients had undergone thoracotomy and a fraction of these lung resection, the surgical group was divided into patients managed with or without a thoracotomy. There were demographic differences between the groups. The surgical group managed without a thoracotomy was comparable to the conservative group. However, the patients undergoing thoracotomy were significantly older (62 vs. 52, p=0.001) than the conservative patients and the patients operated without a thoracotomy (51, p=0.010). They were also smokers and had more pre-existing lung disease. Surgically managed patients operated with thoracotomy had a significantly higher NISS (34 vs. 27, $p<0.01$) and worse outcome concerning residual lung function, compared to patients managed conservatively or surgically without thoracotomy. Patients managed surgically without a thoracotomy had a tendency towards better lung function than patients managed conservatively, although this was not statistically significant.

Table 9 *Estimated CT-lung volume and lung function.*

Follow-up	**Variable**	**Surgical Management**		**Conservative Management**
		- Thoracotomy (n=18)	**+Thoracotomy (n=34)**	**(n=40)**
Initial CT	CT Lung volume (l)	3.39 (1.30–6.33)	2.56 (1.43–4.69)	2.92 (1.53–6.97)
	Pneumothorax volume (l)	0.76 (0.50–1.02)	0.13 (0.01–0.62)	0.09 (0.02–0.62)
Six weeks	Predicted FVC (%)	91.7±18.2[a]	76.8±16.0	85.7±16.0[c]
	Predicted FEV1 (%)	94.9±21.1[a]	69.2±14.7	84.9±18.6[c]
	Predicted PEF (%)	101.3±26.4[a]	82.2±20.6	92.3±27.1
	MIP (cm H_20)	88.3±27.9[a]	64.4±27.9	86.6±26.3[c]
	MEP (cm H_20)	108.4±44.8	94.2±29.3	130.6±36.9[c]
Six months	CT Lung volume (l)	6.60 (3.87–8.77)[a]	5.30 (2.11–7.40)	5.51 (1.81–8.03)
	Predicted FVC (%)	98.5±17.3[a]	80.2±17.1	91.5±16.2[c]
	Predicted FEV1 (%)	98.1±14.5[a]	74.6±17.1	92.6±18.5[c]
	Predicted PEF (%)	100.1±22.9	85.5±24.2	101.1±24.5[c]
	MIP (cm H_20)	92.8±33.5	73.9±36.8	102.2±28.2[c]
	MEP (cm H_20)	118.7±40.7	104.2±38.6	154.8±48.1[b,c]
One year	Predicted FVC (%)	97.5±16.2[a]	83.4±18.3	92.3±16.2[c]
	Predicted FEV1 (%)	96.1±15.6[a]	77.4±17.7	92.3±17.1[c]
	Predicted PEF (%)	105.5±17.0	92.9±20.3	101.6±26.1
	MIP (cm H_20)	95.8±34.9	78.0±28.4	104.4±29.0[c]
	MEP (cm H_20)	119.8±41.5	107.7±37.9	157.1±41.7[b,c]

Continuous variables are shown as mean with SD and compared with T-test or shown as median with range and compared with Mann-Whitney U test. CT=Computed Tomography, FVC=Forced Vital Capacity, FEV1=Forced Expiratory Volume in 1 second, PEF=Peak Expiratory Flow, MIP=Maximal Inspiratory Pressure, MEP=Maximal Expiratory Pressure

[a]Difference in the surgical management group between patients treated with or without a thoracotomy ($p<0.05$).

[b]Difference between patients treated surgically without a thoracotomy and patients managed conservatively ($p<0.05$).

[c]Difference between the surgical management group treated with a thoracotomy and conservatively management group ($p<0.05$).

Lung volumes estimated on CT comparing initial CT with CT six months post trauma, improved significantly in all subgroups of patients. However, the increase in CT-volume was significantly greater in the patients stabilized without a thoracotomy than in patients operated with a thoracotomy (3.1 vs. 2.4, p=0.040) or in patients treated conservatively (3.1 vs. 2.3, p=0.028).

Despite differences in age and injury burden, no significant difference in physical activity, physical function and QoL was found between the groups six weeks, six months and one year after trauma. Similarly, shoulder function and breathing movement was equal between the groups. Breathing movements were decreased on the injured side compared to the non-injured side in both groups. Patients with bilateral flail chest and/or bilateral chest wall stabilization were excluded from this analysis. However, upper thoracic excursion and lateral flexion was consistently better in the conservative group. Patients in the conservative group experienced more pain and were prescribed a higher dose of morphine the first months' post trauma. None of the conservatively managed patients had returned to heavy physical work after six weeks, compared to 18% in the surgical group.

6 GENERAL DISCUSSION

The aim of this thesis was to address the issue of surgical management of rib fractures, through studying the association of MOI with different chest wall injury patterns, evaluating radiological models for prediction of lung function and assessing short- and long-term outcomes of surgery.

The term flail chest is widely used as a criterion for inclusion in many clinical studies on the outcome of chest wall surgery.[25,78,79,82-86,88-90,92] However, though several studies use the AIS definition of FC,[23,78,79,83-85,92] some use their own definition of segmental injuries,[82,86,88] or refer exclusively to paradoxical chest movement,[25] whilst others remain unclear.[89,90] It is questionable to rely solely on clinical grounds for diagnosing FC as this will reduce the likelihood of identifying the condition. The clinical diagnosis of FC depends on the location of the flail segment, typically the condition is seen in patients with sternal and anterior chest wall injuries as described in Paper I and as evident by the early descriptions from the 40s and 50s.[34-36] The mechanism of injury determines the location of rib fractures and the chest wall injury pattern, producing different types of flail segments with the occurrence of unilateral or bilateral injuries (Paper I). Defining different types of flail segments is important, in order to be able to suspect and identify associated injuries pertaining to the specific flail segment and in planning a surgical procedure. It is surprising that the anatomical AIS definition of FC[23] does not include the sternum as this is an integral part of the thoracic cage. This thesis has therefore broadened the AIS definition of FC[23] to include sternal flail segments and thus it is more preferable to use the term unstable thoracic cage injury rather than FC.

Traffic accidents and falls were found to be equally, the most common MOIs in patients operated for multiple rib fractures and unstable thoracic cage injuries in Paper I. This is in contrast to previous studies which suggest that traffic accidents are the most common MOIs in thoracic trauma.[12,13,15,18,19,26-28] The difference can be explained by a mean age of 58 years in the patients studied, and a low prevalence of traffic accidents in Sweden.[113] Isolated chest wall injuries were seen in 12% of patients in Paper I, which is in accordance with previous studies,[12,15,18] and were found to be predominantly associated with falls. In contrast, polytrauma was associated with traffic accidents, and particularly frontal collision MVC was associated with the most severe injuries. Injury burden as defined by ISS[32] and NISS[94], vary according to the type of MOI rather than the age of the patient, with the highest values seen in traffic accidents. However, as the prevalence of different MOIs differ according to age with falls being more common in patients >64 years of age, elderly patients will present with lower ISS[32] and NISS[94] levels. There were surprisingly no significant difference found in ISS[32] and NISS[94] values between falls from the same level and falls from height (Paper I). Therefore, low energy impact should not imply that one can rule out serious trauma to the thorax. In fact, the MOI in 24% of patients operated for multiple rib fractures and unstable thoracic cage injuries was fall from the same level. Suspecting serious injury after fall from the same level is in contradiction to widely used triage criteria which often only include patients falling from height in order to trigger a trauma team activation. Care should be taken not to under-triage the patient presenting with thoracic trauma and at risk of developing physiological derangement.[20]

