General Information:

Study Title: A Multi-Institutional, Retrospective Review for Validation of the Cirrhosis Outcomes Score in Trauma (COST)

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Background and Significance:

Liver disease affects one out of every 10 people in the United States. This number is likely underestimated as many cases of liver disease, particularly compensated cirrhosis, go undiagnosed. In 1990, cirrhosis was identified as an independent predictor of poor outcomes in trauma patients. However, current trauma injury grading systems, such as injury severity scores (ISS) and trauma injury severity score (TRISS), do not take into account liver dysfunction as a risk factor. A score that includes the degree of liver dysfunction would enhance the ability of ISS or TRISS to predict mortality in trauma patients with cirrhosis. While the Child-Pugh (CTP) classification system was historically used to quantify the severity of liver dysfunction, the model for end-stage liver disease (MELD – Tbili, Cr, INR, Na) score is now widely used as an index of liver disease severity, for survival prediction, for surgical risk stratification, and for prioritization of organ allocation. The MELD score is more readily available than the CTP score for the prediction of mortality in trauma patients. Several prior studies have investigated combining trauma injury grading systems with known liver dysfunction scales. Corneille et al found ISS + MELD and ISS + CTP were stronger predictors of mortality than ISS alone for both.

Inaba et al found each unit increase in the MELD score was associated with an 18% increase in the odds of mortality, adjusted odds ratio 1.18.

In our pilot study, a total of 318 cirrhotic trauma patients were analyzed of which the majority were males who suffered blunt trauma. The primary outcome of mortality in-patient, 30-days, 60-days, 90-days, and 1-year was evaluated. COST which was defined as the simple sum of Age, ISS, and MELD was associated mortality on regression analysis, in increasing intervals. A regression analysis of the three individual variables did not demonstrate a need to weigh the components of the score. Adding the individual variables in a weighted fashion did not significantly improve the AUROC and it would add significant complexity to the score calculation. The primary aim of this MIT is to review the risk factors and outcomes of cirrhotic trauma patients to validate the proposed COST mortality prediction model created at Atrium Health Wake Forest Baptist. Secondary goals include elucidating the impact of cirrhosis on morbidities, hospital/ICU LOS, and ultimate patient disposition. Achieving the specific goals of this proposed trial will further our understanding for the prognosis of cirrhotic trauma patients and improve goals of care discussions with patients and their families.

Purpose and Objectives:

We constructed a simple clinical mortality prediction model in cirrhotic trauma patients: Cirrhosis Outcomes Score in Trauma (COST). COST is defined as the sum of age, ISS, and MELD. We hypothesize a higher COST score will correlate with increased mortality in cirrhotic trauma patients.

The primary aim of this study is to review the risk factors and outcomes of cirrhotic trauma patients to validate the proposed COST mortality prediction model created at Atrium Health Wake Forest Baptist. There is not currently a readily available tool to assess trauma outcomes in cirrhotic patients.

We are proposing a multi-institutional, retrospective trial of trauma patients with cirrhosis. This trial would occur in hospitals within the United States. Since this is a retrospective review, there would be no alterations to patient care, and patient care decisions would be determined by the treating team at each individual hospital. A multi-institutional trial is needed to fill gaps in knowledge concerning the outcomes for cirrhotic trauma patients. COST is highly predictive of mortality in cirrhotic trauma patients at 90-days. It is easy to calculate real time in the clinical setting and it may be useful in optimizing goals of care discussions.

Specific aims of this trial include, but are not limited to:

1. To determine risk factors for cirrhotic trauma patients
2. To determine morbidities for cirrhotic trauma patients
3. To determine in-patient, 30-day, 60-day, 90-day, and 1-year mortality for cirrhotic trauma patients

By addressing the above specific aims, we hope to validate this prediction model and the care of cirrhotic trauma patients.

