Outcome after surgical stabilization of rib fractures versus nonoperative treatment in patients with multiple rib fractures and moderate to severe traumatic brain injury (CWIS-TBI)

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BACKGROUND: Outcomes after surgical stabilization of rib fractures (SSRF) have not been studied in patients with multiple rib fractures and traumatic brain injury (TBI). We hypothesized that SSRF, as compared with nonoperative management, is associated with favorable outcomes in patients with TBI.

METHODS: A multicenter, retrospective cohort study was performed in patients with rib fractures and TBI between January 2012 and July 2019. Patients who underwent SSRF were compared to those managed nonoperatively. The primary outcome was mechanical ventilation-free days. Secondary outcomes were intensive care unit length of stay and hospital length of stay, tracheostomy, occurrence of complications, neurologic outcome, and mortality. Patients were further stratified into moderate (GCS score, 9–12) and severe (GCS score, ≤8) TBI.

RESULTS: The study cohort consisted of 456 patients of which 111 (24.3%) underwent SSRF. The SSRF was performed at a median of 3 days, and SSRF-related complication rate was 3.6%. In multivariable analyses, there was no difference in mechanical ventilation-free days between the SSRF and nonoperative groups. The odds of developing pneumonia (odds ratio [OR], 0.59; 95% confidence interval [95% CI], 0.38–0.98; $p = 0.043$) and 30-day mortality (OR, 0.32; 95% CI, 0.11–0.91; $p = 0.032$) were significantly lower in the SSRF group. Patients with moderate TBI had similar outcome in both groups. In patients with severe TBI, the odds of 30-day mortality was significantly lower after SSRF (OR, 0.19; 95% CI, 0.04–0.88; $p = 0.034$).

CONCLUSION: In patients with multiple rib fractures and TBI, the mechanical ventilation-free days did not differ between the two treatment groups. In addition, SSRF was associated with a significantly lower risk of pneumonia and 30-day mortality. In patients with moderate TBI, outcome was similar. In patients with severe TBI a lower 30-day mortality was observed. There was a low SSRF-related complication risk. These data suggest a potential role for SSRF in select patients with TBI. (*J Trauma Acute Care Surg.* 2021;90: 492–500.

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Over 15% of polytraumatized patients have both severe thoracic trauma and traumatic brain injury (TBI).[1] In the intensive care unit (ICU), rib fractures (42%) and TBI (39%) are the injuries with the highest prevalence.[2] While TBI is the leading cause of mortality, thoracic trauma is listed second and accounts for 25% of injury-related deaths annually.[3,4] In patients with multiple rib fractures, 15% to 26% have concurrent TBI; the presence of both injuries is associated with poor outcomes, including longer mechanical ventilation and prolonged ICU length of stay (LOS).[4,5] Rib fractures are seen in up to 39% of patients who have sustained blunt thoracic trauma and a debilitation and lethal complication is pneumonia.[3] Rib fractures are associated with pneumonia rates of 17% to 77%, with increased rates in elderly patients and patients with more rib fractures.[6–10] In addition, the combination of severe thoracic trauma and severe TBI (i.e., an Abbreviated Injury Scale [AIS] score of 3 or higher) are risk factors for the development of pneumonia which is one of the strongest independent predictors of in-hospital mortality in polytraumatized patients.[1]

Because of proven beneficial outcomes in patients with severely displaced rib fractures or flail chest, the use of surgical stabilization of rib fractures (SSRF) has increased considerably over the last decade and has become an important modality in rib fracture management.[11–13] As patients with TBI might confound outcome measures due to an increased risk of prolonged duration of mechanical ventilation, high mortality rate, and complications, such as pneumonia, these patients are typically excluded in studies on outcome of SSRF in patients with multiple rib fractures.[7,9,13,14] Also, the unclear prognosis of TBI patients, irrespective of their underlying thoracic injury, has historically been an exclusion criteria among various studies on the outcome of SSRF. One theoretical concern is that patients with TBI might deteriorate perioperatively because of an increase in intracranial pressure secondary to patient positioning and anesthetics. A survey among thoracic, orthopedic, and trauma surgeons showed that even patients with moderate TBI (Glasgow Coma Scale [GCS] score at admission of 9 to 12) were the least likely to be recommended for SSRF, regardless of abnormal pulmonary variables.[15] Thus, while SSRF may be less frequently offered to patients with TBI, the possible benefit of SSRF in this type of patient has not been studied. Specifically, the respiratory benefits achieved by SSRF in the setting of severe chest wall injuries may be of sufficient magnitude to mitigate the negative effects of TBI and ultimately still improve outcomes in this specific patient population.

The primary aim of this study was to determine the effect of SSRF versus nonoperative treatment of rib fractures on the number of ventilator-free days in adults who sustained both multiple severe rib fractures and moderate or severe TBI. Secondary aims were to determine the effect of treatment on the ICU-LOS, hospital LOS (HLOS), tracheostomy rate, occurrence of complications, neurological outcome, and (in-hospital and 30 days) mortality. We hypothesized that SSRF is associated with favorable outcomes versus nonoperative management in patients with coexisting moderate to severe TBI.

METHODS

Design and Participants

The Chest Wall Injury Society TBI study (CWIS-TBI) was a multicenter, retrospective cohort study conducted by CWIS and involved 19 trauma centers. The Chest Wall Injury Society is an international surgical society founded in 2016 and comprised of approximately 250 trauma, thoracic, and orthopedic surgeons with a specific interest in the management of chest wall trauma (www.cwisociety.org). Members of CWIS were invited for participation if they expressed interest based on information on the CWIS website and a personal e-mail consisting of a short and full-length study protocol. After approval for each individual participating center by the local medical research ethics committee or institutional review board, local investigators identified patients. This was done by searching the hospital's electronic patient files which were registered with specific diagnosis treatment combinations and by searching the national/regional/state trauma registry for admitted patients with a registered AIS) for rib or sternum fractures in combination with an AIS score of 3 or higher of the head. Each hospital used the best local option to identify eligible patients.

Inclusion criteria were: (1) 18 years or older at time of index trauma; (2) three or more fractures of ribs 3 to 10 with either a flail chest or bicortical displacement of at least three fractured ribs, as diagnosed on computed tomography (CT) scan; (3) moderate or severe TBI (GCS ≤12 at admission with posttraumatic intracranial changes, as diagnosed on CT scan); 4) trauma sustained between January 1, 2012, and July 1, 2019; (5) blunt force thoracic trauma; (6) admission to participating hospital within 7 days after trauma with documented GCS at first presentation.

