The Elusive Randomized Control Trial

Jose J. Diaz, MD, CNS, FACS, FCCM
Professor of Surgery
Division Acute Care Surgery
R Adams Cowley Shock Trauma Center
University of Baltimore Maryland
Baltimore, MD
disclosure

- Acute Innovations
- DePuy Synthes
Historical: Small Frag. Plates circa 2000
What is lacking in the data?

- Outcomes?
  - Mortality
  - Ventilator days
  - Incidence of HAP/VAP
  - LOS/ ICU LOS

- Procedure?
  - Approach / Surgical incisions
  - Under the scapula
  - Extent of stabilization
  - Anterior / posterior

- Quality of Life?
  - Return to work
Flail Chest
Flail chest injuries: a review of outcomes and treatment practices from the National Trauma Data Bank.

Flail chest injury 3,467 patients;

- Age was 52.5 years with 54% lung contusions.
- Management: epidural catheters in 8% and surgical fixation of the chest wall in 0.7% of the patients.
- Mechanical ventilation 59% (mean of 12.1 days)
  - ICU admission 82% (mean of 11.7 days)
- Chest tubes 44%, and 21% required a tracheostomy.
- Complications: pneumonia in 21%, ARDS 14%, sepsis 7%, and death 16%.
- 99% of these patients treated nonoperatively, and only a small proportion (8%) received aggressive pain management with epidural catheters.

Surveyed opinion of American trauma, orthopedic, and thoracic surgeons on rib and sternal fracture repair

- EAST, Orthopedic Trauma Association, & thoracic surgeons (THS) affiliated with teaching hospitals in the United States
- 238 trauma surgeons (TRS), 97 orthopedic trauma surgeons (OTS), and 70 THS completed the survey
- 82% of TRS, 66% of OTS, and 71% of THS thought rib fracture repair was indicated in selected patients.
- Greater proportion of surgeons thought that sternal fracture repair was indicated in selected patients (89% of TRS, 85% of OTS, and 95% of THS).
- Chest wall defect/pulmonary hernia (58%) and sternal fracture nonunion (>6 weeks) (68%) were the only 2 indications accepted by a majority of respondents.
- 26% of surgeons reported they had performed or assisted on a chest wall fracture repair,
- 22% of surgeons were familiar with published RTC of the surgical repair of flail chest.
- Surgeons who thought rib fracture or sternal fracture repair was rarely indicated, 91% and 95% specified that a RCT confirming efficacy would be necessary to change their negative opinion.
- Barriers: lack of expertise among TRS, lack of research of optimal techniques, and a dearth of RTC.

STANDARD OF CARE
Pitfalls associated with open reduction and internal fixation of fractured ribs.

- Rib fracture is exceedingly common and remains a leading cause of death in patients with chest injury.
- Probability of death increases by 19% with each broken rib, and the probability of death increases further with age.
- Treatment is centered on pain control and early mobilization to provide adequate pulmonary hygiene.
- Recently, many studies have found mortality benefit to operation fixation (ORIF) of ribs in select patients.
  - Remains underutilized partly due to lack of familiarity with its technique and pitfalls by trauma surgeons, in particular.

Injury. 2015 Dec;46(12):2335-40.
Benefits of surgical stabilization of severe rib fractures

- Patients with rib fractures who have SSRF have less RH compared with similar MMRF patients. Although not a singular reason to perform SSRF, this clinical benefit should not be overlooked.

- Surgical group was significantly less likely to receive prolonged mechanical ventilation or die within 28 days than the control group

- Surgical rib fixation within 10 days of hospital admission may improve outcomes in patients with traumatic rib fractures.
Analysis of bone healing in flail chest injury: do we need to fix both fractures per rib?

- 3-month CT scans were assessed for degree of healing and presence of residual deformity at the fracture fixation site.
- Follow-up CT was performed in 52 of the 60 patients.
- 3 months after surgery, 86.5% of the patients had at least partial healing with good alignment and adequate fracture stabilization.
- Hardware failure was noted in 5 patients (9.6%) and occurred with the absorbable prostheses only.
- 6 patients - preoperative overlapping or displacement showed no improvement in deformity despite fixing the lateral fractures.
- Callus formation and bony bridging between adjacent ribs was often noted in the rib fractures not fixed (28 of 52 patients, 54%)
- 3D CT chest at 3 months after rib fixation indicates that a philosophy of fixing only one fracture per rib in a flail segment does not avoid deformity and displacement, particularly in posterior rib fractures.