Under-triage of the elderly is especially common,[114] despite research showing the increased risk of mortality in the elderly trauma patient with rib fractures.[17,30,115,116] Since the possibility of managing rib fractures surgically is still quite novel many clinicians that care for the elderly patient with chest wall trauma may not be aware of the treatment possibilities available. As a result, the focus of care may be on the underlying medical conditions, which are of importance. However, the patient is unlikely to be admitted as a trauma alert and will therefore not undergo a CT but instead most likely a simple CXR to diagnose pneumothorax and pleural fluid. Considering the development of modern treatment of chest wall injuries, it is inappropriate to perform a radiological examination that will not be able to rule out neither intra-thoracic injuries nor provide the clinician with an overview of the chest wall injury.[45,49] In fact, the elderly trauma patient may have more to gain from surgical stabilization of chest wall injuries than the young patient, as this decreases the risk of pneumonia. Although the elderly patient may be frail at the time of the trauma with an increased risk of mortality, the patient may respond and benefit from appropriate resuscitation but require a higher level of care to survive.[117] Therefore, it is important to be proactive in the resuscitation and management of the elderly trauma patient in order to produce the best possible outcome. There are of course patients where interventions should be limited. But complications due to under-resuscitation and neglect should not be used as a reason for conservative management.

Rib fractures are often associated with abdominal solid organ injuries.[54,55] Concomitant abdominal organ injuries were found in 25% of patients included in Paper I. It is therefore important to not only perform a selective CT of the thorax when investigating the patient with chest wall trauma, but to include the whole trunk as in a WBCT protocol. Although there has been evidence to suggest that performing a selective CT instead of a WBCT does not increase in-hospital mortality,[118] relevant incidental findings are missed with selective examination.[119] The CT is useful not only for diagnosing injuries but for assessing the lung volume. Previous studies have used CT for estimating lung volume in pulmonary disease,[120] pre-operative prediction of volume in lung transplant surgery,[121] and for quantification of pulmonary contusions in trauma for predicting the development of ARDS.[40-42] The estimation of CT-lung volume can be done automatically with the help of computer software and aid the clinician in the initial assessment of the patient. As most trauma patients with chest wall injuries will have difficulty to perform lung function tests, CT-lung volume can be used as a marker for lung function as shown in Paper III. There was a significant difference between CT-lung volumes at initial CT compared to six months post trauma, regardless of whether or not the patient was under positive pressure ventilation, had pneumothorax or lung contusions on initial CT (papers III-IV). The improvement cannot solely depend on the surgical management of the rib cage with reduction of chest wall deformity, since improvement was also seen in conservatively managed patients. However, in patients operated without a thoracotomy the improvement in CT-lung volume was significantly greater than in patients managed with a thoracotomy or in patients manged conservatively. Reducing chest wall deformity without performing thoracotomy gives the best outcome. Although, the patients undergoing thoracotomies had significantly higher NISS[94] and more comorbidities and were therefore not comparable. It is unclear if the difference in results is due to pre-existing morbidity, injury burden in the thorax or the thoracotomy with or without minor lung resection. In order to evaluate if CT-lung volume estimation is useful as a tool in the decision-making process, it should be added to an algorithm and studied prospectively.

The indication for surgery in papers I-II was multiple rib fractures and unstable thoracic cage injuries, whereas in papers III-IV it was solely unstable thoracic cage injuries. The indication for surgery of chest wall injuries has been debated and current guidelines mainly support surgery for FC as this may decrease the LOS on mechanical ventilator, and the incidence of pneumonia and mortality.[122,123] Studies focusing on patients with FC and pulmonary contusions have found no benefit with surgery.[86,90] However, the basis for these studies is a diagnosis of pulmonary contusion on initial CT. Since contusions often develop over time and are underdiagnosed on initial CT,[124] it is possible that these studies only included patients with the most severe lung injuries, requiring mechanical ventilation. Most studies have excluded patients with severe TBI, often defined as a decreased level of consciousness or AIS>3,[79,82,83,85,87-90] as they require longer time on mechanical ventilator,[27] While, it may be argued that optimizing the patients' respiration will be positive for the outcome. Currently there is no data to support a decreased time spent on mechanical ventilator with surgery of FC in patients with severe TBI. One may hypothesize that if the patient is expected to remain on mechanical ventilator in the ICU for at least 14 days, during which time callus forms, then surgery may be unnecessary.

Twenty-eight per cent of patients with unstable thoracic cage injuries included in Paper IV required mechanical ventilation in ICU at some point, regardless of whether or not surgical stabilisation was performed. This is lower than the 35-72% seen in previous studies comparing surgically and conservatively managed patients.[78,83] The timing of surgery is of importance if the aim is to decrease LOS on mechanical ventilator and in ICU. Patients were operated median day 4 in Paper IV and a late operation was associated with pneumonia, longer LOS on mechanical ventilator and in ICU. The overall LOS in hospital was significantly longer in the surgically managed patients than the conservatively managed controls. An earlier operation may have had a greater impact on the LOS on mechanical ventilator, in ICU and in the hospital. Previous studies have shown shorter LOS and reduced incidence of tracheostomy in patients operated within 72 hours.[25,83-85,87,88] As the endpoint of the study was to reduce the need of mechanical ventilation through surgery, patients should have undergone operation within a pre-defined time. The cases of pneumonia seen in the surgical group may have been prevented with an early procedure. Although chest wall surgery should take place after life-threatening injuries and physiological derangement is controlled, it is not elective surgery in the trauma patient. However, a delay in surgery may not only be due to limited resources but an intentional watchful waiting approach by the clinician, as a way to assess if the patient deteriorates and requires surgery. The problem with the delay, is that by the time the patient goes to surgery, the pulmonary physiology may have deteriorated beyond the point that an early surgery might have prevented, and so there is less to gain from surgery. As suggested in previous studies surgery for chest wall trauma should be performed within 72 hours and possibly within 48 hours.[25,83-85,87,88] Therefore, the patient with unstable thoracic injuries needs to be referred early, before respiratory insufficiency ensues, to a trauma centre for appropriate assessment and management.

Chest wall surgery involves a field commonly shared by the thoracic surgeon, the orthopedic surgeon and the trauma surgeon. Regardless of local practice concerning the management of the patient with severe chest wall injuries, the responsible surgeon needs to have a basic knowledge of fracture management and thoracic surgery with a trauma surgeons' holistic perspective on the optimal care of the trauma patient, and be ready to address any concomitant injuries. Patients included in this thesis were operated using titanium plates (MatrixRIB™ Fixation System, DePuy Synthes, West Chester, USA). The surgical technique for stabilizing chest wall injuries differ between studies and there is no consensus in the optimal type of stabilization, although most centers use plates. The differences in surgical approach used makes comparison between studies difficult. Most centers aim to convert a flail segment to a non-flail segment by only stabilizing one of the fractures on each rib. However, this may not prevent deformity and one may risk stabilizing too few fractures.[125] On the other hand, stabilizing too many fractures may cause rigidity and stiffness in the chest wall.[126] Replacing titanium plates with more flexible plates may decrease the long-term effects of surgery. Ideally the plate used should allow minor movement in the fracture site to promote healing but not so much as to cause pain. One may hypothesize that although the anatomical titanium plate is designed to be used on ribs it may be too stiff. The plate that initially causes stability short-term may result in long-term rigidity.

