Study Protocol Title:

Can we be FASTeR? A prospective study utilizing right sided roll to improve sensitivity of the FAST examination

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List of Abbreviations:

FAST - Focused Assessment with Sonography in Trauma Exam
ATLS - Acute Trauma Life Support
FASTeR - FAST exam with Right sided roll
CT - Computed Tomography
PHI - Protected Health Information
REDCap - Research Electronic Data Capture
OR – Operating Room
RUQ – Right Upper Quadrant
LUQ – Left Upper Quadrant
MRH – Memorial Regional Hospital
MOI- Mechanism of Injury
MRI – Magnetic Resonance Imaging
ACS – American College of Surgeons

Introduction

This document is a protocol for a human research study. This study is to be conducted according to US and international standards of Good Clinical Practice in accordance with applicable Federal regulations, International Conference on Harmonization guidelines, and institutional research policies and procedures.

Background Information and Scientific Rationale

Summary of Previous Pre-clinical Studies/Relevant Clinical Studies

Rapid diagnosis and management of intra-abdominal hemorrhage after blunt trauma is critical in the triage and assessment of trauma patients (1). The Focused Assessment with Sonography in Trauma examination (FAST) is an efficient, bedside, non-ionizing, non-invasive method for assessing hemoperitoneum (the presence of blood in the peritoneal cavity), in traumatically injured patients. The FAST is taught during the Acute Trauma Life Support (ATLS) Course, and is the gold standard for the initial assessment of abdominal and chest trauma (2). FASTs have excellent specificity (94.7-99.6% in most series), however sensitivity is low (20-60%) (3-5). Improving the sensitivity of the FAST would allow for earlier detection and management of life-threatening intra-abdominal hemorrhage for innumerable trauma patients.

FASTs are typically performed with the patient in the standard position, lying flat on their back. The right upper quadrant (RUQ), left upper quadrant (LUQ) and suprapubic region are scanned and evaluated for hemoperitoneum. If fluid is found in any of these views, the patient is emergently taken to the operating room (OR) to treat the intra-abdominal hemorrhage.

It has been previously shown that a standard FAST is most likely to detect hemoperitoneum in the RUQ in Morison's pouch, the space on the right side of the body that separates the liver and the right kidney (hepatorenal recess) (2). A recent pilot by Pigneri et al., compared standard FAST exam to FAST exam after the patient had been rolled onto their right side; this modified evaluation method was termed **F**ocused **A**ssessment with **S**onography in **T**rauma **e**xamination after **R**ight sided roll (FASTeR). The rationale was this position likely uses gravity to collect intra-abdominal fluid into Morison's pouch, thus making it possible to visualize small volumes of fluid that would otherwise be undetectable when the patient is lying flat (6). This study demonstrated earlier identification of intra-abdominal fluid with the FASTeR when compared to the standard FAST (6).

Rationale

All patients are rolled onto one side or the other during normal trauma evaluation. Changing practice to turn the patient onto the right side for a modified FAST, or FASTeR, can potentially increase exam sensitivity without delaying care. Our goal is to perform a large, multicenter study to evaluate the impact of FASTeR versus the standard

FAST in hemodynamically unstable trauma patients. We plan to prospectively collect data for creation of a multicenter database; enrolled subjects would undergo both the standard FAST and when appropriate (see Methods) a FASTeR. Our aim is to determine the sensitivity and specificity of the FAST and FASTeR, and determine which exam was more accurate in recognizing hemoperitoneum. Exam results will be confirmed with computed tomography (CT) imaging or operative findings.

Potential Risks and Benefits

Potential Risks

There are no expected medical risks to the study participants in excess of the normal risks of the FAST, which is minimal.

Potential Benefits

If the FASTeR is shown to detect small volumes of hemoperitoneum earlier than was previously possible with the FAST, patients may directly benefit from earlier diagnosis and treatment. Early identification of hemoperitoneum has been shown to be strongly correlated with increased survival rates (1).

Study Objectives

Primary Objective

To calculate and compare the sensitivity and specificity of detecting hemoperitoneum in the RUQ for the standard FAST and the FASTeR in the research subjects. Actual injury complex will be confirmed by CT or operative findings.

Secondary Objective

To calculate and compare the false positive rate, false negative rate, positive predictive value, negative predictive value, and positive and negative likelihood ratios for the standard FAST and FASTeR. Exam results for individual subjects will be compared to see if there is a significant difference in result accuracy.

Study Design

This is a prospective multicenter study. Detailed responsibilities for the lead (Memorial Regional Hospital) and satellite centers below.

