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Review

Operative versus nonoperative treatment of multiple simple rib fractures: A systematic review and meta-analysis

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ABSTRACT

Purpose: Surgical rib stabilization in flail chest is proven to be beneficial over nonoperative treatment in terms of rate of pneumonia, Intensive Care (IC) length of stay (ICLOS) and mechanical ventilation days. The aim of this systematic review and meta-analysis was to evaluate the effect of operative versus nonoperative treatment on the occurrence of pneumonia and other relevant clinical outcomes in patients with multiple simple rib fractures.

Methods: A search was performed in Embase, Medline Ovid, Cochrane Central, Web of Science, and Google Scholar. The primary outcome was the occurrence of pneumonia. Secondary outcomes were duration of mechanical ventillation, ICLOS, hospital length of stay (HLOS), mortality, and wound infections. Publication bias was assessed using funnel plots for the outcome measures and random-effect models were used when heterogeneity of data on outcome measures was significant ($I^2 \geq 40\%$).

Results: The search resulted in 592 unique records, of which 14 studies on 13 cohorts were included. The 14 studies comprised five prospective and nine retrospective cohort studies with a cumulative total of 4565 patients. Meta-analysis showed a significant decrease of the occurrence of pneumonia (n=2659 patients; risk ratio, RR=0.66; 95% confidential interval [CI] 0.49 to 0.90; p=0.008), mortality (n=4456 patients; RR=0.32; 95% CI 0.19 to 0.54; p<0.001), and HLOS (n=648 patients; mean difference, MD=−5.78 days; 95% CI −10.40 to −1.15; p=0.01) in favor of operative treatment. No effect of operative treatment was found for the duration of mechanical ventilation (n=113 patients; MD=−6.01 days; 95% CI =−19.61 to 7.59; p=0.39), or ICLOS (n=524 patients; MD=−2.93 days; 95% CI −8.65 to 2.80; p=0.32). The postoperative wound infection rate ranged from 0 to 9.4%.

Conclusion: Surgical treatment of multiple simple rib fractures may result in a significant reduction of pneumonia, mortality, and hospital length of stay. A reducing effect of treatment on the duration of mechanical ventilation and IC length of stay, was not demonstrated. However, due to nonstandard or absent definitions of outcome measures as well as heterogenous patient groups and the observational design of studies, results must be interpreted with caution and high-quality studies are needed.

Introduction

Rib fractures are common injuries in both trauma- and non-trauma centers and occur in up to 10–35% of patients after sustaining blunt chest trauma [1,2]. Rib fractures are associated with pulmonary morbidity such as pneumonia in 17–77% of patients and a mortality rate around 10%, with increased rates in the elderly and those with a higher number of rib fractures [1,3–9]. Multiple rib fractures can result in a flail chest, which is defined as fracture of three or more consecutive ribs, in two or more places, creating a unstable or flail segment [8,10]. Patients may also suffer from multiple simple rib fractures without a flail segment.

The traditional treatment of multiple rib fractures has a supportive approach, also known as nonoperative treatment. Nonoperative treatment consists of multimodal systemic or locoregional pain management, bronchodilator inhalers, pulmonary physical therapy, oxygen support, and if necessary mechanical ventilation [11]. Nevertheless, 64% of the patients experience thoracic pain and up to 71% develop disabilities long term after nonoperative treatment [9]. Furthermore, there is a prolonged Intensive Care length of stay (ICLOS) and hospital length of stay (HLOS) in

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Table 1
Search strategy per data-bank as performed on May 7, 2019.

Database	Total (N=1023)	Deduplicated (N=592)
Embase.com (Embase, Medline)	364	357
Medline (OVID)	320	135
Cochrane Central	26	14
Web of Science	213	50
Google Scholar	100	36

Embase.com: ('rib fracture'/de/mj OR (((rib*) NEAR/3 (fracture*) NEAR/3 (multiple*)) OR 'rib fractures'):ab,ti) AND ('orthopedic surgery'/de OR 'fracture fixation'/exp OR (fixation* OR splint* OR immobili* OR stabili* OR nail*):ab,ti) AND ('treatment outcome'/exp OR 'clinical effectiveness'/de OR 'hospitalization'/de OR 'prospective study'/de OR 'longitudinal study'/exp OR 'retrospective study'/de OR 'cohort analysis'/de OR (outcome* OR effectiv* OR efficacy OR failur* OR hospitali* OR stay* OR cohort* OR prospecti* OR retrospect* OR 'follow up' OR longitudinal):ab,ti)
Medline Ovid SP: ("Rib Fractures"[mh] OR multiple rib fracture*[tiab] OR "rib fractures"[tiab]) AND ("Orthopedic Procedures"[mh] OR Fracture Fixation[mh] OR fixation*[tiab] OR splint*[tiab] OR immobili*[tiab] OR stabili*[tiab] OR nail*[tiab]) AND ("Treatment Outcome"[mh] OR "Hospitalization"[mh] OR "Length of Stay"[mh] OR "Cohort Studies"[mh] OR outcome*[tiab] OR effectiv*[tiab] OR efficacy[tiab] OR failur*[tiab] OR hospitali*[tiab] OR stay*[tiab] OR cohort*[tiab] OR prospecti*[tiab] OR retrospect*[tiab] OR "follow up"[tiab] OR longitudinal[tiab])
Cochrane Central (trials): ((((rib*) NEAR/3 (fracture*) NEAR/3 (multiple*)) OR 'rib fractures'):ab,ti) AND ((fixation* OR splint* OR immobili* OR stabili* OR nail*):ab,ti) AND ((outcome* OR effectiv* OR efficacy OR failur* OR hospitali* OR stay* OR cohort* OR prospecti* OR retrospect* OR 'follow up' OR longitudinal):ab,ti)
Web of Science: TS=(((((rib*) NEAR/2 (fracture*) NEAR/2 (multiple*)) OR "rib fractures")) AND ((fixation* OR splint* OR immobili* OR stabili* OR nail*)) AND (outcome* OR effectiv* OR efficacy OR failur* OR hospitali* OR stay* OR cohort* OR prospecti* OR retrospect* OR "follow up" OR longitudinal))
Google Scholar: "multiple rib fracture|fractures" fixation|splint|immobilization|stabilization outcomes|effectiveness|efficacy|failure|hospitalization|"length of stay"|cohort|prospective

patients suffering from three or more rib fractures [6]. This association is also seen in the prevalence of pneumonia and mortality; the more rib fractures, the greater the risk of pneumonia and mortality [12–14]. The value of the specific types of analgesic therapies such as epidural or intravenous or nerve blocks seems limited in preventing pneumonia [15].

