DATE:	September 8, 2022
TO:	Katherine Pellizzeri, MD
FROM:	Prisma Health Committee A
PROJECT TITLE:	[1956314-1] The Utility of Serial Hemoglobin Monitoring in Non-Operative Management of Blunt Splenic Injury
REFERENCE #:	
SUBMISSION TYPE:	New Project
ACTION:	APPROVED
APPROVAL DATE:	September 8, 2022
EXPIRATION DATE:	None - Next Report Due Date September 7, 2025
REVIEW TYPE:	Expedited Review
REVIEW CATEGORY:	Expedited review category # *5*

The following items are approved in this submission:

- Prisma Health - IRB Application - Prisma Health - IRB Application (UPLOADED: 09/8/2022)
- Protocol - NOM Blunt Splenic Injury Prospective Study_Protocol_18Aug2022_For IRB Submission.docx (UPLOADED: 09/8/2022)

Thank you for your submission of New Project materials for this project. The Prisma Health Committee A has APPROVED your submission. This approval is based on an appropriate risk/benefit ratio and a project design wherein the risks have been minimized. All research must be conducted in accordance with this approved submission.

This submission has received Expedited Review based on applicable federal regulations.

Please remember that informed consent is a process beginning with a description of the project and insurance of participant understanding followed by a signed consent form. Informed consent must continue throughout the project via a dialogue between the researcher and research participant. Federal regulations require that each participant receives a copy of the consent document.

Please note that any revision to previously approved materials must be approved by this committee prior to initiation. Please use the appropriate revision forms for this procedure.

All UNANTICIPATED PROBLEMS involving risks to subjects or others (UPIRSOs) and SERIOUS and UNEXPECTED adverse events must be reported promptly to this office. Please use the appropriate reporting forms for this procedure. All FDA and sponsor reporting requirements should also be followed.

All NON-COMPLIANCE issues or COMPLAINTS regarding this project must be reported promptly to this office.

This project has been determined to be a MINIMAL RISK project. Based on the risks, this project does not require annual continuing review. The next report due date will be September 7, 2025. If this project completes prior to this date, please submit a status change for project closure to the IRB.

Please note that all research records must be retained for a minimum of three years after the completion of the project.

If you have any questions, please contact Prisma Health IRB at 864-455-8997 or IRB@PrismaHealth.org. Please include your project title and reference number in all correspondence with this committee.

This letter has been electronically signed in accordance with all applicable regulations, and a copy is retained within Prisma Health Committee A's records.

Protocol Version: 18Aug2022

The Utility of Serial Hemoglobin Monitoring in Non-Operative Management of Blunt Splenic Injury

Principal Investigator: Katherine Pellizzeri, MD

Resident: Taylor Harris, MD

Medical Student: Nicolas Poupore

Multicenter Study proposal is: prospective, observational

Background

Non-operative management (NOM) has become the standard of care in trauma centers across the country for treatment of hemodynamically stable patients with low grade blunt splenic injuries (BSI). In hopes of identifying patients early who will fail NOM, institutions frequently order serial hemoglobin (S-Hgb) levels to attempt to treat hemorrhage prior to a decline in hemodynamics. However, patients that fail NOM due to sudden acute blood loss from a clot that becomes disrupted or a sudden tear of a splenic artery from an expanding splenic hematoma, will develop signs and symptoms of shock before they develop a significant drop in their hemoglobin concentration, making serial hemoglobin values less useful.