Patients with any of the following criteria were excluded: (1) rib fractures due to cardiopulmonary resuscitation; (2) patient unfit for surgery due to hemodynamic instability or patient is moribund; (3) previous rib fractures or pulmonary problems, requiring continuous oxygen use at home pretrauma; (4) rib fixation device in situ pre-trauma; (5) preexisting neurological deficit (i.e., GCS score ≤12); (6) congenital thoracic deformity; (7) imprisoned at time of trauma; (8) known pregnancy at time of trauma; (9) clinically transferred to other hospital during primary admission; (10) no posttraumatic intracranial changes on brain CT.

Given the exploratory nature of this study and the lack of data on ventilator-free days in the targeted population, a formal sample size calculation was not made.

Data Collection and Outcome Measures

Data were extracted from the patients' electronic medical files. The primary outcome measure was the number of ventilator-free days during primary hospital admission, defined as the number of days where the patient breathed without assisted breathing.

Secondary outcome measures were ICU-LOS during primary hospital admission, HLOS for the primary admission, rate of and time to tracheostomy performed, the occurrence of complications (e.g., pneumonia within 30 days after trauma as defined according to the Centers for Disease Control and Prevention guidelines,[16] pleural empyema as diagnosed on CT scan within 30 days after trauma and/or pus evacuation[17] and SSRF-related complications, such as thoracic bleeding or wound infection), neurological outcome (i.e., if motor GCS [mGCS] score = 6 was achieved and number of days recovery since it was first <6), and in-hospital and 30-day mortality (including cause of death).

In addition to the outcome measures, the following data were collected: patient characteristics (i.e., age, sex, body mass index [BMI] kg/m^2), smoking at age of trauma (chronic obstructive pulmonary disease and diabetes mellitus), injury-related variables (i.e., mechanism of injury, high-energy trauma or low-energy trauma), type of TBI (epidural hematoma, subdural hematoma [SDH], subarachnoid bleeding, diffuse axonal injury, intraparenchymal hemorrhage, intraventricular hemorrhage [IVH], and brain contusion), TBI severity at hospital admission (moderate [GCS score, 9–12] or severe [GCS score, ≤8]), intracranial hypertension (ICH) (defined as intracranial pressure [ICP] > 20 mm Hg), total number and location of ribs fractured, Injury Severity Score (ISS), presence of a flail chest, pneumothorax, hemothorax, pulmonary contusion, facial fracture, skull fracture, and presence of at least three fractured ribs with bicortical displacement. In addition, the following treatment- and outcome-related variables were collected: treatment (operative or nonoperative), chest tube placement, if operated: surgical delay, rib fixation used, total number of ribs fixated, ICP-reducing therapy performed (including details on the provided therapy), type of additional surgeries required.

Statistical Analysis

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 25 or higher (SPSS, Chicago, IL). Normality of continuous variables was tested with the Shapiro-Wilk test, and homogeneity of variances was tested using the Levene's test. A p value lower than 0.05 was considered statistically significant, and all tests were two-sided. Missing data were not imputed since the rate of missing data per variable was less than 4%, except for "BMI" (13%), "smoking at age of trauma" (28%), and "fracture in every rib region" (11%).

Descriptive analysis was performed to report the data for the entire study population and for the treatment groups. Subgroup analysis was performed for the treatment groups, stratified by TBI severity (moderate or severe). For continuous data, the mean and SD (parametric data) or the median and percentiles (nonparametric data) are reported. Statistical significance of differences between SSRF and nonoperative treatment was assessed using Mann-Whitney U test (nonparametric data). For categorical data, numbers and frequencies were reported per treatment group and compared using χ^2 or Fisher's exact test, as applicable.

After univariate analysis, multivariable analysis through logistic regression and linear regression (for binary and continuous outcomes, respectively) was applied to control for potential confounding. Potential confounders were selected from literature and from the data of the current study. First, a Spearman's rank correlation with outcome measures was determined for the patient demographics and injury characteristics with a known confounding effect (based on literature) or that displayed a p value of 0.2 or lower in the univariate analysis. Next, the effect of these covariates on the odds ratio (OR) or beta value (for logistic regression and linear regression, respectively) was determined. The covariates with a statistically significant correlation with outcome and/or that had a statistically significant OR or beta value in the regression model were BMI, presence of SDH, SAH, IVH, TBI severity, ICH, number of rib fractures, presence of flail chest, pneumothorax, and pulmonary contusion. Since SDH, SAH, and IVH were likely to reflect TBI severity, only the latter was included in the final regression models. Given the multicenter design of the study, participating center was also considered as a confounder. Study center was, however, not included in the final model as it did not statistically correlate with outcome. The final regression model consisted of BMI, TBI severity, presence of ICH, number of rib fractures, presence of flail chest, pneumothorax, and pulmonary contusion. The final crude regression model included the outcome measure as the dependent variable, and SSRF as covariate. In the adjusted analysis, the covariates mentioned above were added as covariates. For binary regression analysis, the OR for SSRF over nonoperative treatment is reported with 95% confidence interval (CI) and p values. For linear regression analysis, the beta value with 95% CI and p value is reported.

RESULTS

In total, 456 (56.1%) of 813 patients with multiple rib fractures and traumatic TBI were included for analysis (Fig. 1).

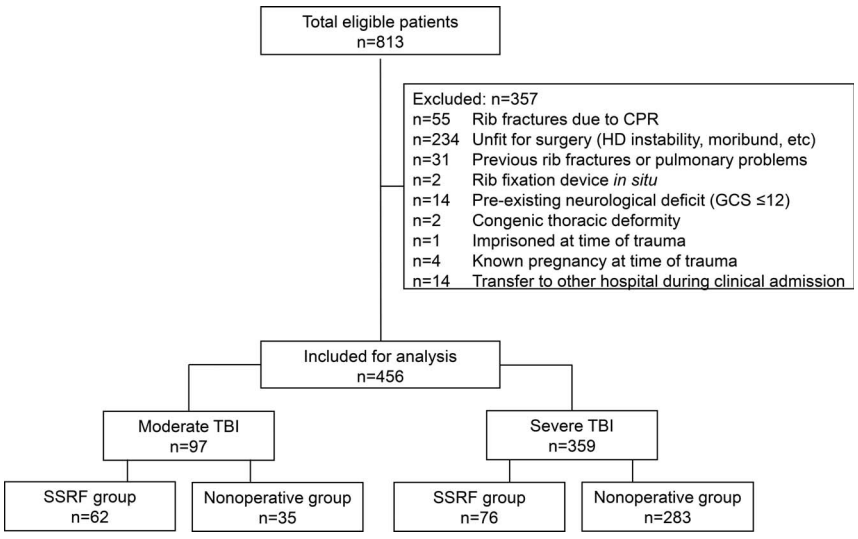

Figure 1. Flowchart of the study.

