A Multicenter, Prospective, Controlled Clinical Trial of Surgical Stabilization of Rib Fractures in Patients with Severe, Non-flail Fracture Patterns (CWIS NON-FLAIL)

NCT: 03221595

Study Protocol and Statistical Analysis Plan

Date: 12/14/2018

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Protocol #: 17-1432 (NCT: 03221595)
Project Title: A Multicenter, randomized controlled trial of surgical stabilization of rib fractures in patients with severe, non-flail fracture patterns (CWIS NON-FLAIL)
Principal Investigator: Fredric M. Pieracci MD, MPH, FACS Version
Date: 12/14/18

I. Hypotheses and Specific Aims:

The objective of this trial is to investigate the efficacy of surgical stabilization of rib fractures (SSRF), as compared to non-operative management, for hospitalized patients with non-flail, severe rib fractures. The study will be conducted within expert, high volume centers that participate in the Chest Wall Injury Society (CWIS). The hypothesis of this trial is that SSRF, as compared to standardized non-operative management, improves pulmonary function, risk of complications, quality of life, pain control, and reduces the need for opioid pain medication among patients with severe, non-flail chest fracture patterns.

II. Background and Significance:

Rib fractures are the most common serious injury following blunt trauma, and occur in approximately 10% of trauma patients [1]. Despite improvements in the care of rib fracture patients, outcomes remain poor and have not changed substantially over the last 15 years [2]. Poor outcomes resulting from rib fractures include both acute complications (e.g., pneumonia, prolonged mechanical ventilation, and death) and chronic disability (e.g., pain, dyspnea, and loss of productivity).

Over the last 10 years, surgical stabilization of rib fractures (SSRF) has emerged as a promising technology for the management of patients with severe chest wall injuries [3]. Conceptually, SSRF applies the fundamental orthopedic principles of reduction and fixation to rib fractures, restoring chest wall stability and minimizing pain with respiration, splinting, and secretion accumulation. The advent of muscle-sparing [4] and even minimally-invasive surgical techniques [5], as well as a relatively low complication rate [6], has improved the appeal of this operation.

To date, three randomized clinical trials (RCTs) [7-9] and three meta-analyses of these and other trials [10-12] have limited their scope to patients with flail chest, a specific clinical diagnosis characterized by paradoxical motion of a portion of the chest wall due to fractures of two or more ribs in at least two places. Flail chest represents the most severe form of chest wall injury, with an associated, very high morbidity and mortality. Each of the aforementioned RCTs, as well as multiple prospective, non-randomized investigations [13, 14], have found a benefit to SSRF as compared to best medical management in this patient population. Accordingly, expert consensus statements have recommended this operation in this subset of patients [3, 15].

Based upon the favorable reported efficacy of SSRF in patients with flail chest, many surgeons have broadened indications to patients with severe, non-flail rib fracture patterns, most commonly ≥ 3 severely displaced fractures. Although these injuries differ anatomically from flail chest, many of the same pathophysiologic principles are at work: namely, painful motion at the fracture sites that cause respiratory compromise, bony bridging [16], and risk of subsequent non-union, chronic pain, and restrictive lung disease. However, it is not clear if stabilization of these fractures confers the same benefits as in the case of flail chest. This lack of efficacy data has been recognized in recent guidelines, which were unable to recommend SSRF for non-flail fracture patterns pending further data [15]. Furthermore, long term quality of life data for both flail and non-flail fracture patterns managed with SSRF are not available.

The use of SSRF is increasing exponentially. Somewhat alarmingly, nearly one half of the procedures were performed in patients without flail chest [17]. A combination of the favorable results observed for SSRF in flail chest, the increasing prevalence of SSRF for non-flail chest, and the lack of quality evidence to support this operation in this patient population, lead to the design of the current RCT.

III. Preliminary Studies/Progress Report:

Our group has previously conducted a similar, single institution, observational study, which included mostly patients with flail chest, but also approximately 20% of patients without flail chest [13]. In this study, SSRF was beneficial. Other groups have reported favorable outcomes with SSRF in non-flail chest patients, although these patients have comprised a small minority of the total patients in the study group [14].

IV. Research Methods

A. Outcome Measure(s):

- **Primary Outcome:**

1. **Chest Wall Specific Quality of Life Questionnaire**: Obtained at two week, one month, and two month follow up visits (**Attachment 1**).

- **Secondary Outcomes:**

2. **Numeric pain score**: Obtained daily while hospitalized, and at two week, one month, and two month follow-up
3. **Narcotic use**: Obtained daily while hospitalized, and at two week, one month, and two month follow-up visits and using a standardized equi-analgesic scale (**Attachment 2**)[18].
4. **Incentive spirometry**: Obtained daily while hospitalized, and at two week, one month, and two month follow-up visits (**Attachment 3**). The best value of three attempts will be used.
5. **Pulmonary function testing**: Obtained once at 2 week follow-up visit

B. Description of Population to be Enrolled:

Inclusion Criteria:

In an effort to identify non-flail rib fracture patients for whom there is relative equipoise for SSRF vs. non-operative management, the CWIS conducted a survey of surgeons who perform SSRF regularly [19]. The survey presented a series of hypothetical trauma patients with non-flail chest, severe rib fractures. Patient age, degree of traumatic brain injury, and number of deranged pulmonary physiologic variables at the time of consideration for surgery were varied, and respondents were asked if they would recommend SSRF. The degree of consensus which most closely approximately true equipoise was 44.8%; this hypothetical scenario involved a patient with

≥ 3 fractures with at least 50% displacement, aged 18 – 80 years, and with either no or mild traumatic brain injury (TBI). This hypothetical patient served as the basis for our inclusion criteria:

1. Hospitalization with ≥ 3 severely displaced (≥ 50% of rib width) acute rib fractures.
2. Two or more of the following pulmonary physiologic derangements (at the time of consideration for enrollment and after best medical therapy).
    a. Respiratory rate > 20 breaths per minute
    b. Incentive spirometry < 50% predicted (**Attachment 3**)
    c. Numeric pain score > 5
    d. Poor cough (as documented by respiratory therapist)
3. Surgery anticipated < 72 hours from injury

Exclusion Criteria:

1. Age < 18 years or ≥ 80 years
2. Flail chest: either radiographic or clinical. Radiographic flail chest is defined on CT chest as ≥ 2 ribs each fractured in ≥ 2 places. Clinical flail is defined as visualization of a segment of chest wall with paradoxical motion on physical exam.
3. Moderate or severe traumatic brain injury (Intra-cranial hemorrhage visualized on CT head with GCS at the time of consideration for enrollment < 12)
4. Intubation
5. Severe pulmonary contusion, defined as Blunt Pulmonary Contusion 18 (BPC18) score > 12 [20].
6. Prior or expected emergency exploratory laparotomy during this admission.
7. Prior or expected emergency thoracotomy during this admission.