A retrospective chart review of patients with BSI between 2013 and 2019 was performed at Prisma Health[1]. In this study, 341 patients were admitted for NOM of their BSI and 37 failed. Patients undergoing arterial embolization were included as requiring operative management. Although 8 of the 37 patients were documented as having a drop of hemoglobin as one of the reasons for failure of NOM, individual chart review identified that only 1 of the 8 had a drop in S-Hgb value as the main event that led to further imaging or a procedure. There were no differences in mortality, ICU or hospital length of stay in patients that failed NOM and had S-Hgb compared to daily Hgb (D-Hgb) values. This retrospective study supports the argument that serial Hgb values may not influence clinical decision-making in NOM of BSI and may not change clinical outcomes. Furthermore, obtaining D-Hgb values instead of S-Hgb values appears to be a safe practice with potential benefits of decreased patient venipunctures, use of resources and cost. In order to confirm these results, a larger prospective multicenter observational study comparing the

outcomes of NOM patients undergoing either daily or serial hemoglobin monitoring is necessary.

Primary Aim

To determine if Serial compared to Daily Hemoglobin monitoring helps identify failure of non-operative management earlier

Secondary Aims

To determine whether monitoring Serial Hemoglobin values compared to Daily monitoring in the NOM group affects clinical outcomes or mortality.

To determine what factors helped identify failure of NOM in patients undergoing Serial compared to Daily Hemoglobin monitoring.

To determine if there are patient subgroups that may benefit from the practice of monitoring Serial Hemoglobin values.

Inclusion Criteria

Patients 18 years or older
Patient identified to have Blunt Splenic Injury (BSI)
Patients that were admitted for non-operative management of their BSI
Admission and monitoring at a Level 1 or 2 trauma center with IR capabilities
Centers with current practice of Serial (q6 hours) or Daily Hemoglobin measurements

Exclusion Criteria

Prisoners
Patients under the age of 18
Patients that died prior to admission
Patients that died of non-abdominal causes within 30 days of admission

Therapeutic Interventions

Operative Management to include any abdominal operation or arterial embolization

Primary Outcome

The rate of failure of NOM in patients monitored with S-Hgb and D-Hgb values

Secondary Outcomes

Clinical outcomes, including mortality, hospital and ICU length of stay, amount of blood transfusions or massive transfusion protocols, and interventions for patients undergoing NOM with S-Hgb and D-Hgb monitoring

Factors that helped identify F-NOM in patients undergoing S-Hgb and D-Hgb monitoring

Patient-dependent factors and clinical factors on presentation in patients undergoing NOM with S-Hgb and D-Hgb monitoring, and comparisons of clinical outcomes related to specific subgroups

List specific variables to be collected & analyzed

Institutions will be asked to contact us within 24 hours of one of their patient's failing NOM and the reason for their failure. To ensure that institutions are prospectively reporting the reasons for failure of NOM, institutions will be contacted on a weekly basis to determine if they had any patients who failed NOM and the reason(s) for failure. The following data will be collected when either an institution contacts us with a patient who failed NOM following a splenic injury, or at our weekly contacts to institutions:

Gender
Age (age above 89 aggregated into one category)
BMI
Comorbidities
Physical exam, vitals, fluid and blood product requirements, ETOH and the need for mechanical ventilation on initial assessment
Findings on initial imaging
Splenic and associated injuries
Hemoglobin values and their timing
Clinical management- OM vs NOM
Success or failure of NOM and the reasons for failure
Type of intervention for those that underwent OM
Mortality

ICU and hospital LOS
Total number of blood transfusions

Data collection and statistical analysis plan

The data will be collected using RedCap Database. Investigators from outside institutions will be given remote access to upload de-identified data to our database. Prisma Health will be the lead site of this multicenter study through the Eastern Association for the Surgery of Trauma (EAST). EAST is a medical association made up of American trauma surgeons. Participating centers will submit this protocol, and all study materials, to their respective institutional review boards (IRBs). Each participating center will send their IRB approval letter to the lead site before they are added to the REDCap database, which is a HIPAA compliant research database. Sites will input data directly into the REDCap database hosted by Prisma Health. No protected health information (PHI) will entered into the database or shared between sites. A master key which links the subject names with the study identification codes will be maintained at the local investigative site until the study has ended and all the information has been collected and verified with the hospital chart.