The most common exclusion criterion was unfit (e.g., hemodynamic instability) or moribund patient at hospital admission (n = 234). A total of 111 (24.3%) patients were treated with SSRF. The SSRF group had a significantly higher median BMI (28 (P_{25}–P_{75}, 25–31) versus 26 (P_{25}–P_{75} 23–29) kg/m^2; $p = 0.008$) than the nonoperative group. Other patient demographics were similar in both treatment groups (Table 1). With regard to the brain injury characteristics, the SSRF group suffered subdural hematoma (n = 41, 36.9% vs. n = 202, 58.6%; $p < 0.001$), subarachnoid hemorrhage (n = 60, 54.1% vs. n = 240, 69.6%; $p = 0.004$), ICH (n = 12, 10.8% vs. n = 89, 26.5%; $p < 0.001$), and severe TBI (n = 76, 68.5% vs. n = 283, 82.0%; $p = 0.003$) significantly less often than the nonoperative group. Brain contusion was more frequently present in the SSRF group (n = 26, 23.4% versus n = 43, 12.5%; $p = 0.009$; Table 1). The SSRF group required ICP reducing therapy

TABLE 1. Demographics and Injury Characteristics of Patients With Moderate or Severe TBI and Rib Fractures Treated Operatively (SSRF) or Nonoperatively

	n*	Overall (N = 456)	n*	SSRF (n = 111)	n*	Nonoperative (n = 345)	*p*
Patient characteristics							
Age (y)	456	50 (37–63)	111	50 (37–61)	345	50 (37–63)	0.786
Sex (male)	455	349 (76.7%)	110	80 (72.7%)	345	269 (78.0%)	0.300
BMI (kg/m^2)	398	26 (24–30)	100	28 (25–31)	298	26 (23–29)	**0.008**
Smoking at age of trauma	328	131 (39.9%)	83	38 (45.8%)	245	93 (38.0%)	0.243
COPD	456	27 (5.9%)	111	11 (9.9%)	345	16 (4.6%)	0.061
Diabetes mellitus	456	49 (10.7%)	111	14 (12.6%)	345	35 (10.1%)	0.482
Injury characteristics							
HET	450	408 (90.7%)	110	100 (90.9%)	340	308 (90.6%)	1.000
Epidural hematoma	456	38 (8.3%)	111	6 (5.4%)	345	32 (9.3%)	0.239
Subdural hematoma	456	243 (53.3%	111	41 (36.9%)	345	202 (58.6%)	**<0.001**
Subarachnoid hemorrhage	456	300 (65.8%)	111	60 (54.1%)	345	240 (69.6%)	**0.004**
DAI	456	90 (19.7%)	111	21 (18.9%)	345	69 (20.0%)	0.891
Intraparenchymal hemorrhage	456	132 (28.9%)	111	34 (30.6)	345	98 (28.4%)	0.718
IVH	456	40 (8.8%)	111	5 (4.5%)	345	35 (10.1%)	0.082
Brain contusion	456	69 (15.1%)	111	26 (23.4%)	345	43 (12.5%)	**0.009**
TBI severity at admission	456		111		345		
Moderate (GCS score, 9–12)		97 (21.3%)		35 (31.5%)		62 (18.0%)	**0.003**
Severe (GCS score, ≤ 8)		359 (78.7%)		76 (68.5%)		283 (82.0%)	
ICH	447	101 (22.6%)	111	12 (10.8%)	336	89 (26.5%)	**<0.001**
No. ribs fractured	456	8 (6–11)	111	9 (8–12)	345	8 (5–11)	**<0.001**
ISS	456	34 (27–41)	111	33 (27–41)	345	34 (27–41)	0.938
Additional injury							
Flail chest	449	221 (49.2%)	111	86 (77.5%)	338	135 (39.9%)	**<0.001**
Pneumothorax	456	346 (75.9%	111	94 (84.7%)	345	252 (73.0%)	**0.015**
Hemothorax	454	246 (54.2%)	110	67 (60.9%)	344	179 (52.0%)	0.124
Pulmonary contusion	452	337 (74.6%)	111	85 (76.6%)	341	252 (73.9%)	0.617
Facial fracture	456	169 (37.1%)	111	41 (36.9%)	345	128 (37.1%)	1.000
Skull fracture	455	186 (40.9%)	111	42 (37.8%)	344	144 (41.9%)	0.506
Fracture in every rib region	405	141 (34.8%)	100	48 (48.0%)	305	93 (30.5%)	**0.002**
≥100% displacement of ≥3 ribs	441	301 (68.3%)	109	81 (74.3%)	332	220 (66.3%)	0.125
Treatment characteristics							
Chest tube required	456	330 (72.4%)	111	99 (89.2%)	345	231 (67.0%)	**<0.001**
ICP reducing therapy required	456	172 (37.7%)	111	26 (23.4%)	345	146 (42.3%)	**<0.001**
Additional surgeries performed							
Facial surgery	456	34 (7.5%)	111	13 (11.7%)	345	21 (6.1%)	0.061
Clavicle surgery	456	16 (3.5%)	111	8 (7.2%)	345	8 (2.3%)	**0.032**
Thoracotomy	456	19 (4.2%)	111	8 (7.2%)	345	11 (3.2%)	0.096
Laparotomy	456	54 (11.8%)	111	11 (9.9%)	345	43 (12.5%)	0.612
Pelvic surgery	456	46 (10.1%)	111	11 (9.9%)	345	35 (10.1%)	1.000
Long bone surgery	456	109 (23.9%)	111	33 (29.7%)	345	76 (22.0%)	0.124
Spine surgery	456	45 (10.1%)	111	6 (5.4%)	345	40 (11.6%)	0.070

COPD, chronic obstructive pulmonary disease; DAI, diffuse axonal injury; HET, high-energy trauma.
*Provides the exact number of patients for which the parameter was known.
Data are shown as median (P_{25}-P_{75}) or as n (%); bold *p* values are considered statistically significant.

significantly less frequently than the nonoperative group (n = 26, 23.4% versus n = 146, 42.3%; $p < 0.001$).

The SSRF group sustained a median of 9 (P_{25}–P_{75}, 8–12) rib fractures versus 8 (P_{25}–P_{75}, 5–11) in the nonoperative group ($p < 0.001$) and had a flail chest or pneumothorax more often (n = 86, 77.5% vs. n = 135, 39.9%; $p < 0.001$ and n = 94, 84.7% versus n = 252, 73.0%; $p = 0.015$, respectively). The ISS and rate of performed additional surgeries were similar in both groups. Patients in the subgroups stratified by TBI severity who underwent SSRF had a significantly higher number of rib fractures, more often a flail chest and required a chest tube more often than the nonoperative group (Supplemental Table S1, http://links.lww.com/TA/B829). The nonoperative group with severe TBI had a higher BMI and more often SDH and SAH than the SSRF group (Supplemental Table S1, http://links.lww.com/TA/B829).

