Computer Modelling Using Prehospital Vitals Predicts Transfusion and Mortality

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Abstract

Objective: Test computer-assisted modeling techniques using prehospital vital signs of injured patients to predict emergency transfusion requirements, number of intensive care days, and mortality, compared to vital signs alone. **Methods:** This single-center retrospective analysis of 17,988 trauma patients used vital signs data collected between 2006 and 2012 to predict which patients would receive transfusion, require 3 or more days of intensive care, or die. Standard transmitted prehospital vital signs (heart rate, blood pressure, shock index, and respiratory rate) were used to create a regression model (PH-VS) that was internally validated and evaluated using area under the receiver operating curve (AUROC). Transfusion records were matched with blood bank records. Documentation of death and duration of intensive care were obtained from the trauma registry. **Results:** During the course of their hospital stay, 720 of the 17,988 patients in the study population died (4%), 2,266 (12.6%) required at least a 3-day stay in the intensive care unit (ICU), 1,171 (6.5%) required transfusions, and 210 (1.2%) received massive transfusions. The PH-VS model significantly outperformed any individual vital sign across all outcomes (average AUROC = 0.82), The PH-VS model correctly predicted that 512 of 777 (65.9%) and 580 of 931 (62.3%) patients in the study population would receive transfusions within the first 2 and 6 hours of admission, respectively. **Conclusions:** The predictive ability of individual vital signs to predict outcomes is significantly enhanced with the model. This could support prehospital triage by enhancing decision makers' ability to match critically injured patients with appropriate resources with minimal delays. **Key words:** transfusion; vital signs; mortality; prehospital care

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Introduction

Injuries cause approximately 4.3 million deaths worldwide each year,[1,2] and treating patients with traumatic injuries is resource intensive, requiring a diverse system of care and personnel.[3,4] Tools that facilitate the matching of patients with their anticipated medical needs early in the triage process are valuable in the allocation of health care resources as well as the timing of therapeutic interventions.[4–8] Specifically, if the need for emergency surgery or blood products could be predicted with high accuracy, a receiving trauma center could be notified of a patient's impending transport, enabling the trauma staff to prepare definitive hemorrhage control procedures, assemble an operating room team, and request blood products.[9,10] Currently, our best triage tools require vital signs to be combined with advanced imaging, laboratory results, or in-person clinical evaluation, limiting the range of triage decisions made in advance of hospital arrival.[9]

We hypothesized that computer-assisted modeling techniques that incorporate the prehospital vital signs of trauma patients could predict the need for emergency transfusion, the number of intensive care days, and the risk of death better than a single vital sign alone. If our hypothesis is true, this new approach would allow immediate and appropriate mobilization of resources, particularly trauma team activation and availability of blood products, before a patient arrives at the hospital.

METHODS

Study Setting and Population

This study was conducted at the R Adams Cowley Shock Trauma Center (STC), a Level 1 trauma center in Baltimore, Maryland. Approval was expedited by the Institutional Review Boards of the University of Maryland School of Medicine and the U.S. Air Force by expedited review without the need to obtain patient informed consent. We abstracted routinely collected standard vital signs (systolic blood pressure [SBP, millimeters of mercury], heart rate [HR, beats per minute], respiratory rate [RR, breaths per minute]), patient care, and outcome data from the STC's trauma registry for patients admitted between 2006 and 2012. Transfusion data, including the time, type, and the number of units of packed red blood cells (pRBC) administered, were obtained from the trauma center's blood bank database.

Selection of Participants and Derivation of the Cohort

Inclusion criteria for this study were age ≥18 years, admission directly from the scene of injury, and complete prehospital vital signs (PH-VS) data. If there were multiple sets of prehospital vital signs available, we used the first set reported. Patients who died within 15 minutes after arrival and those who were transferred from other institutions were excluded. Information about blood product use and trauma registry data were linked using STC patient identifier, medical record number (MRN), time of arrival within 24 hours, age, sex, and mode of transportation.

Definitions of Model Variables and Outcomes

The univariate vital signs and outcomes used in this analysis were SBP, HR, RR, and shock index (SI, defined as HR divided by contemporaneous SBP),[11,12] which was calculated on all patients. The outcomes for prediction included the use of universal donor, Group O un-cross-matched (Ucx) packed red cell units (pRBCs) administered within the first hour of care, pRBCs used in the first 2 hours after admission (RC_2), massive transfusion type MT1(≥5 units pRBC in the first 4 hours of care), MT2 (≥10 units pRBC in the first 12 hours of care), MT3 (≥10 units in the first 24 hours of care), ICU length of stay ≥3 days and ≥ 7 days, and in-hospital mortality. By convention, the time of blood product issue by the blood bank is used as a surrogate marker for time of transfusion of fully cross-matched units.

