Background

In the United States alone, more than 3 million individuals suffer non-fatal injuries annually with greater than half of all multiply injured patients suffering thoracic injuries.(1) Rib fractures are the most common thoracic injury and represent a complicated clinical problem present in nearly 10% of all injured patients.(2, 3) Short-term complications including lung consolidation, pneumonia, and empyema are all associated with rib fractures and result in long inpatient hospital stays and an increased mortality. Rib fractures often result in the development of chronic pain. Chronic pain development among trauma patients at our institution has been documented at rates upwards of 80%, significantly greater than the general population.(4) Aside from the addiction and tolerance associated with continued opiate therapy, chronic pain is a major public health issue that results in significant health resource utilization, decreased quality of life, and lost work productivity.

Prevention of many short-term complications relies on optimal pain control to promote normal respiratory mechanics and effort. While opiate medications have long been the therapeutic backbone, they can produce respiratory depression, nausea, emesis, pruritus, and/or sedation preventing optimal pain control.(3, 5) To offset such problems, many regional adjuncts are utilized with varying degrees of success. Despite many years of research, the optimal analgesic approach applicable for all patients remains elusive. Research from our institution recently demonstrated poor acute pain control increases the development of chronic pain. The majority of research on optimization of rib fracture pain control has focused on regional anesthesia techniques, which provide isolated benefits in the setting of a multiply injured trauma patient.

The Clinical Practice Guidelines for the Management of Pain, Agitation, and Delirium in Adult Patients in the Intensive Care Unit by Barr et al. published in January 2013 were adopted as the most recent standard of care for the clinical management of pain. The mainstay of acute pain management, albeit postoperative, traumatic, or idiopathic, has been opiate based therapy. Utilization of ketamine therapy as an adjunct in the management of acute pain is minimally discussed in these guidelines with some previous retrospective and small prospective studies to support its use noted. Ketamine infusions are currently part of our standard opiate tolerant pain management pathways. However, its use has been reserved for individuals who fail traditional opiate therapy. This trial aims to re-think how we approach acute pain management thru early implementation of ketamine infusion therapy. In our model of acute pain management we move ketamine from an adjunct therapy to the forefront of therapeutic intervention through which we hope to decrease the overall opiate requirements and side effects among trial patients.

As previously stated, chronic pain is a significant contributor to decreased quality of life following injury. Historically, clinicians were taught that the pain and disability of rib fractures resolves in 6 to 8 weeks. However, more recent studies have demonstrated that a large number of patients report significant chest wall pain and overall disability at or beyond 8 weeks of injury.(19,20) In one prospective observational study, the most predictive indicator of both prolonged pain and disability was the pain intensity within the first several days after injury.(19) With the use of early ketamine infusion therapy in the acute injury phase, we also hope to decrease the development of chronic pain and improve quality of life after rib fractures.

Hypothesis

Early utilization of ketamine infusion therapy among adult and elderly patients with rib fractures will improve patient reported pain control.

Specific Aims:

S.A.1: Characterize the efficacy of ketamine infusions in the management of acute thoracic pain associated with rib fractures.

- Hypothesis 1A: Utilization of ketamine infusion therapy among rib fracture patients will lead to decreased patient reported thoracic numeric pain scores compared to controls.

- Hypothesis 1B: Ketamine infusion therapy will lead to decreased total opiate consumption (standardized to morphine equivalent units) in the first 24 and 48 hours compared to controls.

S.A.2: Characterize the impact of ketamine infusion therapy on the development of chronic pain and quality of life in trauma patients who suffer rib fractures.

Hypothesis 2A: Improved rib fracture and global pain control through early ketamine infusion therapy will decrease the rate of chronic pain development and improve quality of life.**Methods**

A prospective randomized, double blinded study of adult blunt trauma patients with associated rib fractures admitted to the trauma service will be conducted. The experimental arm of the study will receive ketamine infusion therapy while the control arm receives saline placebo infusions at an equivalent rate. All patients will be managed with adjunct therapy including opiates in accordance with the thoracic trauma protocols (see Appendix I for further details). This study will focus on adult blunt trauma patients who have associated rib fractures. The focus on adult rib fracture patients stems from an injury pattern in which there is a high incidence of prolonged narcotic utilization and development of chronic pain. Potential subjects will be screened according to the previously listed inclusion and exclusion criteria.

All blunt trauma patients with associated rib fractures will be screened. All patients will be enrolled into our standard thoracic trauma pathway (see Appendix I. TPP.0046) with scheduled medications as listed in the protocol. All individuals will undergo Intercostal Nerve Block (ICNB) (see Appendix II) in the Emergency Department or on admission to the Intensive Care Unit (ICU). In addition to scheduled medications per thoracic trauma protocol, all patients will receive adjunct narcotic therapy. Patients will be screened by the clinical and pharmacy staff following the diagnosis of rib fractures for eligibility. Patients enrolled into the study will be randomized into either the experimental or control arm of the study. The Investigational Drug Services (IDS) department will randomize all enrollees and handle administration of all study drugs. Study assignment and blinding will be held by the Investigational Drug Services department. The infusate will be mixed by the IDS department and all bags will be labeled “Ketamine / Placebo.” The IDS department will have unique bag identifiers, which will allow them to identify which bags have active ketamine and which are placebo in case of emergency. A sign stating “RIB FRACTURE PATIENT” – Please document “Thoracic Pain Scores” will be hung outside the subject’s room. The sign serves as a reminder to those who are providing patient care that they need to record thoracic pain scores as part of SoC for treating rib fractures with Ketamine infusion (see Appendix VI).