Performing a thoracotomy in conjunction with chest wall stabilization may aid in identifying and managing intra-thoracic injuries and removing residual haemothorax (Paper I). An alternative is a more minimally invasive approach using VATS. At present it is difficult to integrate minimally invasive surgery with VATS, as the commercially available plates and tools are not designed for a thoracoscopic approach of stabilization.[123] Patients undergoing thoracotomy in Paper IV had a worse outcome concerning estimated CT-lung volume and lung function. However, the patients in the thoracotomy group were not comparable to the conservative group as they were older, had more pre-existing lung disease and a significantly higher NISS. It is possible that the added surgical insult of a thoracotomy and minor lung resection performed in some patients may have influenced these results. However, regardless of the approach it is important to identify intra-thoracic injuries that need to be addressed. Diaphragmatic injuries were found in 18% of patients undergoing thoracotomy in conjunction with ORIF. The sensitivity for diagnosing diaphragmatic injuries on CT was found to be 14%. These injuries are important to diagnose and treat as they can lead to late complications with herniation which is associated with a high mortality, especially on the left side.[127,128] The diaphragmatic injuries associated with rib fractures[127] should not be confused with the diaphragmatic ruptures rarely seen in blunt trauma.[129] Instead, they rather resemble penetrating injuries to the diaphragm, caused by dislocated penetrating rib fractures. It can be proposed that patients with dislocated lower rib fractures (Zone 2 and 3) on the left side should be investigated invasively for the presence of concomitant diaphragmatic injuries, especially if there is an abdominal organ injury present on the other side of the diaphragm.

Previous studies on the surgical management of FC have mainly focused on managing respiratory insufficiency in order to minimize the need for mechanical ventilation and reduce complications like tracheostomy, pneumonia and mortality.[25,78,79,82-86,88-90,92] Considering the heterogeneity in trauma patients it is possible that they can be divided into several subgroups, where according to pre-existing lung disease, higher injury burden and associated injuries they will require mechanical ventilation to different degrees, regardless of surgery. Voggenreiter et al. attempted such a study on the outcome of surgery in patients with or without pulmonary contusions.[86] However, the subgroups were too small for all the necessary statistical analyses to be done. The challenge with performing a study with subgroup analyses, is the need for including large data material. In order to do so a multi-center study will need to be planned. But before this can be undertaken there needs to be an internationally recognized system for classifying chest wall injuries and flail segments, and the operative technique needs to be more standardized. Any operation may not be better than no operation.

The median time spent on mechanical ventilator for patients in Paper IV in need of mechanical ventilation, was 8 days. This is shorter than what has previously been described for patients managed conservatively for flail chest.[25,79,82,85-87,89,90] There may be several reasons for the discrepancies. The initial resuscitation of the trauma patient has evolved in recent years through minimizing the administration of large volumes of crystalloid fluids with the early administrating of blood products in case of shock. The aim of the resuscitation is to maintain adequate perfusion until bleeding is controlled.[130] This trend of "permissive hypotension" started already in the 90s after a study by Bickell *et* al.,[131] showing improved survival with delayed fluid resuscitation. Although the study pertains to penetrating trauma it has been extrapolated to include also blunt poly-trauma. Avoiding fluid overload may have a positive effect on lung physiology in trauma patients with unstable thoracic cage injuries by minimizing swelling and decreasing pulmonary edema, thus optimizing the injured patient balancing on the threshold for requiring mechanical ventilation. However adequate fluid needs to be administered and there is no evidence for a better outcome with fluid restriction.[132] Other advances in ICU care, such as less invasive monitoring techniques, avoidance of excessive sedation and a multidisciplinary approach to treatment, have also been made that improve the care of the trauma patient.[133]

Patients managed surgically for chest wall injuries heal gradually with improvement in symptoms associated with pain, physical function, lung function and QoL during the first year after surgery (Paper II). However, after one year 13% of patients complain of chest pain and 47% experience local discomfort. The proportion of patients with chronic pain is less than has previously been described in conservatively managed patients.[60,66] When comparing surgically and conservatively managed patients prospectively (Paper IV), it was found that conservatively managed patients have significantly more pain the first months after trauma and were prescribed higher doses of opioids. Although, no difference was seen between the groups after one year. Pain at rest was present in 5–6% of patients and local discomfort in 35% of patients regardless of treatment. The difference in results when comparing surgically managed patients in Papers II and IV may be due to the development of the surgical technique with less invasive surgery. However, the prevalence of pain was also low in the conservative group compared to previous studies.[60,66] Thoracic Epidural Analgesia (TEDA) was used for pain control during hospital care to the same extent in both surgically and conservatively managed patients. The reduction in acute pain may influence long-term pain.[68] It would be interesting to study the pain experienced in relation to chest wall injury patterns and associated injuries, to discover if certain injuries are more prone to causing long-term morbidity.

The benefits of surgery seem to be in the first months' post trauma with decreased pain, less problems with self-care and a quicker return to heavy physical work (Paper IV). Surgery of chest wall injuries does not seem to have either a positive or a negative long-term effect on the patient. No difference was found between the groups concerning physical activity, disability and QoL, despite the surgically managed group being older and more severely injured. The patients included in the follow-up were seen by a physiotherapist. Being included in the study meant additional assessment apart from the study protocol with the opportunity to provide the patient with tools to improve their physical condition. As patients in both groups had remaining pain and limitation in their physical function, they may have benefitted from an individualized multi-professional rehabilitation approach.

Movement of the chest wall was found to be decreased on the operated side initially but improved with time, and after one year, movement was increased on the operated side compared to the non-operated side (Paper I). In patients with bilateral injuries, no significant differences in chest wall movement was found between the operated and non-operated side (Paper III). When comparing surgically and conservatively managed patients, both groups showed a decreased movement on the side of the flail segment but there was no significant difference between the two groups (Paper IV). As patients were only followed for up to a year after the trauma, it is unknown if the breathing movements change in a longer perspective. Although, the instrument comparing breathing movement between sides is highly sensitive, measuring in mm, which may not be considered to be clinically relevant. It does however show us the differences which may be associated with the chest wall stiffness experienced by the patient. Surgically managed patients may experience more stiffness, as evident by decreased upper thoracic excursion and lateral flexion in operated patients (Paper IV). Although, the rigidity may be partly due to the healing process.[60] However, it is important to develop implants that allow for stabilization without adding to rigidity.

Lung function, concerning FVC and PEF, improved gradually with time and was normalized in surgically managed patients one year after surgery (Paper II). Although, FEV1 remained decreased, which is consistent with other studies.[82] Surgically managed patients treated with a thoracotomy had reduced residual CT-lung volume and lung function at follow up compared to patients managed conservatively or surgically without a thoracotomy. Conservatively managed patients could produce consistently higher MEP.

It´s possible that surgery has a negative impact on the soft tissues in the thoracic cage and cause a negative effect on the expiratory muscles. However, there seem to be differences between patients operated with or without a thoracotomy and this topic mandates further study.

Surgery is not without adverse effects. Some patients required re-operations, either due to post-operative bleeding or delayed surgery for removal of implants due to infection or pain. These are complication that follow surgical management. In, contrast patients in the conservatively managed group underwent surgery for the control of empyema and for the use of ECMO due to respiratory insufficiency.