Institutions will be asked to contact us within 24 hours of one of their patient's failing NOM and the reason for their failure. To ensure that institutions are prospectively reporting the reasons for failure of NOM, institutions will be contacted on a weekly basis to determine if they had any patients who failed NOM and the reason(s) for failure. Other data such as demographics and outcomes can be obtained retrospectively.

Will determine if patients who failed NOM in the S-Hgb group were more likely to have a decrease in hemoglobin as a reason for their failure vs patients in the daily hemoglobin group. Will also determine if patients in the S-Hgb group had decreased incidences of hypotension prior to operative management.

Serial and Daily hemoglobin measurement groups will be compared in bivariate analyses using the Chi-square test or Fisher's Exact test for categorical data and Student's T-test or the Wilcoxon Rank Sum test for continuous data. Multiple logistic regression analysis will be used assess the adjusted association of hemoglobin measurement group to NOM failure.

Method for sample size calculation: Inference for a single proportion, comparing to a known proportion, power of 80%, α of 0.05, and a 1-sided test.

The assumption for known proportions is based on the fact that 8 of the 37 failures in NOM (21.6%) had a drop in Hg initially felt to contribute to failure. Detailed chart review, however, revealed that only one of those drops in Hgb led to a change in clinical management (2.7%). Thus, only 10% of those patients had a "clinically significant" drop in Hgb.

Based on the sample size calculation table below, we estimate the need to enroll at least 109 NOM failure patients in each group (serial vs daily Hgb) to detect an absolute difference of 10% (clinically significant) based on an assumed known proportion of 20%

Assumed proportion of failures related to Hgb drop	**Clinically important difference**	**Number of NOM failures needed for study in each group (serial or daily)**
0.03	10%	32
0.05		44
0.10		69
0.15		91
0.20		109
0.25		125

Outline consent procedures here, if applicable

We are requesting a waiver of informed consent and a waiver of documentation of informed consent. Patients will be in acute care/trauma surgery service, and the only information that will be collected prospectively is the reason for failure of NOM. Other data will be obtained retrospectively. Institutions will be asked to adopt the hemoglobin collection frequency that most closely resembles their current practice. Surgeons will treat their patients based upon their own clinical judgement. Participants will not be required to participate in any study visits, and all data points will be collected through the electronic medical record system, as this is an observational study.

Succinctly outline a risk/benefit analysis

The biggest risk of this study concerns the security of protected health information. All data uploaded to the redcap database to be analyzed will be de-identified.

It is unlikely that there will be any immediate benefit to the patients participating in this study, but future care will likely be enhanced. The result of this study may answer the question of whether monitoring labs more frequently positively impacts outcomes for patients with BSI undergoing NOM. If this is not found to be of benefit, de-implementation of this practice can decrease patient venipunctures and discomfort, potentially decrease acute blood loss anemia from frequent lab draws, as well as decrease cost and use of hospital resources. Furthermore, if this practice negatively impacts outcomes, then de-implementation should improve patient care.

Include a brief listing of key references

1) Poupore, NS, Boswell ND, Baginski B, Cull J, Pellizzeri K. The Utility of Serial Hemoglobin Monitoring in Non- operative Management of Blunt Splenic Injury. *The American Surgeon*, 2021, 0(0):1–6, doi:10.1177/00031348211048829. Accepted for publication.
2) Olthof DC, Joosse P, van der Vlies CH, de Haan RJ, Goslings JC. Prognostic factors for failure of nonoperative management in adults with blunt splenic injury. *Journal of Trauma and Acute Care Surgery*. 2013;74(2):546-557. doi:10.1097/ta.0b013e31827d5e3a
3) Peitzman AB, Heil B, Rivera L, et al. Blunt splenic injury In Adults: MULTI-INSTITUTIONAL study of the Eastern Association for the surgery of trauma. *The Journal of Trauma: Injury, Infection, and Critical Care*. 2000;49(2):177-189. doi:10.1097/00005373-200008000-00002
4) Stassen NA, Bhullar I, Cheng JD, et al. Selective nonoperative management of blunt splenic injury. *Journal of Trauma and Acute Care Surgery*. 2012;73(5). doi:10.1097/ta.0b013e3182702afc