ADULT PROTOCOL:

A total of 100 patients aged 18 – 64 years old will be enrolled into the study. The 50 patients randomized to the experimental arm will receive early ketamine infusion therapy at a rate of 2.5 mcg/kg/min. All ketamine infusions will be calculated based on ideal body weight (IBW), unless actual body weight is less than ideal. IBW will be calculated for males as 50kg + 2.3*(number of inches above 5 feet) and for women as 45.5kg + 2.3*(number of inches over 5 feet). The 50 patients randomized to the control arm will receive placebo saline solution at a rate equivalent. Time zero will be defined as the time at which the “ketamine / placebo” infusion is begun. For inclusion in the study, initiation of ketamine / placebo infusions must take place within 12 hours of presentation to Froedtert Memorial Lutheran Hospital (FMLH). Ketamine infusions will be prepared by the IDS service but will be hung and administered by the inpatient nursing staff. Ketamine infusion therapy will be continued for 48 hours. At 6-8 hours post-ICNB all subjects will be assessed for need for repeat ICNB. Need for repeat ICNB will be defined by a thoracic specific numeric pain score greater than seven. Between 8-10 hours post-ketamine infusion initiation, subjects who have thoracic specific pain scores above six will be evaluated for epidural placement by the RAAPS service.

ELDERLY PROTOCOL:

An additional seventy-two patients will be enrolled aged 65 and older (see sample size calculation outlined in c.2.3). Thirty-six patients randomized to the experimental arm will receive ketamine infusion therapy at 2 mcg/kg/min. Ketamine dose is calculated based on ideal body weight (IBW), unless actual body weight is less than ideal. IBW will be calculated for males as 50kg + 2.3*(inches over 5 feet) and for women as 45.5kg + 2.3*(inches over 5 feet). Thirty-six patients randomized to the control arm will receive placebo solution. Time zero is defined at initiation of the “ketamine / placebo” infusion. Ketamine / placebo infusions must begin within 12 hours of presentation to Froedtert Memorial Lutheran Hospital (FMLH). Ketamine/placebo therapy will be continued for 48 hours. At 6-8 hours post-ICNB all subjects will be assessed for repeat ICNB, defined by a thoracic specific numeric pain score greater than seven. At 8-10 hours post-ketamine/placebo initiation, those with thoracic pain scores above seven will be evaluated for epidural placement by the RAAPS service.

All Patient Daily Screening:
Each individual will undergo daily screening by the trauma and anesthesia rounding teams for complications during the infusion. Specific infusion related complications that will be screened daily include: Respiratory Depression, Nausea / Emesis, Itching / Hives, presence of disturbing dreams / Hallucinations / Delusions, Blurred vision, Dizziness, and Confusion (Utilizing the Confusion Assessment Method currently employed at Froedtert). Additionally, nursing staff currently assess sedation and nausea at a per shift minimum. Should any concerns for infusion related complications be encountered by nursing staff, a member of the trauma and/or anesthesia care teams will assess the patient. Trauma attending’s are available 24/7 should any serious concerns arise.

Elderly Patient Daily Assessment Supplement:
All subjects will be assessed daily or more frequently for delirium. The institutional CAM and CAM-ICU Delirium screens, which have been validated in the literature, will be utilized prior to 7-12-2016 (see appendices IV and V) . and the Nu-DESC which went into effect at FMLH on 7-12-2016 will be used as well (Appendix V figure 2). Subjects may remove oneself from the trial or be un-blinded should he/she, pharmacy, and/or clinical staff deem it medically necessary. Medical necessity is determined by inability to treat without knowledge of trial assignment; otherwise treating staff will assume all patients have received ketamine. All adverse events will be recorded and if necessary subjects will be un-blinded in the event of a serious adverse event.

A subject will be allowed to remove himself/herself from the study or be un-blinded should he/she, pharmacy, anesthesia, and/or surgical staff deem it medically necessary. All adverse events will be recorded and if necessary subjects will be un-blinded in the event of a serious adverse event. The research team will monitor all study patients for any adverse event trends. Patients will be followed through the time of discharge.

Safety Protocol and Protection of the Elderly: Rates of delirium in elderly trauma patients is higher than the average adult trauma patient with rates up to 30% quoted in the literature.(6) Interestingly previous work has found thoracic trauma to be a protective factor for the development of delirium, speculated due to more frequent nursing care.(6) Additionally, one of the concerns with ketamine is the dissociative properties which are beneficial in the treatment of pain but a concern for the development of delirium. Studies looking at ketamine in elderly patients have demonstrated the drug side effect profile similar among all patients with some increased dissociation in elderly individuals.(7-12) As a result of these concerns, the study will have an extensive patient safety monitoring plan in place.

All individuals enrolled into the study prior to 7/12/2016 will be screened prior to therapy utilizing the confusion assessment method (CAM) which has been previously validated in the literature and is an institutional practice currently utilized in both the ICU and on the general wards.(13-18) There are two different versions of the CAM currently utilized in Froedtert Memorial Lutheran Hospital specific to location. The general ward CAM is outlined in Appendix IV while a separate CAM-ICU is designated for utilization in all intensive care units and is outlined in Appendix V. Both the CAM and CAM-ICU tools are simple easy to utilize tools that can be administered by nursing staff, aids, residents, or clinical faculty. Currently in the ICU the CAM tool is administered by the nursing staff to all patients as a screening method for delirium. The CAM-ICU will be administered in the ICU per current nursing protocol. Additionally, both the trauma and anesthesia

RAAPS teams in charge of patient care will administer the CAM-ICU for all ICU patients during daily rounds to screen for the presence of delirium. As a result of this, all patients in the ICU will undergo at least three CAM-ICU screens daily to help address delirium concerns. All patients admitted to the floor prior to 7/12/2016 will undergo CAM screening by both the trauma and anesthesia RAAPS teams during daily rounds to screen for the presence of delirium. Additionally, should any nurse or house staff have concerns for the possibility of delirium, the CAM tool will be available for their utilization.

