Predicting High-Intensity Resuscitation Needs in Injured Patients Following Hemostasis

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Abstract

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Introduction: Best practices for the resuscitation of injured patients following hemostasis are poorly defined. The post-hemostasis phase of care is characterized by a wide range of physiologic derangements and multiple therapeutic modalities used to address them (e.g., blood products, intravenous crystalloids, and vasoactive medications). Using a cohort of injured patients from an academic level-one trauma center who required an immediate intervention in the operating room or angiography suite following arrival to the emergency department, we sought to define high-intensity resuscitation (HIR) in this post-hemostasis phase of care; we hypothesized that those who would go on to such a resuscitation could be identified, using only data commonly available at the time of ICU admission.

Methods: Hemodynamic, laboratory, and procedure data were extracted for consecutive injured patients (2016-19) admitted to the trauma ICU following an emergent procedure in either the operating room or angiography suite. Significant resuscitation thresholds were defined as the approximate top decile of blood product (≥3 units) and crystalloid (≥4 Liters) use in the initial

twelve hours of ICU care and persistent vasoactive medication use (between ICU hours 2-12). The primary outcome was a composite of *any* of these three modalities. Predictive modeling was performed using logistic regression with predictor variables selected using Least Absolute Shrinkage and Selection Operator (LASSO) estimation. Models were trained using 70% of the cohort and tested on the remaining 30%; their predictive ability was evaluated using area under receiver operator curves in the testing cohort. Continuous variables were depicted with medians and interquartile ranges and proportions as percentages.

Results: Six-hundred-and-five (605) subjects were analyzed. A total of two-hundred-and-fifteen (36%) required at least one of the three HIR criteria (11% received ≥ 3 units of blood product, 15% ≥ 4L crystalloid, and 24% required persistent vasopressors). Predictor variables selected by LASSO included: shock index, lactate, base deficit, hematocrit, and INR. Area under receiver operator curves for HIR prediction achieved a value of 0.82.

Conclusions: Data available at ICU admission following hemostasis can predict subsequent HIR. Following prospective validation, use of this model may facilitate triage, nursing ratio determination, and resource allocation.

Introduction:

Prior to definitive hemostasis in injured patients, there is wide consensus supporting the administration of a balanced blood product resuscitation, minimizing crystalloid infusion, and expeditious hemostasis.[1-6] This practice uniformity has allowed for identification of risk factors for high-intensity resuscitation (HIR), i.e. high blood product needs, and the development of clinical decision support tools to predict patients that will require massive transfusion.[7-9] The ability or inability to anticipate resuscitation needs has implications on triage effectiveness, resource allocation, and preventing delay in time sensitive interventions (e.g., initiation of massive transfusion protocol or procedural hemostasis in the operating room or with interventional radiology).[10] Following hemostasis, many patients continue to have significant physiologic derangements and resuscitation needs; however, optimal resuscitation practices in this critical phase of care are poorly defined and our ability to predict which patients will require continued HIR is limited to clinical gestalt.[11,12]

Challenges with predicting resuscitation needs in the post-hemostasis phase of an injured patient's trajectory are driven by a relative lack of evidence to define best practice and the multiple therapeutic modalities by which post-hemostasis resuscitation can be performed (e.g., blood product transfusion, intravenous crystalloid infusion, and/or vasoactive medications).[11] The practical implications of this uncertainty regarding post-hemostasis resuscitation needs include: reactive clinical decision making, potential delays in treatment due to underappreciation of ongoing physiologic derangements, and underinformed bedside staffing deployment (e.g. nursing ratios). To address these issues, improved understanding of current resuscitation practice and how resuscitation needs in critical care environments are associated with clinical parameters following hemostasis are needed.

To address these knowledge gaps, we evaluated a cohort of severely injured patients admitted to Harborview Medical Center (Seattle, WA) from January 2016 to December 2019 who required an immediate procedure in the operating room or angiography suite as a result of their injuries and subsequently required critical care within the Trauma Surgical Intensive Care Unit (TSICU). This cohort was used to describe the spectrum of post-hemostasis resuscitation requirements and build prediction models to determine those who would go on to require HIR using data available at the time of TSICU admission. We sought to use this cohort to define HIR in the post-hemostasis phase of care and hypothesized that using only vital sign, laboratory, and procedure data available at the time of ICU admission that we could predict which subjects would go on to require HIR.

Methods:

Study Subjects & Data Management

Data from consecutive injured subjects admitted to Harborview Medical Center (Seattle, WA) between January 1, 2016, and December 31, 2019, were collected from the institutional trauma registry and electronic medical record. Patients with burn injuries were excluded. Inclusion in our analysis required sujects be injured, greater than 18 years old, requiring a procedure either in the operating room or angiography suite immediately following initial assessment in the emergency department, and being admitted to the TSICU directly from their procedure(s). Immediate procedure was defined as a subject's initial disposition from the emergency department being a procedural unit (operating room or angiography). Exclusion criteria included patients: transferred from another institution, admitted to Medical or Neurologic specific critical care environments, following drowning, or those who were missing ICU crystalloid data. The use of

deidentified patient data from the trauma registry was performed after review and approval of the University of Washington's Institutional Review Board.