Evidence suggests that surgical stabilization of a flail chest is beneficial with regards to pneumonia rate, ICLOS, and number of ventilation days [16]. The effect of surgical stabilization for multiple simple rib fractures is still a matter of debate since high level of evidence is lacking. Almost all current studies combined patients with and without a flail chest. Therefore, the aim of this systematic review and meta-analysis was to evaluate the effect of operative versus nonoperative treatment on the occurrence of pneumonia, the duration of mechanical ventilation, ICLOS, HLOS, mortality, and wound infections as reported in patients with multiple simple rib fractures.

Methods

Search strategy

Databases Embase, Medline OVID, Cochrane Central, Web of Science, and Google scholar were searched systematically for cohort studies comparing operatively and nonoperatively treated patients with multiple simple rib fractures. This systematic review was conducted using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [17]. A protocol was written before initiation of this review. The literature search was performed by a professional librarian on May 7, 2019. The search terminology combined various terms for multiple simple rib fractures, outcomes and different treatments with this type of injury (Table 1).

Study selection, inclusion and exclusion criteria

For inclusion, studies had to compare operative with nonoperative treatment, and report on pneumonia, duration of mechanical ventilation, HLOS, ICLOS, mortality, or occurrence of wound infections in patients with multiple simple rib fractures. Multiple rib fractures was defined as having sustained three or more fractured ribs of ribs 1–12, regardless of side, site, adjacentness, dislocation or level of the fractured rib (1st, 2nd, etc.). Exclusion criteria were studies describing populations in which 50% or more of patients had a flail chest (as evidence is already available showing the beneficial effect of operative treatment regarding pneumonia rate, ICLOS, and mechanical ventilation days over nonoperative treatment [16]), studies that did not compare operative with nonoperative treatment of multiple simple rib fractures, studies that did not report on any of the outcomes of interest, studies in pediatric patients, animal studies, meta-analyses or literature reviews, and manuscripts that were not available to us in full text as no outcome measures or study characteristics could be collected. No language criterion was used. The titles and abstracts of the records were screened independently by three authors for eligibility and any disagreement was resolved by consensus. When an author used the same population in multiple publications, the population was only used once in this review, unless the manuscripts reported different outcome measures. The same authors used the same procedure when reviewing the full text manuscripts. Finally, a manual search of the reference lists of all included studies was performed, in order to avoid any missing relevant publication.

Quality assessment and evaluation of publication bias

The methodological quality of the included studies was assessed using a modified quality assessment for cohort studies derived from the Newcastle-Ottawa Scale (NOS) [18]. Studies were scored for various items by three authors independently and scored 0 when not reported, 1 when reported but inadequate, and 2 adequately reported. This then results in a score ranging from zero to 16 points, with a higher score indicating better quality. Any disagreement was resolved by consensus. Publication bias was determined based upon funnel plots.

Outcomes measures

The primary outcome was the occurrence of pneumonia. Secondary outcome measures were duration of mechanical ventilation, ICLOS, HLOS, mortality, and the occurrence of wound infections.

Data collection

Three authors independently extracted the following data from the included studies: author name, publication year, study period, study design, sample size for operative and nonoperative group, number of patients without a flail chest, number of male patients, age, number of rib fractures, duration of follow-up, surgical technique, and time to surgery. The corresponding authors of the manuscripts were contacted by e-mail and requested for raw data on the subgroup of patients without a flail chest, when the provided data were inadequate for meta-analysis. If they did not respond after two weeks a final reminder was sent.

Data analysis

Meta-analysis of the primary and secondary outcomes was performed using ReviewManager (Review Manager (RevMan) [Computer program]. Version 5.3. Copenhagen: The Nordic Cochrane