8. Prior or expected emergency craniotomy during this admission.
9. Spinal cord injury
10. Pelvic fracture that has required, or is expected to require, operative intervention during this admission.
11. The patient was unable to accomplish activities of daily living independently prior to injury (e.g., dressing, bathing, preparing meals).
12. Pregnancy.
13. Incarceration.

C. Study Design and Research Methods

Study type:

Multicenter, randomized, non-blinded, clinical trial, with reserved option to collect data prospectively on subjects who decline randomization.

Study Arms:

1. Standardized best medical management of rib fractures
2. Standardized best medical management of rib fractures plus surgery (SSRF)

Recruitment

Historically, about 50% of patients choose not to be randomized in trials that assign patients to either surgery or not [21]. This is due to many reasons; but one important one is the hesitancy to be randomized to an operation or not. This concern is of course understandable, and our plan for this trial is to prepare for this degree of declination and have a plan in place to still use these patients' de-identified information for research (if they consent to it) to better understand of the optimal treatment of patients with severe rib fractures. We also want to maximize the likelihood that the study will be completed in a timely fashion in the ethical interest of the subjects.

We believe that it is methodologically appropriate to collect patients' information who do not wish to be

randomized given the following conditions, all of which we have been carefully incorporated into the study design:

1. Subjects will first be asked if they are interested in hearing about a research study related to the treatment of their rib fractures prior to discussing randomization. If they decline, the discussion of enrollment will end there,Those receptive to participation will be informed up-front of randomization and the possibility of observation status should they decline randomization. In addition to discussion by study personal, a video will be displayed to clarify the study intervention and mission [attachment 6]. This video will be shown to all patients who are approached for consent. It begins by outlining the option for randomization in the trial. It next describes the option for observation should randomization not be desired. This video will be supplemented by our research personnel, who will reinforce the study design, and then ask the patient to verbalize the information back. This is intended to minimize the risk of coercion.
2. Patients are approached for consent only after meeting 16 inclusion/exclusion criteria, which have been carefully specified in the protocol. This process will, by design, create a very similar group of patients with similar injury patterns and physiology, regardless of their decision to be randomized or not. In a recent trial, we found no significant clinical differences between patients who agreed to and declined randomization to a pain medication for rib fractures in our SICU (the same patient population as for the current trial) [22] Finally, any clinically relevant differences that may occur between patients who elect randomization vs. those who do not will be identified and controlled for in regression analyses.
3. In order to minimize confounding (specifically, selection bias), patients in the observation arm will first be analyzed separately from those who are randomized, looking for significant differences in clinically relevant variables. Furthermore, when and if patients are ultimately grouped together for analysis (for example, randomized operative and observational operative), the randomized variable will be reported and controlled for using regression analysis. In the data analysis phase, four groups of patients will be reported: 1) those randomized to surgery, 2) those randomized to no surgery, 3) those observed who elect surgery and 4) those observed who elect no surgery

Participating Centers:

Recently, the CWIS was formed as an international group of expert chest wall surgeons (www.cwisociety.org). The CWIS membership is comprised of experienced, high volume SSRF surgeons with established successful protocols, pathways, and outcomes of patients with severe rib fractures. This group is also academic, published, and driven to conduct high quality research to refine the indications for SSRF. Participating centers were identified through the CWIS research committee based upon these criteria.

Standardization of management protocols

Both groups (SSRF and medical management) will receive identical non-operative management, including standardized analgesic and pulmonary toilet protocol.

Standardized analgesia will include 1) standing acetaminophen 650 mg PO Q6h; 2) standing ibuprofen 600 mg PO q6H; 3) standing gabapentin 300 mg PO tid 4) one of the following locoregional modalities a) thoracic epidural catheter; 2) pain catheter (i.e., on-Q pump); c) liposomal bupivacaine rib blocks. Beyond these medications, narcotics will be administered as needed and abstracted as an outcome variable. Additional modalities (e.g., IV ketamine) will be discouraged but abstracted when used. All of these are medications that are dictated by our clinical protocol for all patients with rib fractures. None of these medications will be used for research purposes only i.e. all rib fracture patients will receive all of these medications whether they are in the trial or not because they are clinically indicated. Standardized pulmonary toilet will include hourly incentive spirometry and cough assist q4 hours.

For the SSRF group, the surgery will be standardized as follows: 1) flexible bronchoscopy on all patients; 2) muscle sparing incision whenever possible; 3) repair of all displaced fractures of ribs 3-8; 4) pleural irrigation with 500 mL sterile saline; 5) pleural drainage with either straight chest tube or silastic drain (18F – 24F); 6) loco-regional anesthesia using one of the above modalities.

Randomization:

Randomization will be accomplished at the lead study center (Denver, CO) using a standard function in Microsoft Excel that randomly chooses either the number 0 or 1. Each center will receive their own randomization log, such that approximately 50% of subjects from each center are randomized to surgery.

Of note, we anticipate a relatively high rate of declining randomization (approximately 50%). As such, we have incorporated a secondary, observational option for patients who decline randomization. In this arm, the decision to perform SSRF will be clinical, and left to the patient and their treatment team. Whatever that decision is, patients will be asked if they agree to prospective data collection, including the same endpoints as thoserandomized.

Sample size calculation, trial feasibility, and projection duration:

Sample size calculations for the primary and secondary outcome variables are shown below. The largest N total of 74 was selected and rounded up to 100 to maximize the likelihood of obtaining a significant difference. The mean annual number of SSRF performed per study center on patients who meet study criteria is 18. Assuming a 40% study decline rate, this would involve each center enrolling 11 patients over a one year time (lead site can enroll up to study total of 100 in the event the other centers have low enrollment numbers.) The study is thus feasible and powered to achieve target sample size in one year

Outcome variable	Mean (SD) non-op	Mean (SD) op	Alpha	Beta	N / group	N total
Numeric pain score	3 (3)	5 (3)	0.05	0.80	37	74
Incentive spirometry (mL)	650 (300)	850 (300)	0.05	0.80	24	48
FEV1 % pred (PFTs)	67% (20%)	85% (20%)	0.05	0.80	16	42
Overall QOL	6 (2)	8 (2)	0.05	0.80	17	34

Study Conduct:

The study will be conducted and reported in accordance with the recommendations of the Consolidated Standards of Reporting Trials Statement [23] and registered with the U.S. National Institutes of Health (clinicaltrials.gov). The study will be approved by the Colorado Multiple Institution Review Board (COMIRB) and each sub site's IRB. An independent data safety monitoring committee, comprised of 3 members that are all not involved with the trial (and where the majority of the 3 will be unaffiliated with the Chest Wall Injury Society)will submit written reports to COMIRB and the study sponsor after the first 50 patients have been enrolled, followed by increments of 50 enrollments, thereafter. Adverse events will be recorded and reported to both the data safety monitor and COMIRB. No interim analysis is planned.