In conclusion, the decision to perform surgery on rib fractures following trauma in a patient should be individualized. The decision should take into account pre-existing comorbidities, likelihood of prolonged mechanical ventilation for other reasons, associated injuries, the ability to perform adequate surgery and within appropriate time, and last but not least the patient's own wish. Although this thesis does not support the notion that chest wall surgery decreases the need for mechanical ventilation, we can offer the patient a surgery that will reduce the incidence of pneumonia and decrease pain during the first months' post trauma with no difference in long-term adverse outcome compared to conservatively managed patients.

Methodological Considerations

Trauma patients are an inherently heterogenous group which poses a challenge when performing clinical research. This can be counteracted by including large sets of patient data. However, the prevalence of flail chest and unstable thoracic cage injuries is merely 2.6% and only 64 patients were eligible for inclusion at Sahlgrenska University Hospital during the three-year inclusion period in Paper IV. The low level of inclusion was anticipated and therefore Karolinska University Hospital Solna was asked to participate as a control group. A randomized-controlled trial covering both hospitals would have been preferable but could not be performed as surgery had not yet been established at KS. Several factors may influence the results, pre-existing pulmonary disease, age, differences in disease burden and associated injuries which influence the need of and LOS on mechanical ventilator, in

ICU and in the hospital. The heterogenic nature of patient and trauma demographics may also influence long-term outcome concerning the experience of pain, activity, disability and QoL. Often the baseline physiology and psychology of the trauma patient is unknown but may still impact the outcome. In order to consider all the factors that influence outcome measures and to have enough patients to be able to stratify the data, for instance concerning pulmonary contusions and TBI, several thousand patients will need to be included in a prospective randomized-controlled trial. A study of this magnitude will need to include >10 centers and continue for several years. Before such a study can be undertaken there needs to be a recognized international nomenclature for the classification of chest wall injuries. In addition, the operative approach from the decision of which fractures to stabilize, to the manner of incision and the implants used, needs to be standardized.

The association of MOI and chest wall injury patterns have been studied retrospectively (Paper I). There are some limitations to this study as it only includes patients undergoing ORIF, which may therefore represent a selected group of patients with the most severe chest wall injuries. Also, some of the data included was dependent on information recorded in radiological files, surgical procedure records and hospital files. The method described for defining the location of rib fractures, could be sensitive to the arm positioning at the time of CT, as having arms above the head effectively tilts the scapula anteriorly. This was not taken into account when retrospectively studying the CT images. Although, 211 patients were included in the study, which can be considered to be a large number when studying surgical management of rib fractures, there were too few patients in each subgroup to perform more advanced analyses. The study is therefore largely descriptive in nature. However, Paper I, contributes valuable information as it is a unique in-depth study of the association of MOI with different patterns of chest wall injuries. An internationally recognized nomenclature of chest wall injuries is lacking. Defining rib fractures and flail segments according to location will improve the understanding of these injuries and facilitate comparison of results from different studies.

The long-term outcome of surgery for multiple rib fractures and flail chest was assessed in a prospective longitudinal study (Paper II). This is largely a descriptive study of the healing process one year after surgery and the major limitation is the lack of a control group. However, the study comprises a detailed follow-up with the assessment of residual pain, breathing movements, lung function, range of motion in the thorax, disability and QoL.

Estimation of CT-lung volumes pre- and post-operatively in patients with FC, and correlating these to lung function results was performed in a cross-sectional study (Paper III). Limitations in the study include different slice thickness of the images assessed, requiring the use of two different methods of calculating CT-lung volume. However, the methods were compared and found to be in agreement. This is the first study on trauma patients to estimate CT-lung volume and correlate the findings to lung function tests.

Paper IV, as described above, this is a prospective controlled study of the surgical management of unstable thoracic cage injuries. The inclusion into the study was terminated prematurely as KS started to operate selected trauma patients and there was a concern for selection bias. In an unorthodox fashion the study was instead expanded to involve all patients eligible for inclusion during the inclusion period concerning hospital parameters. The patients that had been included from the beginning were followed for one year. The patients in the follow-up were not comparable, the KS patients were younger with less severe thoracic trauma. However, this is the first study to prospectively compare CT-lung volumes, breathing movements and range of motion between surgically and conservatively managed patients with unstable thoracic cage injuries.

7 CONCLUSIONS

- Distinctive chest wall injury patterns can be identified in thoracic trauma as a result of different mechanisms of injury, and is associated with different probabilities of extra-thoracic injuries.

- Patients managed with surgical plate fixation for multiple rib fractures recover gradually with improvement in pain, physical function, lung function and QoL, during the first post-operative year.

- Estimates of lung volume on CT increase significantly when comparing immediate post-trauma CT with CT after six months, and can be used as a marker for lung function.

- No difference in LOS on mechanical ventilator and in ICU is seen between surgically and conservatively managed patients, despite surgically managed patients having more severe thoracic injuries.

- Patients managed surgically for unstable thoracic cage injuries have less pneumonia and experience less pain and discomfort during the first months' after trauma, compared to conservatively managed patients.

- There is no considerable difference in long-term outcome between patients managed surgically compared to conservatively for unstable thoracic cage injuries, one year after trauma.

8 FUTURE PERSPECTIVES

- There is a need for developing an internationally recognized nomenclature for the classification of chest wall injuries. This would be helpful in comparing results from different studies. And it is also a necessary basis for studying the appropriate number and location of rib fractures to stabilize, and for establishing which fractures are prone to non-union.
- The surgical approach to chest wall injuries needs to be more standardized. This encompasses the decision of which ribs to operate, how many fractures to stabilize, to the manner of incision and the implants used. The use of thoracotomy or VATS needs to be implemented in the surgical procedure of patients at risk of diaphragmatic injury. In addition, minimally invasive techniques, including the development of appropriate implants, need to be established in order to produce stability in the chest wall with minimal soft tissue dissection and a reduction in the morbidity associated with surgery.
- The role of early surgery in the patient with unstable thoracic cage injuries, not presently in need of mechanical ventilation, needs to be studied further to see if surgery will prevent deterioration and the development of respiratory insufficiency, and the need for mechanical ventilation.
- The estimation of CT-lung volume as a marker for lung function should be assessed as part of an algorithm in a prospective study, in order to find predictors for selecting patients who benefit most from surgery.
- The role of surgery in the management of multiple painful rib fractures and in chronic painful non-united fractures mandates further research.
- Furthermore, the benefits of an individualized multi-professional assessment and rehabilitation of the patient with severe chest wall trauma should be evaluated further.

ACKNOWLEDGEMENTS

I would like to thank the University of Gothenburg and Sahlgrenska University Hospital, and their representatives, for giving me the opportunity to write this doctoral thesis.

Associate Professor **Hans Granhed**, my main supervisor, for inviting me to work with trauma at Sahlgrenska University Hospital, teaching me basic orthopaedic techniques and sharing his vast knowledge and experience in fracture surgery, giving me the freedom to develop the operative technique and encouraging me along the way.

Professor **Monika Fagevik Olsén**, my co-supervisor, for sharing both enjoyable and stressful clinic visits where we learnt from our patients whilst teaching me basic spirometry and physiotherapy assessment, and discussing scientific issues, as well as providing me with direction when needed.

My co-authors. **Rauni Rossi Norrlund** for great ideas, always being enthusiastic and quick to respond, and sharing a love for Mumin. **David Pazooki** for welcoming me into the Trauma Team at Sahlgrenska University Hospital and teaching me chest wall surgery. **Lena Sandström** for keeping track of the patients included at Karolinska University Hospital Solna. **Lisa Strömmer** for participation, collaboration and sharing a goal to improve trauma care on a national level. **Yao Xiao** and **Olof Brattström** for helping with retrieving patient data.