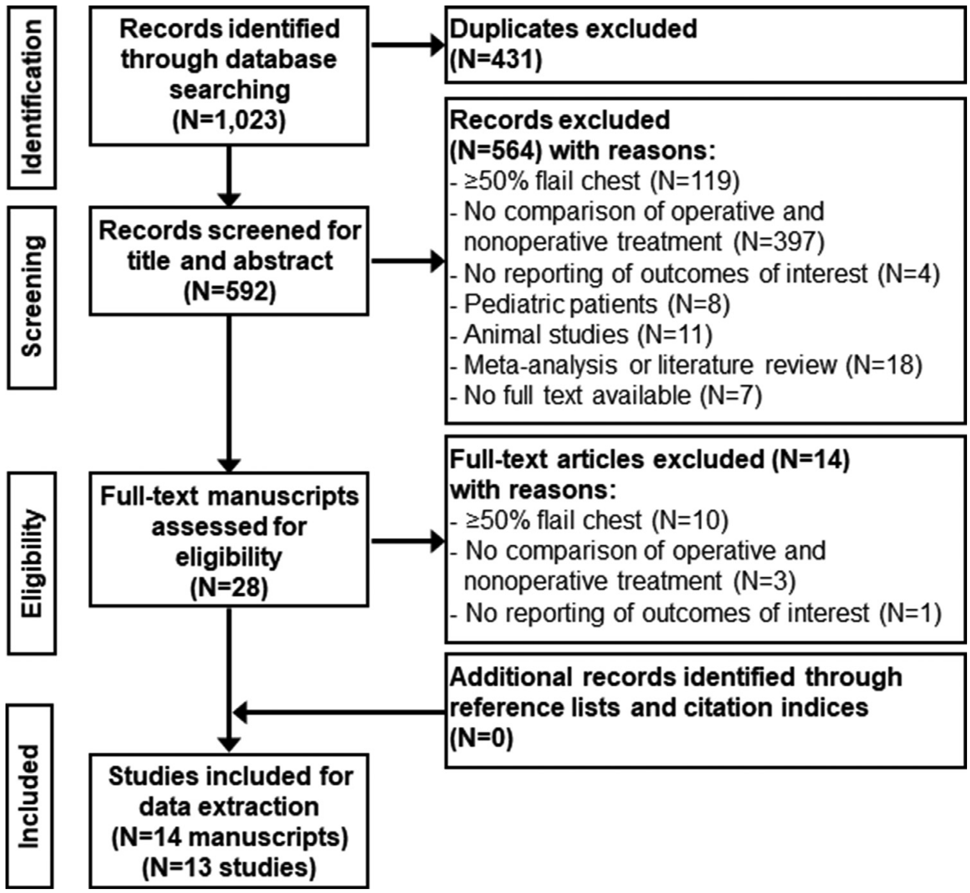

Fig. 1. Study flow chart.

Centre, The Cochrane Collaboration, 2014). Pooled risk ratio's and mean differences were calculated for binary and continuous variables, respectively. Both are reported with their 95% confidence intervals (CI) and p-value. Subgroup analysis on the outcome measures was performed for different cut-off values of the percentage of patients with multiple simple rib fractures per study (*i.e.,* studies with 60% or more, 70% or more, or 85% of patients without a flail chest). Heterogeneity was quantified with Cochran's Q test and I^2 statistic, a fixed effects model was used when the I^2 was $< 40\%$. A random-effects model was used for the pooled analysis when the I^2 was $\geq 40\%$. A p-value <0.05 was considered statistically significant.

Results

Search results

A total of 1023 records were retrieved (364 from EMBASE, 320 from Medline Ovid, 26 from Cochrane Central, 216 from Web of Science, and 100 from Google Scholar; Fig. 1). After removal of duplicate records (n=431), 592 unique records were screened for eligibility. The most common reasons for exclusion of records was because they did not compare operative with nonoperative treatment of multiple rib fractures (n=400) or because over 50% of the population had a flail chest (n=129). Two studies did not report the rate of patients with a flail chest [19,20]. The corresponding authors were contacted, and one author confirmed they excluded patients with a flail chest [19]. Finally, 14 manuscripts reporting on 13 different cohorts with a total of 4565 patients fulfilled the inclusion criteria [21–27,19,28–33]. Two publications were written on the same study, but reported on complementary data [24,25].

Study characteristics

Study characteristics are shown in Table 2. From the included manuscripts, five studies were prospective cohort studies [22,23,27,30,32], nine were retrospective studies on eight different cohorts [21,24–26,19,28,29,31,33]. The mean age per study varied from 37 years to 73 years [26,19]. The mean ISS per study varied from 16 to 31 [23,29].The mean number of rib fractures varied from 3 to 8 [21,22]. The percentage of patients without a flail chest per study varied from 54% to 100% [24–26,19]. The percentage operatively treated patients per study varied from 4.5% to 52.5% [22,32]. Most studies used plates for rib fixation (Table 2).

Quality Assessment and evaluation of publication bias

The detailed outcome of the methodological quality assessment, based on the Newcastle-Ottawa Quality assessment scale is shown in Table 3. The average score of the quality assessment was 9 points (range 5–12). The funnel plots did not raise substantial concern for publication bias (Supplemental Figure S1).

Pneumonia

Pneumonia was reported for both treatment groups in eight studies, totaling 2659 patients [21,23,25,19,28–30,33]. Only one study diagnosed pneumonia based upon a standardized definition, namely of the Center for Disease Control and Prevention [21,34]. Overall, 41 out of 530 patients (7.7%) in the operative group and 189 out of 2129 (8.9%) in the nonoperative group developed pneumonia. The forest plot of the meta-analysis comparing operative

Table 2
Overview of included studies comparing operative versus nonoperative treatment.

Author (year)	Study period	Study design	Sample size operated n	Sample size not operated n	Nr. of patients with simple MRF n (%)	Nr. of male patients n (%)	Mean age in years (SD/range)	Mean ISS (SD/range)	Mean Nr. of rib frac-tures(SD/range)	Mean Follow-up (range)	Surgical technique	Mean time to surgery(SD/range)
De Moya *et al.* (2011) [21]	July 2009-June 2010	Retrospective cohort	16	32	28 (58)	40 (83)	46 (14.7)	O=24 (7) NO=25 (9)	8 (3.4)	29 days	plates	5 days (1-10)
Khandelwal *et al.* (2011) [22]	July 2009 - June 2010	Prospective cohort	32	29	59 (97)	40 (66)	46.4	NA	3.2	30 days	plates	12 days
Granhed *et al.* (2014) [23]	September 2010-July 2012	Prospective cohort	60	153	157 (74)	NA	57 (19-86)	O=21.7 (10.8) NO=30.9 (13.3)	7.5 (2-14)	1 year	plates and intramedullary splints	median 4 days (1-59)
Majercik *et al.* (2015) [24,25]*	January 2009 - June 2013	Retrospective cohort	137	274	223 (54)	328 (80)	55 (18.4)	O=21 (10.7) NO=22 (11.8)	5.2 (2)	2 years	plates	NA
Qiu *et al.* (2016) [26]	January 2006-May 2013	Retrospective cohort	65	59	124 (100)	88 (70.9)	37.03	NA	3.34	6 months	plates	NA
Tarng *et al.* (2016) [27]	January 2010 - December 2012	Prospective cohort	12	53	56 (86)	64 (98)	47.3 (14.4)	O=21.2 (4.1) NO=26.1 (6.0)	7.33 (1.15)	21 months (18-24)	TEN	4 days
Fitzgerald *et al.* (2017) [19]	2003-2015	Retrospective cohort	23	50	73 (100)	NA	72.8	O=20.7 (15.7-25.7) NO=18.5 (14.3-22.7)	3.5	4 months	plates	NA
Uchida *et al*, (2017) [28]	April 2007-March 2015	Retrospective cohort	10	10	14 (70)	14 (70)	O=63 (51-72), NO=57 (53-75)	NA	O=5 (4-6.5), NO=4 (2-7)	NA	plates	4 days (1-7.5)
Kane *et al*. (2018) [29]	2007-2016	Retrospective cohort	116	1000	1041 (93)	NA	48.08	O=20.9 (11.4) NO=15.9 (11.5)	NA	NA	plates	NA
Majeed *et al.* (2018) [30]	January 2017-March 2018	Prospective cohort	21	22	32 (74)	37 (86)	51.35 (13.75)	NA	NA	3 months	plates	NA
Fokin *et al.* (2019) [31]	2011-2017	Retrospective cohort	87	87	122 (70)	129 (74)	O=55.9 NO=55.4	O=19.9 NA=19.9	O=7 NO=6.4	NA	plates	4.5 days
Marasco *et al.* (2019) [32]	January 2012-April 2015	Prospective cohort	67	1415	1309 (88)	1098 (74)	53.6 (19.2)	O=17 (13-24) NA=24 (14-30)	NA	24 months	NA	NA
Shibahashi *et al.* (2019) [33]	2004-2015	Retrospective cohort	147	588	456 (62)	536 (73)	O=59.57 (17.13) NO=60.31 (18.22)	O=26.2 (11.7) NA=26.4 (12.7)	NA	NA	NA	NA