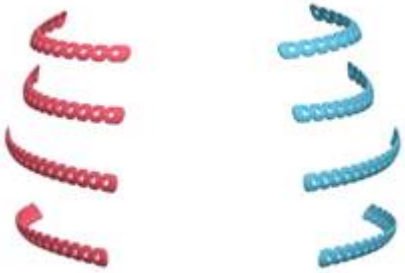
Each satellite site will contact the lead site PI or RC to obtain approval to proceed with consenting each subject, based on a review of the patient's injury mechanism, fracture pattern, and inclusion/exclusion criteria.

D. Description, Risks and Justification of Procedures and Data Collection Tools:

Surgical stabilization of rib fractures:

This is an approximately two hour operation that occurs under general anesthesia. Fractures of ribs 3-10 are repaired using thin, titanium plates through small incisions that minimize muscle division. These plates are the width of a typical rib and vary in length (**Attachment 4**). These plates are applied directly to the bone, across the fractures, typically on the outside of the rib Once the fractures are reduced, the plates are permanently fixed in place with screws, allowing the fractured pieces of rib to realign.

There are several different companies that make and supply these plates and there may be a few different options available in a single hospital, depending on what the business contracts are with the suppliers for their hospital and what is in stock on the day of the operation. The device and the procedure in which to use them are all essentially the same across all brands. All are made out of titanium, all are about the width of a pen and vary in length depending on the extent of the patient's fracture pattern, and all are permanently fixed on place with screws. Below are two different companies that at used at Denver Health and Hospital.



DePuy Synthes

KLS Martin

This trial does not dictate the use of a specific hardware system for the operation. There are currently four companies that offer FDA-approved rib fixation systems: DePuy Synthes, KLS Martin, Zimmer Biomet, and Acute Innovations. This is not an investigation of the superiority/inferiority of any particular hardware system, but rather an investigation of what is the best management of severe non-flail rib fractures: operative or non-operative. Choice of system is left to the discretion of the operating surgeon, as no data exist documenting the superiority of one system over the other. We specifically have not mandated the use of the study sponsor's system in order to create as much distance as possible between the influence of the study sponsor and the research team. In a pre-initiation site survey, all four fixation systems were used among participating centers. Three of the four systems are used at Denver Health Medical Center, depending on availability and surgeon preference. Finally, use of any of the hardware systems will be for an FDA approved indication and patient population, so we do not believe that an IND is required.

During the surgery, any blood that has accumulated in the pleural space will also be irrigated and suctioned out. Loco-regional pain control will also be administered as either rib blocks or an indwelling pain catheter. Finally, bronchoscopy will be performed to suction out any mucous which may have accumulated in the lungs as a result of not taking deep breaths. Risks of surgery include post-operative pain, bleeding, infection, and movement of the plates. Bleeding, infection, and movement of the plates are each very rare, and occur in less than 1% of patients who undergo the procedure. The surgeons at Denver Health have performed approximately 120 operations to treat rib fractures with plates.

Pulmonary function tests:

The subject will be asked to breath into a straw-like tube and values are recorded. This is non-invasive and painless. Some shortness of breath after the test is completed may occur and resolves after a few seconds. The testing is administered by certified respiratory therapists at Denver Health.

Justification of procedures:

SSRF is an established surgery for the treatment of severe rib fractures, and is recognized as such in expert consensus statements [3]. There exists equipoise regarding the benefit of SSRF in the specific study population targeted for this trial [19]

E. Potential Scientific Problems:

The main anticipated problem is a relatively high rate of declining randomization to operative vs. non-operative arms. We anticipate that approximately 50% of eligible patients approached will de- cline randomization. In anticipation of this, we have added an observation arm to the study; patients who decline randomization will be asked permission to collect their data throughout the same two month follow up period. In this case, treatment assignment to operative vs. non-operative is at the discretion of the patient and their treatment team.

Additional problems include coordination of a multiple site study- the investigators have budgeted into the grant a 1.0 FTE research coordinator whose sole responsibility will be this study.

Finally, standardization of management protocols, specifically both operative and non-operative. Standardized protocols will be distributed and monitored for adherence. Furthermore, a site initiation questionnaire has been drafted and will be completed by all centers interested in participation. Centers will be selected based on homogeneity in responses.

A. Data Analysis Plan: A standardized data collection tool will be used (Firefly Labs LLC). A sample data collection tool is attached (**Attachment 5**). All statistical analysis will be conducted using SAS version 9.4 (SAS Inc., Carey, NC). Statistical significance will be defined as $p < 0.05$. The distribution of continuous variables

will be accessed for normality using the Kolmogorov- Smirnov test. Normally distributed continuous variables will be compared using the student's t-test. Non-normally distributed variables will be compared using the Wilcoxon Rank test. Categorical variables will be compared using the chi-squared test, unless expected cell counts were < 10, in which case Fischer's exact test was used.

Patients from both the randomized and observational cohorts will be grouped together in one analysis, and separately in a sub group analysis. The randomized and observed groups will be compared with respect to demographics, injury patterns, and rib fracture severity to unmask any potential biases.

B. Summarize Knowledge to be Gained: SSRF is being performed increasingly outside of the indication of flail chest. Although there may be benefit to SSRF in patients without flail chest, there exists equipoise in this specific patient population as recognized by surveyed members of CWIS. We believe that it is imperative to establish evidence to support this operation in this patient population