Quality of life after major trauma with multiple rib fractures.

- Aimed to document the long-term quality of life in a cohort of major trauma patients with rib fracture injury over 24 months.
- Main outcome measures: quality of life over 24 months post injury assessed using the Glasgow Outcome Scale Extended and SF12 health assessment forms and a pain questionnaire.
- Assessment over 24 months of major trauma patients with multiple rib fractures demonstrated significantly lower quality of life compared with published Australian norms at all time points measured.
- Return to work rates were poor with only 71% of those who were working prior to their accident, returning to any work.

Surgical rib fixation for flail chest deformity improves liberation from mechanical ventilation.

- 2 groups were similar in age, injury severity score, intensive care unit LOS, hospital LOS, total number of rib fractures, and total segmental rib fractures.
- The operative group demonstrated a significant reduction in total ventilator days as compared with the nonsurgical group (4.5 [0-30] vs 16.0 [4-40]; P = .040).
- Patients with SRF were permanently liberated from the ventilator within a median of 1.5 days (0-8 days).

Surgical fixation vs nonoperative management of flail chest: a meta-analysis.

• Results of surgical fixation and nonoperative management for flail chest injuries.
• Systematic review of previously published comparative studies using operative and nonoperative management of flail chest was performed.
• 11 manuscripts with 753 patients met inclusion criteria.
• Only 2 studies were randomized controlled trials
• Surgical fixation resulted in better outcomes for all pooled analyses
  • ventilator days (mean 8 days, 95% CI 5 to 10 days)
  • odds of developing pneumonia (odds ratio [OR] 0.2, 95% CI 0.11 to 0.32)
  • decreased ICU days (mean 5 days, 95% CI 2 to 8 days)
  • mortality (OR 0.31, 95% CI 0.20 to 0.48)
  • septicemia (OR 0.36, 95% CI 0.19 to 0.71)
  • tracheostomy (OR 0.06, 95% CI 0.02 to 0.20)
  • chest deformity (OR 0.11, 95% CI 0.02 to 0.60)

# Meta-Analysis

## Operative Management of Rib Fractures in the Setting of Flail Chest

*A Systematic Review and Meta-Analysis*

Jennifer A. Leinicke, MD, MPH, Leisha Elmore, MPH, Bradley D. Freeman, MD, and Graham A. Colditz, MD, DrPH

