A multicenter, prospective, controlled clinical trial of surgical stabilization of rib fractures in patients with severe, nonflail fracture patterns (Chest Wall Injury Society NONFLAIL)

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BACKGROUND: The efficacy of surgical stabilization of rib fracture (SSRF) in patients without flail chest has not been studied specifically. We hypothesized that SSRF improves outcomes among patients with displaced rib fractures in the absence of flail chest.

METHODS: Multicenter, prospective, controlled, clinical trial (12 centers) comparing SSRF within 72 hours to medical management. Inclusion criteria were three or more ipsilateral, severely displaced rib fractures without flail chest. The trial involved both randomized and observational arms at patient discretion. The primary outcome was the numeric pain score (NPS) at 2-week follow-up. Narcotic consumption, spirometry, pulmonary function tests, pleural space complications (tube thoracostomy or surgery for retained hemothorax or empyema >24 hours from admission) and both overall and respiratory disability-related quality of life (RD-QoL) were also compared.

RESULTS: One hundred ten subjects were enrolled. There were no significant differences between subjects who selected randomization (n = 23) versus observation (n = 87); these groups were combined for all analyses. Of the 110 subjects, 51 (46.4%) underwent SSRF. There were no significant baseline differences between the operative and nonoperative groups. At 2-week follow-up, the NPS was significantly lower in the operative, as compared with the nonoperative group (2.9 vs. 4.5, $p < 0.01$), and RD-QoL was significantly improved (disability score, 21 vs. 25, $p = 0.03$). Narcotic consumption also trended toward being lower in the operative, as compared with the nonoperative group (0.5 vs. 1.2 narcotic equivalents, $p = 0.05$). During the index admission, pleural space complications were significantly lower in the operative, as compared with the nonoperative group (0% vs. 10.2%, $p = 0.02$).

CONCLUSION: In this clinical trial, SSRF performed within 72 hours improved the primary outcome of NPS at 2-week follow-up among patients with three or more displaced fractures in the absence of flail chest. These data support the role of SSRF in patients without flail chest. (*J Trauma Acute Care Surg.* 2020;88: 249–257. Copyright © 2019 Wolters Kluwer Health, Inc. All rights reserved.)

LEVEL OF EVIDENCE: Therapeutic, level II.

KEY WORDS: Rib fractures; surgical stabilization of rib fractures; clinical trial.

Surgical stabilization of rib fractures (SSRF) is now used worldwide in the management of patients with severe chest wall injuries.[1] Conceptually, SSRF applies the basic orthopedic principles of reduction and fixation to rib fractures, restoring chest wall stability and mitigating pain, respiratory failure, and subsequent nonunion. The advent of muscle-sparing techniques,[2,3] as well as a relatively low complication rate,[4,5] has contributed to a rapid rise in the use of SSRF, from 0.7%[6] to 5.8%[7] of patients with a diagnosis of flail chest.

To date, the vast majority of data supporting the efficacy of SSRF have been limited to patients with flail chest, although this condition is defined variably.[8–11] Outcomes of patients with nonflail fractures patterns (most commonly ≥3 displaced fractures) have been reported, but only when analyzed together with flail chest patients.[3,12–14] Accordingly, consensus statements have conditionally recommended SSRF in patients with flail chest, and specifically cautioned against its use otherwise.[15,16]

In practice, many surgeons have broadened their indications for SSRF to routinely include nonflail rib fracture patterns. Although these injuries differ anatomically from flail chest, many of the same pathophysiologic principles apply. However, it remains unclear if stabilization of these fractures is beneficial to patients. Particularly concerning is the disproportionate increase in the use of SSRF in patients without flail chest observed predominately at lower and nontrauma level designated centers.[1]

The objective of this clinical trial was to investigate the efficacy of SSRF specifically in patients with nonflail, severe rib fracture patterns. We hypothesized that SSRF, as compared with nonoperative management, improves pain control, narcotic consumption, pulmonary function, risk of complications, and quality of life (QoL).

METHODS

This was a multicenter, prospective, controlled clinical trial conducted by the Chest Wall Injury Society (CWIS)[17] and involving 12 U.S. academic trauma centers. Centers were selected for participation via completion of an online survey addressing several institution-specific aspects of rib fracture management.[18] Requirements for trial participation were greater than 200 annual admissions of patients with rib fractures, protocolized admission and analgesic pathways for rib fracture patients, and a minimum annual volume of 12 SSRF cases.

The membership of CWIS was surveyed a priori regarding perceived indications for SSRF in patients without flail chest to determine a patient population for which there was equipoise between operative and nonoperative management strategies.[19] The scenario that returned the value closest to equipoise (46.1% of respondents recommended SSRF) was used to formulate inclusion and exclusion criteria for this trial.