F. References:

1. Fabricant L, Ham B, Mullins R, Mayberry J: **Prolonged pain and disability are common after rib fractures**. *American journal of surgery* 2013, **205**(5):511-515; discusssion 515-516.
2. Mayberry JC, Kroeker AD, Ham LB, Mullins RJ, Trunkey DD: **Long-term morbidity, pain, and disability after repair of severe chest wall injuries**. *The American surgeon* 2009, **75**(5):389-394.
3. Pieracci FM, Majercik S, Ali-Osman F, Ang D, Doben A, Edwards JG, French B, Gasparri M, Marasco S, Minshall C *et al*: **Consensus statement: Surgical stabilization of rib fractures rib fracture colloquium clinical practice guidelines**. *Injury* 2017, **48**(2): 307-321.
4. Pieracci FM, Rodil M, Stovall RT, Johnson JL, Biffl WL, Mauffrey C, Moore EE, Jurkovich GJ: **Surgical stabilization of severe rib fractures**. *The journal of trauma and acute care surgery* 2015, **78**(4):883-887.
5. Pieracci FM, Johnson JL, Stoval RT, Jurkovich GJ: **Completely Thoracoscopic, Intrapleural Reduction and Fixation of Severe Rib Fractures**. *Trauma Case Reports* 2015.
6. Doben AR, Eriksson EA, Denlinger CE, Leon SM, Couillard DJ, Fakhry SM, Minshall CT: **Surgical rib fixation for flail chest deformity improves liberation from mechanical ventilation**. *Journal of critical care* 2014, **29**(1):139-143.
7. 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**. *The Journal of trauma* 2002, **52**(4):727-732; discussion 732.
8. Marasco SF, Davies AR, Cooper J, Varma D, Bennett V, Nevill R, Lee G, Bailey M, Fitzger- ald M: **Prospective randomized controlled trial of operative rib fixation in traumatic flail chest**. *Journal of the American College of Surgeons* 2013, **216**(5):924-932.
9. Granetzny A, Abd El-Aal M, Emam E, Shalaby A, Boseila A: **Surgical versus conservative treatment of flail chest. Evaluation of the pulmonary status**. *Interactive cardiovas- cular and thoracic surgery* 2005, **4**(6):583-587.
10. Leinicke JA, Elmore L, Freeman BD, Colditz GA: **Operative management of rib fractures in the setting of flail chest: a systematic review and meta-analysis**. *Annals of surgery* 2013, **258**(6):914-921.
11. Slobogean GP, MacPherson CA, Sun T, Pelletier ME, Hameed SM: **Surgical fixation vs nonoperative management of flail chest: a meta-analysis**. *Journal of the American Col- lege of Surgeons* 2013, **216**(2):302-311 e301.
12. Coughlin TA, Ng JW, Rollins KE, Forward DP, Ollivere BJ: **Management of rib fractures in traumatic flail chest: a meta-analysis of randomised controlled trials**. *The bone & joint journal* 2016, **98-B**(8):1119-1125.
13. Pieracci FM, Lin Y, Rodil M, Synder M, Herbert B, Tran DK, Stoval RT, Johnson JL, Biffl WL, Barnett CC *et al*: **A prospective, controlled clinical evaluation of surgical stabilization of severe rib fractures**. *The journal of trauma and acute care surgery* 2016, **80**(2):187-194.
14. Majercik S, Cannon Q, Granger SR, VanBoerum DH, White TW: **Long-term patient outcomes after surgical stabilization of rib fractures**. *American journal of surgery* 2014, **208**(1):88-92.
15. 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**. *The journal of trauma and acute care surgery* 2017, **82**(3):618-626.
16. Marasco S, Liew S, Edwards E, Varma D, Summerhayes R: **Analysis of bone healing in flail chest injury: Do we need to fix both fractures per rib?** *The journal of trauma and acute care surgery* 2014, **77**(3):452-458.

17. Kane ED, Jeremitsky E, Pieracci FM, Majercik S, Smith SR, Doben AR: **Surgical Stabilization of Rib Fractures: Increasing at an Alarming Rate?** *Oral Presentation at 47th Annual Meeting of the Western Trauma Association, March 5-10, Snowbird, UT* 2017.
18. Barr J, Fraser GL, Puntillo K, Ely EW, Gelinas C, Dasta JF, Davidson JE, Devlin JW, Kress JP, Joffe AM *et al*: **Clinical practice guidelines for the management of pain, agitation, and delirium in adult patients in the intensive care unit**. *Critical care medicine* 2013, **41**(1):263-306.
19. 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**. *International Orthopedics* 2017, **In press**.
20. Tyburski JG, Collinge JD, Wilson RF, Eachempati SR: **Pulmonary contusions: quantifying the lesions on chest X-ray films and the factors affecting prognosis**. *The Journal of trauma* 1999, **46**(5):833-838.
21. Treweek S, Mitchell E, Pitkethly M, Cook J, Kjeldstrøm M, Johansen M et al**. Strategies to improve recruitment to randomized controlled trials**. Cochrane Database of Systematic Reviews 2010,Issue 4. Art. No.: MR000013
22. Pieracci et al. **A randomized controlled trial of the efficacy of Gabapentin versus placebo for adjuvant pain control following acute rib fractures**. 2017. Prepublication.
23. Moher D, Schulz KF, Altman D: **The CONSORT statement: revised recommendations for improving the quality of reports of parallel-group randomized trials**. *Jama* 2001, **285**(15):1987-1991.

Severe Rib Fracture Quality of Life Questionnaire

Study ID: _____

Date: _____

Question	
1	Were you working before your injury? [ ]YES [ ]NO *and* Are you currently working? [ ]YES [ ]NO
2	Please fill in the ONE circle that best describes you

- o Stay in bed all day, feel helpless and hopeless about life
- o Stay in bed at least half the day, have no contact with the outside world
- o Get out of bed but don't get dressed. Stay at home all day
- o Get dressed in the morning. Minimal activites at home. Contact with friends via e-mail, phone
- o Do simple chores around the house. Minimal activities outside of home two days a week
- o Struggle but filfill daily home responsibilities. No outside activity. Not able to work/volunteer
- o Work/volunteer limited hours. Take part in limited social activities on weekends.
- o Work/volunteer for a few hours daily. Can be active at least five hours a day. Can make plans to do simple activities on weekends
- o Work/volunteer at least six hours daily. Have energy to make plans for one evening social activity during the week. Active on weekends
- o Work/volunteer/active eight hours a daily. Take part in family life. Outside social activities limited.
- o Go to work/volunteer each day. Normal daily activities each day. Have a social life outside of work. Take an active part in family life.

3 Over the last month, my rib pain has: [ ]Decreased [ ]Stayed the same [ ]Increased

4 Please fill the ONE circle per line that best describes you, from 0 - 5

	0	1	2	3	4	5	
I had EXCELLENT health before I broke my ribs	o	o	o	o	o	o	I was in POOR health before I broke my ribs
I am back to my NORMAL health since before injury	o	o	o	o	o	o	My health is much WORSE after my rib injury
My chest does NOT feel tight at all	o	o	o	o	o	o	My chest feels VERY tight
I walk up a flight of stairs and am NOT breathless	o	o	o	o	o	o	I walk up a flight of stairs and am VERY breathless
I have NO mucus in my chest at all	o	o	o	o	o	o	My chest is completely FULL of mucus
I NEVER cough	o	o	o	o	o	o	I cough ALL the time
I sleep SOUNDLY	o	o	o	o	o	o	I DON'T sleep because of my chest condition
I have A LOT of energy	o	o	o	o	o	o	I have NO energy at all
I am CONFIDENT leaving home	o	o	o	o	o	o	I am NOT at all confident leaving my home
Since my injury, emotional problems NEVER stop me from doing normal daily activities	o	o	o	o	o	o	Since my injury, I have emotional problems that ALWAYS stop me from doing my normal daily activities
Since my injury, physical problems like pain and muscle weakness, NEVER stop me from doing normal daily activities	o	o	o	o	o	o	Since my injury, physical problems like pain and muscle weakness, ALWAYS stop me from doing my normal daily activities

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Attachment 2

Narcotic	Dose	Unit	route
Hydromorphone	1.5	mg	IV
Hydromorphone	7.5	mg	PO
Fentanyl	100	mcg	IV
Morphine	10	mg	IV
Morphine	30	mg	PO
Oxycodone (Percocet)	20	mg	PO
Hydrocodone (Vicodin)	30	mg	PO