All individuals enrolled into the study after 7/12/2016 will be screened using the Nursing Delirium Screening Scale (Nu-DESC) per hospital change.

Any patient that screens positive on a CAM or Nu-DESC assessment by nursing staff or other non-physician staff would mandate a clinical evaluation by the anesthesia and trauma clinical teams. Should a patient screen positive for delirium utilizing the appropriate CAM or Nu-DESC assessment by a clinical team (i.e. anesthesia or trauma), the patient will be assessed by other rounding clinical team (i.e. anesthesia or trauma). Should both CAM or Nu-DESC screens be positive for the presence of delirium, the patient will be withdrawn from the study with cessation of the ketamine/placebo solution immediately. Additionally, the traditional delirium workup for the presence of infection or other underlying cause will happen in parallel with cessation of the ketamine/placebo solution. Given the short half-life of ketamine, approximately 15 minutes, if the ketamine/placebo solution is the cause of the altered mental status, patient should improve shortly. If the patient does not improve, continued delirium workup will continue in congruence with the current standard of care.

In the event that the two clinical CAM or Nu-DESC assessments are in disagreement with the presence of delirium, a clinical workup for delirium in congruence with the current standard of care will be initiated. However, the ketamine/placebo infusion will continue with repeat assessment in one hour by the clinical teams. If both team CAM or Nu-DESC assessments screen positive or disagreement remains as to the delirium status of the patient, the patient will be withdrawn from the trial with cessation of the ketamine/placebo solution. In the event both teams agree no delirium is present, the patient’s therapy will be continued according to study protocol. For the duration of the trial, should any questions as to the presence of delirium or whether the ketamine/placebo infusion should be stopped arise, there will always be an available clinical research staff (i.e. research resident, trauma staff, or anesthesia staff) that is heavily involved in the trial available for questions 24/7.

All individuals who require withdrawal from the study with cessation of the ketamine/placebo solution will be reported to the Investigational Drug Services department for monitoring of drug safety. Should the IDS department have concern for the safety of ketamine utilization in this elderly patient population, a formal IRB report will be filed with no further enrollment of patients until final IRB consensus is reached.

All aspects of the safety protocol for the protection of elderly patients in general along with study specific protections will be incorporated as a part of resident, staff, and nursing education efforts prior to enrollment of patients into the trial.

Unblinding Protocol: Breaking of blinding for any subject should only be performed for medical emergency conditions in which the identification of the subject's treatment assignment is critical for proper medical care. In all cases, it should be assumed the subject received active drug. In such rare and special circumstances where the selection of a treatment approach for the medical emergency would differ based on whether the subject was on active or placebo, the investigator should contact the Medical Affairs Associate at the CRO acting as the designated medical contact for the permission to unblind. The representative or back-up will be available 24 hours a day. If a decision is made to unblind a subject's assignment, the investigator will utilize the IVRS to request the subject's treatment group. Only the investigator will be unblended to the subject's treatment group and he/she will be responsible for documenting the time, date, and reason for code break. Under these circumstances, study treatment would be discontinued, but all efforts would be made to ensure the remaining per protocol safety and efficacy evaluations were conducted. The investigator will ensure that only study staff involved in the immediate medical treatment of the subject are aware of the unblinding and will ensure, whenever possible, that all other study staff involved in the remaining assessments remain blinded. If applicable, the investigator will

document the date and time other study staff were unblended. In the situation where a non-study physician requires emergency unblinding in order to provide urgent care to the subject, the Medical Monitor or back-up will be contacted to discuss and then, if needed, the treatment code will be provided. The Medical Monitor or backup is available 24 hours a day, 7 days a week.

Unblinding: Breaking of blinding for any subject should only be performed for medical emergency conditions in which the identification of the subject's treatment assignment is critical for proper medical care. In all cases, it should be assumed the subject received active drug. In such rare and special circumstances where the selection of a treatment approach for the medical emergency would differ based on whether the subject was on active or placebo, the investigator should contact the medical representative or back-up. The representative or back-up will be available 24 hours a day. If a decision is made to unblind a subject's assignment, the investigator will contact the Investigational Drug Services Department to request the subject's treatment group. Only the investigator will be unblinded to the subject's treatment group and he/she will be responsible for documenting the time, date, and reason for code break. Under these circumstances, study treatment would be discontinued, but all efforts would be made to ensure the remaining per protocol safety and efficacy evaluations were conducted. The investigator will ensure that only study staff involved in the immediate medical treatment of the subject are aware of the unblinding and will ensure, whenever possible, that all other study staff involved in the remaining assessments remain blinded. If applicable, the investigator will document the date and time other study staff were unblinded. In the situation where a non-study physician requires emergency unblinding in order to provide urgent care to the subject, the Medical Monitor or back-up will be contacted to discuss and then, if needed, the treatment code will be provided. The Medical Monitor or backup is available 24 hours a day, 7 days a week.

Pain Assessments: The study design is based on the utilization of IV narcotics on an hourly basis for adjunctive pain management in accordance with the current trauma protocols and study overview. The utilization for IV narcotics on all patients out thru 24 hours’ post-infusion ensures the proper nursing interaction with patients. While IV narcotics are not required to be administered each hour, a nursing assessment hourly is necessary in order to determine need for IV narcotic administration. Should the patient request narcotics or it is deemed necessary by the nursing staff this would be recorded in the electronic medical record. All pain assessments by the nursing staff would be recorded into the EMR for patient care purposes and for research team recording. It is unreasonable to except hourly nursing pain assessments for the duration of the hospitalization which is why the primary endpoint of the study is the assessment of the 12-24 hour period. Additionally, the design accounts for the possibility that some time points might not have pain assessments. The utilization of the AUC pain analysis as detailed in the data analysis section describes how this accounts for missing data points. Extensive nursing education on the importance of ensuring hourly assessments by either the nurse or aid will be stressed.