Memorial Regional Hospital (lead)

1. Maintain database for enrolled MRH subjects. Data collected will include HIPAA identifiers (included in outcome measures) to monitor our own data integrity.
2. As lead center, MRH will aggregate and analyze collected data from satellite centers which will be submitted without HIPAA identifiers.
3. MRH to manage subjects meeting inclusion criteria according to our institutional patient management protocols.
4. MRH to adhere to IRB protocol and application as submitted.

Satellite Centers

1. Each center must apply and receive IRB approval from their respective IRB(s).
2. Each center is responsible for their own data integrity, as outlined in their approved IRB protocol and application.
3. Each center to provide IRB outcome or waiver letter to the lead center.
4. Each center to complete the data sharing agreement specific to this study.
5. Each center to provide care according to their institutional patient management protocols.
6. Each center to submit de-identified data to the lead center for analysis.

Subject Selection

Inclusion Criteria

1. Patients over 18 and under 89 years of age who present as a trauma activation with clinical history or physical signs of blunt abdominal trauma and hemodynamic instability

Exclusion Criteria

1. Patients under 18 and over 89 years
2. Pregnant women
3. Patients with prohibitive right sided chest trauma
4. Patients in extremis undergoing salvage maneuvers (chest compressions or emergent surgical intervention) which prevents performance of an ultrasound examination
5. Patients who leave against medical advice or are otherwise removed from the medical system before their work up has been completed

Sample Size

50 participants at MRH and 250 participants total for all sites.

Research Design

This is a prospective multicenter study, where MRH will act as the lead center. Each contributing center is responsible for obtaining IRB approval and maintaining data integrity outlined in their approved IRB protocol and application from their respective institutions. Once IRB approval has been obtained, we will begin enrolling trauma patients prospectively into a registry. The participating centers for this study represent a diverse set of trauma centers and emergency departments and include institutions with varying trauma verifications (e.g. ACS and State), sizes, geographical/metropolitan locations, and resource availability to ensure inclusivity.

Since this is a prospective observational study, data will be collected prospectively without altering the manner in which the patients are managed by the surgeon and institution. Accordingly, an informed consent waiver is requested. Patients will be given a flyer with information about the study (see additional documents). Data will be collected for a two year period with interim analysis when specific enrollment targets are met. All data will be recorded on a data sheet and transferred to a secured database (REDCap) without patient identifiers.

Patients with clinical history or physical signs suspicious for blunt abdominal trauma will undergo the standard FAST in the emergency department as per ATLS protocol. During the secondary survey, all patients are rolled for examination of their back and removal of the rigid spine board, per ATLS. In our study, we will standardize this practice so that all patients are rolled onto their right side for this portion of the examination. Patients with extensive right sided chest trauma will be excluded at the discretion of the Trauma Surgeon. After the right sided roll to remove the back board, a repeat ultrasound examination of the RUQ will be performed.

All participating centers, including MRH, will collect and submit the following data to the database for each enrolled subject: age, gender, initial trauma bay vital signs, mechanism of injury, results of the FAST, results of the FASTeR, and injury complex as confirmed by CT imaging or operative findings for their respective centers. Both the CT scan and any surgical intervention that the participant undergoes as a study subject will be performed through routine standard of care procedures. The database will not contain HIPAA identifiers.

MRH will record our internal subject medical record numbers and dates of admission to verify data fields and monitor our own data integrity. All data will be de-identified prior to publication.

Study Outcome Measures (Endpoints)

The study outcome measures will be recorded using the "*Multicenter Study: Can we be FASTeR? A multicenter study utilizing Right sided roll to improve sensitivity of the FAST examination*" data collection form. The patient medical record number (MRN) will be

recorded by hand on the tool for all MRH enrolled subjects only; subject data will be cross-checked with the electronic records in order to maximize data integrity.

1. Number of patients admitted and discharged from MRH between the timeframe (October 16, 2017- October 16, 2019) who present as a trauma activation with clinical history or physical signs of blunt abdominal trauma and hemodynamic instability
    a. MRN (recorded by hand), internal use only
    b. Admission date (recorded by hand), internal use only
2. Demographics (e.g. age, gender)
3. Admission vital signs (e.g. heart rate [bpm], blood pressure, respiratory rate, oxygen saturation)
4. Results (positive or negative) of the FAST (RUQ, LUQ, surprapubic)
5. Results of the FASTeR (RUQ)
6. Method where final injury complex determined (if applicable)
    a. Operative findings
    b. CT scans
    c. Other imaging (e.g. MRI, x-ray, ultrasound)
7. Final injury complex (if applicable)
    a. Liver injury
    b. Splenic injury
    c. Gastrointestinal injury (type)
    d. Genitourinary injury (type)
    e. Vascular/mesenteric injury (type)
    f. Pancreatic injury
    g. Other (type)
8. Outcome of hemoperitoneum confirmed by imaging or operative findings