---

**TABLE 2. Characteristics of Studies Comparing Operative to Nonoperative Management of Flail Chest**

<table>
<thead>
<tr>
<th>Author</th>
<th>Location</th>
<th>Study Design</th>
<th>n: Operative Patients</th>
<th>n: Nonoperative Patients</th>
<th>Outcomes Reported</th>
<th>Timing of Operative Intervention</th>
<th>Quality Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ahmed et al⁵</td>
<td>UAE</td>
<td>Cohort</td>
<td>26</td>
<td>38</td>
<td>DMV, ICULOS, mortality, tracheostomy</td>
<td>12–24 h after ICU admission</td>
<td>Fair</td>
</tr>
<tr>
<td>Karev⁶</td>
<td>Ukraine</td>
<td>Cohort</td>
<td>40</td>
<td>93</td>
<td>DMV, pneumonia, mortality</td>
<td>Within 24 h of hospital admission</td>
<td>Moderate</td>
</tr>
<tr>
<td>Voggenreiter et al⁷</td>
<td>Germany</td>
<td>Cohort</td>
<td>20</td>
<td>22</td>
<td>DMV, pneumonia, mortality</td>
<td>Not specified</td>
<td>Moderate</td>
</tr>
<tr>
<td>Tanaka et al⁸</td>
<td>Japan</td>
<td>RCT</td>
<td>18</td>
<td>19</td>
<td>DMV, ICULOS, pneumonia, tracheostomy</td>
<td>Mean 8.2 ± 4.1 d after admission; randomized d 5</td>
<td>Moderate</td>
</tr>
<tr>
<td>Balci et al⁹</td>
<td>Turkey</td>
<td>Cohort</td>
<td>27</td>
<td>37</td>
<td>DMV, HLOS, mortality</td>
<td>All but 2 patients within 48 h of hospital admission</td>
<td>Moderate</td>
</tr>
<tr>
<td>Granetzny et al¹⁰</td>
<td>Egypt</td>
<td>RCT</td>
<td>20</td>
<td>20</td>
<td>DMV, ICULOS, HLOS, mortality</td>
<td>24–36 h after ICU admission; randomized 24 h after admission</td>
<td>High</td>
</tr>
<tr>
<td>Nirula et al¹¹</td>
<td>USA</td>
<td>Case-control</td>
<td>30</td>
<td>30</td>
<td>DMV, ICULOS, HLOS</td>
<td>Mean 3 d after hospital admission</td>
<td>Moderate</td>
</tr>
<tr>
<td>Althausen et al¹²</td>
<td>USA</td>
<td>Case-control</td>
<td>22</td>
<td>28</td>
<td>DMV, ICULOS, HLOS, pneumonia, tracheostomy</td>
<td>Mean 2.3 d after hospital admission</td>
<td>Moderate</td>
</tr>
<tr>
<td>de Moya et al¹³</td>
<td>USA</td>
<td>Case-control</td>
<td>16</td>
<td>32</td>
<td>DMV, ICULOS, HLOS, pneumonia</td>
<td>Mean 5 d after hospital admission</td>
<td>Moderate</td>
</tr>
</tbody>
</table>

*See Methods section, Data Extraction and Quality Assessment, for detail on determination of Quality Rating.
Operative Management of Rib Fractures in the Setting of Flail Chest
A Systematic Review and Meta-Analysis

Jennifer A. Leinicke, MD, MPH,* Leisha Elmore, MPH,* Bradley D. Freeman, MD,* and Graham A. Colditz, MD, DrPH†

FIGURE 2. Forest plot of the pooled ES in days for the outcome DMV. Pooled ES is $-4.52$ days; 95% CI: $-5.54$ to $-3.50$. $\chi^2$ for heterogeneity $= 13.62$, $P = 0.058$, $I^2 = 48.6$. 

Ann Surg 2013;00:1-8
Operative Management of Rib Fractures in the Setting of Flail Chest

A Systematic Review and Meta-Analysis

Jennifer A. Leinicke, MD, MPH,* Leisha Elmore, MPH,* Bradley D. Freeman, MD,* and Graham A. Colditz, MD, DrPH†

---

**FIGURE 3.** Forest plot of the pooled ES in days for the outcome ICULOS. Pooled ES is \(-3.4\) days; 95% CI: \(-6.01\) to \(-0.80\). \(\chi^2\) for heterogeneity = 15.96, \(P = 0.003\); \(I^2 = 74.9\).
Operative Management of Rib Fractures in the Setting of Flail Chest
A Systematic Review and Meta-Analysis

Jennifer A. Leinicke, MD, MPH,* Leisha Elmore, MPH,* Bradley D. Freeman, MD,* and Graham A. Colditz, MD, DrPH†

FIGURE 6. Forest plot of the pooled RR for the outcome of mortality. Pooled RR is 0.43, 95% CI: 0.28–0.69. $\chi^2$ for heterogeneity $= 0.85, P = 0.932; I^2 = 0.$
Rib fracture fixation for flail chest: what is the benefit?

- Markov transition state analysis performed modeling the outcomes of the standard of care or ORIF-FC (flail chest)
- Incidences of VAP, tracheostomy, sepsis, prolonged ventilation, DVT, PE, wound infection, and postoperative hemorrhage were obtained based from literature review.
- Medicare 2010 reimbursement costs were used for diagnoses and procedures.
- Quality of life improvement factor ranging from 0 to 15% improvement was used to estimate the improvement in pain and functional outcomes related to ORIF-FC.
- Cost-effective treatment was determined, ranging the incidences of VAP and quality of life improvement factor.