Side Effect Assessments: Side effects will be screened for daily by the rounding services. The particular side effects of interest include: nausea (0 = absent, 1 = present, no therapy, 2 = present, therapy effective, 3 = present, therapy ineffective), respiratory depression (defined as RR <8 or SpO2 < 90%), sedation (0= no sedation noted, 1= sedation causing documentation by RN in patient chart, 3=sedation causing increased monitoring in an intensive care unit 4=sedation causing the need for intubation), pruritus (0 = absent, 1 = present, no therapy, 2 = present, therapy effective, 3 = present, therapy ineffective), and the presence of hallucinations and/or disturbing dreams (0=no 1=yes).

Quality of Life Assessment: Following hospitalization, we will follow up with participants at three, six, twelve months, and/or 24 months after enrolling in the study. This follow up interview will occur via telephone call, or in person if the participant is still in the hospital. At each follow up interview, an assessment of quality of life, post-traumatic stress disorder (PTSD), depression, anxiety, and stress will be conducted via the following measures:

1. Depression Anxiety Stress Scales 21 (DASS-21): Assess severity of symptoms of depression, anxiety, or stress.
2. PTSD Checklist for DSM-5 (PCL-5): Assess the 20 symptoms of PTSD listed in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5).

3. Short Form 36 Health Survey version 2 (SF-36v2): Assess health status including physical functioning, vitality, bodily pain, general health perceptions, physical role functioning, emotional role functioning, social role functioning, and mental health.
4. Trauma Quality of Life measure: Assess domains unique to trauma populations, including emotional well-being, functional engagement, recovery / resilience, peritraumatic experience, and physical well-being.

3, 6, 12 and 24 Month Study Procedure: A follow-up assessment will occur via a telephone call or in person. During the interview, subjects will complete the following measures: DASS-21, PCL-5, SF-36v2, and Trauma Quality of Life measure. This will take approximately 15-20 minutes to complete.

For those subjects currently active in the study or who have already completed their participation in the study, we will perform a new verbal telephone consent in order to obtain the quality of life surveys. This document can be found in section 3, titled: "AME #17808 Verbal Consent Telephone Script 2.1.2018"

Inclusion Criteria:

1) Age 18 years or greater– Adult arm = 18 to 64 years of age, Elderly arm = 65 years of age or older
2) Trauma patients admitted to Froedtert Hospital with 3 or more rib fractures documented on plain film or cross-sectional imaging.

Exclusion Criteria:

1) history of adverse reaction to ketamine therapy
2) chronic opioid therapy defined as ≥ 3 weeks of ≥30mg oral morphine equivalents per day
3) current substance abuse with opiates including prescription and/or heroin
4) intubation on arrival or need for urgent intubation on arrival
5) significant traumatic brain injury or suspicion of elevated intracranial pressure resulting in an inability to communicate with staff
6) history of psychosis
7) active delirium
8) glaucoma
9) ischemic heart disease defined as active acute coronary syndrome
10) severe, poorly controlled hypertension
11) concurrent use of monoamine oxidase inhibitors (MAOIs)
12) pregnancy
13) prisoners

Statistical Analysis

Sample Size Analysis:

Adult Study: The primary outcome for this study is a clinically significant difference in pain scores. A clinically significant decrease in acute pain scores is defined as a 2-point interval on the 11-point numeric pain scale. A total enrollment of 52 patients (26 control patients, 26 experimental patients) was calculated utilizing previous institutional data on acute pain scores. A sample size of 52 patients provides an 80% power for the detection of a clinically significant difference in postoperative pain scores. Given confounding factors such as epidural placement and possibility patients may decide to withdraw from the study, a planned sample size of 60 patients will provide a 15% buffer in patient enrollment.

Elderly Study: A planned enrollment of 60 patients provides a 15% buffer. Rates of delirium among all elderly trauma patients are quoted around 30%(35); therefore, a budget is outlined for a total of 72 patients providing a 38% buffer for any perceived patient attrition.

Interim Sample Size Recalculation: The expected variability of the primary outcome was estimated in a slightly different population, thus there is a concern that the actual variability will be different, affecting the overall power of the trial. Thus, an internal pilot will be incorporated into the trial [Friede T, Kieser M (2006) Sample Size Recalculation in Internal Pilot Study Designs: A Review Biometrical Journal, 48(4), 537-555]. When half the patients have been randomized, the primary outcome will be evaluated for them, and a blinded sample size recalculation will be performed using the original target effect size of 2 point difference and the observed standard deviation of the pooled data adjusted for the expected treatment difference using Zucker’s formula:

$$S^2_{adj} = S^2 - (n_1 * d^2)/[4*(n_1-1)],$$

where d=2 is the expected treatment difference. The recruitment will not stop during the recalculation phase, as the originally planned sample size of 26 patients per group will always be recruited. If the recalculation indicates the need for a higher sample size, it will be increased to its calculated value, but not exceeding 39 patients per group (a 50% increase in sample size). This approach maintains the overall type I error rate but protects against moderate underestimation of the between-patient variability.

Analysis: The primary outcome will be the area under curve for the pain trajectory (AUC pain) 12 – 24 hours after initiation of treatment. AUC pain is calculated using the trapezoid rule; linear interpolation will be used between the last pain score before start of the period and first pain score after start of the period to obtain the 12-hour pain score, with a similar calculation for the 24-hour score. This measure can be interpreted as a time-weighted average of pain scores. Demographic and other baseline data as well as outcome measures will be presented overall and by treatment group. Categorical data, such as gender, race, etc., will be presented by frequencies and percentages. Descriptive summary statistics (e.g. frequency, mean, median, range and standard deviation) will be used to present numeric data. The primary outcome will be compared between the two groups using Student’s two-sample t-test.