SSRF was performed at a median of 3 days (P_{25}–P_{75}, 2–5 days) after admission, and did not differ between the moderate TBI (median, 3 days; P_{25}–P_{75}, 1–5 days) and severe TBI group (median, 3 days; P_{25}–P_{75}, 2–5 days; $p = 0.160$).

During SSRF, a median of 4 ribs (P_{25}–P_{75}, 3–5) were fixated, resulting in a ratio of ribs repaired to fractured (rib fixation ratio) of 0.5 (P_{25}–P_{75}, 0.4–0.6). In 39 (36.0%) patients, additional thoracic procedures were performed during SSRF, such as bronchoscopy in 14 (12.6%) patients, VATS in nine (8.1%) patients, diaphragm repair in four (3.6%) patients, pulmonary repair or resection in nine (8.1%) patients and cryoablation in three (2.7%) patients. Complications related to SSRF were seen in four (3.6%) patients and included an intraoperative intracranial pressure increase which required medicinal intervention after which the SSRF was continued in one (0.9%) patient, a postoperative wound infection in two (1.8%) patients and hardware failure in one (0.9%) patient.

Univariate Analysis

In the total cohort, 96.7% patients required mechanical ventilation (n = 441) of which 85 had moderate TBI (87.6% of the moderate TBI group) and 356 had severe TBI (99.2% of

TABLE 2. Univariate and Multivariable in-Hospital Outcome of SSRF Versus Nonoperative Treatment in Patients With Rib Fractures and Moderate or Severe TBI

	Univariate Analysis					Multivariable Analysis					
	SSRF		Nonoperative			Crude Analysis			Adjusted Analysis		
Outcome	N*		N*		*p*	N*	Beta or OR (95% CI)	*p*	N*	Beta or OR (95% CI)	*p*
Ventilator-free days											
All	111	11 (7–20)	345	10 (1–21)	0.069	456	−0.53 (−4.27 to 3.21)	0.781	381	−1.61 (−6.12 to 2.89)	0.483
Moderate TBI	35	12 (7–18)	62	10 (5–23)	0.523	97	−1.95 (−8.67 to 4.77)	0.566	79	−0.47 (−9.60 to 8.65)	0.918
Severe TBI	76	11 (7–20)	283	10 (1–21)	**0.034**	359	0.14 (−4.39 to 4.67)	0.952	302	−1.77 (−7.03 to 3.49)	0.508
ICU-LOS											
All	111	12 (7–19)	345	14 (7–22)	0.209	456	−2.23 (−4.67 to 0.01)	0.051	381	−2.03 (−4.56 to 0.49)	0.114
Moderate TBI	35	8 (5–15)	62	12 (5–15)	0.209	97	−2.96 (−6.79 to 0.87)	0.128	79	−1.83 (−5.72 to 2.07)	0.353
Severe TBI	76	14 (8–20)	283	14 (7–22)	0.824	359	−1.23 (−3.93 to 1.47)	0.373	302	−1.86 (−4.92 to 1.21)	0.234
HLOS											
All	111	21 (14–32)	345	22 (13–38)	0.990	456	−2.82 (−7.29 to 1.65)	0.215	381	−3.82 (−9.15 to 1.51)	0.159
Moderate TBI	35	19 (13–24)	62	19 (13–30)	0.784	97	−5.43 (−13.11 to 2.24)	0.163	79	−4.84 (−14.73 to 5.06)	0.333
Severe TBI	76	23 (16–34)	283	23 (13–39)	0.536	359	−0.99 (−6.43 to 4.45)	0.721	302	−3.11 (−9.43 to 3.22)	0.334
Pneumonia											
All	111	38 (34.2%)	345	164 (47.5%)	**0.016**	456	0.58 (0.37–0.90)	**0.015**	381	0.59 (0.35–0.98)	**0.043**
Moderate TBI	35	6 (17.1%)	62	28 (45.2%)	**0.007**	97	0.25 (0.09–0.69)	**0.007**	79	0.35 (0.11–1.14)	0.082
Severe TBI	76	32 (42.1%)	283	136 (48.1%)	0.368	359	0.79 (0.47–1.31)	0.357	302	0.69 (0.39–1.25)	0.221
mGCS score recovery to 6											
All	103	96 (93.2%)	324	243 (75.0%)	**<0.001**	427	4.57 (2.04–10.25)	**<0.001**	356	4.54 (1.77–11.69)	**0.002**
Moderate TBI	30	28 (93.3%)	52	45 (86.5%)	0.475	82	2.18 (0.42–11.24)	0.353	65	N.D.	N.D.
Severe TBI	73	68 (93.2%)	272	198 (72.8%)	**<0.001**	345	5.08 (1.97–13.10)	**0.001**	291	5.95 (1.91–18.53)	**0.002**
In-hospital mortality											
All	111	8 (7.2%)	345	68 (19.7%)	**0.002**	456	0.32 (0.15–0.68)	**0.003**	381	0.40 (0.15–1.04)	0.061
Moderate TBI	35	4 (11.4%)	62	9 (14.5%)	0.765	97	0.76 (0.22–2.68)	0.669	79	N.D.	N.D.
Severe TBI	76	4 (5.3%)	283	59 (20.8%)	**0.001**	359	0.21 (0.07–0.60)	**0.004**	302	0.30 (0.08–1.06)	0.061
30-d Mortality											
All	111	7 (6.3%)	345	64 (18.6%)	**0.001**	456	0.30 (0.13–0.67)	**0.003**	381	0.32 (0.11–0.91)	**0.032**
Moderate TBI	35	4 (11.4%)	62	9 (14.5%)	0.765	97	0.76 (0.22–2.68)	0.669	79	N.D.	N.D.
Severe TBI	76	3 (3.9%)	283	55 (19.4%)	**0.001**	359	0.17 (0.05–0.56)	**0.004**	302	0.19 (0.04–0.88)	**0.034**

*Provides the exact number of patients for which the outcome measure was known. The multivariable analysis shows the effect of SSRF over nonoperative treatment. In the corrected analysis, BMI, TBI severity, ICH, number of rib fractures, flail chest, pneumothorax, and pulmonary contusion were entered as covariate.

ORs and beta values are shown with 95% confidence interval; bold *p* values are considered statistically significant.

N.D., not determined.