ISS, injury severity score; MRF, multiple rib fractures; NA, not available; NO, nonoperative group; O, operative group; SD, standard deviation; TEN, titanium elastic nails.
*, these are two studies reporting on the same cohort.

Table 3
Quality assessment scores of the included studies.

Author (year)	Aim stated	Consecutive enrolment	Prospective data collection	Appropriate endpoints	Unbiased assessment	Appropriate FU time	Loss-to-FU <5%	Sample size	Total score
De Moya (2011) [21]	2	1	1	2	0	0	2	1	9
Khandelwal *et al.* (2011) [22]	1	1	2	1	2	1	2	0	10
Granhed *et al.* (2014) [23]	2	1	2	2	0	1	0	0	8
Majercik *et al.* (2015) [24,25]	2	1	0	2	0	0	2	0	7
Qiu *et al.* (2016) [26]	1	0	0	2	2	2	2	0	9
Tarng *et al.* (2016) [27]	1	2	2	2	0	1	2	0	10
Fitzgerald *et al.* (2017) [19]	2	2	2	2	0	2	0	0	10
Uchida *et al.* (2017) [28]	1	0	0	2	2	2	2	0	9
Kane *et al.* (2018) [29]	1	1	2	2	2	2	2	0	12
Majeed *et al.* (2018) [30]	2	0	1	1	0	1	0	0	5
Fokin *et al.* (2019) [31]	2	1	0	2	0	1	0	0	6
Marasco *et al.*. (2019) [32]	2	2	2	2	0	2	1	0	11
Shibahashi *et al.* (2019) [33]	1	2	1	1	0	0	0	2	7

and nonoperative treatment for studies including 50% or more patients with multiple simple rib fractures is shown in Fig. 2A. The plot showed moderate heterogeneity between the studies (I^2=38%). A significant difference between groups was found in favor of the operative group (risk ratio [RR] 0.66, 95% confidential interval [CI] 0.49 to 0.90; p=0.008). Subgroup analysis of studies with an increasing proportion of patients with multiple simple rib fractures showed a persistent pooled risk ratio below 1, but an increase of the confidence interval with loss of statistical significance due to the small number of available studies (Fig. 2B–D).

Mechanical ventilation days

The duration of mechanical ventilation was reported in eight studies (n=2456 patients) [21,23,25,27,28,30–32]. This outcome measure was expressed in days by all studies without further elaboration. Six of these studies could not be included in the meta-analysis, because they did not provide the means and standard deviation for the two treatment groups separately [23,25,28,30–32]. This resulted in complete data for 113 patients. The forest plot of the meta-analysis of mechanical ventilation comparing operative and nonoperative treatment is shown in Fig. 2E. The plot shows much heterogeneity of effects between studies (I^2=94%). The pooled mean difference (MD) across the two studies was −6.01 days (95% CI −19.61 to 7.59) for the overall effect, which was not statistically significant (p=0.39). Subgroup analysis of studies with an increasing proportion of patients with multiple simple rib fractures, made pooling impossible as only one study remained available, with statistically significant shorter duration of mechanical ventilation in the operative group (Fig. 2F–H).

ICLOS

The ICLOS was reported in eight studies (n=3389 patients) [21,24,27,19,28,29,31,32]. This outcome measure was expressed in days by all studies without further elaboration. Five of these studies could not be included in the meta-analysis due to incomplete data reporting, resulting in complete data for 524 patients [19,28,29,31,32]. The forest plot of the meta-analysis of ICLOS comparing operative and nonoperative treatment is shown in Fig. 3A. The plot shows much heterogeneity of effects across the studies (I^2=93%). One of the three studies in the meta-analysis showed a statistically significantly shorter ICLOS in the operative group with a mean difference of −8.70 days [27]. The pooled MD across the three studies was −2.93 days (95% CI −8.65 to 2.80) for the overall effect, which was not statistically significant (p=0.32). Subgroup analysis of studies with an increasing proportion of patients with multiple simple rib fractures made pooling impossible as only one study remained available, with statistically significant shorter ICLOS for the operative group (Fig. 3B–D).

HLOS

The HLOS was reported in nine studies (n=2267 patients) [21,23,24,26,27,19,29–31]. This outcome measure was expressed in days by all studies without further elaboration. Five of these studies could not be included in the meta-analysis due to incomplete data reporting, resulting in complete data for 648 patients [23,19,29–31]. The forest plot of the meta-analysis of HLOS comparing operative and nonoperative treatment is shown in Fig. 3E. The plot shows much heterogeneity of effects across the studies (I^2=95%). Two of the four studies in the meta-analysis showed a statistically significantly shorter hospital length of stay in the operative group with a mean difference ranging from −4.84 to −20.38 days [26,27]. The pooled MD across the four studies was −5.78 days (95% CI −10.40 to −1.15) for the overall effect, which was statistically significant (p=0.01). Subgroup analysis of studies with an increasing proportion of patients with multiple simple rib fractures showed a persistent shorter HLOS. With only two studies available for pooling, significant difference in HLOS was lost from 60% or more patients with multiple simple rib fractures (Fig. 3F–H).