Data on subject demographics, injury characteristics, clinical outcomes, ICU admission dates and times, hemodynamics, laboratory values, procedure data, and blood product, crystalloid, and vasoactive medication utilization data were collected. All crystalloid fluids (boluses, maintenance fluids, and rider fluids) were captured. For the purposes of our analyses, ICU admission time after transfer from a procedural unit (operating room or angiography suite) served as the start of the post-hemostasis resuscitation phase of care. Blood product, crystalloid, and vasopressor utilization were catalogued over the initial 12-hours of ICU admission. This twelve-hour window was selected based on prior work in this cohort examining crystalloid administration as well as for its pragmatism in representing a common length of nursing and/or intensivist shifts.[13,14] Continuous data conveyed as median with interquartile range and proportions as percentages. Comparisons between groups were performed using chi-square and Wilcoxon rank sum tests.

Resuscitation Metrics & Associated Clinical Outcomes

Subjects requiring HIR were defined as requiring any of the following in the initial 12 hours following ICU admission 1) ≥ 4 liters of crystalloid (approximate top decile) or 2) ≥ 3 units of blood products (whole blood, packed red blood cells, plasma, or platelets; approximate top decile), or 3) vasoactive medication (phenylephrine, norepinephrine, vasopressin, epinephrine, or dobutamine) between hours 2-12 of ICU admission. Vasopressor requirement in the first two hours of ICU admission alone were not considered a significant resuscitation requirement, rather an anesthetic adjunct to augment blood pressure following anesthesia exposure.[15] For the purposes of

prediction – the primary outcome of interest was a composite of any of these three. Additionally, models for each individual component of the composite HIR outcome were created.

Significant Resuscitation Prediction Modeling & Performance Evaluation

Initial ICU admission vital signs (heart rate and systolic blood pressure) were extracted for all subjects – any subject for whom these values were not recorded within 1 hour of admission (the institutional nursing documentation standard) were treated as missing. For calculation of shock index (Heart Rate / Systolic Blood Pressure) at the time of ICU admission, the difference in time stamps from heart rate and blood pressure measurements were calculated to ensure a close temporal relationship existed between these measurements and that a valid ratio could be interpreted. Initial admission ICU laboratory values were extracted for all subjects. Any subject for whom these values were not available within a window 1 hour before and 2 hours following ICU admission were considered missing. For subjects with multiple values in this window, the mean of available values was used. Patients with missing predictor data were excluded from prediction modeling.

Least absolute shrinkage and selection operator (LASSO) estimation with k-fold cross validation (k=5) using the '*caret'* package in R was performed to determine which predictor variables would be included in the model.[16,17] All available predictors ICU admission: shock index, lactate, base deficit, hematocrit, platelet count, creatinine, and INR as well as pre-ICU admission procedure duration were included in the LASSO estimation analysis.

Logistic regression modeling using the LASSO-selected variables were used to predict HIR. For each of these logistic regression models, area under the receiver operating curves (AUROC) were created to quantify the sensitivity and specificity for predicting the primary, composite HIR outcome and the individual components thereof. For the purposes of model training and testing,

our cohort was divided randomly with 70% of the cohort used to train the predictive model and 30% to test them.[18] All statistics and graphic generation were performed using R Studio (Version 1.4.1717; Boston, MA).

Results:

Study Subjects

Six-hundred-and-five (605) subjects were included in our analysis (CONSORT Diagram **Figure 1**; Cohort Demographics and Variable Overview **Table 1**). Overall, subjects were predominantly male (79%), severely injured (ISS: 26 [IQR: 17-38]) and contained an approximately 3:2 mix of blunt and penetrating mechanisms. 133 (22%) had severe head injuries (AIS Head ≥3). Inpatient mortality of the entire cohort was 11%.

Resuscitation Metrics & Associated Clinical Outcomes

The distributions of crystalloid, blood product, and vasoactive medication use in the study cohort are shown in **Figure 2.** In the initial twelve hours following TSICU admission, 88 (15%) received ≥ 4 L of intravenous crystalloid, 67 (11%) received ≥ 3 units of blood product, and 143 patients (24%) required vasoactive medications between ICU hours two and twelve. Two-hundred-and-fifteen (36%) developed any combination of these three (primary outcome). Depiction of overlapping high-intensity resuscitation requirements among these patients can be found in **Figure 3**. Clinical parameters and outcome associations with high-intensity resuscitation are depicted in **Table 2**. Among subjects who died during their inpatient care, median time from hospital admission to death was 140 hours (IQR: 83-407) in the group that did not require HIR compared to 58 hours (IQR: 19-129) in the HIR subjects (p=0.002).