Dr **Grażyna Söderbom** for great friendship, good discussions, valuable advice, and for checking my language and helping me to improve my writing.

Former Head of Department of Surgery, Professor **Hans Lönroth** for giving me the opportunity, freedom and support to develop trauma care within the department, in Sahlgrenska University Hospital and in Västra Götaland Region, as well as the possibility to learn and develop my own skills in clinical research.

Professor Emeritus **Bo Svennerholm**, Department of Virology and Professor **Magnus Gisslén**, Department of Infectious Diseases, for taking a young medical student under their wings many years ago, and introducing her to research and scientific thinking.

Current Head of Department of Surgery, **Erik Johnson,** and Head of Emergency and Trauma Surgery, **Hans Axelsson**, for giving me time to finish this work.

Bertil Leidner, the artistic radiologist, for creating the cover.

A big thank you to former and present members of the Trauma Team at Sahlgrenska University Hospital, **Ragnar Ang**, **Per Örtenwall**, **Josefine Gustafsson**, **Karin Sillén**, **Martin Stenerös**, **Pieter Van Wyk**, **Carl-Jacob Holmberg** and **Rasha El-Ahmad**. Your support and hard work through the years has meant more than I can express!

Slavica Janeva, my friend and colleague, who first lured me to come and work at Sahlgrenska University Hospital.

My colleagues at Sahlgrenska University Hospital who have helped and supported me through the years.

My friends and relatives for encouragement and love.

I want to thank my amazing, three big sisters **Rosanna**, **Yvonne-Marie** and **Vivian**–who knows what I would have become without you. Last but not least I also want to thank my father Professor Emeritus **Chrys** C. Caragounis who always encouraged me in my studies and taught me by example to work hard and live with integrity.

This book is dedicated to my mother **Sophia** Caragounis who was quite firm in her belief that rib fractures did not require surgery, unfortunately she passed away before she had the opportunity to read this book….

REFERENCES

1. World Health Organization. Injuries and violence: the facts 2014. Switzerland 2014 ISBN 978-92-4-150801-8.
2. World Health Organization. World health statistics 2018: monitoring health for the SDGs, sustainable development goals. *Geneva* 2018 ISBN 978-92-4-156558-5.
3. Socialstyrelsen. Statistikdatabas för yttre orsaker till skador och förgiftningar. 2018.
4. Socialstyrelsen. Statistikdatabas för dödsorsaker. 2018.
5. Brattström O. SweTrau Svenska Traumaregistret Årsrapport 2017. 2018.
6. Baker CC, Oppenheimer L, Stephens B, Lewis FR, Trunkey DD. Epidemiology of trauma deaths. *American journal of surgery.* 1980;140(1):144-150.
7. Demetriades D, Murray J, Charalambides K, et al. Trauma fatalities: time and location of hospital deaths. *Journal of the American College of Surgeons.* 2004;198(1):20-26.
8. Ndiaye A, Chambost M, Chiron M. The fatal injuries of car drivers. *Forensic Sci Int.* 2009;184(1-3):21-27.
9. Soreide K, Kruger AJ, Vardal AL, Ellingsen CL, Soreide E, Lossius HM. Epidemiology and contemporary patterns of trauma deaths: changing place, similar pace, older face. *World J Surg.* 2007;31(11):2092-2103.
10. Hodgson NF, Stewart TC, Girotti MJ. Autopsies and death certification in deaths due to blunt trauma: what are we missing? *Can J Surg.* 2000;43(2):130-136.
11. Callcut RA, Kornblith LZ, Conroy AS, Robles AJ, Meizoso JP, Namias N. The Why & How Our Trauma Patients Die: A Prospective Multicenter Western Trauma Association Study. *Journal of Trauma and Acute Care Surgery.* 2019;Epub Ahead of Print.
12. Ziegler DW, Agarwal NN. The morbidity and mortality of rib fractures. *The Journal of trauma.* 1994;37(6):975-979.
13. Ciraulo DL, Elliott D, Mitchell KA, Rodriguez A. Flail chest as a marker for significant injuries. *Journal of the American College of Surgeons.* 1994;178(5):466-470.
14. Flagel BT, Luchette FA, Reed RL, et al. Half-a-dozen ribs: the breakpoint for mortality. *Surgery.* 2005;138(4):717-723; discussion 723-715.
15. Narayanan R, Kumar S, Gupta A, et al. An Analysis of Presentation, Pattern and Outcome of Chest Trauma Patients at an Urban Level 1 Trauma Center. *Indian J Surg.* 2018;80(1):36-41.

16. Holcomb JB, McMullin NR, Kozar RA, Lygas MH, Moore FA. Morbidity from rib fractures increases after age 45. *Journal of the American College of Surgeons.* 2003;196(4):549-555.
17. Bergeron E, Lavoie A, Clas D, et al. Elderly trauma patients with rib fractures are at greater risk of death and pneumonia. *The Journal of trauma.* 2003;54(3):478-485.
18. Sirmali M, Turut H, Topcu S, et al. A comprehensive analysis of traumatic rib fractures: morbidity, mortality and management. *European journal of cardio-thoracic surgery : official journal of the European Association for Cardio-thoracic Surgery.* 2003;24(1):133-138.
19. Demirhan R, Onan B, Oz K, Halezeroglu S. Comprehensive analysis of 4205 patients with chest trauma: a 10-year experience. *Interact Cardiovasc Thorac Surg.* 2009;9(3):450-453.
20. Committe on Trauma ACoS. ATLS® Advanced Trauma Life Support® Student Course Manual. 2018(10th Edition).
21. Boffard KD, IATSIC. Manual of Definitive Surgical Trauma Care. 2016(4th Edition).
22. Mattox KL, Wall MJ, Tsai P, Moore E, Feliciano D. Trauma: Trauma thoracotomy: principles and techniques. *McGraw-Hill.* 2013;7th edition:461-467.
23. Gennarelli TA WEB, IL: Association for the Advancement of Automotive Medicine. The Abbreviated Injury Scale 2005 - Update 2008. 2008.
24. Galan G, Penalver JC, Paris F, et al. Blunt chest injuries in 1696 patients. *European journal of cardio-thoracic surgery : official journal of the European Association for Cardio-thoracic Surgery.* 1992;6(6):284-287.
25. Ahmed Z, Mohyuddin Z. Management of flail chest injury: internal fixation versus endotracheal intubation and ventilation. *The Journal of thoracic and cardiovascular surgery.* 1995;110(6):1676-1680.
26. Schulz-Drost S, Krinner S, Langenbach A, et al. Concomitant Sternal Fracture in Flail Chest: An Analysis of 21,741 Polytrauma Patients from the TraumaRegister DGU(R). *Thorac Cardiovasc Surg.* 2017;65(7):551-559.
27. Dehghan N, de Mestral C, McKee MD, Schemitsch EH, Nathens A. Flail chest injuries: a review of outcomes and treatment practices from the National Trauma Data Bank. *The journal of trauma and acute care surgery.* 2014;76(2):462-468.
28. Shorr RM, Crittenden M, Indeck M, Hartunian SL, Rodriguez A. Blunt thoracic trauma. Analysis of 515 patients. *Ann Surg.* 1987;206(2):200-205.
29. Stawicki SP, Grossman MD, Hoey BA, Miller DL, Reed JF, 3rd. Rib fractures in the elderly: a marker of injury severity. *Journal of the American Geriatrics Society.* 2004;52(5):805-808.