Rib fracture fixation for flail chest: what is the benefit?

- Cost effectiveness:
  - $15,269 for ORIF-FC compared with $16,810 for standard of care.
- Quality of life improvement factor was set to 0%
  - ORIF-FC the most cost-effective strategy.
- ORIF-FC remained the most cost-effective strategy by $8,400 when the incidence of VAP after ORIF was as high as 22%.
- Despite the additional cost of surgery, rib fracture fixation dominates the standard of care and should be considered in the management of appropriate flail chest patients.

Utility of three-dimensional computed tomography for the surgical management of rib fractures.

- (3D) CT adds valuable information to the preoperative plan for fixation of rib fractures.
- Retrospective cohort of 35 consecutive adult patients with flail chest requiring surgery, we evaluated the intraobserver and interobserver reliability of plain radiographs, 2D CT and 3D CT, for the identification of rib fractures and identified how often the surgical plan changed with the addition of the information provided by the 3D CT.
- 2 fellowship-trained orthopedic trauma surgeons who regularly operate on rib fractures in their clinical practice and were not involved in the treatment of the study population evaluated the radiographic data.
- Intraobserver and interobserver reliability was excellent for both 2D CT and 3D CT and was the highest for 2D CT.
- Overall, 2D CT had the highest diagnostic accuracy for detecting rib fractures as compared with plain radiographs and 3D CT.
- 3D CT changed the surgical tactic in 65.7% of the cases

Surgical versus nonsurgical interventions for flail chest.

- Thoracic trauma (TT) is common among people with multiple traumatic injuries. One of the injuries caused by TT is the loss of thoracic stability resulting from multiple fractures of the rib cage, otherwise known as flail chest (FC). A person with FC can be treated conservatively with orotracheal intubation and mechanical ventilation (internal pneumatic stabilization) but may also undergo surgery to fix the costal fractures.

- SEARCH METHODS: We ran the search on the 12 May 2014. We searched the Cochrane Injuries Group's Specialised Register, the Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library), MEDLINE (OvidSP), EMBASE Classic and EMBASE (OvidSP), CINAHL Plus (EBSCO), ISI WOS (SCI-EXPANDED, SSCI, CPCI-S, and CPSI-SSH), and clinical trials registers. We also screened reference lists and contacted experts.

- SELECTION CRITERIA:
  - Randomized controlled trials of surgical versus nonsurgical treatment for people diagnosed with FC.

- DATA COLLECTION AND ANALYSIS:
  - Two review authors selected relevant trials, assessed their risk of bias, and extracted data.

Surgical versus nonsurgical interventions for flail chest.

- 3 studies that involved 123 people.
- The methods used for blinding the participants and researchers to the treatment group were not reported, but as the comparison is surgical treatment with medical treatment this bias is hard to avoid.
- There was no description of concealment of the randomization sequence in two studies.
- All three studies reported on mortality, and deaths occurred in two studies.
- There was no clear evidence of a difference in mortality between treatment groups (risk ratio (RR) 0.56, 95% confidence interval (CI) 0.13 to 2.42);
  however, the analysis was underpowered to detect a difference between groups.
- Out of the 123 people randomized and treated, six people died;
- the causes of death were pneumonia, pulmonary embolism, mediastinitis, and septic shock.
- Among people randomized to surgery, there were reductions in pneumonia (RR 0.36, 95% 0.15 to 0.85; three studies, 123 participants), chest deformity (RR 0.13, 95% CI 0.03 to 0.67; two studies, 86 participants), and tracheostomy (RR 0.38, 95% CI 0.14 to 1.02; two studies, 83 participants).
- Duration of mechanical ventilation, length of intensive care unit stay (ICU), and length of hospital stay were measured in the three studies.
- Due to differences in reporting, we could not combine the results and have listed them separately.
- Chest pain, chest tightness, bodily pain, and adverse effects were each measured in one study.

AUTHORS' CONCLUSIONS:
- There was some evidence from three small studies that showed surgical treatment was preferable to nonsurgical management in reducing pneumonia, chest deformity, tracheostomy, duration of mechanical ventilation, and length of ICU stay.
- Further well-designed studies with a sufficient sample size are required to confirm these results and to detect possible surgical effects on mortality.