High-Intensity Resuscitation Prediction Modeling & Performance Evaluation

LASSO estimation identified five predictor variables to be included in our logistic regression prediction models. These included TSICU admission: 1) shock index, 2) lactate, 3) INR, 4) base deficit, and 5) hematocrit. The relative predictive importance of each variable included in LASSO analyses can be found in **Supplemental Figure 1**. The logistic regression model utilizing these LASSO selected predictor variables (**Supplemental Table 1**) achieved an AUROC of 0.82 for the composite outcome (**Figure 4**). By comparison the AUROC for the individual components of the composite outcome using the same predictor variables were: ≥ 4 L of intravenous crystalloid in first 12 hours in ICU: AUROC 0.71, ≥ 3 units of total blood product in first 12 hours in ICU: AUROC 0.83, and vasoactive medication administration between ICU hours 2 and 12: AUROC 0.70.

Discussion:

To our knowledge, this work is the first to describe the heterogeneous and multi-modality resuscitative needs of injured patients following hemostasis, define "high-intensity" resuscitation in this phase of care, and predict high-intensity, post-hemostasis resuscitation using only data available at the time of critical care admission. Our analysis demonstrated a wide range in resuscitation requirements and overlapping use of three main therapeutic modalities – blood products, crystalloid, and vasopressors. As expected, those identified as requiring high-intensity resuscitation had significantly worse outcomes with respect to inpatient mortality, critical care length of stay, and total length of stay. More importantly, we were able to create a novel prediction model using only commonly available hemodynamic and laboratory data at the time of TSICU admission that accurately identifies patients who will go on to require HIR. This model has comparable sensitivity and specificity to models used to predict massive transfusion in the pre-hemostasis phase of care.[7-9]

The ability to accurately predict which patients will require HIR could have significant utility in enhancing physician/nursing triage capabilities, resource allocation, and early prognostication. In the wake of the SARS-CoV-2 pandemic, institutional resources for intensive care unit staffing availability and patient to nursing ratios have been challenging.[19,20] If a prediction model for HIR could be successfully incorporated into critical care practice, patient placement and nursing assignment ratios could be proactively adjusted. Additionally, patients requiring high-intensity resuscitation were more than four times more likely to die than those who did not require high-intensity resuscitation and died much more rapidly (Median time to death: 58 hours vs. 140 hours). While early establishment of code status and goals of care are important for all patients, patients identified early as being likely to require HIR provides an early prompt to clinicians to have these conversations with patients and families early and engage palliative care services when appropriate. Finally, models like the one presented here are amenable to being integrated into electronic medical records where they can passively collect the data required to predict HIR needs and generate alerts for critical nurses and intensivists if a given patient is at high risk of requiring HIR thereby decreasing the cognitive load on these providers when triaging their multiple patient care responsibilities.

These results should be interpreted in the context of several important limitations. The retrospective nature of our study prevented the capture of potentially important variables (e.g., damage control procedures, transitions to comfort-directed care, pre-TSICU admission imaging results, or granular pre-critical care factors like crystalloid volume or blood products received pre-hospital, in the emergency department, or during an emergency procedure) and outcomes (e.g., return to IR/OR for hemostasis). While prospective validation of this model is needed, the novelty of this predictive model using only commonly available variables present on critical care

admission needs to be considered. Second, shock index had the highest level of relative importance of any variable included in LASSO-facilitated creation of our prediction model (**Supplemental Figure 1**). While there is a body of literature describing the association of shock index with mortality and resuscitation requirements in injured patients, the use of shock index in the post-hemostasis/ICU phase of care has not been validated.[21-24] Third, the definition of "high-intensity" post-hemostasis resuscitation though novel, is arbitrary based on our high-volume, institutional practice. The thresholds for blood product and crystalloid use were selected as they approximate the top decile of each therapeutic modality in our study cohort, and while we expect that our practice is comparable to like centers, prospective multi-center validation of such a prediction model will likely require adjustment. Finally, missing hemodynamic and lab data was an issue in our cohort (0-18.5% of included predictor variables were missing); while this is attributable to our pre-defined acceptable time windows for predictor variables to be considered representative of ICU admission physiology rather than true missingness, it is nonetheless possible that this missing data introduces bias (e.g., patients with more severe physiologic derangements may have their initial vital signs recorded outside of the one hour post admission window because nurses responsible for charting vital signs are occupied providing care). Standardized timing of vital sign and laboratory studies coordinated by research personnel will be performed in the prospective validation study.