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Inclusion criteria were: (1) hospitalization with three or more ipsilateral, bicortical, severely displaced, acute fractures of ribs 3 to 10. Severe displacement was defined as 50% or greater of rib width measured on axial CT chest imaging. The three severely displaced fractures did not need to be consecutive.; (2) two or more of the following pulmonary physiologic derangements, measured after initiation of locoregional anesthesia: (i) respiratory rate of 20 or greater breaths per minute, (ii) incentive spirometry (IS) less than 50% predicted, (iii) numeric pain score (NPS) greater than 5/10, and (iv) poor cough (as documented by respiratory therapists not involved in the trial); and (3) SSRF expected less than 72 hours from injury. The time between injury and SSRF was selected based upon recently published studies.[20,21]

Exclusion criteria were: 1) flail chest, defined as either clinical (paradoxical motion of a segment of the chest wall observed on physical examination) or radiographic (≥2 consecutive ribs each fractured in ≥2 places on CT chest); (2) younger than 18 years or 80 years or older; 3) moderate or severe traumatic brain injury (intracranial hemorrhage visualized on CT head with Glasgow Coma Scale score ≤ 12); (4) acute ventilator-dependent respiratory failure; (5) severe pulmonary contusion, defined as Blunt Pulmonary Contusion 18 (BPC18) score greater than 12[22]; (6) prior or expected emergency exploratory laparotomy, thoracotomy, or craniotomy during the index admission; (7) spinal cord injury; (8), pelvic fracture that had required, or was expected to require, operative intervention; (9) inability to accomplish activities of daily living independently prior to injury; (10) life expectancy less than 6 months; (11) pregnancy; (12) incarceration; and (13) enrollment longer than 72 hours from injury.

The trial consisted of both randomized and observational arms. This methodologic decision was made a priori and based on previously described high rates of declination of randomization for both surgical trials in general and SSRF trials specifically.[23,24] Eligible subjects were shown a standardized informational video that explained the purpose of the study, as well as the option for either randomization or observation.[25] In the case that randomization was selected by the patient, the site was provided with their next allocation by the lead trial center. Each study center followed an independent, block randomization schema. In the case of observation, the patient and clinical team had an informed discussion about the patient's preferred treatment course (SSRF vs. nonoperative); however, the final decision was made by the patient. The clinical team was specifically instructed to inform patients that there was no evidence to support one treatment strategy over the other. Data were analyzed on an intention to treat basis; subjects initially enrolled in the nonoperative arm who ultimately underwent SSRF were included in the nonoperative group.

The SSRF operation was standardized across sites to include general anesthesia, muscle sparring incisions, and pleural drainage. All fractures of ribs 3 to 10 were repaired whenever possible. Selection of implant system was left to the discretion of the operating surgeon.

Nonoperative management modalities were standardized as follows for both the operative and nonoperative groups: (1) acetaminophen 650 mg orally each 6 hours; (2) ibuprofen 600 mg orally each 6 hours; (3) gabapentin 300 mg orally thrice daily; (4) one of the following locoregional analgesic modalities, present at the time of enrollment: (i) thoracic epidural catheter, (ii) continuous infusion of a local anesthetic (i.e., on-Q pump), (iii) liposomal bupivacaine rib blocks, or (iv) paravertebral blocks or catheter. Choice of locoregional modality was left to the discretion of the clinical team. Narcotics were administered as needed and abstracted as an outcome variable.

The independent variable was SSRF. The primary dependent variable was the NPS at a 2-week follow-up visit. Additional in hospital outcomes included narcotic requirements (measured daily at 10:00 AM using equianalgesic dosing[26]), bedside IS (measured daily at 10:00 AM), pleural space complications, hospital length of stay (LOS), intensive care unit LOS, and mortality. Pneumonia was defined according to Centers for Disease Control and Prevention (CDC) guidelines.[27] A pleural space complication was defined as either retained hemothorax or