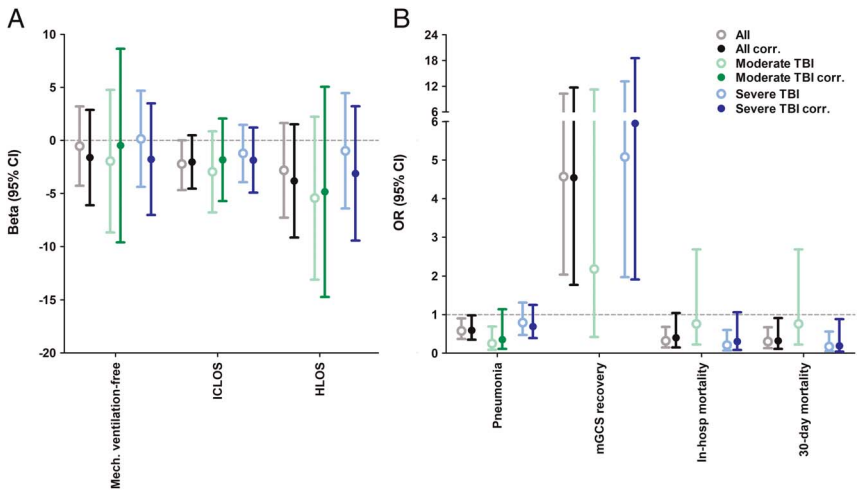

Figure 2. Forrest plots for the effect of SSRF over nonoperative treatment for (A) continuous and (B) binary outcomes in all patients as well as in patients with moderate or severe TBI, based on (un)adjusted regression models. Unadjusted and adjusted beta values and ORs (for continuous and binary outcomes, respectively) are shown. For binary outcomes, nonoperative treatment served as reference group. In the adjusted analysis, BMI, TBI severity, ICH, number of rib fractures, flail chest, pneumothorax, and pulmonary contusion were entered as covariate.

the severe TBI group). For patients with severe TBI, the number of ventilator-free days was significantly higher after SSRF (median, 11 days; P_{25}–P_{75}, 7–20 days) than after nonoperative treatment (median, 10 days; P_{25}–P_{75}, 1–21 days; $p = 0.034$). The ICU-LOS and HLOS were similar between the two treatment groups in both the total cohort as well as in the subgroups of patients with moderate or severe TBI (Table 2). The rate of pneumonia was significantly lower in both the total cohort as well as in patients with moderate TBI when comparing the SSRF group with the nonoperative group (n = 38, 34.2% vs. n = 164, 47.5%; $p = 0.016$, and n = 6, 17.1% vs. n = 28, 45.2%; $p = 0.007$, respectively). Recovery of mGCS score to 6 in patients, in which this had been less than 6, was significantly more frequent in the total cohort and in patients with severe TBI when comparing the SSRF group with the nonoperative group (n = 96.2, 93.2% vs. n = 243, 75.0%; $p < 0.001$ and n = 68, 93.2% vs. n = 272, 72.8%; $p < 0.001$). In the total cohort, this mGCS recovery score to 6 was achieved after a median of 3 days (P_{25}–P_{75}, 1–8 days) in the SSRF group versus 4 days (P_{25}–P_{75}, 2–14 days) in the nonoperative group ($p = 0.020$). Both the in-hospital and 30-day mortality rates were significantly lower in the SSRF group in both the total cohort and in patients with severe TBI than in the nonoperative group.

Multivariable Analysis

Overall Cohort

In the adjusted analysis, the number of ventilator-free days did not differ between the two treatment groups (beta, −1.61; 95% CI, −6.12 to 2.89 days; $p = 0.483$; Table 2 and Fig. 2). The odds of developing pneumonia (OR, 0.59; 95% CI, 0.35–0.98; $p = 0.043$) and odds of 30-day mortality (OR, 0.32; 95% CI, 0.11–0.91; $p = 0.032$) were significantly lower and rate of mGCS score recovery to 6 (beta, 4.54; 95% CI, 1.77–11.69 days; $p = 0.002$) significantly higher in the SSRF group. The ICU-LOS, HLOS, and the other outcome measures were similar in the SSRF and nonoperative group (Tables 2 and 3 and Fig. 2).

Moderate TBI

In patients with moderate TBI, the number of ventilator-free days did not differ between the two treatment groups (beta −0.47; 95% CI, −9.60 to 8.65 days; $p = 0.918$; Table 2 and Fig. 2). The odds of developing pneumonia and of mortality were similar in both treatment groups. No difference in ICU-LOS, HLOS, and the other outcome measures was demonstrated.

Severe TBI

In patients with severe TBI, the number of ventilator-free days was similar in both groups (beta, −1.77; 95% CI, −7.03 to

TABLE 3. In-Hospital Outcome in Patients With Moderate or Severe TBI and Rib Fractures Treated Operatively (SSRF) or Nonoperatively

		All			Moderate TBI			Severe TBI		
	N*	SSRF (n = 111)	Nonop. (n = 345)	*p*	SSRF (n = 35)	Nonop. (n = 62)	*p*	SSRF (n = 76)	Nonop. (n = 62)	*p*
Tracheostomy performed	456	35 (31.5%)	135 (39.1%)	0.176	6 (17.1%)	16 (25.8%)	0.450	29 (38.2%)	119 (42.0%)	0.600
Time to tracheostomy (days)	456	9 (5–12)	10 (7–15)	0.125	5.8 (SD, 4.2)	10.0 (SD 5.2)	0.120	10 (6–13)	11 (7–15)	0.363
Pleural empyema	456	1 (0.9%)	5 (1.4%)	1.000	1 (2.9%)	1 (1.6%)	1.000	0 (0.0%)	4 (1.4%)	0.583
Time until mGCS score = 6 (days)	456	3 (1–8)	4 (2–14)	**0.020**	2 (1–4)	3 (1–8)	0.092	4 (2–9)	5 (2–15)	0.178

Data are shown as N (%), mean (SD), or as median (P_{25}-P_{75}); bold *p*-values are considered statistically significant.
*Provides the exact number of patients for which the outcome measure was known.
FU, follow-up; Nonop, nonoperative treatment; SEPS; subdural evacuation port system.

3.49 days; $p = 0.508$; Table 2 and Fig. 2). The odds of 30-day mortality (OR, 0.19; 95% CI, 0.04–0.88; $p = 0.034$) was significantly lower and the rate of mGCS score recovery to 6 (beta, 5.95; 95% CI, 1.91–18.53 days, $p = 0.002$) significantly higher in the SSRF group. The odds of developing pneumonia, the HLOS, ICU-LOS, and the other outcome measures were similar in both treatment groups.

DISCUSSION

This multicenter retrospective cohort study is the first to examine SSRF versus nonoperative treatment on in-hospital outcome in patients with multiple rib fractures and TBI (GCS score, ≤ 12). Although there was no difference in the primary outcome of ventilator-free days, this study demonstrated that the SSRF group had, after multivariable analysis, a significantly lower odds of developing pneumonia and of 30-day mortality than the nonoperative group. In patients with severe TBI, SSRF was associated with a significantly lower odds of 30-day mortality. The HLOS, and ICU-LOS were similar in both treatment groups. Furthermore, SSRF in patients with TBI is a safe procedure which can be performed relatively early after admission, without perioperative neurological impairment and a low complication rate.