In conclusion, this work represents an advance in our understanding of the post-hemostasis phase of care. Simple laboratory and hemodynamic data available at the time of ICU admission are predictive of which patients will require HIR which has implications on patient outcomes, our prognostic capabilities, and resource utilization in critical care environments.

Table 1. Cohort Demographics and Variable Overview

Characteristic	**N = 605**[1]
Age	39 (28, 52)
Sex (Male)	480 (79%)
Race	
Asian	50 (8.3%)
Black	110 (18%)
Native American	16 (2.6%)
Unknown/Not Recorded	22 (3.6%)
Pacific Islander	10 (1.7%)
White	397 (66%)
Disposition from Emergency Department	
Angiography Suite	42 (6.9%)
Operating Room	563 (93%)
Trauma Mechanism	
Blunt	351 (58%)
Penetrating	250 (41%)
Other	4 (0.7%)
Injury Severity Score	26 (17, 38)
Head Abbreviated Injury Score	
0	426 (70%)
1	3 (0.5%)
2	43 (7.1%)
3	36 (6.0%)
4	23 (3.8%)
5	73 (12%)
6	1 (0.2%)
ICU Admission Lactate (mmol/L)	3.00 (1.96, 4.40)
ICU Admission Base Deficit (mmol/L)	-0.9 (-3.7, 0.8)
ICU Admission Platelet Count (thousand)	154 (119, 197)
ICU Admission Hematocrit (%)	32.7 (29.0, 36.0)
ICU Admission Creatinine (mg/dL)	0.79 (0.66, 0.99)
ICU Admission INR	1.30 (1.20, 1.40)
ICU Admission Shock Index[2]	0.77 (0.63, 0.94)
Procedure Duration (Hours)	1.98 (1.32, 2.80)

[1]Median (IQR); n (%)
[2]Time between ICU Admission Heart Rate and Systolic Blood Pressure documentation: Median 0 minutes, Mean 1.2 minutes, Range 0-39 minutes

Table 2. Clinical Parameters & Outcome Associations with High Intensity Resuscitation

Characteristic	Did Not Require HIR N = 390[1]	Required HIR N = 215[1]	p-value[2]
Injury Severity Score	22 (14, 34)	34 (22, 50)	**<0.001**
Hospital Length of Stay (Days)	10 (6, 23)	16 (7, 33)	**0.001**
ICU Length of Stay (Days)	4 (3, 6)	8 (4, 17)	**<0.001**
Ventilator Days	2 (1, 3)	5 (2, 12)	**<0.001**
In-Hospital Mortality	19 (4.9%)	49 (23%)	**<0.001**

[1] Median (IQR); n (%)