Model Evaluation and Validation

The multivariate model used in this analysis was based on the PH-VS, and to avoid overfitting, parsimonious models were built through stepwise logistic regression. The Wald Chi-square test was used to determine whether a variable should be included (forward step; p-value < 0.2) or excluded (backward step; p-value > 0.3).[13] The resulting areas under the receiver operating curve (AUROC[14,15]) were used to evaluate the models' performance in predicting mortality, ICU admission, and blood product use.[16]

To internally validate the model and gauge its generalizability, a 10-fold repeated 10 times cross-validation with stratified sampling scheme was used.[17] The entire set of PH-VS data was randomly divided into 10 equal-sized non-overlapping data subsets. A stratified sampling strategy was used in separating the data set to preserve the prevalence of positive outcomes from the original date set. The model was initially trained over ten cycles, each cycle consisting of model training using 9 of the previously defined subsets and with the remaining set used for validation testing. After iterating over all 10 data subsets, this procedure was repeated another 9 times, for a total of 100 training and validation testing cycles. The average AUROC from all training and testing cycles was calculated for each end point. The model was considered to be stable when it generated less than a 10% difference in the AUROCs across the training and validation data subsets. Delong's method was used to compare AUROCs. A p-value < 0.05 was considered statistically significant.[18]

RESULTS

Characteristics of the Study Subjects

There were 17,988 patients who had complete sets of vital signs and were merged with the blood use database to form the study population (Figure 1). The mean prehospital vitals were HR = 92.0 ± 21.5 beats per minute, SBP = 136.8 ± 28.6 mmHg, RR = 18.6 ± 4.6 breaths per minute, with a shock index = 0.69 ± 0.21 (Table 1). Most injuries (11,085 of 17,988, [61.6%]) were minor (Injury Severity Score [ISS[19,20]]<9), with 11,112 (61.8%) and 1,308 (7.3%) of patients receiving blunt and penetrating injuries, respectively. Depending on the definition used, 1–2% of patients received massive transfusions (MT1 = 2.01%, MT2 = 1.05%, MT3 = 1.17%), 6.51% received at least one blood component, 12.6% of the patients in our data set were admitted to our ICU, and 4% died.

Table 2 summarizes the ROC analysis of univariate vital sign discrimination power and the predictive performance of multivariable regression models. For simplicity, we only reported the average AUROC over the training set. SI was the best-performing univariate

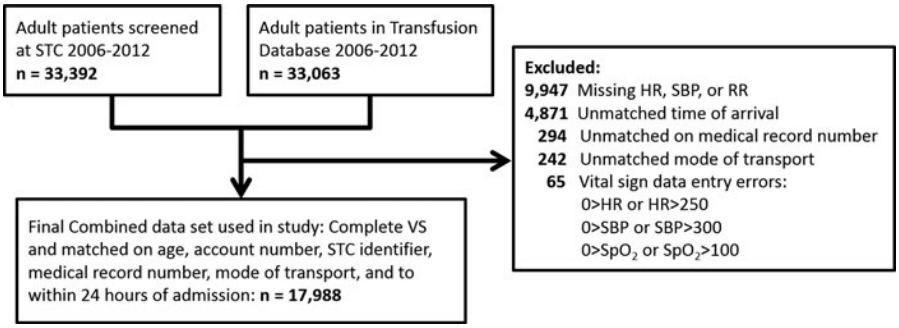

FIGURE 1. Consort diagram showing the derivation of the study cohort. HR = heart rate; SBP = systolic blood pressure; RR = respiratory rate; SpO_2 = percent peripheral oxygen saturation; STC = Shock Trauma Center; VS = vital signs.

vital sign across most outcomes ($p < 0.0001$). The PH-VS model outperformed the univariate vital signs across all outcomes, including mortality and all definitions of massive transfusion (average model AUROC = 0.82, $p < 0.0001$ for all comparisons). The PH-VS model correctly predicted that 512 of 777 (65.9%) and 580 of 931 (62.3%) patients in the study population would receive transfusions within the first 2 and 6 hours of admission, respectively.

TABLE 1. General study population demographics.