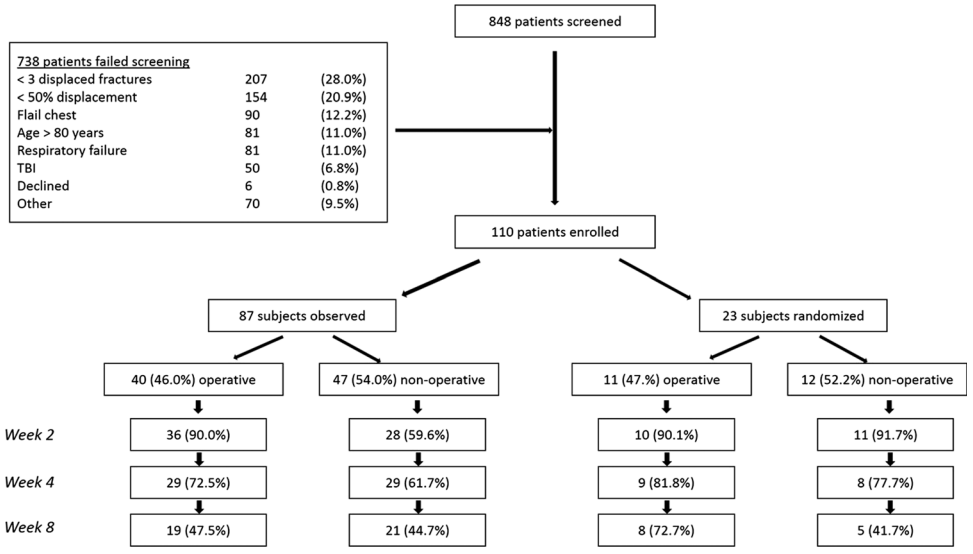

Figure 1. Derivation of the final sample, including portion of subjects in randomized vs. observational arms, operative vs. nonoperative groups, and follow-up visits. TBI, traumatic brain injury.

empyema necessitating a procedural intervention (e.g., tube thoracostomy or video-assisted thoracoscopic surgery) longer than 24 hours after admission. Narcotic requirements, IS, and QoL were also measured at 2 weeks, 1 month, and 2 months of follow-up visits. Pulmonary function tests were obtained at the 2-week follow-up visit. The QoL instrument was administered as a composite of the American Chronic Pain Association Quality of Life Scale[28] and the Chronic Pulmonary Disease Assessment Test,[29,30] modified to relate to rib fractures specifically. Both overall QoL (range, 1–11) and respiratory disability (range, 0–50; higher being worse), were abstracted. The QoL instrument is available as Supplemental Digital Content, Figure 1, http://links.lww.com/TA/B520. Data collection occurred via an online system managed by an independent bioinformatics company (Firefly, Inc., Iowa City, IA).

Sample size calculations were performed *a priori* for the outcomes of NPS, IS, forced expiratory volume in 1 second (FEV1), and QoL. The NPS returned the largest sample size (n = 74), and was thus selected and rounded up to 100 subjects to account for attrition. Specifically, we hypothesized that SSRF would decrease the mean NPS at the 2-week follow-up visit from 5 to 3 (standard deviation = 3), with alpha and beta error levels set to 0.05 and 0.80, respectively.[31,32]

The trial was registered with the U.S. National Institutes of Health (www.clinicaltrials.gov NCT03221595), institutional review board approval was obtained by each study center, and informed consent was obtained from each subject. A site initiation call was performed by the research coordinator (K.L.) with each of the satellite sites, during which the standardized aspects of nonoperative management, operative technique, and subject follow-up were described in detail via a slide presentation.

TABLE 1. Comparison of Baseline Parameters in Randomized vs. Observational Subjects (A) and Operative vs. Nonoperative Groups (B)