[2] Wilcoxon rank sum test; Pearson's Chi-squared test

Figure 1: CONSORT Diagram for subject inclusion/exclusion

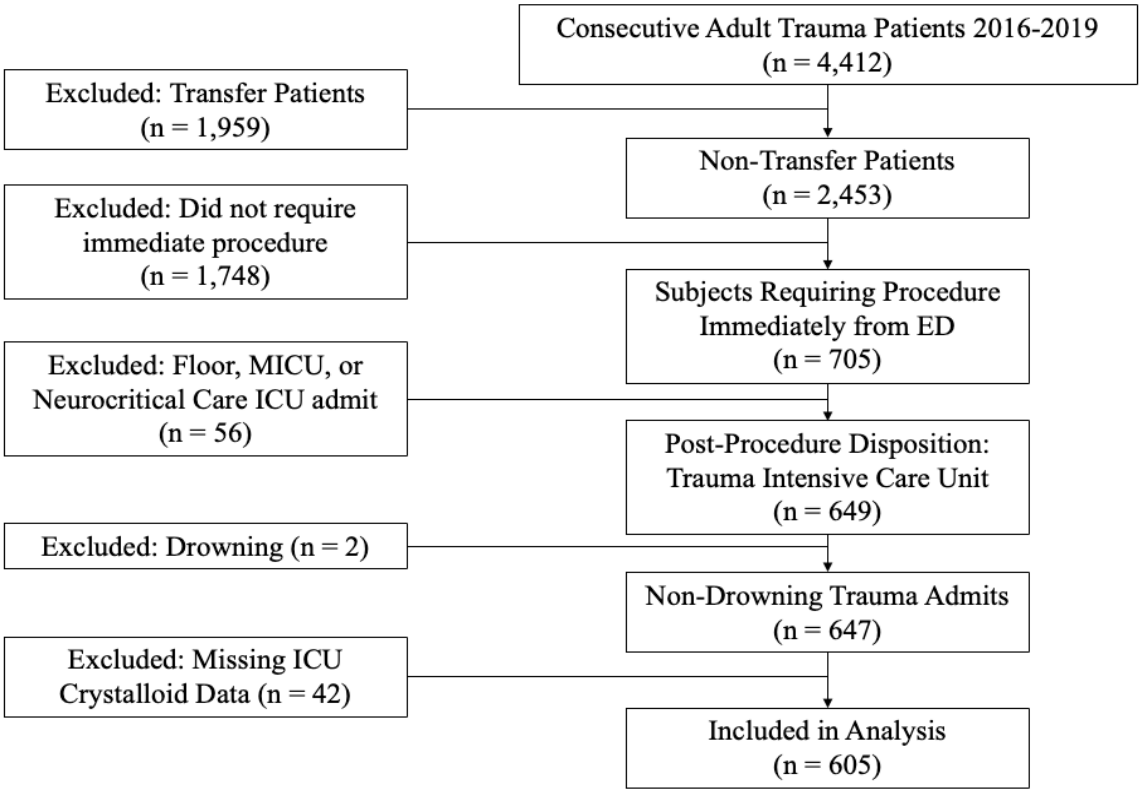
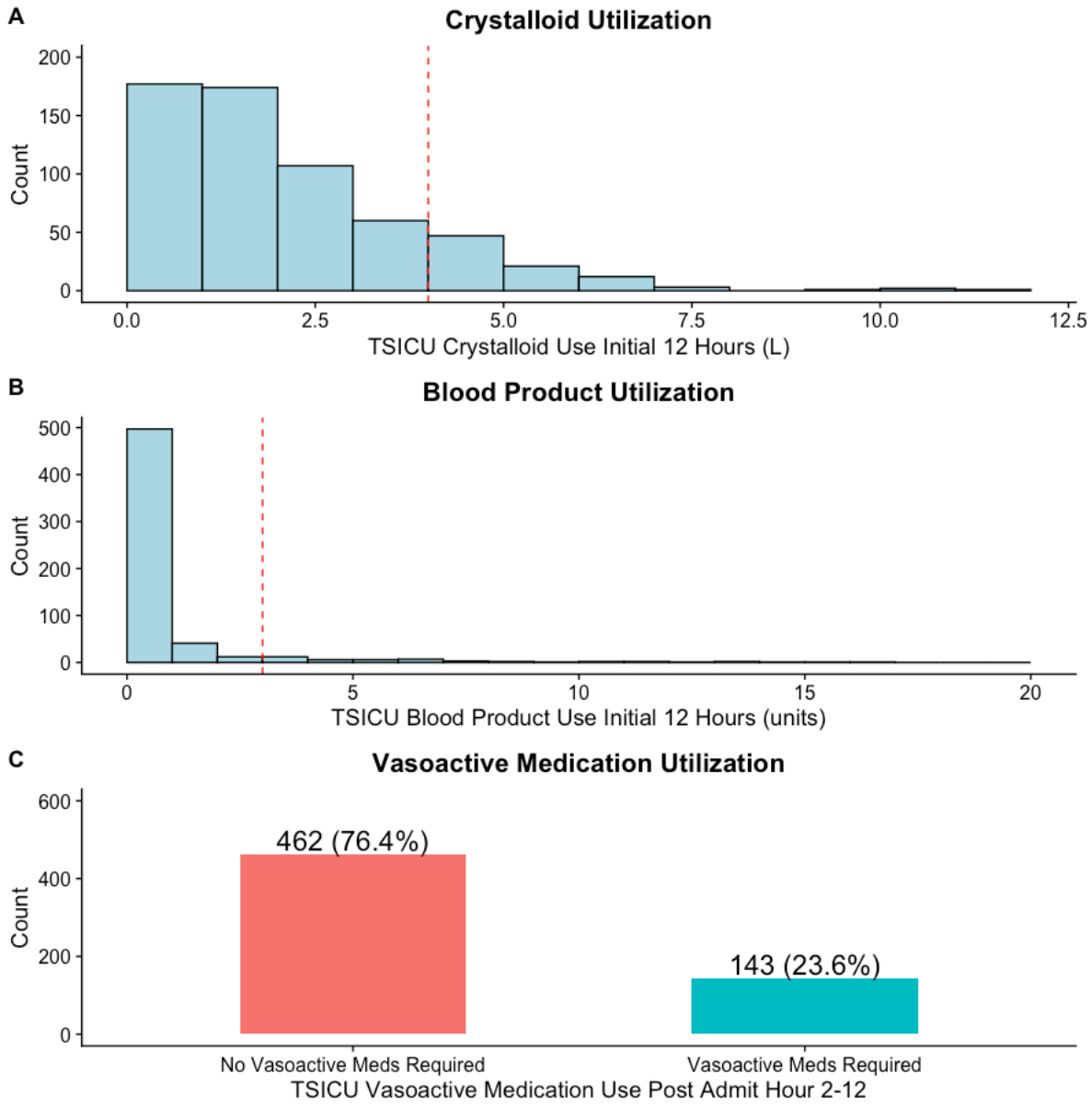
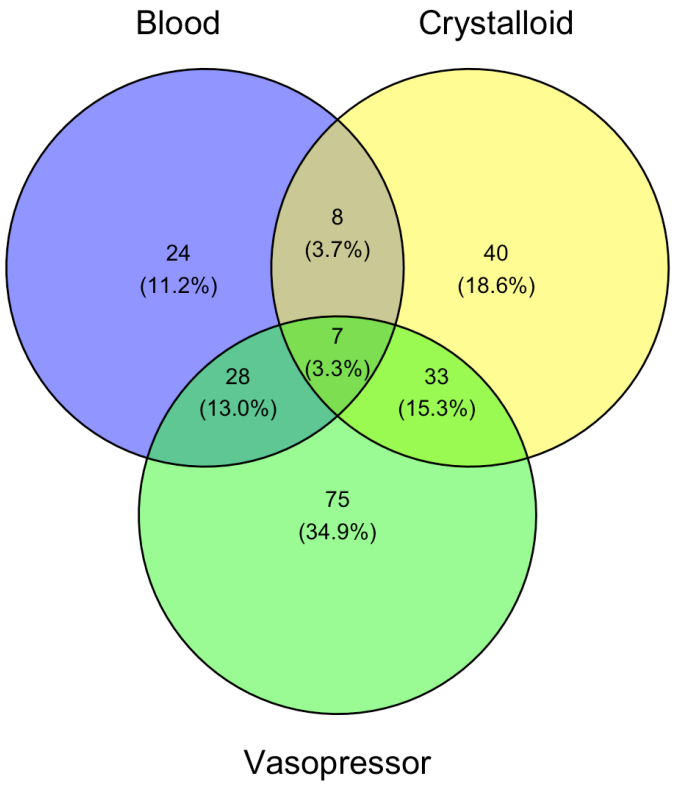