Eastern Association for the Surgery of Trauma
Advancing Science, Fostering Relationships, and Building Careers

SERIAL VS. DAILY HEMOGLOBIN IN THE NON-OPERATIVE MANAGEMENT OF BLUNT SPLENIC INJURIES
EAST MULTICENTER STUDY
DATA COLLECTION TOOL

Multicenter Study: _____

Enrolling Center: _____
Enrolling Co-investigator: _____

Demographics:

Age: _____ Sex:_____ BMI: _____

Comorbidities:

Alcohol Use Disorder	YES	NO
Anticoagulant Therapy	YES	NO
Antiplatelet Therapy	YES	NO
Bleeding Disorder	YES	NO
Cirrhosis	YES	NO
Current Smoker	YES	NO

Initial assessment data:

ISS:

GCS:

HR:

SBP:

DBP:

Crystalloid (L):

MTP:	YES	NO
TBI:	YES	NO
Mechanical Ventilation:	YES	NO
ETOH:	YES	NO

Imaging findings data:

Transfusions	# of units
pRBC	
FFP	
Whole blood	

Hemoperitoneum: YES NO

CT Blush: YES NO

Traumatic injuries data:

Grade of Splenic Injury: 1 2 3 4 5

Isolated Splenic Injury: YES NO
Solid Organ Injury: YES NO
Other Abdominal Injury: YES NO
MSK Injury: YES NO
Chest Wall Injury: YES NO
Blunt Cerebrovascular Injury: YES NO
Spine Injury: YES NO

Hemoglobin Data

Time from admission		Serial	Daily	Last hemoglobin reviewed at the time of F- NOM (if applicable)
	1st Hemoglobin (admission)			
	2nd Hemoglobin			
	3rd Hemoglobin			
	4th Hemoglobin			
24 hours	5th Hemoglobin			
	6th Hemoglobin			
	7th Hemoglobin			
	8th Hemoglobin			
48 hours	9th Hemoglobin			
	10th Hemoglobin			
	11th Hemoglobin			
	12th Hemoglobin			
72 hours	13th Hemoglobin			
	14th Hemoglobin			
	15th Hemoglobin			
	16th Hemoglobin			
96 hours	17th Hemoglobin			
	18th Hemoglobin			
	19th Hemoglobin			
	20th Hemoglobin			
120 hours	21st Hemoglobin			

Clinical decision-making

Non-operative or Operative Management: OM NOM

OM:

Surgical Intervention (circle one below)
- Exploratory Laparotomy
- Splenectomy
- Splenorraphy
- Arterial Embolization

NOM:

Success Failure

F-NOM:

Day of Hospitalization # FNOM:

Reason(s) for F-NOM (circle and rank all that apply)
- Hemodynamic changes
- Hemoglobin drop
- Acute Abdomen
- Death (secondary to abdominal causes)

Choice of OM after failure (circle one below)
- Exploratory Laparotomy
- Splenectomy
- Splenorraphy
- Arterial Embolization

Outcomes:

Death YES NO

Total Transfusions:
- pRBC
- FFP
- Whole blood

ICU Length of Stay:

Hospital Length of Stay:

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EAST MULTICENTER STUDY
DATA DICTIONARY

Serial vs. Daily Hemoglobin in the Non-Operative Management of Blunt Splenic Injuries – Data Dictionary

Data Entry Points and appropriate definitions / clarifications:

Entry space	Definition / Instructions
Standard Study Questions	
Age	Age of patient enrolled
Case Information	
Sex	Sex of Patient enrolled
BMI	Body Mass Index of Patient enrolled. Weight is in kilograms and height is meters. The formula for BMI is kg/m^2.
Pre-existing Conditions/Comorbidities	
ALCOHOL USE DISORDER	Diagnosis of alcohol use disorder documented in the patient medical record. Additional Information • Present prior to injury. • Consistent with American Psychiatric Association (APA) DSM 5, 2013. • A diagnosis of Alcohol Use Disorder must be documented in the patient's medical record.
ANTICOAGULANT THERAPY	Documentation in the medical record of the administration of medication (anticoagulants, antiplatelet, agents, thrombin inhibitors, thrombolytic agents) that interferes with blood clotting. ANTICOAGULANTS ANTIPLATELET AGENTS THROMBIN INHIBITORS THROMBOLYTIC AGENTS Fondaparinux Tirofiban Bevalirudin Alteplase Warfarin Dipyridamole Argatroban Reteplase Dalteparin Anagrelide Lepirudin, Hirudin Tenacteplase Lovenox Eptifibatide Drotrecogin alpha kabikinase

Pentasaccaride Dipyridamole Dabigatran tPA
APC Clopidogrel
Ximelagatran Cilostazol
Pentoxifylline Abciximab
Rivaroxaban Ticlopidine
Apixaban Prasugrel
Heparin Ticagrelor
Additional Information
• Present prior to injury.
• Exclude patients whose only anticoagulant therapy is chronic Aspirin.

BLEEDING DISORDER

A group of conditions that result when the blood cannot clot properly.
Additional Information
• Present prior to injury.
• A Bleeding Disorder diagnosis must be documented in the patient's medical record (e.g. Hemophilia, von Willenbrand Disease, Factor V Leiden).
• Consistent with American Society of Hematology, 2015.

CIRRHOSIS

Documentation in the medical record of cirrhosis, which might also be referred to as end stage liver disease.
Additional Information
• Present prior to injury.
• If there is documentation of prior or present esophageal or gastric varices, portal hypertension, previous hepatic encephalopathy, or ascites with notation of liver disease, then cirrhosis should be considered present.
• A diagnosis of Cirrhosis, or documentation of Cirrhosis by diagnostic imaging studies or a laparotomy/laparoscopy, must be in the patient's medical record.

CURRENT SMOKER

A patient who reports smoking cigarettes every day or some days within the last 12 months.
Additional Information
• Present prior to injury.
• Exclude patients who report smoke cigars or pipes or smokeless tobacco (chewing tobacco or snuff).

Initial assessment data

NOTE = Vital signs are first documented recordings in the trauma bay, not verbally presented from Emergency Medical Services

ISS	Injury Severity Score. Total score is out of 75
GCS	Glasgow Severity Score. Total score is out of 15.
HR	Heart Rate. Measurements in Beats per minute.
SBP	Systolic Blood Pressure. Measurement in mmHg.
DBP	Diastolic Blood Pressure. Measurement in mmHg.
Crystalloid Liters	Total amount of fluid given in trauma bay and en route tn hospital.
pRBC Units	Total amount of packed red blood cell units given in trauma bay and en route to hospital. Measurements in units
Whole blood Units	Total amount of whole blood given in trauma bay and en route to hospital. Measurements in units
MTP	Massive Transfusion Protocol activated
If MTP, how many coolers:	Total numbers of coolers used in the trauma bay if Massive Transfusion Protocol was activated
TBI	Traumatic Brain Injury.
Mechanical Ventilation:	Patient was mechanically ventilated on arrival to the trauma bay or was intubated in the trauma bay.
ETOH:	Positive alcohol screening.

Imaging findings data:

Hemoperitoneum:	On CT scan, radiology note of hemoperitoneum in the abdomen.
CT blush:	On CT scan, contrast extravasation from the spleen is noted. This includes both intracapsular and extracapsular.

Traumatic injuries data:

Grade of Splenic Injury:	Grades consist of I, II, III, IV, and V. Please use 2018 AAST updated version of splenic injuries. Grades can be noted radiographically or intraoperatively.
Isolated splenic injury:	Only splenic injury noted of significance
Solid Organ injury:	Injury to another solid organ in the abdomen. This included liver, pancreas, adrenals, and kidneys
Other abdominal injury:	Injury to the abdomen that does not fit into solid organ injury above.