	(A) Randomized vs. Observational			(B) Operative vs. Nonoperative		
Parameter	**Randomized**	**Observational**	**SMD**	**Operative**	**Nonoperative**	***p***
N	23	87		51	59	
Operative	11 (47.8%)	40 (45.5%)	0.04			
Demographics						
Age (years)	55.3	54.5	0.09	54.6	55.3	0.85
Male	19 (86.4%)	63 (72.4%)	−0.35	39 (76.5%)	43 (74.1%)	0.83
Current smoker	5 (21.7%)	26 (29.6%)	−0.11	11 (21.6%)	19 (32.2%)	0.28
COPD or asthma	4 (17.4%)	7 (8.0%)	0.11	7 (13.7%)	3 (5.1%)	0.18
BMI > 30 kg/m^2	4 (17.4%)	19 (21.6%)	−0.11	12 (23.5%)	11 (19.0%)	0.49
Injury Pattern						
Fall	10 (43.5%)	28 (31.8%)	0.23	21 (41.2%)	17 (28.8%)	0.23
MVC	6 (26.1%)	26 (29.9%)	−0.08	13 (25.5%)	19 (31.7%)	0.53
ISS	12.5	13.0	0.10	13	14	0.80
Admission GCS score	14.5	14.8	−0.12	15	15	0.43
ICH	2 (8.7%)	8 (9.1%)	−0.02	3 (5.9%)	7 (11.9%)	0.33
Facial fracture	2 (8.7%)	7 (8.0%)	0.02	4 (7.8%)	5 (8.3%)	1.00
Spine fracture	6 (26.1%)	26 (29.6%)	−0.08	14 (27.5%)	18 (30.0%)	0.83
Pelvis fracture	2 (8.7%)	8 (9.1%)	0.02	4 (7.8%)	5 (8.5%)	1.00
Long bone fracture	1 (4.4%)	15 (17.1%)	−0.42	7 (13.7%)	9 (15.0%)	1.00
Solid organ injury	3 (13.0%)	17 (19.3%)	−0.18	12 (23.5%)	8 (13.6%)	0.22
BCVI	0	1 (1.1%)	−0.15	1 (2.0%)	0 (0.0%)	0.46
Chest wall injury						
Number of ribs fractured	6	7	−0.17	7	7	0.25
RibScore	2	2	−0.14	2	2	0.40
BPC18	2	2	−0.06	2	2	0.60
Hemothorax	8 (34.8%)	28 (31.8%)	0.15	22 (43.4%)	15 (25.4%)	0.07
Pneumothorax	10 (43.5%)	50 (56.8%)	−0.28	30 (58.8%)	30 (50.9%)	0.45
Chest tube <24 hours from admit	3 (13.0%)	12 (13.8%)	0.05	7 (13.7%)	8 (13.6%)	0.98
Clavicle fracture	3 (13.0%)	11 (12.5%)	0.01	5 (9.8%)	9 (15.3%)	0.57
Scapula fracture	5 (21.7%)	12 (13.6%)	0.21	8 (15.7%)	9 (15.0%)	1.00
*Loco-regional modality**						
Thoracic epidural catheter	8 (34.8%)	38 (43.7%)	0.57	24 (47.1%)	22 (37.3%)	0.62
Continuous intercostal nerve block	8 (34.8%)	19 (21.8%)		13 (25.5%)	14 (23.7%)	
Para vertebral block or catheter	3 (13.0%)	14 (16.1%)		6 (11.8%)	11 (18.6%)	
Liposomal bupivacaine rib block	6 (26.1%)	16 (18.4%)		9 (17.6%)	13 (22.0%)	

COPD, chronic obstructive pulmonary disease; BMI, body mass index; MVC, motor vehicle collision; GCS, Glasgow Coma Scale; ICH, intracranial hemorrhage; BCVI, blunt cerebrovascular injury; BPC18, blunt pulmonary contusion 18 score. (*), numbers do not sum to 110 because two subjects received more than one modality during the course of hospitalization.

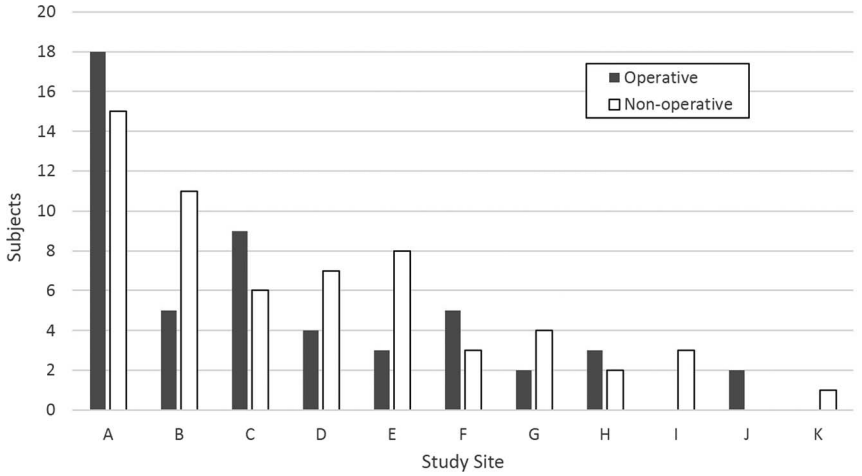

Figure 2. Subject enrollment by trial site, including portion of subjects in the operative vs. nonoperative groups.

During the enrollment phase of the trial, an online informational text messaging channel was used on which information was reiterated and clarification questions were posed and addressed (Slack Technologies, Inc., San Francisco, CA). The trial underwent oversight by a three person data safety monitoring board (DSMB) comprised of a trauma, thoracic, and orthopedic surgeon. An interim analysis was performed at 50% enrollment to access for harm.

Multiple investigators, including the principle investigator (PI) (F.M.P.), possessed potential conflicts of interest with industry. Furthermore, the trial was funded by an investigator (F.M.P.) initiated research grant from Depuy, Synthes, Inc. (Raynham, MA). Because of these potential conflicts, the trial was reviewed by the University of Colorado Office of Regulatory Research and a management plan was implemented a priori. The plan included the following: (1) the PI did not consent subjects; (2) the PI was not involved in data collection; (3) the PI was not involved in data analysis; (4) all data analyses were performed by an independent biostatistician not involved with either CWIS or the sponsor; (5) financial relationships between investigators and industry were disclosed to both subjects and their providers via a standardized letter; (6) no DSMB members were involved with the sponsor; (7) the majority of DSMB members were not CWIS members; and (8) the sponsor had no involvement in study design, data collection, data analysis, or article drafting.