Figure 2: TSICU Crystalloid, Blood Product, and Vasoactive Medication Distributions in Study Cohort



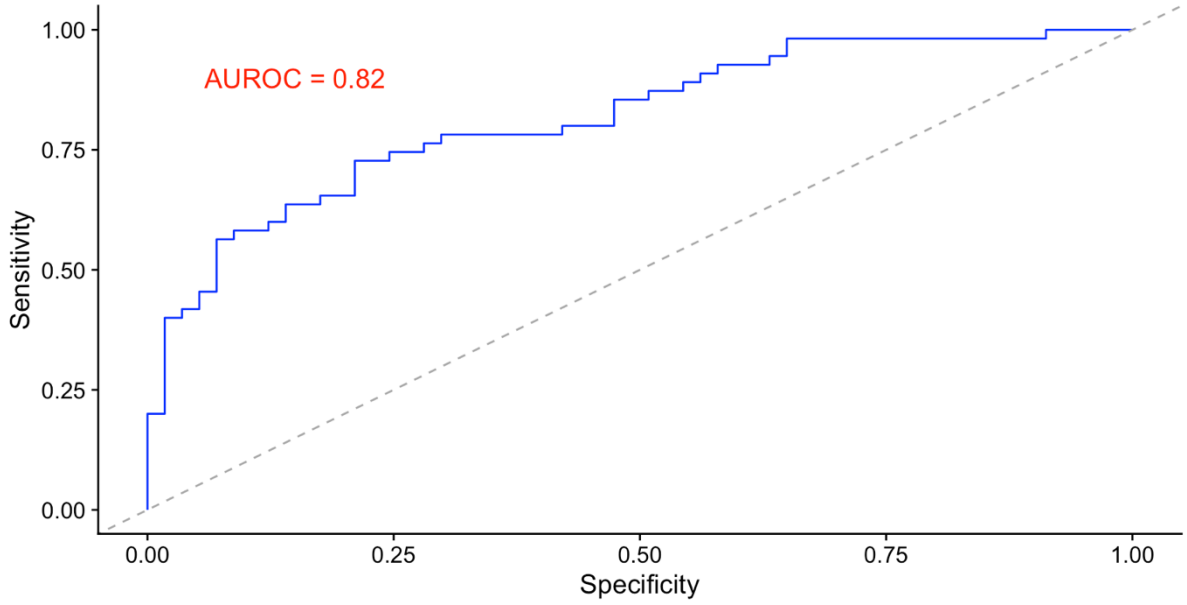
Distributions of different resuscitative modalities in study cohort. A) Intravenous crystalloid distribution. Dashed red line at 4 liters represents threshold for high intensity resuscitation based on crystalloid use B) Blood product distribution. Dashed red line at 3 units represents threshold for high intensity resuscitation based on blood product use. Five subjects with > 20 units of total blood product use are excluded from this histogram C) Vasoactive medication distribution.