Attachment 3

Nomogram for predicted incentive spirometry (mL) calculations

FEMALE

HEIGHT IN INCHES

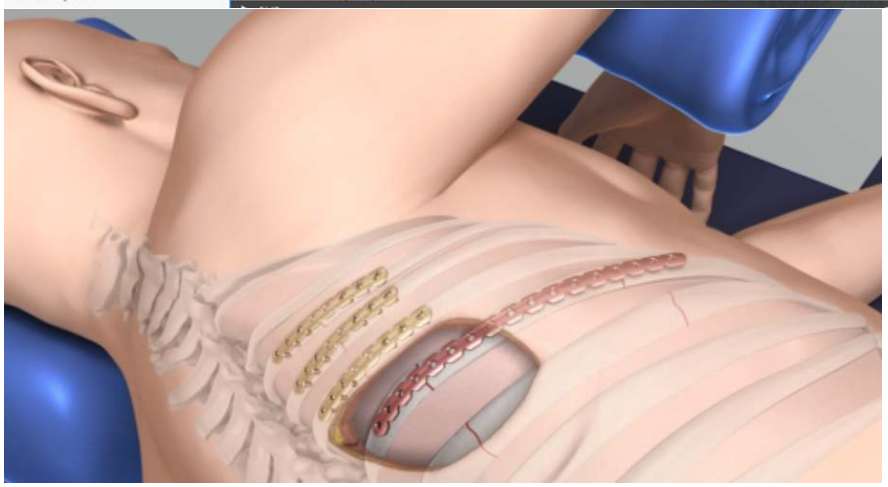
AGE IN YEARS	58"	60"	62"	64"	66"	68"	70"	72"	74"
20	1900	2100	2300	2500	2700	2900	3100	3300	3500
25	1850	2050	2250	2450	2650	2850	3050	3250	3450
30	1800	2000	2200	2400	2600	2800	3000	3200	3400
35	1750	1950	2150	2350	2550	2750	2950	3150	3350
40	1700	1900	2100	2300	2500	2700	2900	3100	3300
45	1650	1850	2050	2250	2450	2650	2850	3050	3250
50	1600	1800	2000	2200	2400	2600	2800	3000	3200
55	1550	1750	1950	2150	2350	2550	2750	2950	3150
60	1500	1700	1900	2100	2300	2500	2700	2900	3100
65	1450	1650	1850	2050	2250	2450	2650	2850	3050
70	1400	1600	1800	2000	2200	2400	2600	2800	3000
75	1350	1550	1750	1950	2150	2350	2550	2750	2950
80	1300	1500	1700	1900	2100	2300	2500	2700	2900