All statistical analyses were done using SAS 9.4 (SAS Institute, Cary, NC). A single-interim analysis was performed at n = 67. Using the O'Brien-Fleming spending function the *p* value for declaring significance at this final analysis was set at *p* less than 0.045 in two-tailed tests. Numerical variables are expressed as mean (standard deviation) when normally distributed, and as median (interquartile range) when skewed. For the latter variables, box plots were used for graphing results. Categorical variables were expressed as frequencies and percentages. Normal distribution was assessed by the Kolmogorov-Smirnov test and visual inspection of histograms. We initially compared randomized to observational subjects regarding relevant baseline characteristics using standardized mean differences (SMD)[33]; SMD greater than 0.20 was considered a relevant imbalance. Once randomized and observational subjects were combined, we again assessed imbalances in baseline risk factors using SMD and statistical testing (Mann-Whitney test for numerical

TABLE 2. Comparison of NPS (A), Narcotic Consumption (B), and Spirometry (C) Between the Operative and Nonoperative Groups

	(A) NPS				(B) Narcotic Consumption				(C) Spirometry			
	N	Operative	Nonoperative	*p*	N	Operative	Nonoperative	*p*	N	Operative	Nonoperative	*p*
Hospital day 1	35,49	7.5	7.0	0.75	35,50	2.6	1.6	0.05	31,44	39.0%	39.5%	0.69
Hospital day 2	46,56	6.3	6.0	0.74	45,58	2.0	2.0	0.61	43,54	40.0%	41.5%	0.73
Hospital day 3	47,52	5.3	5.9	0.17	47,56	1.5	1.6	0.67	44,53	46.0%	49.0%	0.32
Hospital day 4	47,50	5.3	6.1	0.09	47,50	1.5	1.5	0.74	44,44	48.5%	49.5%	0.67
Hospital day 5	46,40	5.0	5.9	0.13	46,39	1.3	2.3	0.59	44,37	59.0%	51.0%	0.60
Hospital day 6	42,32	4.7	5.8	0.05	43,33	1.3	2.0	0.59	41,32	52.0%	49.0%	0.40
Hospital day 7	35,29	4.7	6.3	<0.01	34,30	1.0	2.3	0.10	32,27	55.0%	54.0%	0.39
Day of discharge	50,54	4.1	5.2	0.04	48,57	0.5	0.8	0.21	47,50	55.0%	49.0%	0.28
2 week follow-up	43,31	2.9	4.5	<0.01	31,17	0.5	1.2	0.05	42,29	87.0%	90.0%	0.41
4 week follow-up	35,30	2.4	3.3	0.03	20,14	0.3	1.5	0.13	35,27	100.0%	100.0%	0.72
8 week follow-up	26,19	1.5	3.3	0.02	10,8	0.2	0.5	0.08	24,18	100.0%	97.5%	0.17

N refers to the number of patients for whom data was available in the operative, followed by the nonoperative group.

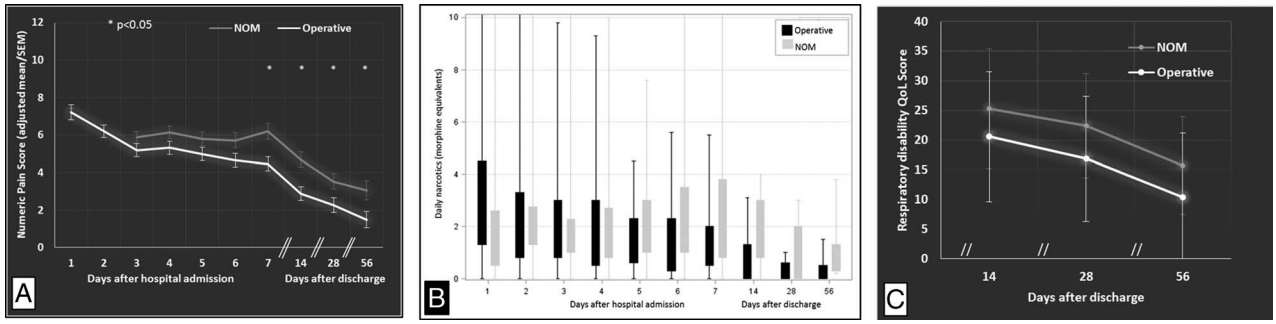

Figure 3. NPS (*A*), narcotic consumption (*B*), and respiratory disability-related quality of life (*C*) for the operative, as compared with the nonoperative (NOM) groups.