Mortality

Mortality was reported in 11 studies (n=4456 patients) [23,25–27,19,28–33]. Three studies elaborated on the reason and timing of their mortality rate [23,26,30]. The forest plot of the meta-analysis of mortality comparing operative and nonoperative treatment is shown in Fig. 4A. Overall mortality was 13 out of 745 (1.7%) in

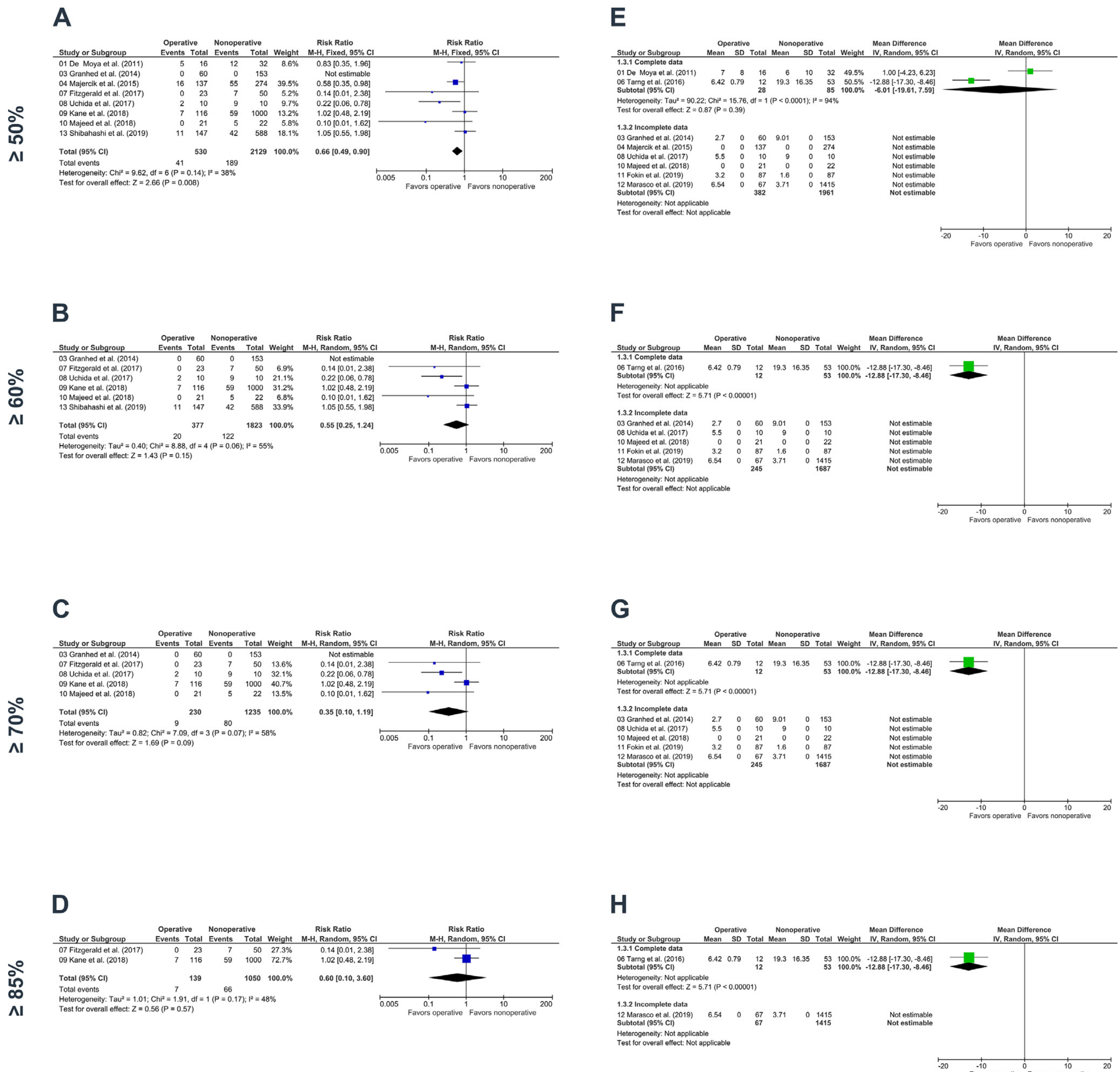

Fig. 2. Forest plots detailing the risk ratio for pneumonia (A-D) and the mean difference for duration of mechanical ventilation (E-H) for operative versus nonoperative treatment of multiple simple rib fractures.
Forest plots are shown for increasing cut-off values for multiple simple rib fractures, i.e., ≥50% (A, E), ≥60% (B, F), ≥70% (C, G), and ≥85% (D, H). CI, Confidence Interval; IV, Inverse Variance; M-H, Mantel-Haenszel; SD, Standard Deviation.

the operative group and 194 out of 3711 (5.2%) in the nonoperative group. The plot shows slight heterogeneity of effects across the studies (I^2=22%). The pooled risk ratio (RR) across the 11 studies showed statistically significantly less mortality in the operative group (RR 0.32; 95% 0.19 to 0.54; P<0.001). Subgroup analysis of studies with higher percentages of patients without a flail chest, showed a significant pooled risk ratio of around 0.32, up to studies including 85% of patients without a flail chest (Fig. 4B–D).

Wound infections

Wound infections was reported as outcome measure in four studies (n=123 operatively treated patients), ranging from 0 to 9.4% (Table 4) [22,23,28,30]. Two studies reported wound infections. One study only mentioned three superficial wound infections without any further information on treatment and outcome [22]. The other study reported one deep infection resulting in a fracture related infection which was treated with a reoperation at seven months after initial trauma and antibiotics for three months after which the infection resolved [23].

Table 4
Occurrence of wound infections after operative treatment of multiple simple rib fractures.