MSK injury:	Musculoskeletal injury. This includes injuries to bones and muscles in the extremities (arms and legs)
Chest Wall Injury:	Injury to the chest wall, including rib fractures
Blunt Cerebrovascular Injury:	Injury to the cerebrovascular structures secondary to blunt force trauma
Spine Injury:	Injury to the spine. This includes vertebral fractures.

Hemoglobin Data

Note = please mark at which point patients are transitioned from serial Hemoglobin lab values to daily

Serial Hemoglobin:	Serial refers to hemoglobin measurements every 6 hours. Hemoglobin can be measured on Hemoglobin/Hematocrit, complete blood count, or point of care.
Daily Hemoglobin:	Daily refers to hemoglobin measurements every 24 hours. Hemoglobin can be measured on Hemoglobin/Hematocrit, complete blood count, or point of care.
1st Hemoglobin:	This is first hemoglobin measurement noted during the hospitalization on admission.
2nd – 21st Hemoglobin:	This is second through twenty first hemoglobin during the hospitalization in chronological order. Continue to record hemoglobin values until patient is discharged or 21st hemoglobin has been recorded.

Last Hemoglobin reviewed at the time of F-NOM: Please check the box next to the last hemoglobin reported in the chart that was reviewed when a patient failed non-operative management

Management Data

Non-operative Management:	This means the patient was admitted to the hospital from the trauma bay without undergoing a surgical operation. Surgical operations include arterial embolization, splenectomy, exploratory laparotomy, and splenorraphy.
Operative Management:	This means the patient was brought directly to the operating room or interventional radiology suite from the trauma bay. Operations include arterial embolization, splenectomy, exploratory laparotomy, and splenorraphy. Patient can go to CT scanner before operating room or interventional radiology suite and still be included in the operative management group.
Failure Non-operative management:	Failure means that the patient that initially was deemed appropriate to non-operative management now requires an operation. These operations include arterial embolization, splenectomy, exploratory laparotomy, and splenorraphy. There is no time period needed for a patient to be admitted. The intention to admit as stated about in non-oeprtive management and then a change in plans constitutes a failure. Death also constitutes a failure of non-operative management
Success Non-operative management:	Success means the patient was initially deemed appropriate for non-operative management and did not undergo any of these operations

	during their hospitilizations: arterial embolization, splenectomy, exploratory laparotomy, and splenorraphy. Patient must be discharged from hospital to be considered a success.
Day of Hospitalization # F-NOM:	Please note on which day of hospitalization the patient failed non-operative management. Day of admission is hospitalization day #1.
Reason for F-NOM:	Check all the reasons that apply and rank them by effect on clinical decision making for patients that failed non-operative management.
Hemodynamic changes:	This refers to blood pressure and heart rate changes
Hypotension	This refers to an adult systolic blood pressure less than 90 mmHg
Hemoglobin drop:	This refers to a changes in hemoglobin
Acute abdomen:	This refers to an acute abdomen noted in physical exam of the patient
Death:	Patient expired in the hospital. Please note if the death was due to abdominal trauma or nonabdominal trauma (eg, patient goes comfort care secondary to brain injury)

Outcomes

Complications (check all that apply)

NOTE = for calculation of all complication days, day of admission = hospital day #1

Death:	Patient expired during this admission or within 30 days of admission from any cause
Total transfusions:	This is the total number of transfusions of packed red blood cells, fresh frozen plasma and whole blood during their hospitalization. Do not include transfusions in the trauma bay here. Do include the amount of transfusions in the operating room.
ICU Length of Stay:	Length of Stay in days. Admission is hospitalization day #1
Hospital Length of stay:	Length of Stay in days. Admission is hospitalization day #1. Include stay in ICU in this number.