Traumatic brain injury is considered a traditional contraindication for SSRF as TBI increases the risk of pneumonia regardless of other injuries, as well as the duration of mechanical ventilation, ICU-LOS, and HLOS based on slow neurological recovery. Also, patients with TBI might deteriorate neurologically perioperatively and the neurologic outcome is difficult to predict.[12,13,18] Accordingly, the main impediment to ventilator liberation has been traditionally considered to be the TBI as opposed to the chest wall injury, rendering SSRF theoretically of little benefit. Furthermore, no published data are available on the effect of SSRF compared with nonoperative treatment in the patient with TBI. Because of this non–evidence-based consensus, participating centers, while forerunners in the field of SSRF, might have been discrete in performing SSRF at an early stage. However, early (within 48 hours) fixation of rib fractures is associated with shorter duration of mechanical ventilation, HLOS, and ICU-LOS in various patient groups without TBI.[14,19–21]

The mortality rate in patients who sustain TBI is high and known to be approximately 25% in polytraumatized patients.[1,22] The in-hospital and 30-day mortality rate in the current study cohort for all nonoperatively treated patients with rib fractures and TBI was 19.7% and 18.6%, respectively. In the entire SSRF group, the mortality rates decreased with 12.5% for in-hospital mortality and 12.3% for 30-day mortality. Patients with severe thoracic injury on CT may have a three times higher odds of 30-day mortality.[23] In this study, after correcting for the TBI severity and presence of ICH, an odds ratio of 0.32 for 30-day mortality for the entire SSRF group and an odds ratio of 0.19 for the SSRF group with severe TBI was found. This indicates a possible beneficial effect of stabilizing the severely injured chest wall by SSRF on the mortality rate of patients with concomitant multiple rib fractures and TBI. Thus, TBI should no longer be seen as a contraindication to SSRF.

Both the presence of TBI and multiple rib fractures are known risk factors for the development of pneumonia.[1,8,24,25] Surgical stabilization of rib fracture is known to decrease the rate of pneumonia and has been studied extensively in patients with multiple rib fractures and a flail chest.[26,27] The SSRF group in this cohort had a median of one additional fractured rib and 37.6% more often a flail chest than the nonoperative group. Although having more severe thoracic injury than the nonoperative group, the rate of pneumonia was 13.3% lower in the SSRF group than in the nonoperative group in the total cohort and 28.1% lower in patients with moderate TBI. After logistic regression, the odds of developing pneumonia in the SSRF group was 0.59 for the total cohort. No effect of SSRF on the pneumonia rate was found in the group with severe TBI. A possible explanation for the lack of this beneficial effect in the SSRF group with severe TBI might be the lengthy mechanical ventilation which these patients often require. This consequently increases the risk of ventilator-associated pneumonia of which rates of 45 to 60% have been found in these patients.[28,29] Due to the similar number of ventilator-free days in the SSRF group and nonoperative group of the patients with severe TBI, a comparable rate of ventilator-associated pneumonia could be expected.

While SSRF was associated with significantly lower odds of developing pneumonia and 30-day mortality, the number of ventilator-free days was similar in both groups in the total cohort. As no distinction was made in mechanical ventilation mode, SSRF could have improved respiratory mechanics, allowing for a quicker wean to a less invasive ventilation mode such as pressure support. This might have decreased the odds of developing pneumonia in the SSRF group in this acute phase or decreased pain and consequently added to the prevention of pneumonia after extubation.

In addition, the apparent beneficial effect of SSRF on the odds of developing pneumonia and 30-day mortality in the total study cohort, did not significantly decrease HLOS and ICU-LOS. After correction for the potential confounders, these outcome measures were found to be statistically similar but suggest a modest positive effect of an almost 4 days decrease for HLOS and 2 days decrease for ICU-LOS in favor of the SSRF group in the total cohort.

A possible explanation for the similar HLOS and ICU-LOS might be the extensive other injuries of these patients. With a similar rate of additional surgeries performed and a high median ISS greater than 30 in the SSRF and nonoperative group of the total cohort, the exact effect of these extracranial and extrathoracic injuries on the HLOS and ICU-LOS is unclear.

The current study demonstrated that SSRF in patients with TBI is a safe procedure and does not introduce additional neurological damage perioperatively. Four of the 111 patients developed a SSRF-related complication of which only one occurred perioperatively. In this patient, ICP increased during positioning in the operating room, but SSRF could successfully be continued after administration of mannitol and reverse-Trendelenburg positioning. In a patient with TBI, factors related to surgery such as fluid resuscitation overload cause an elevating central venous pressure or prone positioning can result in an increasing ICP requiring prompt intervention.[30] While the effect of SSRF has not been specifically studied in patients with TBI, studies have evaluated the effect of timing of orthopedic fracture fixation in patients with TBI. Some of these studies demonstrated deleterious effects of early fracture fixation due to high rates of perioperative hypotension, increased intracranial pressure and poor neurological outcome possibly due to secondary brain injury.[31] On the other

hand it is suggested that orthopedic injuries should be managed aggressively while maintaining sufficient cerebral perfusion pressure through adequate monitoring and fluid resuscitation, but supporting literature is not clear and low in quality.[32] In the postoperative setting of this study, no iatrogenic neurological damage was found with similar times to mGCS score recovery of 6 in the SSRF group and nonoperative group and a higher rate of mGCS score recovery of 6 in the SSRF group of the total cohort and in patients with severe TBI. This outcome measure does not imply that SSRF improves neurological outcome after TBI compared with nonoperative treatment. It does however suggest that SSRF and the appurtenant perioperative setting is safe and does not deteriorate or slow down neurological recovery after TBI, even when SSRF is performed as early as 3 days after trauma.

The parameter GCS score at admission was chosen to define TBI severity as there currently is no criterion standard.[33] The GCS score is the most widely used measure of TBI severity.[34] However, while this variable has known limitations (e.g., in intoxicated patients), other parameters such as the AIS head also have limitations and a weak correlation with long- and short-term outcome.[35,36] Because of the retrospective nature of this study, GCS score at the time of SSRF or sudden GCS score improvements after admission were not known. However, while AIS head might be a superior indicator for defining TBI severity, which should be evaluated in future research, the GCS score is one of the best severity measurements for immediate clinical care.[37] To correct for nontraumatic reasons leading to a lowered GCS score, the combination of GCS score and presence of intracranial abnormalities on head CT was chosen as an inclusion criterion. This was readily available for all participating centers and of clinical importance during the early posttraumatic phase as SSRF performed within 48 hours is associated with improved outcome.[19] In addition, the logistic regression analysis abstracted and controlled for parameters beyond GCS score that captured severity of TBI, such as the presence of ICH.

