Surgical Fixation vs Nonoperative Management of Flail Chest: A Meta-Analysis

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BACKGROUND: Flail chest is a life-threatening injury typically treated with supportive ventilation and analgesia. Several small studies have suggested large improvements in critical care outcomes after surgical fixation of multiple rib fractures. The purpose of this study was to compare the results of surgical fixation and nonoperative management for flail chest injuries.

STUDY DESIGN: A systematic review of previously published comparative studies using operative and nonoperative management of flail chest was performed. Medline, Embase, and the Cochrane databases were searched for relevant studies with no language or date restrictions. Quantitative pooling was performed using a random effects model for relevant critical care outcomes. Sensitivity analysis was performed for all outcomes.

RESULTS: Eleven manuscripts with 753 patients met inclusion criteria. Only 2 studies were randomized controlled designs. Surgical fixation resulted in better outcomes for all pooled analyses including substantial decreases in ventilator days (mean 8 days, 95% CI 5 to 10 days) and the odds of developing pneumonia (odds ratio [OR] 0.2, 95% CI 0.11 to 0.32). Additional benefits included 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), and chest deformity (OR 0.11, 95% CI 0.02 to 0.60). All results were stable to basic sensitivity analysis.

CONCLUSIONS: The results of this meta-analysis suggest surgical fixation of flail chest injuries may have substantial critical care benefits; however, the analyses are based on the pooling of primarily small retrospective studies. Additional prospective randomized trials are still necessary. (J Am Coll Surg 2013;216:302−311. © 2013 by the American College of Surgeons)

Multiple rib fractures with segmental chest wall instability represents high energy chest trauma with significant morbidity and mortality.[1,2] Treatment of these flail chest injuries has evolved over the past half century. Early strategies used chest wall traction and external stabilization methods,[3] but were later abandoned in favor of internal pneumatic splinting using positive pressure mechanical ventilation. Although mechanical ventilation is the standard of care for flail chest injuries at most North American institutions, several authors have reported excellent results using operative techniques to manage these injuries. Despite recognizing the potential benefits for surgical fixation, operative management has been described as an underused treatment.[4]

The introduction of rib specific plating options has caused increased interest in surgical fixation of multiple rib fractures. Recent studies have described biomechanical testing, implant design, and surgical techniques for several plate designs.[5-8] Despite the increasing access to this technology, strong evidence supporting surgical fixation of flail chest injuries remains sparse. The purpose of this study was to compare the critical care outcomes of surgical fixation to nonoperative management in patients with flail chest injuries using pooled data from previously published comparative studies.

CME questions for this article available at http://jacscme.facs.org

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METHODS

Literature search

In May 2011, a comprehensive literature search was performed using the OVID interface and the following databases: Medline, Embase, Cochrane Database of Systematic Reviews (CDSR), and the Cochrane Central Register of Controlled Trials (CENTRAL). The purpose of the search was to identify published studies comparing operative and nonoperative treatment for flail chest injuries. Search terms included MeSH headings and key words related to fracture fixation, rib fractures, and flail chest. The specific search strategy for each database is detailed in Appendix 1 (online only).

Study selection

Titles from all database searches were combined and a systematic review process was performed independently by 2 reviewers. First, titles were screened for potential relevance to the management of flail chest injuries. The abstracts of selected titles were then screened for further detail to ensure the study included a comparison of operative and nonoperative management of flail chest injuries. If adequate information was not present in the title or abstract, the manuscript was automatically considered for full-text review. Full-text review was performed on all selected abstracts. Final selection of included manuscripts was based on the following inclusion criteria: eligible studies included only human patients with traumatic flail chest injuries; the study must have also compared clinical results of any type of operative treatment to a nonoperative treatment group, and each group must have included more than 10 cases. Finally, the study must have reported clinical outcomes that would allow potential data pooling with other included studies. Basic science studies and interventions for nonacute trauma were excluded. Foreign language manuscripts were translated as necessary, and no publication date restrictions were applied.

Data extraction and statistical analysis

All relevant clinical outcomes data for each included study were extracted independently by 2 authors. A priori, it was hypothesized that ventilator days, ICU duration, pneumonia, mortality, and pulmonary function would be potential outcomes for quantitative pooling. Additional critical care outcomes of interest were identified during the final review and the relevant data were extracted by both reviewers. To facilitate potential quantitative pooling, the sample size, as well as the mean and standard deviation or the number of events for each intervention group were recorded.

Study heterogeneity was assessed using the I^2 statistic and a threshold of greater than 50% was established to represent substantial heterogeneity.[9] The I^2 statistic is reported as the percentage of variability of between-study heterogeneity that is not due to sampling error. Quantifying the amount of between-study heterogeneity is important because it allows the reader to determine how statistically similar the sample populations are, and whether it is appropriate to pool data from these populations. Statistical pooling was performed using a random effects model. This was selected a priori because we expected to pool results from small sample sizes and retrospective study designs, which inherently contain more effect size variability. By design, a random effects model accounts for within- and between-study variability, and is frequently used in meta-analyses of nonrandomized controlled trials.[10,11] For continuous outcomes, the results were reported as a pooled difference in means and its 95% confidence interval (CI); for dichotomous outcomes, a pooled odds ratio (OR) and 95% CI were reported. Finally, the pooled risk difference was used to calculate a number needed to treat (NNT), based on the relationship of 1/(risk difference). Forest plots were generated to graphically display the results of all pooled analyses. This type of plot allows the reader to visualize the effect size and confidence interval for each study, and it weighted contribution to the pooled estimate. Funnel plots were also examined for evidence of bias. A funnel plot can be used to screen for evidence of publication bias or biased estimates from smaller studies. When the results of the included studies are plotted, it should resemble a triangle or inverted funnel, with larger, more precise studies represented narrowly at the peak of the pooled estimate. When the plot does not resemble the inverted funnel, it may represent small study effects that manifest with wide effect estimates, poor precision, or publication bias from the underpowered negative results.