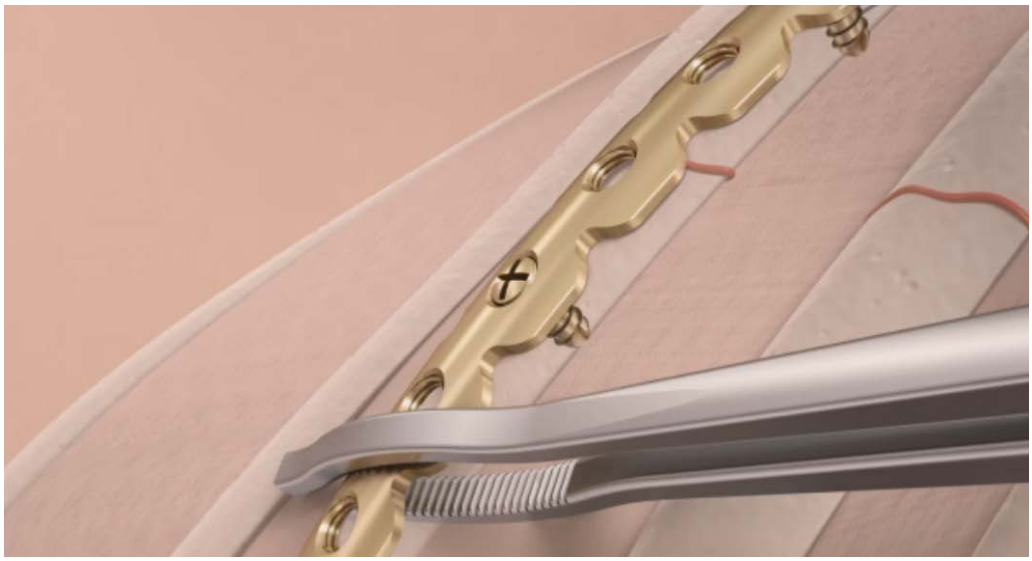
MALE

HEIGHT IN INCHES

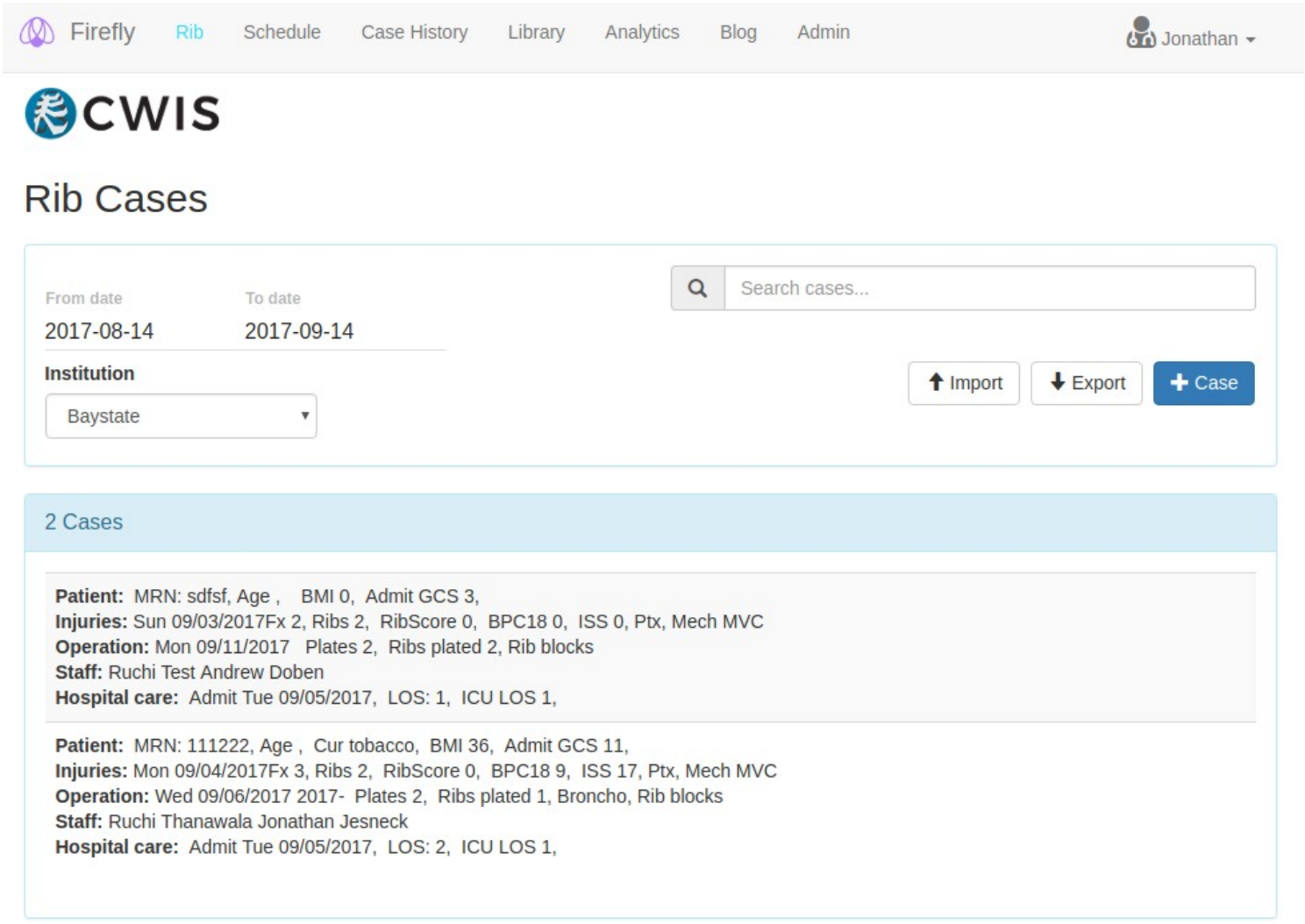
AGE IN YEARS	58"	60"	62"	64"	66"	68"	70"	72"	74"	76"	78"
20	2000	2200	2400	2600	2800	3000	3200	3400	3600	3800	4000
25	1950	2150	2350	2550	2750	2950	3150	3350	3550	3750	3950
30	1900	2100	2300	2500	2700	2900	3100	3300	3500	3700	3900
35	1800	2000	2200	2400	2600	2800	3000	3200	3400	3600	3800
40	1750	1950	2150	2350	2550	2750	2950	3150	3350	3550	3750
45	1700	1900	2100	2300	2500	2700	2900	3100	3300	3500	3700
50	1650	1850	2050	2250	2450	2650	2850	3050	3250	3450	3650
55	1550	1750	1950	2150	2350	2550	2750	2950	3150	3350	3550
60	1500	1700	1900	2100	2300	2500	2700	2900	3100	3300	3500
65	1400	1600	1800	2000	2200	2400	2600	2800	3000	3200	3400
70	1350	1550	1750	1950	2150	2350	2550	2750	2950	3150	3350
75	1300	1500	1700	1900	2100	2300	2500	2700	2900	3100	3300
80	1250	1450	1650	1850	2050	2250	2450	2650	2850	2050	3250

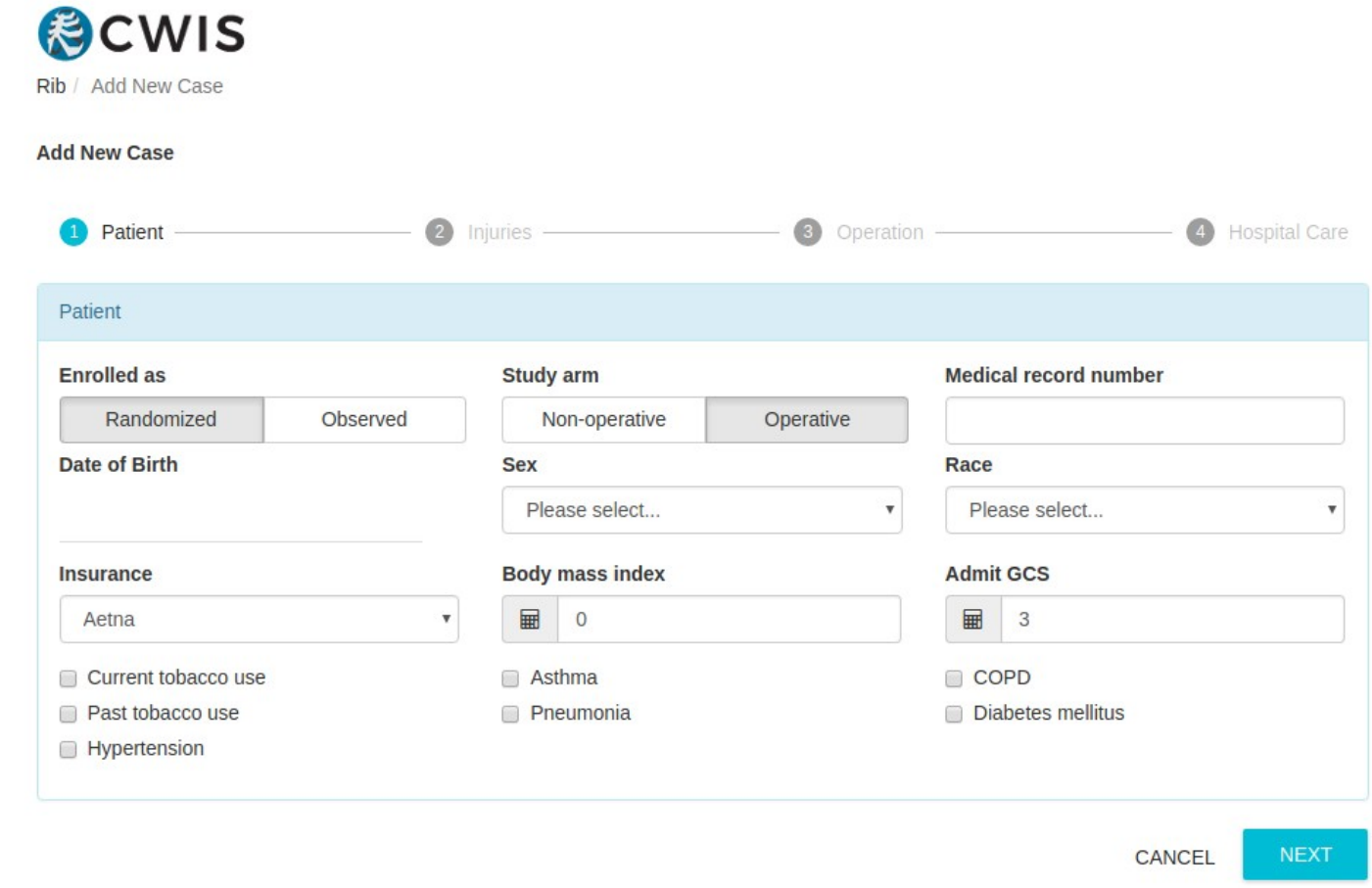
Attachment 4





Attachment 5




CWIS
Rib / Add New Case
Add New Case
1 Patient
2 Injuries
3 Operation
4 Hospital Care
Patient
Enrolled as
Randomized
Observed
Study arm
Non-operative
Operative
Medical record number
Date of Birth
Sex
Please select...
Race
Please select...
Insurance
Aetna
Body mass index
0
Admit GCS
3
Current tobacco use
Past tobacco use
Hypertension
Asthma
Pneumonia
COPD
Diabetes mellitus
CANCEL
NEXT