30. Bergeron E, Clement J, Lavoie A, et al. A simple fall in the elderly: not so simple. *The Journal of trauma.* 2006;60(2):268-273.
31. Van Vledder MG, Kwakernaak V, Hagenaars T, Van Lieshout EMM, Verhofstad MHJ, South West Netherlands Trauma Region Study G. Patterns of injury and outcomes in the elderly patient with rib fractures: a multicenter observational study. *European journal of trauma and emergency surgery : official publication of the European Trauma Society.* 2018.
32. Baker SP, O'Neill B, Haddon W, Jr., Long WB. The injury severity score: a method for describing patients with multiple injuries and evaluating emergency care. *The Journal of trauma.* 1974;14(3):187-196.
33. Chapman BC, Herbert B, Rodil M, et al. RibScore: A novel radiographic score based on fracture pattern that predicts pneumonia, respiratory failure, and tracheostomy. *The journal of trauma and acute care surgery.* 2016;80(1):95-101.
34. Hagen K. Multiple rib fractures treated with a drinker respirator: a case report. *JBJS Am.* 1945;27(2):330-334.
35. Heroy WW, Eggleston FC. A method of skeletal traction applied through the sternum in "steering wheel" injury of the chest. *Ann Surg.* 1951;133(1):135-138.
36. Cohen EA. Treatment of the flail chest by towel clip traction. *American journal of surgery.* 1955;90(3):517-521.
37. Paydar S, Mousavi SM, Akerdi AT. Flail chest: are common definition and management protocols still useful? *European journal of cardio-thoracic surgery : official journal of the European Association for Cardio-thoracic Surgery.* 2012;42(1):192.
38. Vana PG, Neubauer DC, Luchette FA. Contemporary management of flail chest. *The American surgeon.* 2014;80(6):527-535.
39. Miller-Keane. Encyclopedia and Dictionary of Medicine, Nursing and Allied Health. *Saunders.* 2003;7th Edition.
40. Wang S, Ruan Z, Zhang J, Jin W. The value of pulmonary contusion volume measurement with three-dimensional computed tomography in predicting acute respiratory distress syndrome development. *The Annals of thoracic surgery.* 2011;92(6):1977-1983.
41. Mahmood I, El-Menyar A, Younis B, et al. Clinical Significance and Prognostic Implications of Quantifying Pulmonary Contusion Volume in Patients with Blunt Chest Trauma. *Medical science monitor : international medical journal of experimental and clinical research.* 2017;23:3641-3648.
42. Strumwasser A, Chu E, Yeung L, Miraflor E, Sadjadi J, Victorino GP. A novel CT volume index score correlates with outcomes in polytrauma patients with pulmonary contusion. *The Journal of surgical research.* 2011;170({Strumwasser, 2011 #93}2):280-285.

43. Langdorf MI, Medak AJ, Hendey GW, et al. Prevalence and Clinical Import of Thoracic Injury Identified by Chest Computed Tomography but Not Chest Radiography in Blunt Trauma: Multicenter Prospective Cohort Study. *Ann Emerg Med.* 2015;66(6):589-600.
44. Livingston DH, Shogan B, John P, Lavery RF. CT diagnosis of Rib fractures and the prediction of acute respiratory failure. *The Journal of trauma.* 2008;64(4):905-911.
45. Chapman BC, Overbey DM, Tesfalidet F, et al. Clinical Utility of Chest Computed Tomography in Patients with Rib Fractures CT Chest and Rib Fractures. *Archives of trauma research.* 2016;5(4):e37070.
46. Scalea TM, Rodriguez A, Chiu WC, et al. Focused Assessment with Sonography for Trauma (FAST): results from an international consensus conference. *The Journal of trauma.* 1999;46(3):466-472.
47. Montoya J, Stawicki SP, Evans DC, et al. From FAST to E-FAST: an overview of the evolution of ultrasound-based traumatic injury assessment. *European journal of trauma and emergency surgery : official publication of the European Trauma Society.* 2016;42(2):119-126.
48. Rowell SE, Barbosa RR, Holcomb JB, Fox EE, Barton CA, Schreiber MA. The focused assessment with sonography in trauma (FAST) in hypotensive injured patients frequently fails to identify the need for laparotomy: a multi-institutional pragmatic study. *Trauma Surg Acute Care Open.* 2019;4(1):e000207.
49. Turk F, Kurt AB, Saglam S. Evaluation by ultrasound of traumatic rib fractures missed by radiography. *Emergency radiology.* 2010;17(6):473-477.
50. Hurley ME, Keye GD, Hamilton S. Is ultrasound really helpful in the detection of rib fractures? *Injury.* 2004;35(6):562-566.
51. Nummela MT, Bensch FV, Pyhalto TT, Koskinen SK. Incidence and Imaging Findings of Costal Cartilage Fractures in Patients with Blunt Chest Trauma: A Retrospective Review of 1461 Consecutive Whole-Body CT Examinations for Trauma. *Radiology.* 2018;286(2):696-704.
52. Cho SH, Sung YM, Kim MS. Missed rib fractures on evaluation of initial chest CT for trauma patients: pattern analysis and diagnostic value of coronal multiplanar reconstruction images with multidetector row CT. *The British journal of radiology.* 2012;85(1018):e845-850.
53. Talbot BS, Gange CP, Jr., Chaturvedi A, Klionsky N, Hobbs SK, Chaturvedi A. Traumatic Rib Injury: Patterns, Imaging Pitfalls, Complications, and Treatment-Erratum. *Radiographics : a review publication of the Radiological Society of North America, Inc.* 2017;37(3):1004.

54. Park S. Clinical Analysis for the Correlation of Intra-abdominal Organ Injury in the Patients with Rib Fracture. *The Korean journal of thoracic and cardiovascular surgery.* 2012;45(4):246-250.
55. Al-Hassani A, Abdulrahman H, Afifi I, et al. Rib fracture patterns predict thoracic chest wall and abdominal solid organ injury. *The American surgeon.* 2010;76(8):888-891.
56. Berry F. The treatment of injuries to the chest. *American journal of surgery.* 1941;54:280.
57. Jaslow IA. Skeletal traction in the treatment of multiple fractures of the thoracic cage. *American journal of surgery.* 1946;72(5):753-755.
58. Avery EE, Morch ET, Head JR, Benson DW. Severe crushing injuries of the chest; a new method of treatment with continuous hyperventilation by means of intermittent positive endotracheal insufflation. *Q Bull Northwest Univ Med Sch.* 1955;29(4):301-303.
59. Lewis FL, Jr., Thomas AN, Schlobohm RM. Control of respiratory therapy in flail chest. *The Annals of thoracic surgery.* 1975;20(2):170-176.
60. Landercasper J, Cogbill TH, Lindesmith LA. Long-term disability after flail chest injury. *The Journal of trauma.* 1984;24(5):410-414.
61. Wutzler S, Blasius FM, Stormann P, et al. Pneumonia in severely injured patients with thoracic trauma: results of a retrospective observational multi-centre study. *Scandinavian journal of trauma, resuscitation and emergency medicine.* 2019;27(1):31.
62. Van Gent JM, Calvo RY, Zander AL, et al. Risk factors for deep vein thrombosis and pulmonary embolism after traumatic injury: A competing risks analysis. *The journal of trauma and acute care surgery.* 2017;83(6):1154-1160.
63. Nennhaus HP, Javid H, Julian OC. Alveolar and pleural rupture. Hazards of positive pressure respiration. *Arch Surg.* 1967;94(1):136-141.
64. Kumar A, Pontoppidan H, Falke KJ, Wilson RS, Laver MB. Pulmonary barotrauma during mechanical ventilation. *Crit Care Med.* 1973;1(4):181-186.
65. Ranieri VM, Suter PM, Tortorella C, et al. Effect of mechanical ventilation on inflammatory mediators in patients with acute respiratory distress syndrome: a randomized controlled trial. *JAMA.* 1999;282(1):54-61.
66. Beal SL, Oreskovich MR. Long-term disability associated with flail chest injury. *American journal of surgery.* 1985;150(3):324-326.
67. Fabricant L, Ham B, Mullins R, Mayberry J. Prolonged pain and disability are common after rib fractures. *American journal of surgery.* 2013;205(5):511-515; discusssion 515-516.
68. Katz J, Jackson M, Kavanagh BP, Sandler AN. Acute pain after thoracic surgery predicts long-term post-thoracotomy pain. *Clin J Pain.* 1996;12(1):50-55.