While this cohort study is the first, to date, to evaluate the effect of SSRF on in-hospital outcome in patients with multiple rib fractures and TBI, several limitations should be considered when interpreting the outcome.

First, because of the retrospective nature of this study, missing data and underreporting might have affected outcome through information bias. Through data collection in which all variables were obligatory and low-threshold communication as the providing coauthors were CWIS members, there were hardly any missing data concerning the included patients.

Second, while the multicenter design resulted in a large number of patients, the sample size of subgroups might have been too low to detect small but clinically meaningful differences in outcome between treatment groups. Because lower sample size result in larger confidence intervals, this may explain why the lower odds of developing pneumonia found for the total SSRF group was not seen for the moderate and severe TBI subgroups. The size of the total cohort was unclear beforehand. Therefore the use of an adjusted regression model was chosen instead of propensity score matching. The multicenter design might also have affected outcome due to heterogeneity in clinical practice resulting in effect modification or potential confounding of within-center covariates.[38] On the other hand, the multicenter design has made the results more generalizable.

Third, the study was nonrandomized. The mortality difference between the SSRF and nonoperative group might therefore be suggestive of the fact that patients with a better neurological status and consequently prognosis, are more likely to be selected for SSRF, confounding this outcome. With no standardized treatment protocol and the more severe TBI characteristics in the nonoperative group, the treating clinician might have chosen to perform SSRF on the patient in which a better outcome and prognosis was expected. This might have introduced some bias in the outcome, but mimics daily clinic. A possible consequent survival bias was however mitigated by using the number of ventilator-free days instead of the duration of mechanical ventilation as the primary outcome and by performing a linear regression analysis.

Fourth, the presented logistic and linear regression model only included possible confounders which were identified from available literature and the current data. The confounding effect of nonincluded parameters, such as AIS head, is therefore not known. A prospective design with set variables and a standardized treatment protocol might overcome these shortcomings. In addition, because of the retrospective data on in-hospital outcome, future research should focus on the outcome after discharge and cost effectiveness to provide a complete overview on outcome after SSRF in this type of patient. Before conducting expensive and potentially risky prospective studies, such as randomized controlled trials (RCTs), on this issue, it is important to establish through retrospective research that there is, as this study showed, at least equipoise and, specifically, that SSRF does not harm patients with TBI.

In summary, in patients with moderate to severe TBI a difference in the primary outcome of number of ventilator-free days between the SSRF and nonoperative groups was not demonstrated. However, this exploratory study suggests a reduced odds of both pneumonia and 30-day mortality in patients who underwent SSRF as compared with nonoperative treatment. Moreover, SSRF is shown to be a safe procedure with a low complication rate, and TBI should no longer be seen as an absolute contraindication to surgery. Prospective studies should strengthen this conclusion in future research.

AUTHORSHIP

J.T.H.P., E.M.M.V.L., F.M.P., and M.M.E.W. participated in the study design. J.T.H.P., E.M.M.V.L., F.A., Z.M.B., E.C., J.C., D.B.C., P.A.C., W.B.D., A.R.D., E.A.E., J.D.F., D.R.F., B.G., C.H., D.G.H., A.J.K., H.K., K.N.L., S.L., S.F.M., A.G.M., T.N., T.D.O., P.P., A.P.R., V.S., G.R.S., Y.S., J.W., F.M.P., and M.M.E.W. participated in data collection. J.T.H.P., E.M.M.V.L., and M.M.E.W. participated in data analysis. J.T.H.P., E.M.M.V.L., F.M.P., and M.M.E.W. participated in data interpretation. J.T.H.P., E.M.M.V.L., and M.M.E.W. participated in the article development. J.T.H.P., E.M.M.V.L., F.A., Z.M.B., E.C., J.C., D.B.C., P.A.C., W.B.D., A.R.D., E.A.E., J.D.F., D.R.F., B.G., C.H., D.G.H., A.J.K., H.K., K.N.L., S.L., S.F.M., A.G.M., T.N., T.D.O., P.P., A.P.R., V.S., G.R.S., Y.S., M.H.J.V., J.W., F.M.P., and M.M.E.W. participated in critical revisions and accepted the final article version.