Quality of Life Analysis: Independent samples t-tests with multiple correction will be conducted to evaluate whether those who received early ketamine infusion therapy experience significant differences in quality of life, PTSD, depression, anxiety, and stress.

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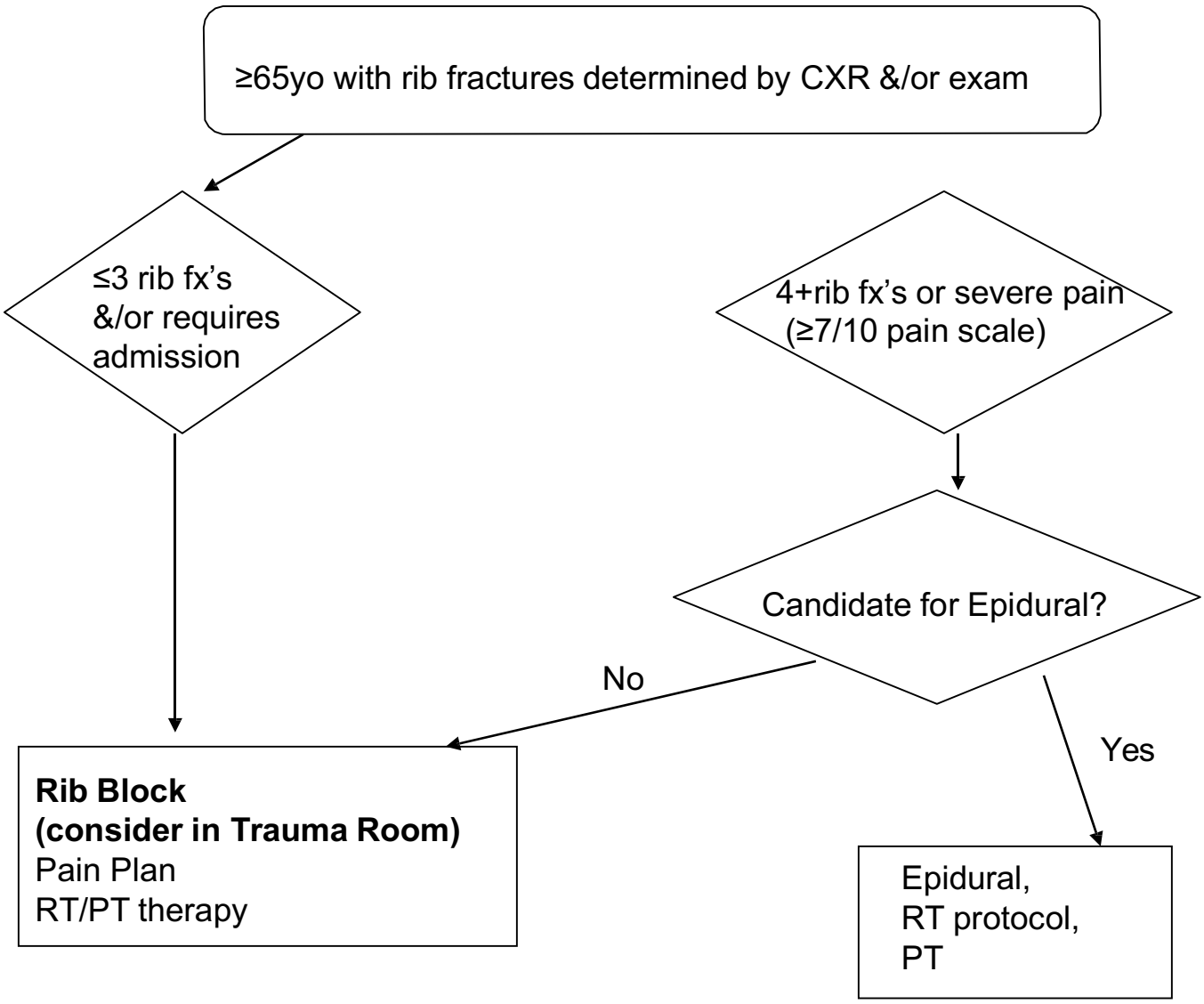
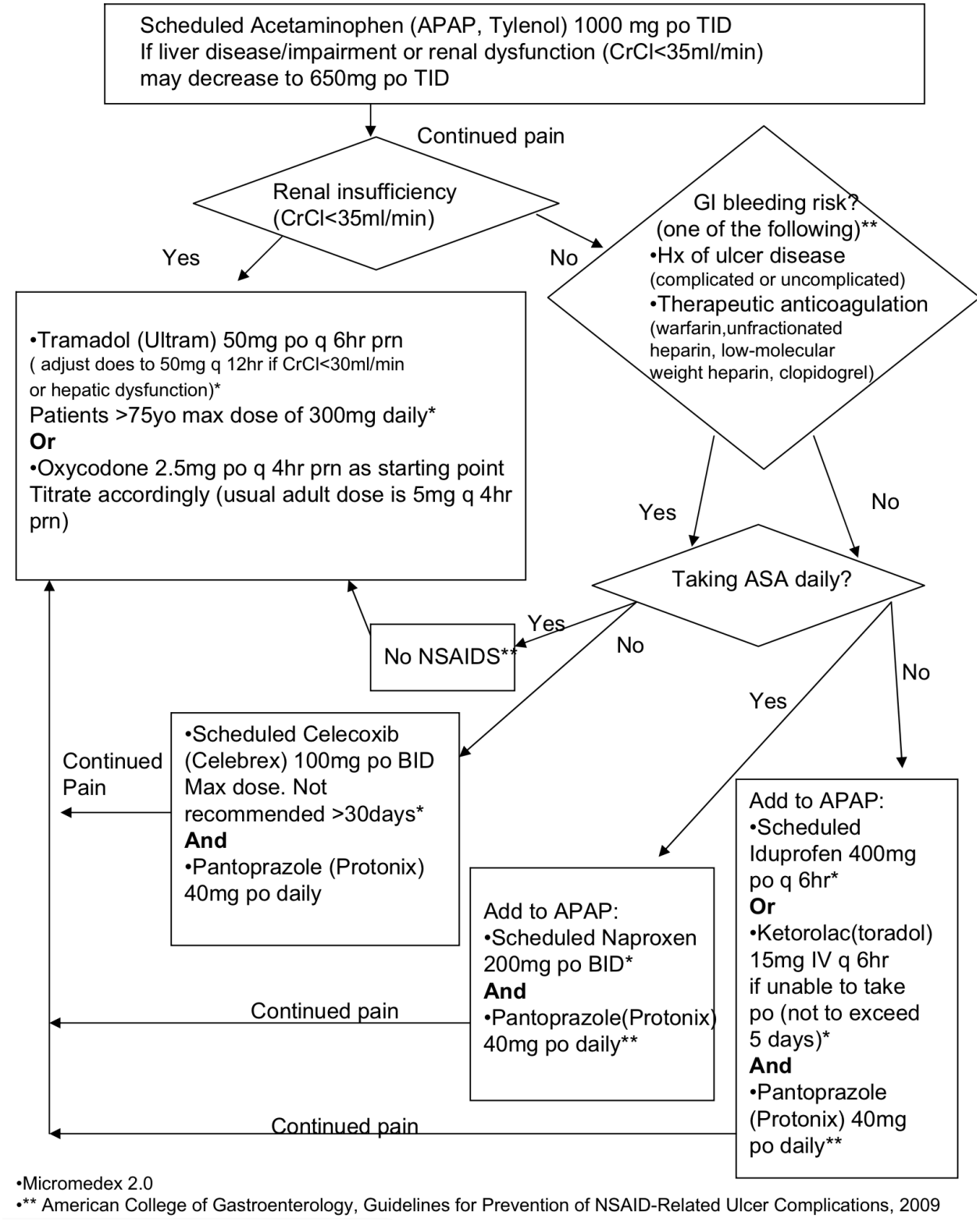
Appendix I. TPP.0043 Geriatric Rib Fracture Management