Additional sensitivity analysis was performed for various aspects of the meta-analysis. Initially, the analyses were repeated, with sequential removal of a single study to determine its influence on the pooled results. Further analyses were also repeated using only the included prospective studies. All statistical analyses were performed using the Comprehensive Meta-Analysis software package (Biostat). Statistical significance was set at $p < 0.05$ for all pooled estimates.

RESULTS

Search results

Appendix 2 (online only) outlines the study flow and selection of included articles. On removal of duplicate

Table 1. Description of Included Studies

First author	Country	Study period	Study design	Sample size	Operative treatment
Ahmed[12]	UAE	1995*	Retrospective	64	K-wires
Balci[13]	Turkey	1991–2000	Retrospective	64	Suture and traction
Borrelly[14]	France	1972–1984	Retrospective	176	Judet struts
Granetzny[15]	Germany	2005*	RCT	40	K-wires or steel wire
Karev[16]	Ukraine	1973–1992	Retrospective	133	Osteosynthesis†
Kim[17]	France	1978–1979	Retrospective	63	Judet struts
Nirula[18]	USA	1996–2000	Case-control	60	Adkin struts
Ohresser[19]	France	1965–1971	Retrospective	14	Osteosynthesis†
Tanaka[20]	Japan	1992–1998	RCT	37	Judet struts
Teng[21]	China	2006–2008	Retrospective	60	Absorbable nail, suture, or titanium plate
Voggenreiter[22]	Germany	1988–1994	Retrospective	42	Isoelastic rib clamp or pelvic reconstruction plate

*Year of publication, no study period described.
†Osteosynthesis implant not described.
RCT, randomized controlled trial; UAE, United Arab Emirates.

publications, 306 titles were reviewed and a total of 11 manuscripts met full inclusion criteria. Table 1 summarizes the included studies. Briefly, a total of 753 patients comprised the pooled study population, with the sample size varying for each outcome of interest. Study periods ranged from 1965 to 2008. Only 2 studies were prospective randomized controlled designs;[15,20] the remainder were retrospective comparative studies. A variety of surgical techniques were used, including Judet struts, K-wires, and plate fixation. Nonoperative management consisted of mechanical ventilation and analgesia, with most studies not reporting their specific mechanical ventilation mode.

The numbers of studies available to pool results for each outcome varied and are summarized in Table 2. One study included 2 separate operative vs nonoperative comparative cohorts based on the presence or absence of pulmonary contusion;[22] these data were combined using a fixed effects model and then used in the quantitative pooling with the other included studies. The most commonly reported outcomes were ventilator days, pneumonia, and mortality. Respiratory function was also commonly reported, but due to significant heterogeneity in the pulmonary function testing used and the time points measured, these results were not amenable to pooled analysis. Similar difficulties were observed attempting to pool other potential functional outcomes; rarely was the same metric used between studies, the time points were not consistent, and most studies did not report any functional outcomes at all.

Study synopses

Ahmed and Mohyuddin (1995)[12]

Ahmed and Mohyuddin[12] retrospectively reviewed 64 patients with a flail chest injury. Twenty-six patients underwent internal fixation, and 38 were treated with ventilation. The groups were similar in age, sex, and injury severity, but no statistical comparisons were reported. The surgically managed group required fewer days of mechanical ventilation, had a shorter mean ICU stay,

Table 2. Summary of Pooled Results

Outcomes	References	Sample size (no. of studies)	Treatment favored	I^2 Statistic, %	Mean decrease (95% CI)	Odds ratio (95% CI)	Risk difference (95% CI)	NNT
Ventilator days	13,15-18,20-22	563 (8)	Operative	48	7.5 (5.0–9.9)	—	—	—
ICU days	15,18,20,21	261 (4)	Operative	0.1	4.8 (1.6–7.9)	—	—	—
Hospital days	13,15,18,21	400 (4)	Operative	33	4.0 (0.7–7.4)	—	—	—
Mortality	12-17,22	582 (7)	Operative	0	—	0.31 (0.20–0.48)	0.19 (0.13–0.26)	5
Pneumonia	12-16,20-22	616 (8)	Operative	4	—	0.18 (0.11–0.32)	0.31 (0.21–0.41)	3
Septicemia	12,14,17,22	345 (4)	Operative	0	—	0.36 (0.19–0.71)	0.14 (0.56–0.23)	7
Tracheostomy	12,13,20	165 (3)	Operative	0	—	0.12 (0.04–0.32)	0.34 (0.10–0.57)	3
Dyspnea	12,19,20	135 (3)	Operative	0	—	0.40 (0.16–1.01)	0.15 (−0.09–0.39)	7
Chest pain	19,20	71 (2)	Nonsignificant	0	—	0.40 (0.01–12.60)	0.18 (−0.46–0.83)	5
Chest deformity	12,13,15,21	228 (4)	Operative	2.1	—	0.11 (0.02–0.60)	0.30 (−0.00–0.60)	3

NNT, number needed to treat (1/risk difference).

had fewer cases of chest infection and sepsis, required fewer tracheostomies, and had a lower mortality rate.