Author (year)	Sample size	Wound infection	
		(N)	(%)
Khandelwal *et al.* (2011) [22]	32	3	9.4%
Granhed *et al.* (2014) [23]	60	1	1.7%
Uchida *et al.* (2017) [28]	10	0	0.0%
Majeed *et al.* (2018) [30]	21	0	0.0%

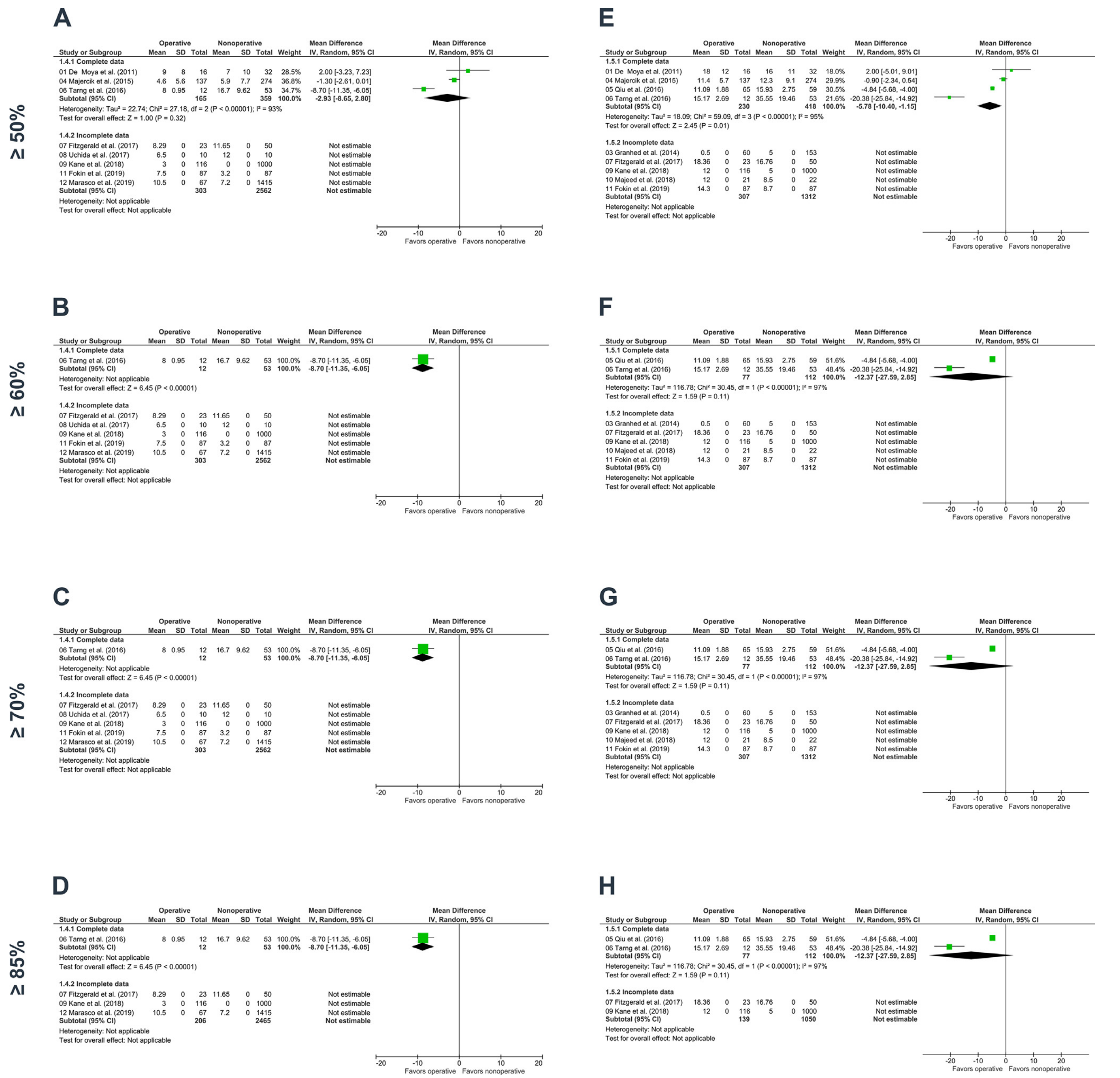

Fig. 3. Forest plots detailing the mean difference for ICLOS (A-D) and HLOS (E-H) for operative versus nonoperative treatment of multiple simple rib fractures.
Forest plots are shown for increasing cut-off values for multiple simple rib fractures, i.e., ≥50% (A, E), ≥60% (B, F), ≥70% (C, G), and ≥85% (D, H). CI, Confidence Interval; IV, Inverse Variance; SD, Standard Deviation.

Discussion

This study showed that operative fixation of multiple simple rib fractures may lead to a reduced risk of pneumonia, mortality, and hospital length of stay. No significant difference in the duration of mechanical ventilation and IC length of stay was demonstrated. As the included studies had observational study designs with heterogenous populations and different or absent definitions of the outcome measures, the data should be interpreted with caution and might not be viewed in terms of causality. The occurrence of pneumonia is of critical importance for the outcome after rib fractures. Battle *et al.* showed in a meta-analysis that pneumonia is one of the significant risk factors for mortality in blunt chest wall trauma patients [12]. The assumed pathomechanism is that pain due to the fractures results in inadequate ventilation and mucus retention concordant to pulmonary contusion resulting in an increased risk of pneumonia. Theoretically, less pain would enable the patient to normalize ventilation and mucus clearance, resulting in a reduced risk of pneumonia. Therefore, adequate pain treatment is mandatory.

Epidural catheters are used most frequently as a mean to control pain and appear superior over other systemic pain management modalities [35,36]. Although thoracic epidural catheters may reduce the mechanical ventilation duration, any benefit in mortality, ICLOS, or HLOS has not been proven [37]. This stresses the need for other pain reducing treatment modalities. Since immobilization of rib fractures prevents the periosteum from movement at the fracture site, surgical fixaton might reduce pain significantly.