CWIS

Rib / Add New Case

Add New Case

Patient — 2 Injuries — 3 Operation — 4 Hospital Care

Injuries and Repairs

Fracture

	Right					Sternum	Left					
	P	Lateral			A		A	Lateral			P	
Rib		LP	LS	LA				LA	LS	LP		Rib
1	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	1
2	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	2
3	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	3
4	☐	☐	☐	☐	☐		☐	☐	☐	☐	☐	4
5	☐	☐	☐	☐	☐		☐	☐	☐	☐	☐	5
6	☐	☐	☐	☐	☐		☐	☐	☐	☐	☐	6
7	☐	☐	☐	☐	☐		☐	☐	☐	☐	☐	7
8	☐	☐	☐	☐	☐		☐	☐	☐	☐	☐	8
9	☐	☐	☐	☐	☐		☐	☐	☐	☐	☐	9
10	☐	☐	☐	☐	☐		☐	☐	☐	☐	☐	10
11	☐	☐	☐	☐	☐		☐	☐	☐	☐	☐	11
12	☐	☐	☐	☐	☐		☐	☐	☐	☐	☐	12

Location Legend
A: Anterior
Lateral
LA: Lateral-anterior
LS: Lateral-straight
LP: Lateral-posterior
P: Posterior
Marker Legend
S: Severe displacement
N: Non-severe displacement

Injury Date

Mechanism

Please select...

Mechanism note

Rib Score

0

BPC 18

0

Injury severity score

0

- ☐ Intracranial hemorrhage
- ☐ Face fracture
- ☐ Clavicle fracture
- ☐ Scapula fracture
- ☐ Spine fracture
- ☐ Spinal cord injury
- ☐ Pelvis fracture
- ☐ Long bone fracture
- ☐ Solid organ injury
- ☐ Blunt cardiovascular injury
- ☐ Hemothorax (on admission)
- ☐ Pneumothorax (on admission)

BACK NEXT

CWIS

Rib / Add New Case

Add New Case

Patient — Injuries — 3 Operation — 4 Hospital Care

Operation

Plates

	Right					Sternum	Left					
	P	Lateral			A		A	Lateral			P	
Rib		LP	LS	LA				LA	LS	LP		Rib
1	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	1
2	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	2
3	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	3
4	☐	☐	☐	☐	☐		☐	☐	☐	☐	☐	4
5	☐	☐	☐	☐	☐		☐	☐	☐	☐	☐	5
6	☐	☐	☐	☐	☐		☐	☐	☐	☐	☐	6
7	☐	☐	☐	☐	☐		☐	☐	☐	☐	☐	7
8	☐	☐	☐	☐	☐		☐	☐	☐	☐	☐	8
9	☐	☐	☐	☐	☐		☐	☐	☐	☐	☐	9
10	☐	☐	☐	☐	☐		☐	☐	☐	☐	☐	10
11	☐	☐	☐	☐	☐		☐	☐	☐	☐	☐	11
12	☐	☐	☐	☐	☐		☐	☐	☐	☐	☐	12

Location Legend
A: Anterior
Lateral
LA: Lateral-anterior
LS: Lateral-straight
LP: Lateral-posterior
P: Posterior

Marker Legend
☐: Plate

OR Date

2017-09-14

OR Start Time

OR End Time

☐ Bronchoscopy
☐ Rib blocks
☐ Lung isolation

☐ Chest tube
☐ Pain catheter

Position

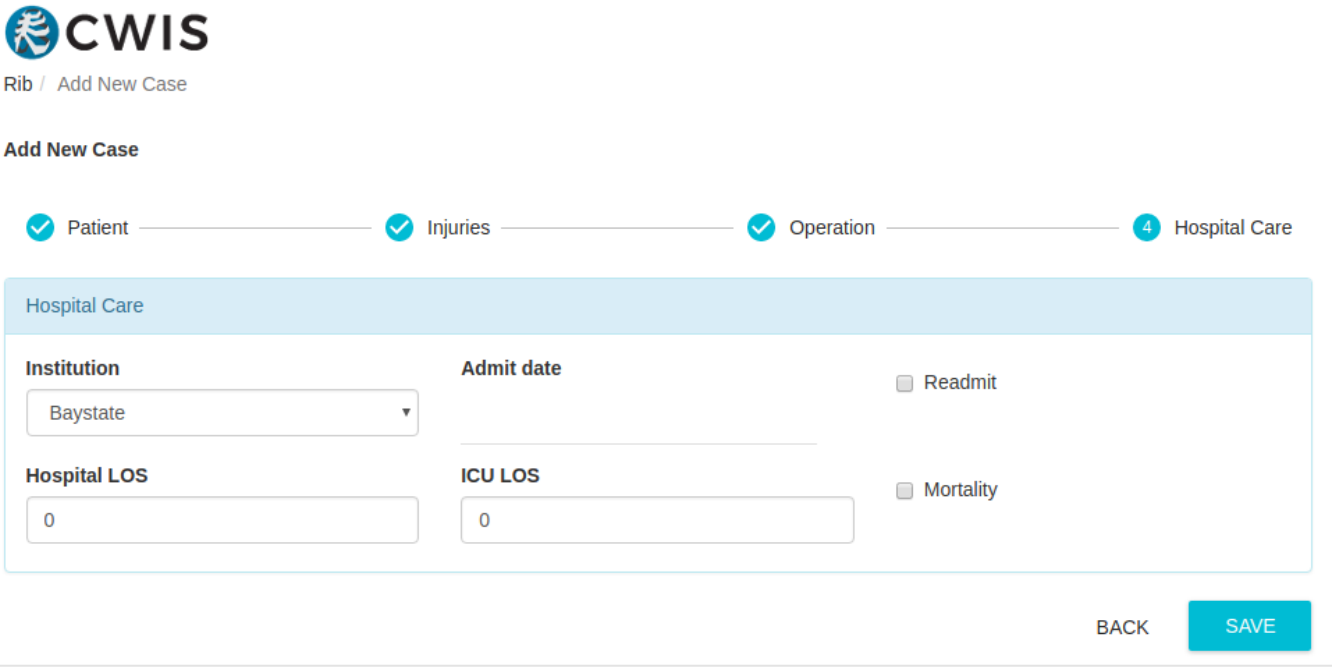
Supine

☐ Evacuation of HTX
☐ Subcutaneous drain

Staff

Select users...