Balci and colleagues (2004)[13]

This study reported on 64 patients in 3 treatment groups presenting with 3 or more segmental rib fractures and paradoxical chest wall motion. Patients were selected for open fixation when clinical dyspnea and blood gas measurements of $PaO_2 < 60$ mmHg and $PaCO_2 > 40$ mmHg were present. Operative patients received open reduction and fixation with silk suture attached to traction. Nonoperative patients were treated with either intermittent positive-pressure ventilation or a non-intermittent positive-pressure ventilation mode of ventilation. For our analysis, the results from both nonoperative ventilatory groups were combined. Based on their results, the authors concluded that operative patients seemed to have mortality, pneumonia, and ventilatory day benefits, despite being sicker than the nonoperative group (Injury Severity Score 21 vs 18).

Borrelly and colleagues (1985)[14]

Borrelly and associates[14] retrospectively reviewed 236 patients with chest instability treated over a 12-year period (1972 to 1984). Patients were treated with mechanical ventilation if mechanical ventilation was necessary for another reason (pulmonary contusion, coma, etc) or if osteosynthesis was technically impossible. Surgical intervention was chosen when these 2 criteria were not met. Osteosynthesis was chosen because of its perceived morbidity benefits. Ninety-seven patients were treated with ventilation; 79 were treated with osteosynthesis. There was a 40% (39 of 97) mortality rate in the ventilation group and 16% (13 of 79) in the operative group. Twenty-one percent of the patients in the nonoperative group (20 of 97) and 13% (10 of 79) of patients in the operative group developed sepsis. The mean number of days of hospitalization in the patients who survived was 44 days in the nonoperative group and 30 days in the operative group.

Granetzny and colleagues (2005)[15]

These authors conducted a randomized controlled trial of nonoperative vs operative treatment of flail chest in 40 patients who had fractures of 3 or more ribs with paradoxical movement. Patients randomized to the nonoperative group were treated with adhesive plaster splint and mechanical ventilation, when required. Patients randomized to surgical fixation were treated 24 to 36 hours after admission and were treated with adhesive plaster splint until surgery. Despite randomization, the nonoperative group was significantly younger than the operative group (36 ± 14.9 years vs 40.5 ± 8.2 years; $p < 0.001$) and the nonoperative group was slightly sicker than the operative group according to the Injury Severity Score (18.0 ± 5.1 vs 16.8 ± 3.5; $p = 0.043$). The operative group had fewer days of mechanical ventilation, shorter ICU stays, shorter overall duration of hospitalization, fewer cases of pneumonia, fewer cases of residual chest wall deformity, and better forced vital capacity at 2 months postoperatively. Mortality was 2 of 20 in the operative group and 3 of 20 in the nonoperative group.

Karev and associates (1997)[16]

This study compared the results of 40 operative and 93 nonoperatively treated patients with flail chest injuries from 1973 to 1992. Operatively treated patients were stabilized with a variety of unspecified extramedullary osteosynthesis implants, typically at the end of other emergency surgical procedures. The specific surgical indications were not explicitly described; however, the authors described an increasing preference toward surgical fixation over the study time period (up to 47% of all flail chest patients). Despite the nonrandomized allocation, similar demographics and ISS were observed between the groups. Operatively treated patients had fewer mechanical ventilation days (2 vs 6), lower incidence of pneumonia (6 of 40 vs 32 of 93), and a decreased incidence of mortality (9 of 40 vs 43 of 93).

Kim and colleagues (1981)[17]

Kim and colleagues[17] conducted a retrospective study of 63 patients with flail chest injuries. Forty-five patients were treated with mechanical ventilation alone, and 18 patients were treated with surgical fixation. The mean age of the nonoperative sample was 58 years, with 16 of the patients aged 65 or older. The mean age of the operative group was 48 years, with an age range of 23 to 70 years. Seventy-seven percent of patients in the nonoperative group had multiple injuries; 66% in the operative group had multiple injuries. The operative group had fewer deaths (4.5% vs 22.3%) and fewer ventilator days (1 ± 3 days vs 18 ± 6 days).

Nirula and coworkers (2006)[18]

This study included 60 patients and is the only report from a North American center. Operative patients during a 4-year period (1996 to 2000) were matched to an equal number of historical controls based on age, ISS, and chest Abbreviated Injury Score. Patients were selected for operative treatment based on ventilatory compromise, thoracic deformity, hypoxemia, and pain. Fixation was performed with Adkin struts. Trends toward decreased ICU days (12.1 ± 1.2 vs 14.1 ± 2.7), hospital days

(18.8 ± 1.8 vs 21.1 ± 3.9), and ventilatory days (6.5 ± 1.3 vs 11.2 ± 2.6) were seen favoring the operative group; however, no result reached statistical significance.

Ohresser and colleagues (1972)[19]

This retrospective study included 92 patients with severe closed chest injuries, 57 of whom were treated with osteosynthesis and 32 who were treated nonoperatively. At 1 year after injury, 10 of 27 (37%) patients in the operative group and 4 of 7 (57%) patients in the nonoperative group reported dyspnea. No acute critical care outcomes were reported for the comparative groups.