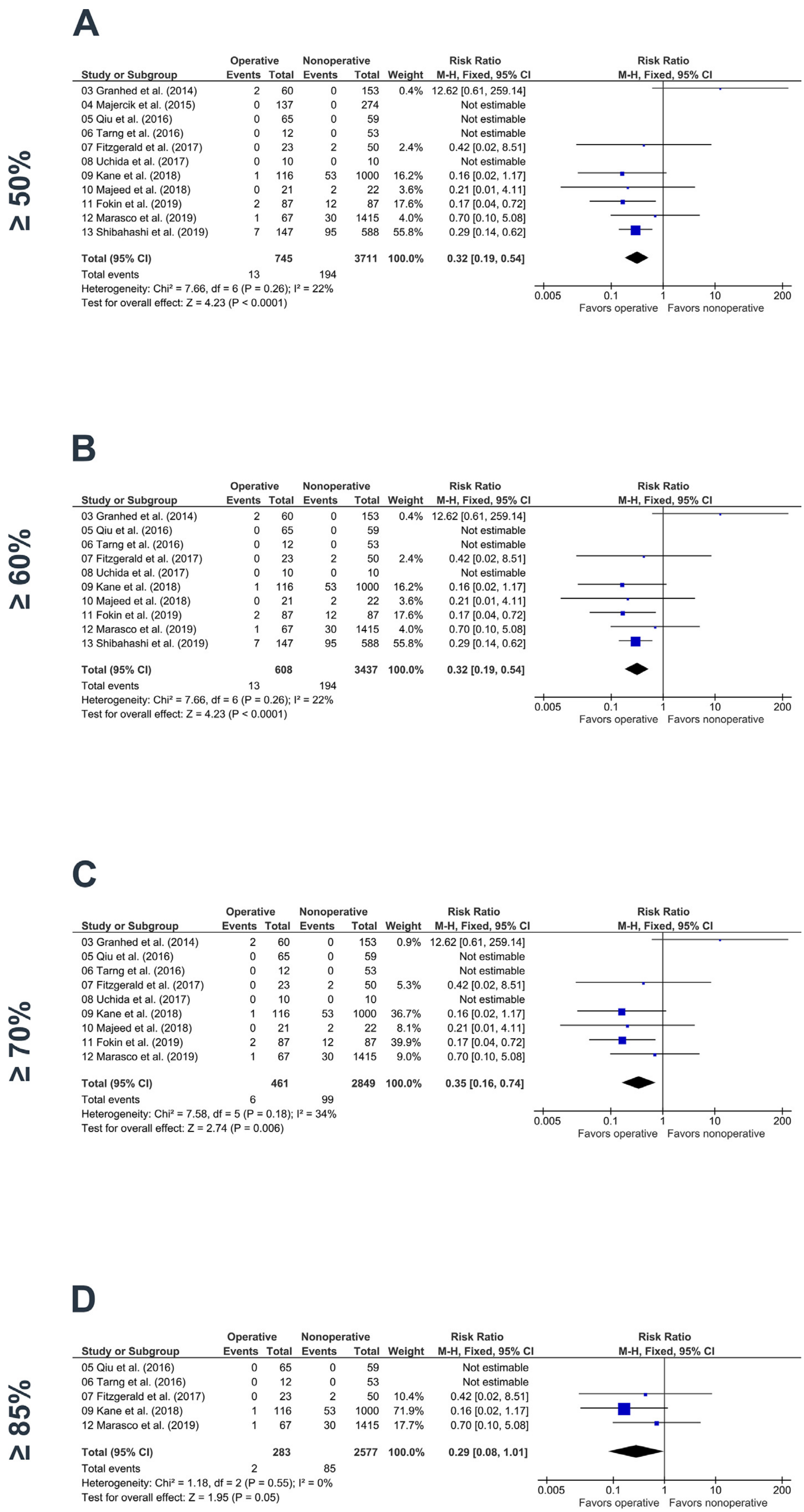

Fig. 4. Forest plots detailing the risk ratio for mortality for operative versus nonoperative treatment of multiple simple rib fractures.
Forest plots are shown for increasing cut-off values for multiple simple rib fractures, i.e., ≥50% (A), ≥60% (B), ≥70% (C), and ≥85% (D). CI, Confidence Interval; M-H, Mantel-Haenszel.

However, studies comparing pain in operatively versus nonoperatively treated patients are rare. They are often retrospective and the results are contradicting [21,22,38,39].

Differences in occurrence of pneumoniae between included studies can be based on differences in or lack of definition. For example, six of the eight studies that reported the outcome of occurrence of pneumonia did not describe their definition of pneumonia [23,19,28–30,33]. In their retrospective study, Majercik *et al.* based their definition of pneumonia on microbiological data but provide no further specification [25]. The definition by DeMoya *et al.* was according to the Center for Disease Control and Prevention's definition and included chest radiographical findings, positive biochemical blood samples, and clinical symptoms [21]. The two studies [21,25] which provided a definition of pneumonia, reported almost half of pneumoniae of all studies combined for the operatively treated group and almost a third of the nonoperatively treated group. These differing and absent definitions of the primary outcome measure might influence the effect of the treatment in these patients.

Although multivariable analysis or metaregression analysis has not been done, the reduction of occurrence of pneumonia and mortality did not result in a reduction in duration of mechanical ventilation and ICLOS. The fact that pneumonia occurred statistically significantly more often in the nonoperative group stresses the possibility that the mechanical ventilation is less often the cause of pneumonia in patients with multiple rib fractures. The effect of treatment on mechanical ventilation, ICLOS, and HLOS must be interpreted with caution regarding the heterogeneity of up to 96% of the meta-analyses. The results for pneumonia and mortality displayed much less heterogeneity (I^2 38 and 22%, respectively) and appear more reliable. The nonstandard definitions of pneumonia might have confounded outcome in these two treatment groups. In addition, of the 11 studies that determined mortality rate, seven studies reported one or more deaths within the treatment groups and only three studies elaborated on the cause of the mortality [23,26,30]. These three studies reported a total of seven deaths of which five had a pulmonary cause such as respiratory failure, pneumonia, or acute respiratory distress syndrome (ARDS). The lack of insight into the causes of mortality in the larger part of the studies potentially introduced bias for this outcome measure and hinders interpretation of causality.