EAST Guidelines for Flail Chest / Pulmonary Contusion

<table>
<thead>
<tr>
<th>Level II</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Trauma patients with PC-FC should not be excessively fluid restricted, but rather should be resuscitated as necessary with isotonic crystalloid or colloid solution to maintain signs of adequate tissue perfusion. Once adequately resuscitated, unnecessary fluid administration should be meticulously avoided. A pulmonary artery catheter may be useful to avoid fluid overload.</td>
</tr>
<tr>
<td>2. Obligatory mechanical ventilation should be avoided.</td>
</tr>
<tr>
<td>3. The use of optimal analgesia and aggressive chest physiotherapy should be applied to minimize the likelihood of respiratory failure and ensuing ventilatory support. Epidural catheter is the preferred mode of analgesia delivery in severe flail chest injury. (see EAST PMG “Analgesia in Blunt Thoracic Trauma)</td>
</tr>
<tr>
<td>4. Patients with PC-FC requiring mechanical ventilation should be supported in a manner based on institutional and physician preference and separated from the ventilator at the earliest possible time. PEEP / CPAP should be included in the ventilatory regimen.</td>
</tr>
<tr>
<td>5. Steroids should not be used in the therapy of pulmonary contusion.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Level III</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. A trial of mask CPAP should be considered in alert, compliant patients with marginal respiratory status</td>
</tr>
<tr>
<td>2. Independent lung ventilation may be considered in severe unilateral pulmonary contusion when shunt cannot be otherwise corrected due to mal-distribution of ventilation or when crossover bleeding is problematic.</td>
</tr>
<tr>
<td>3. Diuretics may be used in the setting of hydrostatic fluid overload as evidenced by elevated pulmonary capillary wedge pressures in hemodynamically stable patients or in the setting of known concurrent congestive heart failure.</td>
</tr>
<tr>
<td>4. Surgical fixation may be considered in severe unilateral flail chest or in patients requiring mechanical ventilation when thoracotomy is otherwise required.</td>
</tr>
</tbody>
</table>
SURGICAL FIXATION OF RIB FRACTURES

SUMMARY
Rib fractures are a common injury in patients sustaining blunt trauma to the chest. While most rib fractures heal uneventfully with conservative methods, some patients require more invasive treatment to prevent future pulmonary complications. Surgical fixation of rib fractures has long been a controversial mode of treatment that has recently gained support in certain clinical circumstances. While most research on the operative treatment of rib fractures takes place in the context of flail chest, various case reports and retrospective studies document its success for other select indications.

RECOMMENDATIONS
- Level 1
  - None
- Level 2
  - Surgical fixation of rib fractures should be considered as the primary treatment in the following patients without severe head or other major organ system injury
    - Flail chest segment
    - Severe chest wall deformity with or without pulmonary herniation
    - Symptomatic fractures of 3 or more consecutive ribs
- Level 3
  - Intramedullary hardware should be employed for fixation of posterior rib fractures to avoid extensive dissection
  - Surgical fixation of rib fractures should be considered for patients with symptomatic malunion or nonunion of rib segments (chronic therapy)
  - Absorbable plates are not recommended for fixation of posterior rib fractures
Internal Fixation of Rib Fracture

Number: 0822

Policy
Aetna considers internal fixation of rib fractures (e.g., MatrixRIB Fixation System, RibLoc Rib Fracture Plating System) medically necessary in cases of severe flail chest failing to wean from a ventilator or when thoracotomy is required for other reasons. Aetna considers internal fixation of rib fractures experimental and investigational for all other indications.

See also CPB 0582 - Titanium Rib (../500_599/0582.html).
This document addresses the open treatment of rib fracture(s) using an internal fixation device.

Investigational and Not Medically Necessary:

The use of an internal rib fixation system is considered investigational and not medically necessary for all indications.
Conclusion

• The current medical rigor of medical evidence”
  • elusive \textit{randomized clinical trial}
  • Patient / injury pattern selection is not standardize
  • Clinical outcomes are not standardized
  • Long term out comes

• Trauma surgeons:
  \textit{I never see these patients back = no news must be good news}