Tanaka and associates (2002)[20]

This is a randomized controlled trial of surgical stabilization vs internal pneumatic stabilization in 37 patients with flail chest injuries requiring mechanical ventilation over a 6-year period. Patients were randomly assigned to a treatment group 5 days after injury. There were no statistically significant differences in age, sex, ISS, site of flail segment, or number of fractures between the 2 groups. The surgical group had significantly fewer cases of pneumonia 21 days after injury, shorter duration of ventilation, shorter duration of ICU stay, and fewer cases of tracheostomy at 21 days after injury. There was no significant difference between the 2 groups with regard to incidence of pneumonia or tracheosotomy at 7 days postinjury. Subjective dyspnea was more common in the nonoperative group than the operative group at 1 year.

Teng and coworkers (2009)[21]

This study of 60 patients occurred between 2006 and 2008. Operative indications included bilateral flail chest injuries, persistent respiratory dysfunction despite nonoperative management, persistent pain, or on retreat of emergent open thoracotomy. Operative fixation was obtained using absorbable nails, suture, or titanium plates. Nonoperative patients received supportive treatment including a commercial rib splint orthosis. Significant decreases were observed in the operative group for ventilatory days (14 vs 20), ICU days (8.7 vs 15.2), hospital days (22.4 vs 17.1), the incidence of pneumonia (4 of 32 vs 12 of 28), and chest wall deformity (0 of 32 vs 18 of 28).

Voggenreiter and colleagues (1998)[22]

Voggenreiter and colleagues[22] reported on 42 patients over a 6-year period (1988 to 1994). Indications for surgical fixation included emergent thoracotomy for intrathroracic injury, paradoxical chest wall motion during weaning from respirator, and severe chest wall deformity. Patients were divided into 4 groups based on the presence or absence of pulmonary contusions and whether they received operative chest wall fixation or nonoperative management. This was the only study to separate patients based on pulmonary contusion and this created small groups for analysis (4 to 18 patients per group). As a result, we disregarded the pulmonary contusion distinction and analyzed the data based on operative and nonoperative treatment. We believed this was consistent with the other included studies, mirrored many surgeons' clinical practice of considering surgical fixation despite the presence of pulmonary contusion, and would also bias the results toward the null hypothesis of no treatment effect.

Pooled outcomes

Minimal study heterogeneity was encountered for most outcomes of interest (Table 2); however, moderate heterogeneity was seen when pooling the ventilator days ($I^2 = 48\%$) and hospital days ($I^2 = 33\%$) data. The secondary analysis of outcomes from the 2 randomized controlled trials revealed minimal heterogeneity for the ventilator days outcome ($I^2 = 0\%$). Because the I^2 statistic was below 50% for all results, we concluded there was minimal between-study heterogeneity and we have reported the pooled analyses for all outcomes of interest. Furthermore, this observation suggests that potential causes of between-study heterogeneity, such as differing publication dates or operative techniques, were not significant.

The pooled mean difference or odds ratio, as well as the number needed to treat for dichotomous outcomes, are also summarized in Table 2. Operative treatment was favored over nonoperative management for all pooled outcomes, including substantial decreases in ventilator days (8 days, 95% CI 5 to 10 days) and the odds of developing pneumonia (odds ratio [OR] 0.18, 95% CI 0.11 to 0.32). The ventilator days and pneumonia outcomes had large sample sizes ($n > 500$) and were pooled from the greatest number of eligible studies. Forest plots for these outcomes are displayed in Figures 1 and 2. These graphs show that the pooled effect and its 95% CI for both outcomes favor operative treatment. Similar plots were seen for the remainder of outcomes of interest. The number-needed-to-treat analyses also revealed large treatment effects from operative management for all study outcomes. Based on the pooled results, a total of 3 patients would need to undergo operative stabilization to prevent 1 case of pneumonia (95% CI 2 to 5).

Funnel plots were analyzed for evidence of bias, and Figures 3 and 4 display the results for the ventilator days and pneumonia outcomes. One study (Kim and colleagues[17]) in Figure 3 is seen as an outlier beyond the funnel plot confidence intervals and may represent biased small study size results pooled in the ventilator

Study Name	Difference in Means	Standard Error	95% CI		p-value
Balci	-4.1	1.2	-6.4	-1.8	0.00
Karev	-4.0	0.2	-4.4	-3.6	0.00
Kim	-17.0	1.5	-19.9	-14.1	0.00
Granetzny	-10.0	2.8	-15.5	-4.5	0.00
Nirula	-4.7	0.5	-5.7	-3.7	0.00
Tanaka	-7.5	1.9	-11.2	-3.8	0.00
Teng	-6.0	3.0	-11.9	-0.1	0.05
Voggenreiter	-16.4	8.1	-32.3	-0.4	0.04
Summary	-7.5	1.2	-9.9	-5.0	0.00

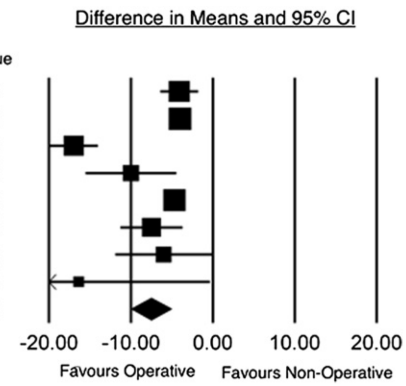

Figure 1. Forest plot and pooled analysis of mean difference in ventilator days. The mean difference in ventilator days is reported for each study (black square) along with its 95% confidence interval (horizontal lines). The size of the square represents the weighted contribution of each study and the black diamond in the Summary line represents the pooled estimate and its 95% CI (width of diamond).

days analysis. No evidence of potential bias was seen for the other pooled outcomes.