variables and Fisher exact test for categorical variables). Adjustment for confounders (relevant imbalances detected with the SMD) was done using linear mixed models accounting for clustering by institution and repeated measures within subjects. Skewed outcomes or outcomes with heteroscedasticity (i.e., unequal variances of compared groups) were transformed using the Box-Cox power transformation (lambda = 0.25 for all). All transformations resulted in normally distributed residuals in the linear mixed models. Interaction terms between SSRF and time were included in the models to assess whether the intervention modified the temporal trends of the outcome. If the interaction's p value was less than 0.045, we proceeded with pairwise contrasts between the two interventions by period. The missing value proportions for relevant demographic and injury description variables were 5% or less, thus no imputation was done.

RESULTS

One hundred ten subjects were enrolled from January 2018 to June 2019. The derivation of the final sample is shown in Figure 1; 738 (87.0%) of 848 patients failed screening; the most common reasons for screening failure were three or less displaced rib fractures (n = 207, 30.3%) and less than 50% displacement of fractures (n = 154, 21.3%). Six patients (0.8%) declined participation. Patients who failed screening, as compared with those who were enrolled, were more likely to be female (34% vs. 25%, respectively), older (58 vs. 55 years, respectively), and less severely injured (Injury Severity Score [ISS], 9 vs. 14, respectively).

Of the 110 subjects enrolled, 23 (20.9%) selected randomization and 87 (79.1%) selected observation. There were no differences noted between subjects who selected randomization as compared with observation with respect to comorbidities, injury patterns, and likelihood of operative intervention (Table 1A); thus, the randomized and observational groups were combined to perform all remaining analyses. There was a higher percentage of male patients in the randomization arm versus the observational arm (86% vs. 72%, respectively).

Of the 110 subjects enrolled, 51 (46.4%) underwent surgery. The distribution of enrollment by study site, as well as the proportion of operative versus nonoperative subjects, is shown in Figure 2. One subject (0.9%) was enrolled in the nonoperative arm (observational cohort) and crossed over to the operative arm due to persistent pain; this subject was analyzed with the nonoperative group.

Of the 110 subjects enrolled, 85 (77.3%) had at least one follow-up visit. There were no significant differences between subjects who followed up, as compared with patients who did not follow-up, with regard to randomization status (22% vs. 17%, respectively, $p = 0.29$), operative arm (48% vs. 31%, respectively, $p = 0.25$), age (43 vs. 46 years, $p = 0.41$), ISS (13 vs. 17, respectively, $p = 0.36$), RibScore[34] (2 for both groups, $p = 0.82$), or number of rib fractures (7 vs. 8, respectively, $p = 0.59$).

Baseline characteristics of subjects in the operative versus nonoperative groups are summarized in Table 1B. Demographics, injury severity, associated injuries, and rib fracture patterns were similar between groups, with the exception of admission hemothorax, which trended toward being more common in the operative, as compared with the nonoperative group (43.4% vs. 25.4%, respectively, $p = 0.07$). All subjects in both groups had some form of locoregional analgesia

TABLE 3. Comparison of Overall QoL, As Well as Respiratory Disability-Related QoL Between the Operative and Nonoperative Groups

	n	Operative	Nonoperative	*p*
Overall QoL (1–11)				
2 week follow-up	42,29	5	5	0.17
4 week follow-up	35,29	8	6	0.13
8 week follow-up	26,21	10	7	0.28
Respiratory disability-related QoL (0–50)				
2 week follow-up	43,29	21	25	0.03
4 week follow-up	30,30	17	22	0.07
8 week follow-up	25,21	16	10	0.27

N refers to the number of patients for whom data was available in the operative, followed by the nonoperative group.

placed on a median hospital day 2 (range, 1–4). Choice of locoregional modality did not vary by either randomization or operative status.

In the operative group, SSRF occurred 2 days after admission (0–3). The median length of surgery was 2.5 hours (1–4), 4 ribs repaired (3–6), and the ratio of ribs repaired to fractured 0.6 (0.5–0.8). All available proprietary fixation platforms were used. Evacuation of hemothorax was performed in 37 (72.6%) cases and pleural irrigation in 39 (76.5%) cases. Additional intraoperative adjuncts included bronchoscopy (n = 40, 78.4%), video-assisted thoracoscopic surgery (n = 19, 37.3%), and placement of a subcutaneous drain (n = 3, 5.9%).