One of the main problems in evaluation of surgical rib fixation is the variety in injury characteristics of the patient population. Multitraumatized patients are often evaluated together with patients with isolated rib fractures. Most studies included multitrauma patients defined as ISS of >16 with mean ISS ranging from 16 to 31 (Table 2) [21,23–25,27,19,29,31–33]. Only five studies also reported the abbreviated injury score (AIS) as specification of the thoracic trauma [21,27,28,32,33]. As a result, it remains unclear in the larger part of the studies if the rib fractures contributed most to the ISS. Also, the number of rib fractures per patient was not available in four studies which only stated including patients with three or more fractured ribs in the Methods section [29,30,32,33]. As the number of rib fractures is a risk factor for pulmonary complications such as pneumonia and mortality, the lack of these data might have influenced these outcome measures [6,8,12,40]. Therefore, ICLOS and HLOS might be influenced by other main contributors of the high ISS. In order to further clarify the outcome of patients with multiple rib fractures, future studies should include patients with isolated rib fractures solely or provide detailed AIS and ISS scores to enable stratifaction for the body-regional AIS score.

In addition, while this study we only included studies with a majority (≥50%) of patients without a flail chest, nine studies did not specify the distribution of these patients into the two treatment groups [22–24,26,27,19,28–30]. Five studies did report this population distribution. Four studies found significantly more patients with a flail chest in the operatively treated group [25,32,31,33]. Only De Moya *et al*. had similar numbers of patients with and without a flail chest in both groups [21]. Significant variability in the thoracic injuries with the more seriously injured patients being in the operative treatment group could have also affected ICLOS and HLOS. Differences in outcome between the two groups must therefore be interpreted with caution. Also, only two studies consisted of 100% patients with multiple non-flail rib fractures [26,19].

In order to correct for the arbitrary cut-off value of including studies with at least 50% of patients with multiple simple rib fractures, subgroup analyses were performed for studies with increasing cut-off values up to 85% of patients with multiple simple rib fractures. This showed the lack of available studies reporting on various outcome parameters. Duration of mechanical ventilation and ICLOS could not be pooled if more than 50% of the patiens had multiple simple rib fractures, and outcome measure HLOS could only be assessed in two studies with 60% or more patients with multiple simple rib ractures. The lower risk ratio of mortality in the operative fixation group remained significant up to the cut-off value of 85%. While showing a persistent pooled risk ratio below 1 for the outcome measure of pneumonia when performing subgroup analysis in studies with higher cut-off values, statistical significance was lost due to the increased confidence intervals. This highlights the need for high quality (randomized) studies in order to assess the true effect of operative rib fixation in patients with multiple simple rib fractures with similar patient and injury characteristics.

Published operative rib fixation guidelines and consensus statements advocate surgery within 72 h post-trauma [41–43]. For example, every additional hospital day before surgery is associated with a 31% increased likelihood of pneumonia [44]. While all surgeries were performed at index admission, only six studies mentioned the time to surgery which ranged from 4 to 12 days [21–23,27,28,31]. As a result, the effect of early operative rib fixation on ICLOS, HLOS, and pneumonia rate might have been influenced and could not be distilled.

This study has several limitations. First, this study was unable to extract data for patients with multiple simple rib fractures only. In order to diminish the influence of patients with a flail chest on the outcome measurements, we excluded studies with ≥50% of patients with a flail chest. However, with patients without a flail chest accounting for 54–100% of the study population, the influence of patients with a flail chest can not be estimated exactly.

Second, this meta-analysis is mainly based on comparative observational studies, often retrospective (Table 2). With nonstandard or absent definitions of pneumonia and mostly no elaboration on the cause of mortality, the precise effect of both treatment options for multiple simple rib fractures could be less accurately measured. Randomized controlled trials are currently absent for patients with multiple simple rib fractures. In addition, for the duration of mechanical ventilation, ICLOS and HLOS, up to over 75% of the included studies did not provide all data that were needed to include them in the meta-analysis. Also, results from case series that enrolled one type of treatment only were excluded, which may have caused inclusion bias. Third, the included studies had variable methodological strength, follow-up, and outcome parameters. As there was no exclusion of studies after quality assessment, this may influence the outcome in an unknown way. Finally, the pooled risk ratio's and mean differences could not be adjusted for potential confounders, such as the number of rib fractures or ISS. The unadjusted pooled estimates reported in this review should therefore be interpreted with caution. Von Hippel *et al*. showed that I^2 should be presented and interpreted with caution in small meta-analyses [45]. Therefore, the heterogeneity that was found may be considered as imprecise and biased. The random-effects model was used because the effect size varied from study to study and this model was more likely to fit the actual sampling distribution [46]. The true effect size might be higher or lower due to differences in case mix.

Correction for most of these flaws in methodology was impossible since the authors of the included studies did not response to the request for missing data and data for patients with multiple isolated rib fractures only. Despite these shortcomings, the presented data suggest a favorable outcome on occurrence of pneumonia and mortality rate comparing operatively with non-operatively treatment in patients with multiple simple rib fractures. Including only studies in which the majority of patients did not have a flail chest suggest some positive effects, but the exact effect remains to be studied in randomized homogenous populations consisting of patients with multiple simple rib fractures only.

This systematic review and meta-analysis shows that operative treatment of multiple simple rib fractures may result in a significant reduction of pneumonia, mortality, and hospital length of stay. However, a reducing effect of treatment on the duration of mechanical ventilation and IC length of stay. The wound infection rate which should be kept in mind as a complication following operative treatment ranges from 0 to 9.4%. The results must be interpreted with caution due to the limitations such as non-standard definitions of outcome measures, heterogenous patient groups, and low-quality observational studies. These limitations, in combination with the promising results, stress the need for randomized controlled trials evaluating outcome after nonoperative and operative treatment in patients with multiple simple rib fractures.

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Decalaration of Competing Interest

Mathieu M.E. Wijffels, Jonne T.H. Prins, Eva J.P. Perpetua Alvino and Esther M.M. Van Lieshout declare that they have no conflict of interest.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.injury.2020.07.009.

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