Figure 3. Breakdown of High-Intensity Resuscitation Requirements



Venn diagram depicting two-hundred and fifteen subjects that required at least one modality of high intensity resuscitation (Blood product ≥3 units or crystalloid ≥ 4 liters in the first 12 hours after TSICU admission or persistent vasopressor use between TSICU hours 2-12).

Figure 4: Area Under Receiver Operator Curve for High Intensity Resuscitation Prediction Model



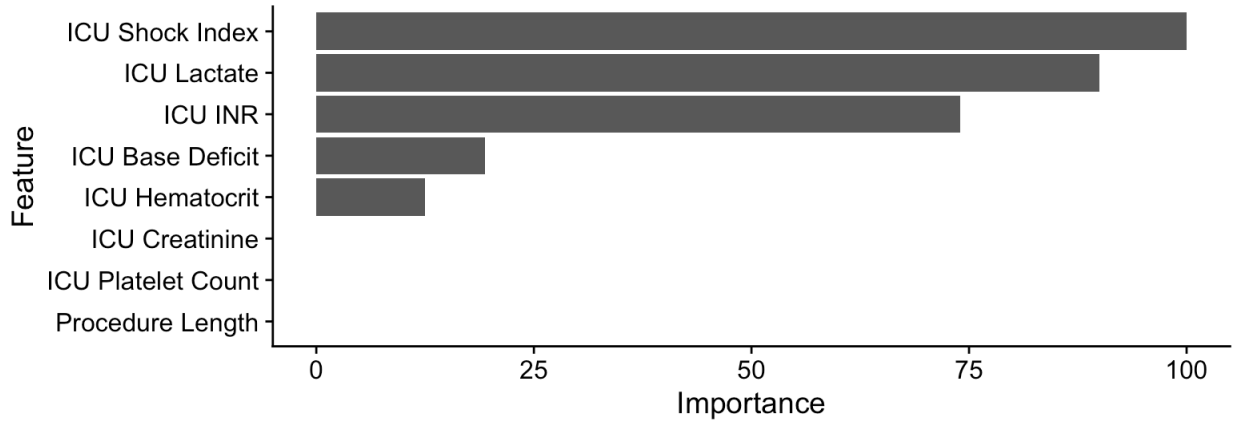
Supplemental Tables & Figures:

Supplemental Table 1: High-Intensity Resuscitation Logistic Regression Prediction Logistic Regression Model

Characteristic	OR[1]	95% CI[1]	p-value
ICU Admission Shock Index	6.55	1.91, 24.1	**0.004**
ICU Admission Lactate (mmol/L)	1.07	0.93, 1.24	0.3
ICU Admission INR	5.65	1.17, 30.5	**0.036**
ICU Admission Base Deficit (mmol/L)	0.96	0.88, 1.04	0.3
ICU Admission Hematocrit (%)	0.98	0.93, 1.03	0.5

[1] OR = Odds Ratio, CI = Confidence Interval

Supplemental Figure 1: LASSO Variable Importance Plot



References:

1. Holcomb JB, Tilley BC, Baraniuk S, et al. Transfusion of plasma, platelets, and red blood cells in a 1:1:1 vs a 1:1:2 ratio and mortality in patients with severe trauma: the PROPPR randomized clinical trial. *Jama*. Feb 3 2015;313(5):471-82. doi:10.1001/jama.2015.12
2. Cannon JW, Khan MA, Raja AS, et al. Damage control resuscitation in patients with severe traumatic hemorrhage: A practice management guideline from the Eastern Association for the Surgery of Trauma. *J Trauma Acute Care Surg*. Mar 2017;82(3):605-617. doi:10.1097/TA.0000000000001333
3. Kasotakis G, Sideris A, Yang Y, et al. Aggressive early crystalloid resuscitation adversely affects outcomes in adult blunt trauma patients: an analysis of the Glue Grant database. *J Trauma Acute Care Surg*. May 2013;74(5):1215-21; discussion 1221-2. doi:10.1097/TA.0b013e3182826e13
4. Robinson BRH, Cohen MJ, Holcomb JB, et al. Risk Factors for the Development of Acute Respiratory Distress Syndrome Following Hemorrhage. *Shock*. Sep 2018;50(3):258-264. doi:10.1097/shk.0000000000001073
5. Holcomb JB, del Junco DJ, Fox EE, et al. The prospective, observational, multicenter, major trauma transfusion (PROMMTT) study: comparative effectiveness of a time-varying treatment with competing risks. *JAMA Surg*. Feb 2013;148(2):127-36. doi:10.1001/2013.jamasurg.387
6. Weykamp MB, Stern K, Brakenridge SC, et al. PREHOSPITAL CRYSTALLOID RESUSCITATION: PRACTICE VARIATION AND ASSOCIATIONS WITH CLINICAL OUTCOMES. *Shock*. Jan 1 2023;59(1):28-33. doi:10.1097/shk.0000000000002039
7. Nunez TC, Voskresensky IV, Dossett LA, Shinall R, Dutton WD, Cotton BA. Early prediction of massive transfusion in trauma: simple as ABC (assessment of blood consumption)? *J Trauma*. Feb 2009;66(2):346-52. doi:10.1097/TA.0b013e3181961c35
8. McLaughlin DF, Niles SE, Salinas J, et al. A predictive model for massive transfusion in combat casualty patients. *J Trauma*. Feb 2008;64(2 Suppl):S57-63; discussion S63. doi:10.1097/TA.0b013e318160a566
9. Yücel N, Lefering R, Maegele M, et al. Trauma Associated Severe Hemorrhage (TASH)-Score: probability of mass transfusion as surrogate for life threatening hemorrhage after multiple trauma. *J Trauma*. Jun 2006;60(6):1228-36; discussion 1236-7. doi:10.1097/01.ta.0000220386.84012.bf
10. Meyer DE, Vincent LE, Fox EE, et al. Every minute counts: Time to delivery of initial massive transfusion cooler and its impact on mortality. *J Trauma Acute Care Surg*. Jul 2017;83(1):19-24. doi:10.1097/TA.0000000000001531
11. Beni CE, Arbabi S, Robinson BRH, O'Keefe GE. Acute intensive care unit resuscitation of severely injured trauma patients: Do we need a new strategy? *J Trauma Acute Care Surg*. Dec 1 2021;91(6):1010-1017. doi:10.1097/ta.0000000000003373
12. Braasch MC, Turco LM, Cole EM, Brohi K, Winfield RD. The evolution of initial-hemostatic resuscitation and the void of posthemostatic resuscitation. *J Trauma Acute Care Surg*. Sep 2020;89(3):597-601. doi:10.1097/TA.0000000000002576
13. Stimpfel AW, Aiken LH. Hospital staff nurses' shift length associated with safety and quality of care. *J Nurs Care Qual*. Apr-Jun 2013;28(2):122-9. doi:10.1097/NCQ.0b013e3182725f09

14. Webster J, McLeod K, O'Sullivan J, Bird L. Eight-hour versus 12-h shifts in an ICU: Comparison of nursing responses and patient outcomes. *Australian Critical Care*. 2019/09/01/ 2019;32(5):391-396. doi:https://doi.org/10.1016/j.aucc.2018.08.004
15. Wu M, Ghassemi M, Feng M, Celi LA, Szolovits P, Doshi-Velez F. Understanding vasopressor intervention and weaning: risk prediction in a public heterogeneous clinical time series database. *J Am Med Inform Assoc*. May 1 2017;24(3):488-495. doi:10.1093/jamia/ocw138
16. Ranstam J, Cook JA. LASSO regression. *British Journal of Surgery*. 2018;105(10):1348-1348. doi:10.1002/bjs.10895
17. Max K. Building Predictive Models in R Using the caret Package. *Journal of Statistical Software*. 11/01 2008;28doi:10.18637/jss.v028.i05
18. Gholamy A, Kreinovich V, Kosheleva O. Why 70/30 or 80/20 relation between training and testing sets: A pedagogical explanation. 2018;
19. Andel SA, Tedone AM, Shen W, Arvan ML. Safety implications of different forms of understaffing among nurses during the COVID-19 pandemic. *J Adv Nurs*. Jan 2022;78(1):121-130. doi:10.1111/jan.14952
20. Lasater KB, Aiken LH, Sloane DM, et al. Chronic hospital nurse understaffing meets COVID-19: an observational study. *BMJ Qual Saf*. Aug 2021;30(8):639-647. doi:10.1136/bmjqs-2020-011512
21. Mutschler M, Nienaber U, Münzberg M, et al. The Shock Index revisited - a fast guide to transfusion requirement? A retrospective analysis on 21,853 patients derived from the TraumaRegister DGU. *Crit Care*. Aug 12 2013;17(4):R172. doi:10.1186/cc12851
22. Biney I, Shepherd A, Thomas J, Mehari A. Shock Index and Outcomes in Patients Admitted to the ICU With Sepsis. *CHEST*. 2015;148(4):337A. doi:10.1378/chest.2281151
23. Cannon CM, Braxton CC, Kling-Smith M, Mahnken JD, Carlton E, Moncure M. Utility of the shock index in predicting mortality in traumatically injured patients. *J Trauma*. Dec 2009;67(6):1426-30. doi:10.1097/TA.0b013e3181bbf728
24. Vandromme MJ, Griffin RL, Kerby JD, McGwin G, Jr., Rue LW, 3rd, Weinberg JA. Identifying risk for massive transfusion in the relatively normotensive patient: utility of the prehospital shock index. *J Trauma*. Feb 2011;70(2):384-8; discussion 388-90. doi:10.1097/TA.0b013e3182095a0a