There was no difference between the operative and nonoperative groups in either hospital (6 days) or intensive care unit (2 days) LOS. Mechanical ventilation was uncommon and did not differ between groups (median ventilator days for each group = 0, $p = 0.79$). Pneumonia was uncommon and did not differ between the operative and nonoperative group (2.0% vs. 6.7%, respectively, $p = 0.37$). Pleural space complications were significantly less common in the operative group as compared with the nonoperative group (0% vs. 10.2%, respectively, $p = 0.02$). Readmission rates did not differ between the operative and nonoperative groups (3.9% vs. 6.8%, respectively). There were no cases of reoperation, hardware infection, or hardware failure following SSRF. There were no mortalities in either group.

The NPS at the 2-week outpatient follow-up (primary outcome) was significantly lower in the operative, as compared with the nonoperative group (2.9 vs. 4.5, respectively, $p < 0.01$). Furthermore, the NPS was significantly lower in the operative, as compared with the nonoperative group at hospital day 7, as well as both the 4-week and 8-week follow-up visits (Table 2A and Fig. 3*A*). There were no significant differences in NPS between groups for hospital days 1 to 6.

Narcotic consumption, shown in Table 2B and Figure 3*B*, trended toward being higher in the operative, as compared with the nonoperative group on hospital day 1 (2.6 vs. 1.6, respectively, $p = 0.05$). However, this trend reversed beginning at hospital day 7, when the amount of narcotic equivalents consumed by the nonoperative, as compared with the operative group, was more than two times higher, (2.3 vs. 1.0, respectively, $p = 0.10$). This finding persisted through the 2-week, 4-week, and 8-week follow-up visits. However, at no point in time did these differences achieve statistical significance.

There were no significant differences in spirometry recordings between the operative and nonoperative groups at any timepoint (Table 2C). Forced expiratory volume in 1 second, obtained at the 2-week outpatient follow-up visit, was equivalent between the operative and nonoperative groups (75.5% vs. 75.8% predicted, respectively, $p = 0.76$).

Quality of life data are summarized in Table 3. There were no significant differences observed in overall QoL between groups at any timepoint. Respiratory disability was reported as significantly lower in the operative, as compared with the nonoperative group, at the 2-week follow-up visit (21 vs. 25, respectively, $p = 0.03$). However, the differences were not statistically significant at the 4-week and 8-week follow-up visits (Fig. 3*C*).

DISCUSSION

This investigation represents the first prospective, multicenter trial of SSRF, and specifically of SSRF in patients without flail chest. The key finding of this study is that SSRF, as compared with nonoperative management, improved the primary outcome of pain control at 2-week follow-up for patients with three or more displaced fractures in the absence of flail chest. As compared with nonoperative management, SSRF also resulted in fewer pleural space complications, and improved self-reported respiratory disability at 2-week follow-up. No differences in additional outcomes during the index hospitalization, spirometry, or follow-up pulmonary function tests were observed. Finally, there was a nonsignificant trend toward decreased narcotic consumption in the operative group. Importantly, SSRF in this trial was performed relatively early (within 72 hours) postinjury.

This project specifically targeted a patient population without either clinical or radiographic flail. Furthermore, to mitigate any potential confounding in outcomes, such as NPS and narcotic consumption, we excluded patients who required other major operations. We also excluded patients with both ventilator-dependent respiratory failure and severe pulmonary contusions to isolate, in so far as possible, the effects of SSRF on pulmonary disability. Finally, we sought to capture any potential benefit of SSRF by (1) requiring clinical pulmonary derangement in addition to radiographic findings for trial inclusion, (2) mandating that the surgery be performed early after injury, and (3) selecting centers experienced in SSRF.

These decisions intentionally resulted in a sample with a relatively low injury severity and, for the most part, isolated displaced rib fractures. It was, therefore, expected that general outcomes, such as respiratory failure, pneumonia, and mortality, would be relatively infrequent and not differ between the operative and nonoperative groups, as they may have in prior studies of severely injured, multiple-trauma patients with flail chest. In the latter cases, the immediate goal of SSRF was to restore chest wall mechanics to the point of independent respiration. By contrast, the main considerations in patients such as ours are pain control and pleural space complications; SSRF significantly improved both of these outcomes in this trial.

We believe the benefits derived from SSRF observed in this trial to be moderate. Decreases in NPS were, on average, 1.5 points. Furthermore, improvements in the respiratory disability-related QoL were on the order of 15%. Decreases in narcotic consumption, though not statistically significant, appeared more substantial, and on the order of a halving of requirements. Accordingly, it is worth noting that the reduction in pain in the operative arm occurred despite (1) undergoing a surgical intervention and (2) taking at least the same quantity of narcotics. This observation is of particular relevance given the current opioid epidemic.[40] Finally, it is our contention that any significant reduction in pain is of clinical importance to patient care.