Sensitivity analyses were also performed for all pooled outcomes. Figures 5 and 6 display representative examples of the forest plot output and summary effect of removing each study on the pooled results for the outcomes of ventilator days and pneumonia. All pooled outcomes were stable to the sequential removal of each included study, including the results from Kim and associates,[17] which were identified as potentially biased. Repeat analysis using only data from the 2 prospective trials could be performed for the ventilator days, ICU days, and pneumonia outcomes. This repeat analysis was based on 77 patients and revealed similarly significant point estimates and conclusions favoring operative treatment (Table 3).

DISCUSSION

This meta-analysis presents results from 11 studies comparing surgical intervention to nonoperative management for the treatment of flail chest injuries. The pooled results suggest substantial benefits to surgical intervention, including decreases in the number of mean ventilator days, ICU days, and hospital days, as well as decreased odds for tracheostomy, pneumonia, chest deformity, mortality, and septicemia. These conclusions were stable to basic sensitivity analysis and repeat analyses using only prospective randomized controlled trial data.

The results from this meta-analysis are consistent with reports from previously published smaller studies included in the quantitative pooling. Many of the pooled studies demonstrated point estimates favoring operative

Study Name	Odds Ratio	95% CI		p-value
Ahmed	0.182	0.053	0.629	0.007
Balci	0.063	0.003	1.146	0.062
Borrelly	0.132	0.056	0.309	0.000
Granetzny	0.111	0.020	0.610	0.011
Karev	0.336	0.128	0.885	0.027
Tanaka	0.034	0.005	0.211	0.000
Teng	0.190	0.053	0.690	0.012
Voggenreiter	0.714	0.185	2.762	0.626
Summary	0.184	0.105	0.324	0.000

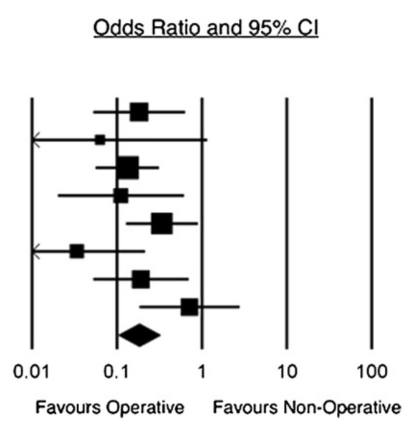

Figure 2. Forest plot and pooled analysis of odds ratio for developing pneumonia. The odds ratio for developing pneumonia is reported for each study (black square) along with its 95% confidence interval (horizontal lines). The size of the square represents the weighted contribution of each study and the black diamond in the Summary line represents the pooled estimate and its 95% CI (width of diamond).

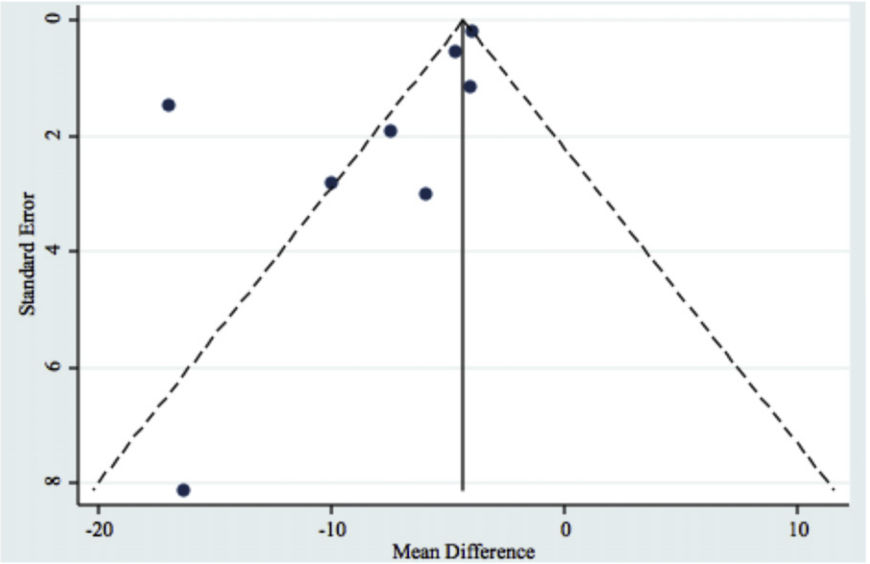

Figure 3. Funnel plot of included studies for pooled analysis of mean difference in ventilator days. For each study, the point estimate of the treatment effect is plotted along the x-axis and the precision of the estimate is plotted on the y-axis. The summary estimate (vertical line) and its 95% confidence interval (diagonal dotted lines) are also represented. One study[14] is seen as an outlier beyond the dotted lines and may represent bias from its small study size.

intervention, but lacked the sample size to ensure statistically significant conclusions for several of their clinical outcomes. Over the years, review articles and expert opinion have outlined the potential indications and benefits of rib fracture fixation; however, many of these reviews have been based on few studies and anecdotal evidence. The results of this study extend the previous literature by providing a systematic review of the available literature and by facilitating a pooled analysis, which provides a more precise measure of the surgical treatment effect across several clinical outcomes.