BACK NEXT


CWIS
Rib / Add New Case
Add New Case
Patient
Injuries
Operation
4
Hospital Care
Hospital Care
Institution
Baystate
Admit date
Readmit
Hospital LOS
0
ICU LOS
0
Mortality
BACK
SAVE

Attachment 6

one•light PICTURES & WORDS SCRIPT SECOND DRAFT	Client: Chest Wall Injury Society Project: CWIS - Non Flail Trial Invitation Date: 11/13/17 Length: 1-2 Min. Contacts: Fredric Pieracci / Kiara Leasia Writer: Fredric Pieracci Producer: Victor Shapiro
Video	**Audio**
Open on CWIS Graphic Logo & Title	Music sting over graphic logo
- *green screen studio* - Dissolve to med-wide shot of Dr. Pieracci in office setting -	Hello – We are showing you this informational video because you are eligible for a clinical research trial. You are eligible for this trial because you have three or more severely broken ribs, and have been admitted to the hospital for this reason.
Cut to med shot – Dr Pieracci turns to camera left	O/C: My name is Dr. Pieracci, and I am the lead investigator for this trial. I'd like to take the next few minutes to explain why you may want to consider participating in our project.
Cut to B-roll shots of - Intubated patient - Physicians conferring over patient CT scans - Patient conducting breathing exercises	O/C: In the past, all patients with rib fractures were treated without surgery. This treatment consisted of pain medications and, in severe cases, a breathing tube and machine. Many patients with severe injuries developed complications such as pneumonia, chronic pain, and chronic breathing difficulties.

Cut to animated visual of plate placement over fractured rib, or video of physicians conferring over CT of already plated ribs – Soften image - dissolve in title: *Surgical Stabilization of Rib Fractures*	V/O: Over the last 15 years, an operation has been developed to place small, permanent plates on the rib fractures to stabilize them, promote healing, and decrease pain. Myself, as well as the investigators at your center, have helped to develop this treatment, known as surgical stabilization of rib fractures.
Dissolve to appropriate visual of flail chest injury – - or - Text title reinforcement: - Flail Chest Plate Repair Discoveries – * Decrease Pain & Complications * Quicker Recovery Time * Safe Surgery * Lower Risk of Complications	V/O: At first, we performed the operation on patients with the most severe form of rib fractures, known as flail chest, and discovered that surgery, as compared to no surgery, decreased pain and complications, and quickened recovery. Also, the surgery has been found to be extremely safe, with a very low risk of complications.
Dr. Pieracci center camera - medium shot	O/C: What we still *do not* know, however, and are attempting to find out with this trial, is if the same benefit from surgery will be seen in patients with rib fractures that *do not* have flail chest - specifically, fractures such as yours.
Cut to CT scan of displaced rib injury comparative to CT of flail chest injury	V/O: These fractures, although not considered a "flail chest," are still severely displaced, as shown here. When we recently surveyed experts in the field of rib fractures, about half of them thought that surgery would help patients in your condition, and the other half did not.
Cut to frame w/ *Chest Wall Injury Society* title > reduce to *CWIS Non-Flail* title > dissolve in map of US > pinpoint cities w/ participating centers > dissolve in *100 patient participants*	V/O: The current trial, named "CWIS NON-FLAIL," is being conducted by the Chest Wall Injury Society, an international organization of experts in treating rib fractures. There are 20 centers like yours enrolling patients in this trial across the US; with a total of 100 patients participating.

Dr. Pieracci center camera - medium shot dissolve to split circle graphi illustrating the concept of randomized selection	O/C: If you join the study, you will be assigned to either receive surgery for your rib fractures, or not. The selection process is completely random - you will have an equal chance to be in the "SURGERY" group or "NO SURGERY" group.
Cut to Synthes animation of rib plating procedure (hopefully!)	V/O: If you are in the surgery group, you will undergo an operation that will take about 2 hours. While you're asleep, expert surgeons will place titanium plates onto your ribs through small incisions, stabilizing the fractures. This operation has been performed in thousands of patients across the world, and surgeons at your center have performed at least 50 of these operations. In fact, centers were carefully selected for this trial based on their expertise with this surgery.
Dr. Pieracci center camera - medium shot	O/C: If you are in the "NO SURGERY" group, you will still receive all of the best, state of the art care for your rib fractures. ~~You will~~ just not receive the rib stabilization surgery.
Dr. Pieracci turns to camera left - medium shot Dissolve to title graphic reinforcement of VO: What to expect during trial: - Daily checkup while in hospital - Case follow up for up to two months - No additional requirements from you - May be asked to perform standard 30 minute breathing test during two week follow up visit – at no additional charge.	O/C: Whether in the "SURGERY" or "NO SURGERY" group, we will follow and check on you at least daily, while in the hospital. V/O: Additionally, we will follow you for up to two months after your injury, along with your treatment team, at your follow up visits. You will not need to do anything extra for being in this trial; we will arrange for our research staff to see you during your already-scheduled visits with your primary treatment team. You may be asked to perform a 30 minute breathing test at your 2 week follow up visit, which is free of charge to you, and usually part of your standard follow up care.

Cut to Dr Pieracci center camera – medium shot Dissolve back to circle graphic displaying randomization with added circle graphic illustrating *observational* group Dissolve to Dr.'s Pieracci & White conferring w patient – (will need setup)	O/C: Each arm of this study involves both risks and benefits, and you should speak with research staff at your hospital to discuss these. If you ultimately decide *not* to be randomized to SURGERY or NO SURGERY, we will still ask that you allow us to collect information about your injury and recovery. In this case, whether you have surgery or not will depend entirely upon what you and your medical team decide is best for you. In this case, you will be in the OBSERVATIONAL arm of our trial.
Cut to Dr Pieracci center camera – medium shot Dissolve to color background w CWIS & Synthes logos – and bulleted list w names of each participating location	V/O: It will not cost you anything to be in this trial. Moreover, the study investigators, such as myself, will not be paid, and have no vested interest in any particular outcome of the trial, other than to advance the care of patients with rib fractures. This trial is being funded by the Chest Wall Injury Society, DePuy Synthes, Inc., and the individual study sites.
Dissolve out previous title information – Dissolve in following: - Participation is completely voluntary - Opt-out at anytime w/o consequence - Discuss trial or any questions you may have w research personnel at your institution.	O/C: You should know that participation in this study is completely voluntary and, if you decide to join, you can opt-out at any point without consequence. I encourage you to ask the research personnel at your institution any additional questions that you may have about the trial.
Cut to Dr Pieracci center camera – medium wide shot	O/C: Thank you for taking the time to listen to this message and please take a moment to think about how your involvement in this trial will be a valuable contribution to the betterment of medical care everywhere. On behalf of all of our study personnel, I wish you a speedy recovery from your injuries, and appreciate your consideration of participating in this important trial. Have a nice day –
CWIS & Synthes (?) Logos	MUSIC STING OUT