Our data showed a significantly decreased incidence of pleural space complications in the operative group, despite a trend toward an increased incidence of admission hemothorax. This finding is consistent with prior retrospective data in patients with flail chest.[41] Hemothorax is common following displaced

rib fractures,[20] and approximately one fifth of cases of retained hemothorax progress to empyema.[42] Multiple factors likely contribute to SSRF mitigating the risk of both retained hemothorax and empyema, including reduction and fixation of the rib fractures, pleural irrigation and, sterile, guided chest tube placement. Decreasing the risk of subsequent pleural space complications should be considered a benefit of SSRF.

Daily spirometry values, FEV1, LOS, and readmission rates were equivalent between the operative and nonoperative groups. These findings underscore the notion that SSRF in this relatively uninjured patient population had a more modest effect on outcomes as compared with patients with flail chest. Specifically, although pain and respiratory disability-related QoL were improved in the operative arm, these improvements were not enough to demonstrably alter pulmonary function, readmission or overall QoL. Ultimately, expectation management based in part on our findings is crucial to an individualized discussion with patients regarding the risks and benefits of SSRF specific to their fracture pattern.

This trial is limited by loss to follow-up, a relatively short follow-up period, and a lack of generalizability beyond both subject and site inclusion criteria. Unequal enrollment across centers may have resulted in unmeasured institutional bias. Attrition resulted in a lack of power when analyzing outcomes at both the 4-week and 8-week follow-up visits. Additional unmeasured covariates that could influence NPS, such as preinjury narcotic use and substance abuse disorder, were not abstracted. Allowing providers to prescribe both narcotics and logo-regional analgesic modality according to their own institutional protocols was a decision made to minimize complexity at the expense of introducing some degree of variability. We did not abstract charge information for this trial, precluding any analysis of the effect of SSRF on hospital, patient, or societal costs.

One additional limitation that warrants specific discussion is the pooling of randomized and observational patients, which has both advantages and disadvantages. Patients who selected operative management may have differed from those who selected nonoperative management in unmeasured ways. Possible reasons for selecting operative management include more pain, as well as a higher level of trust in the medical system. However, these reasons are neither supported by our data (e.g., equivalent baseline NPS between groups) nor should they exaggerate any potential benefit of SSRF.

The decision to include both randomized and observational options in this trial was considered to be a necessary practical concession. The decision was made a priori to successfully complete the trial within a timeline relevant to address an urgent question in the field of SSRF. This reasoning was validated prospectively as nearly 80% of subjects declined randomization. Observational trials, through often viewed as inferior to randomized clinical trials, offer certain unique advantages, including participants being more representative of patients in clinical practice, and timeliness of completion.[43]

In summary, in this multicenter, prospective, clinical trial, we demonstrated a significant improvement in the primary outcome of pain at 2-week follow-up in patients with displaced, nonflail fracture patterns who underwent SSRF, as compared with nonoperative management. We also observed both an elimination of pleural space complications and an improvement in respiratory disability-related QoL at 2-week follow-up after SSRF, as compared with nonoperative management. All other outcomes analyzed did not differ significantly between operative and nonoperative groups, underscoring a more modest benefit to SSRF in this patient population. These data support a role for SSRF in patients without either clinical or radiographic flail chest, with recognition of trial inclusion criteria, including evidence of pulmonary derangements due to the fractures, early surgery, and performance of the operation at an experienced center.

AUTHORSHIP

F.M.P., K.L., A.R.D., E.A.E., S.M., B.S., White participated in the literature search. F.M.P., A.R.D., White participated in the study design. K.L. participated in the data collection. K.L. participated in the data analysis. F.M.P., K.L., Z.B., A.R.D., E.A.E., L.L., S.M., B.S., F.Z., White participated in the data interpretation. F.M.P., K.L., Z.B., A.R.D., E.A.E., L.L., S.M., L.P., B.S., G.S., B.T., F.Z., C.D., Semon, and White participated in the critical revisions.

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DISCLOSURE

F.M.P. is a paid educator (past) and research funding (current) for DePuy Synthes, Inc. E.E. is a paid educator (current) for DePuy Synthes, Inc. L.L. is a paid consultant (current) for Acute Innovations, Inc, KLS Martin, Inc., and DePuy Synthes, Inc. L.P. is a paid educator (current) for DePuy Synthes, Inc. B.S. is a paid educator (current) for Acute Innovations, Inc. Bradley Thomas MD: paid educator (current) for Zimmer Biomet, Inc. A.R.D. is a paid consultant (past) for Zimmer Biomet, Inc. and DePuy, Snthes, Inc. All the other authors declare no conflicts of interest.

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