Based on the pooled results, it appears that surgical fixation of flail chest injuries is superior to nonoperative management for several critical care outcomes. The type of fixation, however, appears to be less important because consistent benefits were seen across a heterogeneous group of surgical implants. The spectrum of operative implants included rigid devices such as plates and struts, to less rigid Kirschner wires, and even sutures. As a result, these meta-analysis data do not facilitate a recommendation for a preferred surgical implant. When selecting a surgical device for flail chest fixation, the surgeon should consider the ease of the operation, the biomechanical properties of the device, the risk for complications, and the implant's cost.

The magnitude of the pooled results is also worth significant discussion. Dyspnea and chest pain were the only outcomes with a nonsignificant odds ratio, and this was likely due to their smaller sample sizes, yet the point estimates and statistical significance still trended toward a protective benefit to operative intervention. Furthermore, the number needed to treat for the dichotomous outcomes analyzed suggested that only a few patients would require operative fixation to prevent several different adverse events. The upper confidence limit for the number needed to treat of most of these outcomes remained below 10 patients. Although not directly studied, the economic and quality of life impact of reducing ventilator duration, ICU length of stay, and multiple adverse events is also likely to be quite substantial.

Despite the overwhelming positive results observed, the results of this meta-analysis must be interpreted in the context of the pooled studies. Overall, the majority of included data were from small retrospective studies. Of the 11 studies, only 2 had more than 100 patients; the 2 randomized controlled trials included had only 37 and 40 patients, respectively. The brief study synopses reported in the Results section also highlight various limitations within each study that threatened the internal validity of each study's results. These included the retrospective design of the 9 studies, which may overestimate the treatment effect because these designs typically used historical controls for their comparison group; if systematic improvements occurred in the institution's delivery of critical care,

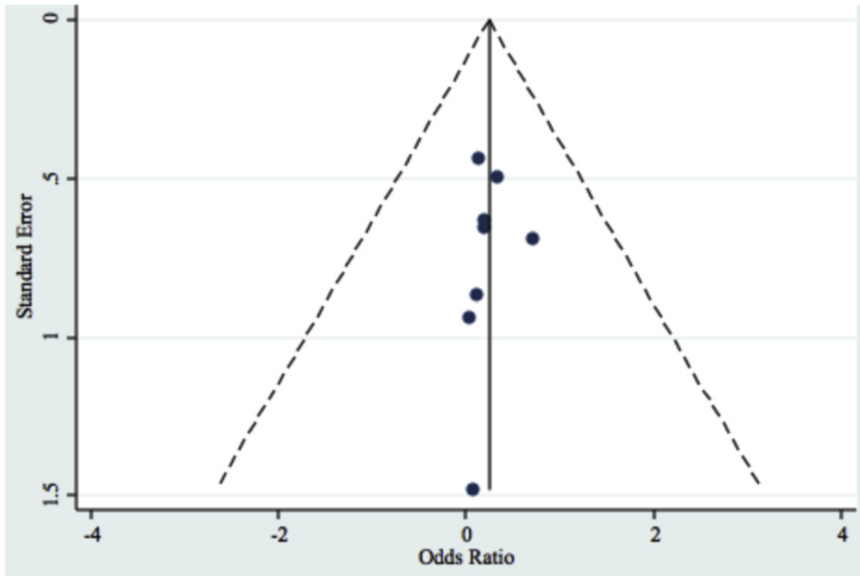

Figure 4. Funnel plot of included studies for pooled analysis of odds ratio for developing pneumonia. For each study, the point estimate of the treatment effect is plotted along the x-axis and the precision of the estimate is plotted on the y-axis. The summary estimate (vertical line) and its 95% confidence interval (diagonal dotted lines) are also represented. No evidence of bias from small study effects is observed.

then the treatment effect of operative intervention would be overestimated. This is certainly possible as improvements are made in antibiotic coverage, mechanical ventilation strategies, and prevention of complications associated with prolonged mechanical ventilation. In addition, the nonrandomized study designs likely experienced elements of selection bias, with certain patients automatically receiving nonoperative care due to the severity of their multisystem injuries; this is likely to overestimate the difference in duration of mechanical ventilation, ICU length of stay, hospital length of stay, morbidity, and mortality between the 2 groups.