	Study Population
Age, mean (σ)	41.6(18.6)
Sex,% male	69
Race, n (%)	
Caucasian	11352(63.1)
African American	5365(29.8)
Asian	13(0.1)
Hispanic	559(3.1)
Native American	135(0.8)
Other	564(3.1)
GCS, mean (σ)	14(2.8)
Prehospital	
HR	92.0(21.5)
SBP	136.8(28.6)
RR	18.6(4.6)
SI	0.69(0.21)
Admission	
HR	89.1(21.5)
SBP	144.3(32.0)
RR	19.3(6.0)
MOI, n (%)	
Blunt	11122(61.8)
Penetrating	1308(7.3)
Inhalation/poisoning	149(0.8)
Other (Burn, crush, other)	249(1.4)
Not recorded	5160(28.7)
ISS, n (%)	
≤9	11085(61.6)
10-15	2376(13.2)
16-24	2280(12.7)
≥25	2247(12.5)
Mortality (%)	4.0
Length of Stay (Days)	3.2
ICU Stay (%)	12.6
Transfusion (%)	6.51
MT1 (%)	2.01
MT2 (%)	1.05
MT3 (%)	1.17

GCS = Glasgow Coma Score; MOI = Mechanism of Injury; ISS = Injury Severity Score; MT1 = massive transfusion type 1 (≥5 units pRBC in the first 4 hours of care); MT2 (≥10 units pRBC in the first 12 hours of care); MT3 (≥10 unit pRBC in first 24 hours after admission).

DISCUSSION

In this retrospective single-center analysis, we found that an analysis of prehospital vital signs by machine learning algorithms can predict transfusion, mortality, length of ICU stay, and the need for trauma team activation, and with higher sensitivity and specificity compared with single measurements of prehospital vital signs If implemented as a part of pre-hospital trauma patient management, these predictions would have an impact on prehospital triage decisions and resource allocation.

Our data show that multivariate models outperform single measurements of vital signs (see Table 2). Compared to reports of other studies[20,21] that incorporated data from the clinical examination, imaging results, or laboratory results to predict trauma patient outcomes, we achieved similar or better AUROC values (0.62,0.91) with measures of VS alone. Our predictions are independent of laboratory values (e.g., lactate concentration, international normalized ratio, hemoglobin level) or advanced imaging studies (Focused Assessment with Sonography for Trauma or computed tomography), which are required by other published outcome prediction tools. Acquisition of this additional information is both time consuming and expensive.[9] Our endpoints are patient-centered (e.g., transfusion, mortality) and are not driven by injury severity score, which can only be determined retrospectively.[21,22] Our results also answer a call by prehospital providers to create decision-support tools that are fast, accurate, and easy to use.[23]

The PH-VS algorithm could be integrated into a website or prehospital care protocols as a predictor of when to administer blood products during patient transport. When a receiving hospital is being notified of the patient transport, physicians could input the pa-

tient's vitals into a cellphone app or computer version of this model, and receive real-time decision support on whether to give or withhold blood products. The model could also be integrated into a device where these calculations are automatically done internally. Indicators for probability of death, ICU admission, or transfusion could be conveyed to the operator by percentages or colors (e.g., worsening prognosis or increasing need for interventions shown by a progression from green, to yellow, and then red). Our findings can be applied rapidly and inexpensively within current trauma triage frameworks, especially the prehospital arena, with minimal infrastructure cost.

Ourmodel demonstrates a method of generating moderate-to-strong predictions about important patient-oriented outcomes (need for transfusion, massive transfusion, ICU care, and mortality) while the patient is at the scene of injury by non-physicians. This would allow first responders to provide more resources to the injured patient earlier in their clinical course. Timely intervention is key, as exsanguination is a major and proximate cause of death after trauma,[24–26] and prehospital transfusion has been associated with improved early outcomes.[27]

Early initiation of transfusion therapy can both maintain oxygen delivery and improve coagulation parameters during transport and early phases of care. The only life-saving interventions are surgical control of the hemorrhage and providing adequate coagulation factors to reverse acute coagulopathy of trauma.[9,] Early administration of plasma is known to improve survival during trauma resuscitation. Because we are a high-volume trauma center with a high demand for blood products, we have plasma we are able to provide blood products to patients essentially on arrival.[28] At our institution, our blood bank prepares blood products, including plasma, for delivery to the patient's bedside within 15 minutes[28] of initiating our massive transfusion protocol. This immediate mobilization is not possible at most medical centers: many will need to thaw multiple units of plasma simultaneously in the setting of massive transfusion, which can take more than 30 minutes to prepare using current protocols and equipment.[28] A recent national survey of Level I and II trauma centers found that plasma was immediately available at only 31% of sites.[29] Of those who had plasma immediately available, 37% stored it outside of the emergency department. The potential time gains provided by the PH-VS model would allow clinicians at these hospitals a head start on these logistical issues to prepare resources before an injured patient arrives at the hospital.