69. McKendy KM, Lee LF, Boulva K, et al. Epidural analgesia for traumatic rib fractures is associated with worse outcomes: a matched analysis. *The Journal of surgical research.* 2017;214:117-123.
70. Dor V, Paoli J, Noirclerc M, Malmejac C, Chauvin G, Pons R. Osteosynthesis of the thoracic wall. Technic, results and indications. Apropos of 19 cases. *Ann Chir.* 1967;Aug-Sept; 21(15):983-996.
71. Bemelman M, Poeze M, Blokhuis TJ, Leenen LP. Historic overview of treatment techniques for rib fractures and flail chest. *European journal of trauma and emergency surgery : official publication of the European Trauma Society.* 2010;36(5):407-415.
72. Sillar W. The crushed chest. Management of the flail anterior segment. *J Bone Joint Surg Br.* 1961;43-B:738-745.
73. Labitzke R, Schmit-Neuerburg K, Schramm G. Indikation zur thoracotomie und rippenstabilisierung beim thoraxtrauma im hohen lebensalter. *Chirurg.* 1980(51):567-580.
74. Judet R. [Costal osteosynthesis]. *Rev Chir Orthop Reparatrice Appar Mot.* 1973;59:Suppl 1:334-335.
75. Sanchez-Lloret J, Letang E, Mateu M, et al. Indications and surgical treatment of the traumatic flail chest syndrome. An original technique. *Thorac Cardiovasc Surg.* 1982;30(5):294-297.
76. Sales JR, Ellis TJ, Gillard J, et al. Biomechanical testing of a novel, minimally invasive rib fracture plating system. *The Journal of trauma.* 2008;64(5):1270-1274.
77. Kruger M, Zinne N, Zhang R, et al. Multidirectional thoracic wall stabilization: a new device on the scene. *The Annals of thoracic surgery.* 2013;96(5):1846-1849.
78. Granhed HP, Pazooki D. A feasibility study of 60 consecutive patients operated for unstable thoracic cage. *J Trauma Manag Outcomes.* 2014;8(1):20.
79. Marasco SF, Davies AR, Cooper J, et al. Prospective randomized controlled trial of operative rib fixation in traumatic flail chest. *Journal of the American College of Surgeons.* 2013;216(5):924-932.
80. Campbell N, Conaglen P, Martin K, Antippa P. Surgical stabilization of rib fractures using Inion OTPS wraps--techniques and quality of life follow-up. *The Journal of trauma.* 2009;67(3):596-601.
81. Fitzpatrick DC, Denard PJ, Phelan D, Long WB, Madey SM, Bottlang M. Operative stabilization of flail chest injuries: review of literature and fixation options. *European journal of trauma and emergency surgery : official publication of the European Trauma Society.* 2010;36(5):427-433.
82. Tanaka H, Yukioka T, Yamaguti Y, et al. Surgical stabilization of internal pneumatic stabilization? A prospective randomized study of management of severe flail chest patients. *The Journal of trauma.* 2002;52(4):727-732; discussion 732.

83. Granetzny A, Abd El-Aal M, Emam E, Shalaby A, Boseila A. Surgical versus conservative treatment of flail chest. Evaluation of the pulmonary status. *Interact Cardiovasc Thorac Surg.* 2005;4(6):583-587.
84. Jayle CP, Allain G, Ingrand P, et al. Flail chest in polytraumatized patients: surgical fixation using Stracos reduces ventilator time and hospital stay. *Biomed Res Int.* 2015;2015:624723.
85. Doben AR, Eriksson EA, Denlinger CE, et al. Surgical rib fixation for flail chest deformity improves liberation from mechanical ventilation. *J Crit Care.* 2014;29(1):139-143.
86. Voggenreiter G, Neudeck F, Aufmkolk M, Obertacke U, Schmit-Neuerburg KP. Operative chest wall stabilization in flail chest--outcomes of patients with or without pulmonary contusion. *Journal of the American College of Surgeons.* 1998;187(2):130-138.
87. Solberg BD, Moon CN, Nissim AA, Wilson MT, Margulies DR. Treatment of chest wall implosion injuries without thoracotomy: technique and clinical outcomes. *The Journal of trauma.* 2009;67(1):8-13; discussion 13.
88. Althausen PL, Shannon S, Watts C, et al. Early surgical stabilization of flail chest with locked plate fixation. *J Orthop Trauma.* 2011;25(11):641-647.
89. Xu JQ, Qiu PL, Yu RG, Gong SR, Ye Y, Shang XL. Better short-term efficacy of treating severe flail chest with internal fixation surgery compared with conservative treatments. *Eur J Med Res.* 2015;20:55.
90. Zhang Y, Tang X, Xie H, Wang RL. Comparison of surgical fixation and nonsurgical management of flail chest and pulmonary contusion. *Am J Emerg Med.* 2015;33(7):937-940.
91. Bhatnagar A, Mayberry J, Nirula R. Rib fracture fixation for flail chest: what is the benefit? *Journal of the American College of Surgeons.* 2012;215(2):201-205.
92. Balci AE, Eren S, Cakir O, Eren MN. Open fixation in flail chest: review of 64 patients. *Asian Cardiovasc Thorac Ann.* 2004;12(1):11-15.
93. Fagevik Olsén M, Pazooki D, Granhed H. Recovery after stabilising surgery for "flail chest". *European journal of trauma and emergency surgery : official publication of the European Trauma Society.* October 2013;39(5):501-506.
94. Osler T, Baker SP, Long W. A modification of the injury severity score that both improves accuracy and simplifies scoring. *The Journal of trauma.* 1997;43(6):922-925; discussion 925-926.
95. Rüedi T BE, Moran CG. AO principles of Fracture Management. *New York, Thime.* 2007;246.