Experimental Design/Methods:

Study Design:
This study is a retrospective review. Institutional Review Board (IRB) approval will be obtained at the Vanderbilt University Medical Center and Wake Forest University Health Sciences, with each participating institution obtaining their own IRB approval. Each center will be responsible for screening, accessing or analyzing data or images based on the inclusion and exclusion criteria. There will be not intervention or interaction with subjects. Variables to be collected are outlined in the data collection form. While care for cirrhosis often extends beyond the initial hospitalization, this study will only include data from the initial hospital admission until discharge. Care after the initial discharge will not be included. As a retrospective study, there is a minimal risk to patients as there will be no alterations to patient care. Study duration for data collection and analysis is anticipated to be 4 years. We anticipate including over 1000 charts, with likely 100-200 at each site.

Study Population:
Patient charts will be included if they meet the stated inclusion criteria. They will similarly be excluded if they meet the stated exclusion criteria as outlined below.

Inclusion Criteria:
1. Age 18 years and greater
2. Traumatic injury
3. History of well-compensated cirrhosis based on known clinical diagnosis
4. Cause of cirrhosis secondary to pre-existing illness: alcohol abuse, hepatitis, NASH, cryptogenic
5. Admission labs (first set of labs obtained during the patient's trauma evaluation) must include CMP and INR

Exclusion Criteria:
1. Age less than 18 years
2. Non-traumatic injury
3. Liver dysfunction secondary to traumatic injury includes patients with a significant liver injury and/or shock liver of critical illness
4. Pregnancy
5. Missing essential labs, ie. CMP and INR

Recruitment and Consent Procedures:
Each institutional PI(s) or their designees will screen and include patient charts. If a patient chart both meets inclusion criteria and does not meet exclusion criteria, they will be included at their treating institution. There will be a waiver of consent requested for this study, and thus undue coercion is not a consideration. A waiver of consent is requested for this trial as it is retrospective, and patients with cirrhosis and trauma are often critically ill and are unable to give consent. Excluding these patients would bias this trial against the sickest patients.

Data Use Agreement:

A data use agreement will be completed with all participating sites, including our partnership with Atrium Health Wake Forest Baptist. A standard data use agreement form will be utilized from the Vanderbilt Contracts Department.

Randomization Procedures:
There is no randomization in this study, as this is a retrospective trial. There is no alteration in patient care provided, and care is according to the treating team at each institution.

Therapeutic Interventions/Procedures:
There is no proposed alteration in patient care with this retrospective trial. Patients will be treated according to the standard at each institution. There will be no therapeutic interventions or procedures which occur specifically due to trial participation. However, interventions/procedures which are performed as part of patients' courses of care may be noted.

Study Variables:
Study variables are as listed in the data collection form. PHI is required to connect medical records together and due to potential inclusion of age >89 as a variable. Initially, MRN will be used to determine inclusion at a participating facility; however, it will not be used in the final data set.

Benefits to Study Participants:
There is no benefit to participants in this trial as this is a retrospective trial, and there will be no alteration in patient care. However, there will be benefit to future patients with cirrhosis through further optimizing care of cirrhotic trauma patients.

Disclosure of Information to Study Participants:
Information will not be disclosed to study participants.

Risks to Study Participants:
This is a minimal risk study, with breach of confidentiality the primary risk. We will guard against breach of confidentiality with the use of a limited-use data set prior to entry into the central multi-institutional trial data collection tool RedCap, which will be maintained by the team at Vanderbilt University Medical Center. The exception is age will be recorded as a variable in this study, including age greater than 89 years if this occurs. There are not alternatives to participation.

Drug/Device Information:
This is a retrospective trial. While patients may undergo therapy with a drug or device during treatment of their cirrhosis in the setting of trauma, choices of drug use and device use will be according to institutional practice. No changes in patient care will occur with this study. This study does not delineate use of a drug or device as part of the study protocol.