Pain Management for Elderly Patient (≥65y) with Rib Fractures



Pain Plan



•Micromedex 2.0
•** American College of Gastroenterology, Guidelines for Prevention of NSAID-Related Ulcer Complications, 2009

Appendix I. TPP.0043 Geriatric Rib Fracture Management cont.

DETAILS

Rib Blocks

Location: Performed in Emergency Dept at tender, fractured rib including one level above and below. Medication: 5 ml of 0.25% Bupivicaine with Epinephrine 1:200,000 utilize 25ga needle, inject just below the rib in the intercostal groove. May repeat every 6-8 hours as needed.

RT/PT

- Order respiratory care consult
- Incentive spirometry every hour independent of RT
- Early mobilization with Physical Therapy

Antihistamines

Use Loratadine (Claritin) or Cetirizine (Zyrtec) Diphenhydramine (Benadryl) is contraindicated

Topicals

If skin intact, may use:

- Methylsalicylate(Ben-Gay/Icy Hot) applied to painful area 3-4 times daily or
- Capsaicin cream/lotion/gel applied to painful area 3-4 times daily

IV Opiods

If needed, start with low does (morphine 1mg or hydromorphone 0.1mg) Hydromorphone is preferred in patients with renal dysfunction Opiod equivalency: oxycodone 20mg orally = morphine10mg IV= hydromorphone 1.5mg IV

Benzodiazepines and muscle relaxants including benzodiazepines, methocarbamol(Robaxin), metaxolone(Skelaxin), cyclobenzaprine(Flexeril) are all contraindicated

Other Considerations

If significant rib displacement and/or flail chest with significant volume loss, rib stabilization should be considered.

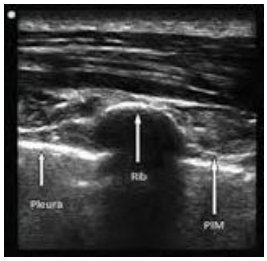
<u>Appendix II</u>. Intercostal Nerve Block Protocol

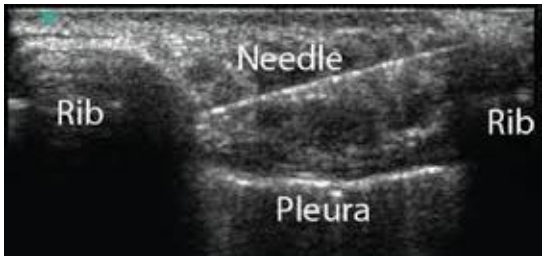
What you will need:

- 0.25% Bupivacaine with 1 : 200,000 epinephrine
- 22 gauge needle (1.5" or spinal per patient size)
- Ultrasound (Optional –utilize high frequency linear probe)
- 10 or 20 mL syringe
- Chloraprep or Betadine prep
- Sterile Gloves

Procedure Outline:

1. Patient should be consented and all questions answered.
2. Pre-Block measurements to be obtained:
    - Global and Thoracic specific numeric pain score
    - Vital Capacity and Incentive Spirometry
3. Identify the location and number of ribs fractured.
4. Calculate the maximum volume of bupivacaine for the patient.
    - Max bupivacaine dose = 3 mg / kg (Volume of 0.25% = **1.2 ml / kg)**
5. Patients should be placed into lateral decubitus position with arm above the head to improve access.
    - Placement of the block proximal to the site of fracture is optimal in all patients.
6. If using:
    - Landmark → Palpate all ribs you plan to block.
    - US → Visualize each of the ribs that you plan to block.
7. Prep the posterior axillary line for all ribs you plan to block.
    - If plan to block posterior, prep the back in a paravertebral fashion.
8. Approach:
    - Landmark Based:
        - Advance needle down onto the rib of interest
        - Withdraw needle slightly. Re-directing the needle caudal, advance down the rib until you feel the need advance just underneath the rib.
        - Advance needle 1-2 mm under the rib and aspirate the syringe.
        - After negative aspiration (i.e. no bubbles or blood), inject 5 mL of solution into rib space.
    - Ultrasound Guided:
        - Visualize the rib and intercostal space of interest with the high frequency ultrasound probe.
        - Note the presence or absence of pneumothorax on ultrasound examination.
            - ✓ Pneumothorax defined by absence of lung sliding on exam.
        - Under direct visualization, advance needle down onto the rib of interest.
            - ✓ Note: Keep tip of needle in view at all times to ensure correct depth.
        - Reposition needle just caudal the rib of interest.
        - Inject 5mL of local anesthetic with needle tip placed just superficial the pleural surface.
        - Withdraw needle and check for pneumothorax at the end of the procedure.





9. Repeat procedure as outlined in step 7 for each fracture including one level above and below known fractures.
10. Post-Block measurements to be obtained. (Note: should be ~15-60 minutes after completion)
    - Global numeric pain score and Thoracic specific numeric pain score.
    - Vital Capacity and Incentive Spirometry.

Appendix III. Acute Pain Management Protocol

Scheduled Medications to start on Admission

- Acetaminophen 1000mg PO q 6 hours
  - If liver disease/impairment or CrCl < 35ml/min ➔ Acetaminophen 650mg q 8 hours
- Ibuprofen 600mg PO q 6 hours OR Ketorolac 15mg IV q 6 hours
  - Patients must have GFR > 60
  - Must have no contra-indication to NSAID therapy (i.e. ASA use, allergy/sensitivity, concurrent ACE inhibitor use, other nephrotoxins, etc.)
  - Ulcer prophylaxis →If on NSAID then Pantoprazole 40mg IV or PO Daily
- Methocarbamol 500mg PO q 6 hours

Intercostal Nerve Block (ICNB) Performed in the Emergency Department or on Admission.

- Please see ICNB protocol for details on how to properly perform an ICNB.
- Pre and Post ICNB: Global and Thoracic Pain scores, Vital Capacity, and Incentive Spirometry measurements.

Ketamine / Placebo Protocol

- Order placed in the Emergency Department upon patient enrollment.
- "Ketamine/Placebo" solution to run at 1.5 mcg/kg/min with NO dosage adjustments.

Opiate Therapy Protocol

- All patients will be placed on IV opiate therapy for at least 24 hours following admission.
- Initial Assessment of Pain on Admission through Numeric Pain Score (NPS)
  - All patients should have both a Global Score and a Thoracic Score.
  - Initial IV opiate medication choice per the discretion of the admitting physician.
  - Initial IV Opiate dosage per the discretion of the admitting physician.
- Reassessment of NPS at 1 hours:
  - If NPS $\geq$ 7 → Dosage of IV opiate should be doubled and administered as 2nd dose.
  - If NPS < 7 → Continue current IV opiate dosing.
- Reassessment of NPS at 2 hours:
  - If NPS $\geq$ 7 → Dosage of IV opiate should be doubled and administered as 3rd dose.
  - If NPS < 7 → Continue current IV opiate dosing.
- Reassessment of NPS hourly / q2 hours:
  - If NPS > 7 → Dosage of IV opiate should be adjusted based on clinical scenario.
  - If NPS < 7 → Continue current IV opiate dosing.

- Reassessment at 6 hours:
  - If Thoracic NPS $\geq$ 7 → Patient should have a repeat ICNB performed.
  - If Thoracic NPS < 7 → Continue current opiate therapy.

- IF patient receives a repeat ICNB:
  - Reassessment at 4 hours post-ICNB and Thoracic NPS $\geq$ 7 → RAAPS to consider Epidural placement
  - Reassessment at 4 hours post-ICNB and Thoracic NPS < 7 → Continue current therapy.
- IF patient DOES NOT receive repeat ICNB:
- Continue reassessments and if Thoracic NPS $\geq$ 7 → Repeat ICNB at time of that assessment.

Appendix IV. Froedtert Confusion Assessment Method (CAM)

Figure 1. Froedtert Memorial Lutheran Hospital General Confusion Assessment Method Assessment.

Feature 1 = Acute onset
1. Is there evidence of an acute change in mental status from the patient's baseline?

Feature 2 = Inattention
1. Did the patient have difficulty focusing attention, for example, being easily distractible, or having difficulty keeping track of what was being said?
a. Not present at any time during interview.
b. Present at some time during interview, but in mild form.
c. Present at some time during interview, in marked form.
d. Uncertain.
2. (If present or abnormal) Did this behavior fluctuate during the interview, that is, tend to come and go or increase and decrease in severity?
a. Yes.
b. No.
c. Not applicable.
3. (If present or abnormal) Please describe this behavior:

Feature 3 = Disorganized thinking
1. Was the patient's thinking disorganized or incoherent, such as rambling or irrelevant conversation, unclear or illogical flow of ideas, or unpredictable switching from subject to subject?