96. Saltin B, Grimby G. Physiological analysis of middle-aged and old former athletes. Comparison with still active athletes of the same ages. *Circulation.* 1968;38(6):1104-1115.
97. Grimby G, Borjesson M, Jonsdottir IH, Schnohr P, Thelle DS, Saltin B. The "Saltin-Grimby Physical Activity Level Scale" and its application to health research. *Scand J Med Sci Sports.* 2015;25 Suppl 4:119-125.
98. Salén B, Spangfort E, Nygren A, Nordemar R. The Disability Rating Index: an instrument for the assessment of disability in clinical settings. *J Clin Epidemiol.* 1994;47:1423-1435.
99. The EuroQol Group. EuroQol-a new facility for the measurement of health-related quality of life. *Health Policy.* 1990;16(3):199-208.
100. Herdman M, Gudex C, Lloyd A, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation.* 2011;20(10):1727-1736.
101. Burstrom K, Sun S, Gerdtham UG, et al. Swedish experience-based value sets for EQ-5D health states. *Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation.* 2014;23(2):431-442.
102. van Hout B, Janssen MF, Feng YS, et al. Interim scoring for the EQ-5D-5L: mapping the EQ-5D-5L to EQ-5D-3L value sets. *Value Health.* 2012;15(5):708-715.
103. Moll J, Wight V. An objective clinical study of chest expansion. *Ann Rheum Dis.* 1972;31:1-8.
104. Viitanen JV, Suni J, Kautiainen H, Liimatainen M, Takala H. Effect of physiotherapy on spinal mobility in ankylosing spondylitis. *Scand J Rheumatol.* 1992;21(1):38-41.
105. Bostrom C, Harms-Ringdahl K, Nordemar R. Relationships between measurements of impairment, disability, pain, and disease activity in rheumatoid arthritis patients with shoulder problems. *Scand J Rheumatol.* 1995;24(6):352-359.
106. Ragnarsdottir M, Kristinsdottir EK. Breathing movements and breathing patterns among healthy men and women 20-69 years of age. Reference values. *Respiration.* 2006;73(1):48-54.
107. Quanjer PH, Tammeling GJ, Cotes JE, Pedersen OF, Peslin R, Yernault JC. Lung volumes and forced ventilatory flows. Report Working Party Standardization of Lung Function Tests, European Community for Steel and Coal. Official Statement of the European Respiratory Society. *Eur Respir J Suppl.* 1993;16:5-40.
108. Moore EE, Malangoni MA, Cogbill TH, et al. Organ injury scaling. IV: Thoracic vascular, lung, cardiac, and diaphragm. *The Journal of trauma.* 1994;36(3):299-300.

109. Moore EE, Cogbill TH, Jurkovich GJ, et al. Organ injury scaling. III: Chest wall, abdominal vascular, ureter, bladder, and urethra. *The Journal of trauma.* 1992;33(3):337-339.
110. Caragounis EC, Fagevik Olsen M, Granhed H, Rossi Norrlund R. CT-lung volume estimates in trauma patients undergoing stabilizing surgery for flail chest. *Injury.* 2019;50(1):101-108.
111. Rosner B. Fundamentals of Biostatistics. *Books/Cole, Boston MA.* 2011(7th).
112. Caragounis EC, Fagevik Olsen M, Pazooki D, Granhed H. Surgical treatment of multiple rib fractures and flail chest in trauma: a one-year follow-up study. *World J Emerg Surg.* 2016;11:27.
113. European Commission: Mobility and transport. Road safety 2016: How is your country doing? *Luxembourg: Publications Office of the European Union.* 2017.
114. Finelli FC, Jonsson J, Champion HR, Morelli S, Fouty WJ. A case control study for major trauma in geriatric patients. *The Journal of trauma.* 1989;29(5):541-548.
115. Campbell-Furtick M, Moore BJ, Overton TL, et al. Post-trauma mortality increase at age 60: a cutoff for defining elderly? *American journal of surgery.* 2016;212(4):781-785.
116. Kodadek LM, Selvarajah S, Velopulos CG, Haut ER, Haider AH. Undertriage of older trauma patients: is this a national phenomenon? *The Journal of surgical research.* 2015;199(1):220-229.
117. Joseph B, Phelan H, Hassan A, et al. The impact of frailty on failure-to-rescue in geriatric trauma patients: A prospective study. *The journal of trauma and acute care surgery.* 2016;81(6):1150-1155.
118. Sierink JC, Treskes K, Edwards MJ, et al. Immediate total-body CT scanning versus conventional imaging and selective CT scanning in patients with severe trauma (REACT-2): a randomised controlled trial. *Lancet.* 2016;388(10045):673-683.
119. Treskes K, Bos SA, Beenen LFM, et al. High rates of clinically relevant incidental findings by total-body CT scanning in trauma patients; results of the REACT-2 trial. *Eur Radiol.* 2017;27(6):2451-2462.
120. Kauczor HU, Heussel CP, Fischer B, Klamm R, Mildenberger P, Thelen M. Assessment of lung volumes using helical CT at inspiration and expiration: comparison with pulmonary function tests. *AJR American journal of roentgenology.* 1998;171(4):1091-1095.
121. Konheim JA, Kon ZN, Pasrija C, et al. Predictive equations for lung volumes from computed tomography for size matching in pulmonary transplantation. *The Journal of thoracic and cardiovascular surgery.* 2016;151(4):1163-1169 e1161.
122. Kasotakis G, Hasenboehler EA, Streib EW, et al. Operative fixation of rib fractures after blunt trauma: A practice management guideline

from the Eastern Association for the Surgery of Trauma. *The journal of trauma and acute care surgery.* 2017;82(3):618-626.

123. Pieracci FM, Majercik S, Ali-Osman F, et al. Consensus statement: Surgical stabilization of rib fractures rib fracture colloquium clinical practice guidelines. *Injury.* 2017;48(2):307-321.
124. Peters S, Nicolas V, Heyer CM. Multidetector computed tomography-spectrum of blunt chest wall and lung injuries in polytraumatized patients. *Clinical radiology.* 2010;65(4):333-338.
125. Marasco S, Liew S, Edwards E, Varma D, Summerhayes R. Analysis of bone healing in flail chest injury: do we need to fix both fractures per rib? *The journal of trauma and acute care surgery.* 2014;77(3):452-458.
126. Campbell N, Richardson M, Antippa P. Biomechanical testing of two devices for internal fixation of fractured ribs. *The Journal of trauma.* 2010;68(5):1234-1238.
127. Kim S, Choi WJ, Lee KH, Byun CS, Bae KS, Park IH. The clinical implications of severe low rib fracture in the management of diaphragm injury: A Case Control Study. *International journal of surgery.* 2017;42:178-182.
128. Degiannis E, Levy RD, Sofianos C, Potokar T, Florizoone MG, Saadia R. Diaphragmatic herniation after penetrating trauma. *The British journal of surgery.* 1996;83(1):88-91.
129. Al-Thani H, Jabbour G, El-Menyar A, Abdelrahman H, Peralta R, Zarour A. Descriptive Analysis of Right and Left-sided Traumatic Diaphragmatic Injuries; Case Series from a Single Institution. *Bulletin of emergency and trauma.* 2018;6(1):16-25.
130. Rossaint R, Bouillon B, Cerny V, et al. The European guideline on management of major bleeding and coagulopathy following trauma: fourth edition. *Crit Care.* 2016;20:100.
131. Bickell WH, Wall MJ, Jr., Pepe PE, et al. Immediate versus delayed fluid resuscitation for hypotensive patients with penetrating torso injuries. *The New England journal of medicine.* 1994;331(17):1105-1109.
132. Simon B, Ebert J, Bokhari F, et al. Management of pulmonary contusion and flail chest: an Eastern Association for the Surgery of Trauma practice management guideline. *The journal of trauma and acute care surgery.* 2012;73(5 Suppl 4):S351-361.
133. Vincent JL. Critical care--where have we been and where are we going? *Crit Care.* 2013;17 Suppl 1:S2.