At our institution, a certain percentage of massive transfusions are initiated with blood products delivered to the patient's bedside, yet the patient ultimately does not receive any transfusions. This is a result of variations in practice and providers, and the fact that the blood bank is often notified the moment a bleeding patient arrives, but before a full assessment is completed. Our hospital's baseline false-positive rate of in-house massive transfusions is approximately 10%.[30] Given that the PH-VS algorithm's false positive rate is 16% for predicting massive transfusion (Table 2), our blood bank finds it reasonable to pre-release of blood products based on the results of our out-of-hospital PH-VS algorithm.[28–30]

The modeling strategy described in this study highlights how machine learning analyses of vital signs can augment human decision making. By using commonly available vital signs, we created tool with test characteristics on par with other commonly used laboratory tests. It is likely that tools using continuous patient monitoring (e.g., ECG, SpO_2, $ETCO_2$) would have even better performance.[7,30–32] Other studies by our investigative team show that analysis of continuous vital signs from trauma patients predicts the need for emergency blood transfusion better than prehospital personnel, bedside nurses, and clinicians during the first 15 minutes of trauma patient resuscitation.[33–35] These findings could prove useful in allowing clinicians to accurately and confidently order major interventions such as massive transfusion, while the patient is being transported to the hospital.

LIMITATIONS

The decision to administer a transfusion is based on many factors that may not be contained in the patient registry used to create our algorithms. Half of the original patient population was eliminated by our requirement for complete sets of vital signs for the database merger, which could have introduced selection bias. However, the likelihood of this bias is mitigated by our observation that the study group and the general trauma center population had similar mortality rates. Injury mechanism was not reported on 28.7% of the subjects included in our study, but this was not one of the variables in our logistic regression model, so this gap in information should not affect our results. Although we internally validated our model to assess their performance, it is necessary to further validate the models using a completely new data set from another center.

CONCLUSIONS

With advances in computer hardware and medical sensory technology, more data can be collected even before patients' arrival at the hospital. Automated processing of patient data can maintain and reveal critical information for diagnostic assistance and clinical guidelines. In a large, single-center trauma population, computer-based analyses of prehospital vital signs were shown to better able to predict a patient's

TABLE 2. AUROC values for individual models based on vital signs.

		Outcome							
		U_{CX}	RC_2	MT_1	MT_2	MT_3	ICU_3	ICU_7	Mortality
Prehospital Vitals	SBP	0.72	0.70	0.75	0.77	0.77	0.57	0.58	0.53
	HR	0.63	0.62	0.69	0.74	0.73	0.53	0.54	0.57
	RR	0.53	0.53	0.55	0.57	0.59	0.53	0.53	0.57
	SI	0.76*	0.74*	0.80*	0.84*	0.83*	0.56	0.57	0.51
Pre-VS Model**	0.85	0.80	0.84	0.87	0.87	0.72	0.73	0.89	

Values refer to the AUROC of each model and each given outcome. UCX = emergency transfusion of Group O un-cross-matched blood; RC2 = packed red blood cell (pRBC) transfusion within 2 hours of admission; MT1 = ≥5 units pRBCs in the first 4 hours of care; MT2 = ≥10 units pRBCs in the first 12 hours of care; MT3 = ≥10 pRBCs in the first 24 hours of care; ICU3 and ICU7 are no less than three and seven day stays in the intensive care unit, respectively.
*Significantly different from other univariate vital signs ($p < 0.0001$). **The AUROCs of the Pre-VS model were significantly higher than the univariate vital signs across all outcomes ($p < 0.0001$).

need for transfusion (including massive transfusion), need for ICU care, and likelihood of death than measurement of a single vital sign. These algorithms hold the potential for saving significant amounts of time along the patient care pathway. The adoption of these techniques by emergency medical systems of hospitals at various levels of trauma care designations could enhance the effectiveness of prehospital triage decisions; reduce mortality and the use of medical and physical resources.

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