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DISCLOSURE

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REFERENCES

1. Hofman M, Andruszkow H, Kobbe P, Poeze M, Hildebrand F. Incidence of post-traumatic pneumonia in poly-traumatized patients: identifying the role of traumatic brain injury and chest trauma. *Eur J Trauma Emerg Surg*. 2020;46(1):11–19.
2. Michetti CP, Fakhry SM, Brasel K, Martin ND, Teicher EJ, Newcomb A, TRIPP study group. Trauma ICU prevalence project: the diversity of surgical critical care. *Trauma Surg Acute Care Open*. 2019;4(1):e000288.
3. Lafferty PM, Anavian J, Will RE, Cole PA. Operative treatment of chest wall injuries: indications, technique, and outcomes. *J Bone Joint Surg Am*. 2011; 93(1):97–110.
4. Ziegler DW, Agarwal NN. The morbidity and mortality of rib fractures. *J Trauma*. 1994;37(6):975–979.
5. Dehghan N, de Mestral C, McKee MD, Schemitsch EH, Nathens A. Flail chest injuries: a review of outcomes and treatment practices from the National Trauma Data Bank. *J Trauma Acute Care Surg*. 2014;76(2):462–468.
6. Tanaka H, Yukioka T, Yamaguti Y, Shimizu S, Goto H, Matsuda H, Shimazaki S. Surgical stabilization of internal pneumatic stabilization? A prospective randomized study of management of severe flail chest patients. *J Trauma*. 2002;52(4):727–732; discussion 32.
7. Marasco SF, Davies AR, Cooper J, Varma D, Bennett V, Nevill R, Lee G, Bailey M, Fitzgerald M. Prospective randomized controlled trial of operative rib fixation in traumatic flail chest. *J Am Coll Surg*. 2013;216(5):924–932.
8. Bulger EM, Arneson MA, Mock CN, Jurkovich GJ. Rib fractures in the elderly. *J Trauma*. 2000;48(6):1040–1046; discussion 6-7.
9. Qiu M, Shi Z, Xiao J, Zhang X, Ling S, Ling H. Potential benefits of rib fracture fixation in patients with flail chest and multiple non-flail rib fractures. *Indian J Surg*. 2016;78(6):458–463.
10. Bergeron E, Lavoie A, Clas D, Moore L, Ratte S, Tetreault S, Lemaire J, Martin M. Elderly trauma patients with rib fractures are at greater risk of death and pneumonia. *J Trauma*. 2003;54(3):478–485.
11. Kane ED, Jeremitsky E, Pieracci FM, Majercik S, Doben AR. Quantifying and exploring the recent national increase in surgical stabilization of rib fractures. *J Trauma Acute Care Surg*. 2017;83(6):1047–1052.
12. Pieracci FM, Majercik S, Ali-Osman F, et al. Consensus statement: surgical stabilization of rib fractures rib fracture colloquium clinical practice guidelines. *Injury*. 2017;48(2):307–321.
13. Kasotakis G, Hasenboehler EA, Streib EW, Patel N, Patel MB, Alarcon L, Bosarge PL, Love J, Haut ER, Como JJ. Operative fixation of rib fractures after blunt trauma: a practice management guideline from the eastern Association for the Surgery of trauma. *J Trauma Acute Care Surg*. 2017;82(3):618–626.
14. Althausen PL, Shannon S, Watts C, Thomas K, Bain MA, Coll D, O'Mara TJ, Bray TJ. Early surgical stabilization of flail chest with locked plate fixation. *J Orthop Trauma*. 2011;25(11):641–647.
15. Pieracci FM, Agarwal S, Doben A, Shiroff A, Lottenberg L, Whitbeck SA, White TW. Indications for surgical stabilization of rib fractures in patients without flail chest: surveyed opinions of members of the Chest Wall Injury Society. *Int Orthop*. 2018;42(2):401–408.
16. Prevention TCoDCa. Pneumonia (ventilator-associated [VAP] and non-ventilator-associated pneumonia [PNEU]) event. 2018 [Available from: https://www.cdc.gov/nhsn/pdfs/pscmanual/6pscvapcurrent.pdf.
17. DuBose J, Inaba K, Okoye O, et al. Development of posttraumatic empyema in patients with retained hemothorax: results of a prospective, observational AAST study. *J Trauma Acute Care Surg*. 2012;73(3):752–757.
18. De Campos JRM, White TW. Chest wall stabilization in trauma patients: why, when, and how? *J Thorac Dis*. 2018;10(Suppl 8):S951–S962.
19. Pieracci FM, Coleman J, Ali-Osman F, Mangram A, Majercik S, White TW, Jeremitsky E, Doben AR. A multicenter evaluation of the optimal timing of surgical stabilization of rib fractures. *J Trauma Acute Care Surg*. 2018; 84(1):1–10.
20. Iqbal HJ, Alsousou J, Shah S, Jayatilaka L, Scott S, Scott S, Melling D. Early surgical stabilization of complex chest wall injuries improves short-term patient outcomes. *J Bone Joint Surg Am*. 2018;100(15):1298–1308.
21. Otaka S, Aso S, Matsui H, Fushimi K, Yasunaga H. Early versus late rib fixation in patients with traumatic rib fractures: a nationwide study. *Ann Thorac Surg*. 2020;110:988–992.
22. van Leeuwen N, Lingsma HF, Perel P, et al. Prognostic value of major extracranial injury in traumatic brain injury: an individual patient data meta-analysis in 39,274 patients. *Neurosurgery*. 2012;70(4):811–818; discussion 8.
23. Dai D, Yuan Q, Sun Y, Yuan F, Su Z, Ding J, Tian H. Impact of thoracic injury on traumatic brain injury outcome. *PLoS One*. 2013;8(9):e74204.
24. Coary R, Skerritt C, Carey A, Rudd S, Shipway D. New horizons in rib fracture management in the older adult. *Age Ageing*. 2019.
25. Flagel BT, Luchette FA, Reed RL, Esposito TJ, Davis KA, Santaniello JM, Gamelli RL. Half-a-dozen ribs: the breakpoint for mortality. *Surgery*. 2005; 138(4):717–723; discussion 23-5.
26. Beks RB, Peek J, de Jong MB, Wessem KJP, Oner CF, Hietbrink F, Leenen LPH, Groenwold RHH, Houwert RM. Fixation of flail chest or multiple rib fractures: current evidence and how to proceed. A systematic review and meta-analysis. *Eur J Trauma Emerg Surg*. 2018.
27. Cataneo AJ, Cataneo DC, de Oliveira FH, Arruda KA, El Dib R, de Oliveira Carvalho PE. Surgical versus nonsurgical interventions for flail chest. *Cochrane Database Syst Rev*. 2015;(7):CD009919.
28. Esnault P, Nguyen C, Bordes J, et al. Early-onset ventilator-associated pneumonia in patients with severe traumatic brain injury: incidence, risk factors, and consequences in cerebral oxygenation and outcome. *Neurocrit Care*. 2017;27(2):187–198.
29. Zygun DA, Zuege DJ, Boiteau PJ, Laupland KB, Henderson EA, Kortbeek JB, Doig CJ. Ventilator-associated pneumonia in severe traumatic brain injury. *Neurocrit Care*. 2006;5(2):108–114.
30. Hariri RJ, Firlick AD, Shepard SR, Cohen DS, Barie PS, Emery JM, Ghajar JBG. Traumatic brain injury, hemorrhagic-shock, and fluid resuscitation—effects on intracranial-pressure and brain compliance. *J Neurosurg*. 1993;79(3):421–427.
31. O'Brien PJ. Fracture fixation in patients having multiple injuries. *Can J Surg*. 2003;46(2):124–128.
32. Giannoudis PV, Veysi VT, Pape HC, Krettek C, Smith MR. When should we operate on major fractures in patients with severe head injuries? *Am J Surg*. 2002;183(3):261–267.
33. Teasdale G, Maas A, Lecky F, Manley G, Stocchetti N, Murray G. The Glasgow Coma Scale at 40 years: standing the test of time. *Lancet Neurol*. 2014; 13(8):844–854.
34. The Brain Trauma Foundation. The American Association of Neurological Surgeons. The joint section on neurotrauma and critical care. Glasgow Coma Scale Score. *J Neurotrauma*. 2000;17(6–7):563–571.
35. Foreman BP, Caesar RR, Parks J, Madden C, Gentilello LM, Shafi S, Carlile MC, Harper CR, Diaz-Arrastia RR. Usefulness of the abbreviated injury score and the injury severity score in comparison to the Glasgow Coma Scale in predicting outcome after traumatic brain injury. *J Trauma*. 2007; 62(4):946–950.
36. Demetriades D, Kuncir E, Murray J, Velmahos GC, Rhee P, Chan L. Mortality prediction of head abbreviated injury score and Glasgow Coma Scale: analysis of 7,764 head injuries. *J Am Coll Surg*. 2004;199(2):216–222.
37. Savitsky B, Givon A, Rozenfeld M, Radomislensky I, Peleg K. Traumatic brain injury: it is all about definition. *Brain Inj*. 2016;30(10):1194–1200.
38. Localio AR, Berlin JA, Ten Have TR, Kimmel SE. Adjustments for center in multicenter studies: an overview. *Ann Intern Med*. 2001;135(2):112–123.