Feature 4 = Altered level of consciousness
1. Overall, how would you rate this patient's level of consciousness?
a. Alert (normal).
b. Vigilant (hyperalert, overly sensitive to environmental stimuli, startled very easily).
c. Lethargic (drowsy, easily aroused).
d. Stupor (difficult to arouse).
e. Coma (unarousable).

Note: The diagnosis of delirium by CAM requires the presence of features 1 and 2 and either 3 or 4.

Figure 1. Froedtert Memorial Lutheran Hospital General Confusion Assessment Method Assessment.

Appendix V. Froedtert Confusion Assessment Method Intensive Care Unit (CAM-ICU)

Figure 1. Froedtert Memorial Lutheran Hospital Intensive Care Unit Confusion Assessment Method Assessment.

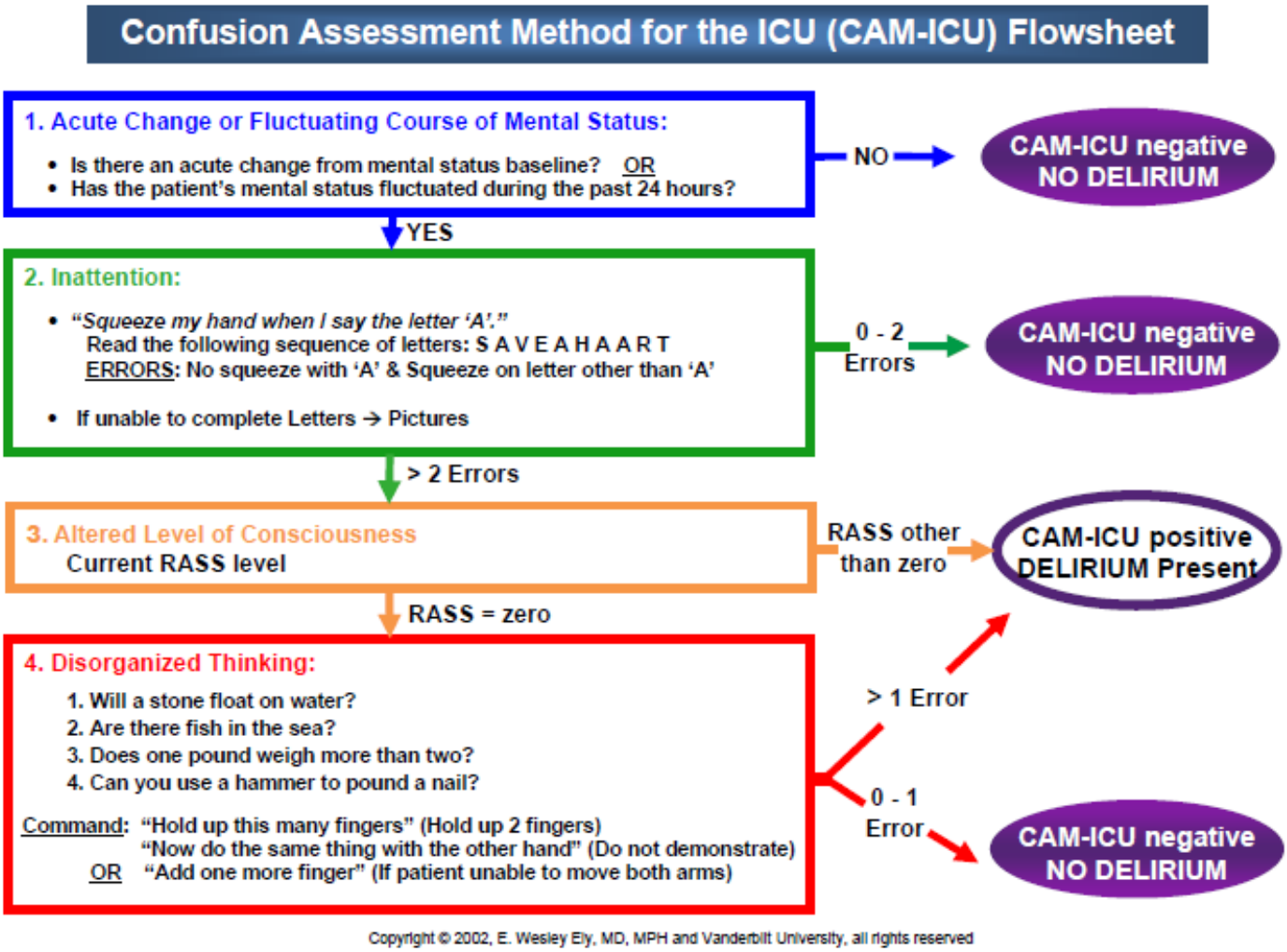


Figure 2. Nursing Delirium Screening Scale (Nu-DESC)

Nursing Delirium Screening Scale (Nu-DESC)

Disorientation
0 - Alert, orientated to person, place and time 1 - Disoriented but easily reoriented 2 - Disoriented x2 or x3, not easily oriented
Inappropriate behavior
0 – Calm and Cooperative 1 – Restless but cooperative 2 - Agitated, pulling at devices, climbing over side rails
Inappropriate communication
0 - Appropriate 1 - Unclear thinking or rambling speech 2 - Incoherence, nonsensical or unintelligible speech
Illusions/Hallucinations
0 - None Noted 1 - Paranoia, fears 2 - Hallucinations, distortions of visual objects
Psychomotor
0 - None 1 - Delayed or slow responsiveness 2 - Excessive sleeping, somnolent, lethargic

NU-DESC >2
Sensitivity=85.7%
Specificity=86.8%

Gaudreau JD, et al. Gen Hosp Psychiatry. 2005;27(3):194-9

Appendix VI: Rib Fracture Sign

RIB FRACTURE PATIENT

Please document

"Thoracic Pain Scores"