Study Name	Statistics with Study Removed				
	Point	Standard Error	95% CI		p-value
Balci	-8.2	1.5	-11.0	-5.4	0.00
Karev	-8.6	2.0	-12.6	-4.5	0.00
Kim	-4.8	0.5	-5.9	-3.7	0.00
Granetzny	-7.2	1.3	-9.8	-4.7	0.00
Nirula	-8.4	2.1	-12.5	-4.3	0.00
Tanaka	-7.5	1.4	-10.2	-4.9	0.00
Teng	-7.7	1.3	-10.3	-5.1	0.00
Voggenreiter	-7.3	1.3	-9.8	-4.8	0.00
Summary	-7.5	1.2	-9.9	-5.0	0.00

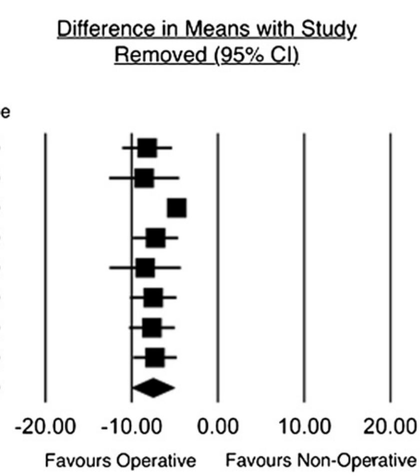

Figure 5. Sensitivity analysis of pooled mean differences in ventilator days. Data from each study were separately removed to determine if the pooled results were sensitive to a single study. Each line displays the pooled estimate (Point) and its 95% confidence interval when its respective study is excluded from the analysis. Minimal variation is observed and all analyses favor operative treatment.

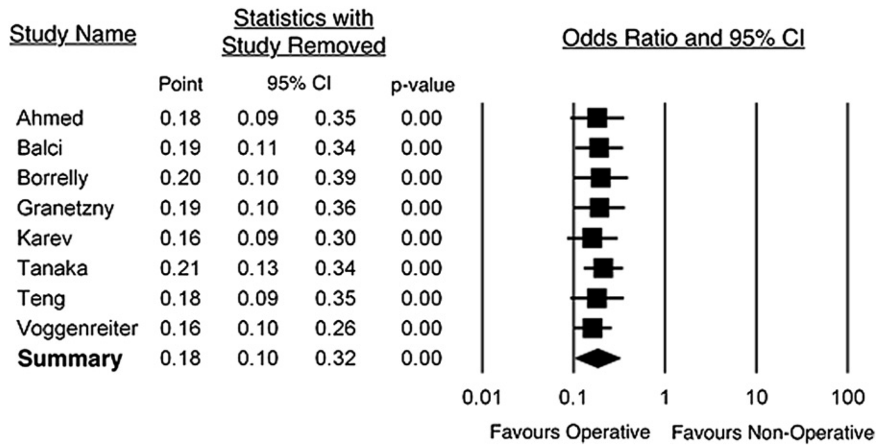

Figure 6. Sensitivity analysis of pooled odds ratio for developing pneumonia. Data from each study were separately removed to determine if pooled results were sensitive to a single study. Each line displays the pooled estimate (Point) and its 95% confidence interval when its respective study is excluded from the analysis. Minimal variation is observed and all analyses favor operative treatment.

Although the results of a meta-analysis dominated by small retrospective studies should be read with caution, there are several aspects of this study design that do strengthen the conclusions. The eligibility criteria placed no restrictions on date or language of publication, and this resulted in several foreign language studies being screened and included. This is important because operative fixation of flail chest injuries has not been the predominant treatment strategy in North America. In fact, only 1 of the included studies was from a North American center. In addition to including several foreign language studies, this meta-analysis used several sensitivity tests to scrutinize the strength of the results. For each clinical outcome, this included repeated "one study removed" analysis to determine if the pooled results were sensitive to the inclusion of data from a single study. The results were also re-examined using only the data from the 2 randomized controlled trials; this separate analysis also demonstrated similar point estimates.

These strengths in data analysis allow the reader to comprehensively interpret the results of this review. This is crucial when considering the ventilator days outcome. The pooled analysis of all eligible studies demonstrated a large treatment effect with moderate study heterogeneity (mean decrease, 7.5 days, $I^2 = 48\%$). There was also a potential for study bias in the data from the study by Kim and colleagues,[17] as demonstrated in the funnel plot. However, multiple analysis methods are able to continue to support the conclusion that operative treatment likely reduces ventilator days. This includes the appropriate use of a random effects model for I^2 heterogeneity of 48%, the minimal change in the point estimate for decrease in ventilator days during sensitivity analysis removing the data from Kim and associates[17] (mean decrease, 4.8 days), and the similar point estimate in the repeated analysis of including only the randomized controlled trial data (mean decrease, 8.3 days).

CONCLUSIONS

In conclusion, the results of this meta-analysis suggested significant benefits to operative treatment compared with nonoperative management of flail chest injuries. These benefits were observed across multiple critical care outcomes and with relatively narrow confidence intervals. Although these results are encouraging, it is important to recognize that the current literature is dominated by small retrospective studies, and changing one's clinical practice based solely on these data is premature. Several important clinical decisions cannot be answered from this study. These include whether patients with

Table 3. Summary of Pooled Results from Prospective Randomized Controlled Trials Only (n = 77)[15,20]

Outcomes	Treatment favored	I^2 Statistic, %	Mean decrease (95% CI)	Odds ratio (95% CI)	Risk difference (95% CI)	NNT
Ventilator days	Operative	0	8.3 (5.2−11.4)	—	—	—
ICU days	Operative	0	6.6 (1.8−11.5)	—	—	—
Pneumonia	Operative	0	—	0.06 (0.02−0.22)	0.54 (0.27−0.81)	2

NNT, number needed to treat (1/risk difference).

pulmonary contusion benefit from rib fracture fixation, and what the minimum amount of chest wall stability is necessary to obtain the observed benefits of surgery. Although this pooled analysis is very encouraging to support operative fixation of flail chest injuries, more definitive prospective randomized controlled trials are necessary to overcome the potential biases discussed. We are aware of 2 such registered clinical trials and look forward to their results (ClinicalTrials.gov identifiers: NCT01367951, NCT01147471.