Safety:
This is a minimal risk study. There will be no alterations in patient care with this study, and patients will be treated according to their institutional standard of care. The major risk in this study is loss of confidentiality, which will be guarded against by using a password protected data

collection tool. We will also be entering mostly de-identified data into the central data collection tool. The exception will be age which will be a collected variable, including age greater than 89 years.

Data Collection/Storage/Monitoring:
Data from each participating institution will be entered into the central data collection tool. This data collection tool is HIPAA compliant and the data will be a limited-use data set with all but the age of the subject being de-identified prior to entry into the central data collection tool, including age greater than 89 years. The team at the Vanderbilt University Medical Center will oversee the central data collection tool after creation of the standardized data entry form and will also monitor the data on a quarterly basis. The RedCap data collection tool requires a username and password for access. Local institutions will store data according to their own local practices and IRB regulations.

Data Safety Monitoring Board:
Since this study is a retrospective trial, there will not be a Data Safety Monitoring Board (DSMB) as there is no alteration in patient care.

Confidentiality:
The major risk in this study is loss of confidentiality. The entered data into the RedCap data collection tool will be de-identified, with the exception of age. Each patient record in the central data collection tool is given a record ID number. While the RedCap central data collection tool is accessible over the internet, access requires a username and password. Local records may be maintained at each institution according to their own protocols for IRB reporting and data storage.

Compensation/Costs:
There will be no compensation for included charts in this trial. There will similarly be no costs incurred for including charts in this trial.

Funding:
There is not funding for this initiative at either site, Vanderbilt University Medical center or Atrium Health Wake Forest Baptist.

Waiver of Consent:
This study will be performed with a waiver of consent, as it is a retrospective study with no alteration in patient care. There is no physical risk to the patient given as there are no alterations in patient care and this is considered a minimal risk study. The main risk to participants is loss of confidentiality, which will be guarded against using the described precautions. This study would not be feasible without a waiver of consent, as patients with cirrhosis in trauma are often critically ill and unable to give consent. These patients may sometimes die, and would then be similarly unable to give consent. Exclusion of these critically ill patients would bias the results of this study by not including the most critically ill.

Data Collection/Statistical Analysis/Justification of Sample Size:

Data Collection:
This is a retrospective trial. Collected variables will include those listed in the data collection form, and the data points will be entered into the RedCap data collection tool. The coordinating center team at the Vanderbilt University Medical Center will maintain the database and evaluate the data on a quarterly basis. They will also be responsible for communication with participating centers and provide the statistician for data analysis.

Initial Data Analysis:
We will perform univariate analysis on the data to determine variable frequencies and sample characteristics. Appropriate bivariate analyses will be performed comparing the association of collected variables and outcomes. More specific analysis may be performed for analysis of time to various therapies, such as with Kaplan-Meier plots and Cox proportional hazards models. Multivariate analysis may be performed to account for the effect of confounding variables.

Specific aims are as follows but are not limited to:

Specific Aim #1: To determine risk factors for cirrhotic trauma patients

Specific Aim #2: To determine morbidities for cirrhotic trauma patients

Specific Aim #3: To determine in-patient, 30-day, 60-day, 90-day, and 1 year mortality for cirrhotic trauma patients

Specific Aim #4: To validate COST

Risk/Benefit Analysis:
Currently, there is no a readily available tool to assess trauma outcomes in cirrhotic patients. The risk factors, morbidities, and mortality of cirrhosis in trauma patients may be beneficial to elucidate to provide better care for future cirrhotic patients. The risk to patients in this trial is minimal as this is a retrospective trial without alterations in patient care. The major risk to patients is loss of confidentiality, which we will guard against as described.

Vulnerable Populations:

1. The status of the included patient chart as an employee/lab personnel, or prisoner will likely not be known from the records reviewed from the study.
2. Cognitively impaired individuals may be included in this study. There will not be direct patient contact with patients who are cognitively impaired.
3. Pregnant patients will be excluded from this trial as their radiographic imaging and medical therapy may differ due to their gravid state from the general patient population.

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