Statistical Analysis Plan

All subjects who meet inclusion criteria and have complete data available will be used for data analysis. The sensitivity and specificity (with confidence intervals) for detecting hemoperitoneum using the standard FAST or the FASTeR versus the actual injury complex findings (CT or operative findings) will be calculated in the research subjects along with the false positive rate, false negative rate, positive predictive value, negative predictive value, and positive and negative likelihood ratios. A McNemar's test will be used to directly compare the accuracy of the FAST and FASTeR results for individual research subjects.

The data pooled from the participating centers will provide a robust data set that will minimize center or physician specific result bias and provide the needed statistical volume as calculated by the power analysis.

Study Procedures

Subject Identification, Recruitment, and Screening

This a prospective multicenter study, which will prospectively record data without altering the manner in which the patients are managed by the surgeon and institution. Accordingly, an informed consent waiver is requested. All data will be recorded on a data sheet and transferred to a secured database (REDCap) without patient identifiers.

Eligibility for study enrollment will be considered for all patients presenting to MRH as a trauma alert during the study period, with a clinical history or physical signs for blunt abdominal trauma who would clinically indicate a standard FAST in the trauma bay as per ATLS protocol. Patients with extensive right sided chest trauma will be excluded at the discretion of the Trauma Surgeon. Both the CT scan and any surgical intervention that the participant undergoes as a study subject will be performed through routine standard of care procedures.

Study Duration

We anticipate a rolling accruement of subjects over a two year period. A sample size calculation (power analysis) was performed to estimate the needed total participant accruement to provide a power of 90% and an alpha of <0.05. Standard FAST should identify up to 60% of subjects with significant intra-abdominal injury. If we assume that the FASTeR will identify hemoperitoneum in 1 of 4 subjects with intra-abdominal injury and previous negative FAST examination, then our needed sample size is 209 subjects. To account for subjects meeting exclusion criteria, we will plan to accrue 250 patients. Given that this sample size calculation was based on estimation regarding the sensitivity of the FASTeR in this patient population, interim analyses regarding primary endpoint will be conducted after 100 subjects have been accrued and again after 200 subjects have been accrued. Subject charts will be reviewed in increments of ten as they are enrolled.

Withdrawal of Subjects

Subjects that are unable to tolerate the position changes described in the protocol will be considered screening failures and will be automatically withdrawn from the study.

Subjects that receive the FASTeR are free to withdraw themselves from the study at any time. They may withdraw from the study by notifying the PI, Dr. Pigneri, directly by phone. The option to withdraw and the contact information for Dr. Pigneri are listed on the study information flyer that will given to all subjects.

Quality Control and Quality Assurance

Study data will be collected and managed using REDCap electronic data capture tools. REDCap (Research Electronic Data Capture) is a secure, web-based application designed to support data capture for research studies, providing 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources (7).

Satellite centers are responsible for getting IRB approval and maintaining their own data integrity as outlined in their respective IRB protocols and applications. The lead center (MRH) will aggregate and analyze deindentified data collected in REDCap.

Ethical Considerations

This study is to be conducted according to US and international standards of Good Clinical Practice, applicable government regulations and Institutional research policies and procedures.

This protocol and any amendments will be submitted to a properly constituted Institutional Review Board (IRB), in agreement with local legal prescriptions, for formal approval of the study conduct.

Confidentiality and Privacy

Information about study subjects will be kept confidential and managed according to the requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA). Subjects may voluntarily withdraw from the program or revoke their authorization to share information related to the research. In the event that a subject revokes authorization to collect or use PHI, the investigator, by regulation, retains the ability to use all information collected prior to the revocation of subject authorization.

Subjects will be assigned a study identification (ID) number that will distinguish subjects; a master code list linking the subject's study ID to patient identifiers will not be shared and will be stored in a separate location from the study data. All data collected will be de-identified and aggregated before sharing. The master code list and study data and will be destroyed following data analysis and study completion. All data will be de-identified prior to publication.

Conflict of Interest

There is no conflict of interest.

Funding Source

None

Publication Plan

The Investigator intends to publish the results of this prospective study in a peer-reviewed journal at an unspecified time in the future. The Investigator will serve as the primary and corresponding author for any future publications related to this proposed study.

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