Author Contributions

Study conception and design: Slobogean, MacPherson, Hameed

Acquisition of data: Slobogean, MacPherson, Sun, Pelletier

Analysis and interpretation of data: Slobogean, MacPherson, Pelletier, Hameed

Drafting of manuscript: Slobogean, MacPherson

Critical revision: Slobogean, Sun, Pelletier, Hameed

REFERENCES

1. Athanassiadi K, Theakos N, Kalantzi N, Gerazounis M. Prognostic factors in flail-chest patients. Eur J Cardiothorac Surg 2010;38:466−471.
2. Ciraulo DL, Elliott D, Mitchell KA, Rodriguez A. Flail chest as a marker for significant injuries. J Am Coll Surg 1994;178:466−470.
3. Hudson TR, McElvenny RT, Head JR. Chest wall stabilization by soft tissue traction: A new method. JAMA 1954;156:768−769.
4. Mayberry JC, Ham LB, Schipper PH, et al. Surveyed opinion of American trauma, orthopedic, and thoracic surgeons on rib and sternal fracture repair. J Trauma 2009;66:875−879.
5. Sales JR, Ellis TJ, Gillard J, et al. Biomechanical testing of a novel, minimally invasive rib fracture plating system. J Trauma 2008;64:1270−1274.
6. Bottlang M, Helzel I, Long W, Madey S. Anatomically contoured plates for fixation of rib fractures. J Trauma 2010;68:611−615.
7. Campbell N, Conaglen P, Martin K, Antippa P. Surgical stabilization of rib fractures using Inion OTPS wraps−techniques and quality of life follow-up. J Trauma 2009;67:596−601.
8. Hasenboehler EA, Bernard AC, Bottiggi AJ, et al. Treatment of traumatic flail chest with muscular sparing open reduction and internal fixation: description of a surgical technique. J Trauma 2011;71:494−501.
9. Higgins JPT, Thompson SG, Deeks JJ, et al. Measuring inconsistency in meta-analysis. BMJ 2003;327:557−560.
10. Friedemann C, Heneghan C, Mahtani K, et al. Cardiovascular disease risk in healthy children and its association with body mass index: systematic review and meta-analysis. BMJ 2012; 345:e4759.
11. Moja L, Piatti A, Pecoraro V, et al. Timing matters in hip fracture surgery: patients operated within 48 hours have better outcomes. a meta-analysis and meta-regression of over 190,000 patients. PLoS ONE 2012;7:e46175.
12. Ahmed Z, Mohyuddin Z. Management of flail chest injury: internal fixation versus endotracheal intubation and ventilation. J Thorac Cardiovasc Surg 1995;110:676−680.
13. Balci AE, Eren S, Cakir O, Eren MN. Open fixation in flail chest: review of 64 patients. Asian Cardiovasc Thorac Ann 2004;12:11−15.
14. Borrelly J, Aazami MH. New insights into the pathophysiology of flail segment: the implications of anterior serratus muscle in parietal failure. Eur J Cardiothorac Surg 2005;28: 742−749.
15. Granetzny A, Abd El-Aal M, Emam E, et al. Surgical versus conservative treatment of flail chest. Evaluation of the pulmonary status. Interact Cardiovasc Thorac Surg 2005;4: 583−587.
16. Karev DV. Operative management of the flail chest. Wiad Lek 1997;50:205−208.
17. Kim M, Brutus P, Christides C, et al. Résultats compares du traitement des volets thoraciques: stabilization penumatique interne classique, nouvelle modalité de la ventilation artificielle, agrafage. J Chir 1981;118:499−503.
18. Nirula R, Allen B, Layman R, et al. Rib fracture stabilization in patients sustaining blunt chest injury. Am Surg 2006;72: 307−309.
19. Ohresser PH, Amoros JF, Leonardelli M, et al. Les sequelles fonctionnelles des traumatismes fermes du thorax. Poumon Coeur 1972;28:145−150.
20. 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. J Trauma 2002;52:727−732.
21. Teng JP, Cheng YG, Ni D, et al. Outcomes of traumatic flail chest treated by operative fixation versus conservative approach. J Shanghai Jiaotong University (Medical Science) 2009;29:1495−1498.
22. Voggenreiter G, Neudeck F, Aufmkolk M, et al. Operative chest wall stabilization in flail chest−outcomes of patients with or without pulmonary contusion. J Am Coll Surg 1998;187:130−138.

Appendix 1. Search Strategy per Database

Medline

- (Rib fractures or flail chest) *AND*
- Bone plate, fracture fixation, splints, biocompatible materials, polymers, surgical mesh, polypropylenes, absorbable implants, prostheses and implants/ or
- May 5, 2011, n = 167

Embase

- (Flail chest or rib fracture) *AND*
- Bone plate, plate fixation, osteosynthesis, fracture fixation, osteosynthesis material, biocompatible materials, polymers, surgical mesh, polypropylenes, absorbable implants, prostheses and implants/ or
- May 5, 2011, n = 249

Cochrane (CDSR or CENTRAL)

- Flail chest or rib fracture
- May 5, 2011, n = 18

Appendix 2.