Anomaly Detection Outperforms Logistic Regression in Predicting Outcomes in Trauma Patients

Zachary D. W. Dezman, MD, MS, Chen Gao, PhD, Shiming Yang, PhD, Peter Hu, PhD, Li Yao, MS, Hsiao-Chi Li, PhD, Chein-I. Chang, PhD, Colin Mackenzie, MD

Abstract

Objective: Recent advancements in trauma resuscitation have shown a great benefit of early identification and control of hemorrhage, which is the most common cause of death in injured patients. We introduce a new analytical approach, anomaly detection (AD), as an alternative method to the traditional logistic regression (LR) method in predicting which injured patients receive transfusions, intensive care, and other interventions. **Methods**: We abstracted routinely collected prehospital vital sign data from patient records (adult patients who survived more than 15 minutes after being directly admitted to a level 1 trauma center). The vital signs of the study cohort were analyzed using both LR and AD methods. Predictions on blood transfusions generated by these approaches were compared with hospital records using the respective areas under the receiver operating characteristic curves (AUROC). **Results**: Of the patients seen at our trauma center between January 1, 2009, and December 31, 2010, 5,464 were included. AD significantly outperformed LR, identifying which patients would receive transfusions of uncrossmatched blood, transfusion of blood between the time of admission and 6 hours later, the need for intensive care, and in-hospital mortality (mean AUROC = 0.764 and 0.720, respectively). AD and LR provided similar predictions for the patients who would receive massive transfusion. Under the stratified 10 fold times 10 cross-validation test, AD also had significantly lower AUROC variance across subgroups than LR, suggesting AD is a more stable predictions model. **Conclusions**: AD provides enhanced predictions for clinically relevant outcomes in the trauma patient cohort studied and may assist providers in caring for acutely injured patients in the prehospital arena. **Keywords**: trauma; transfusion; vital signs; logistic regression; anomaly detection

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Address correspondence to Zachary D. W. Dezman, MD, MS, University of Maryland School of Medicine, Emergency Medicine, 110 Paca, 6th Floor, Baltimore, Maryland 21201. E-mail: zdezman@em.umaryland.edu

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Introduction

Uncontrolled hemorrhage is responsible for two-thirds of the 4.3 million deaths worldwide that will occur as a result of traumatic injury this year.[1,2] Recent advancements in trauma care have shown that early and aggressive interventions can help control bleeding and improve survival.[3–7] The United States trauma system exists to triage injured patients to the appropriate level of care, but it is expensive to maintain a multiple networks of prehospital providers, nurses, physicians, and surgeons in a state of constant readiness.[8–11] Inappropriately over-triaging is costly in a financial sense; under-triage increases patient morbidity and mortality. Furthermore, the current American College of Surgeons Committee on Trauma guideline on the use of vital signs to determine prehospital interventions cannot be made more specific without missing some high-risk patients.[12] Lives and resources could be saved if there was a tool that could rapidly identify patients with life-threatening hemorrhage.

The current standard is expert clinical judgment, but there is a large degree of disagreement between different providers.[13] Scoring systems and clinical support tools have been developed to help physicians predict which patients will need what services, but these have all relied on a combination of physician evaluation, lab testing, or imaging, eliminating the possibility for early and appropriate interventions in the field by prehospital providers.[14] Prior efforts by our group have focused on working within the existing trauma system framework by analyzing large groups of regularly collected vital signs (heart rate [HR], systolic blood pressure [SBP], diastolic blood pressure [DBP], and respiratory rate [RR]) to make clinical predictions tools.[14–16] Prediction models using logistic regression (LR) can readily identify the abnormal vital signs most commonly associated with patients with unfavorable outcomes, but they require roughly equal proportions of both positive and negative cases to achieve sufficient prediction power; LR is limited when the event of interest is rare.[15] In modern trauma centers, only a small proportion of patients receive transfusions (3–5%) and fewer still die (1–3%).[16,17] While it is possible to compensate for these shortcomings by increasing the weight of a particular outcome or by using a balanced sampling method,[15] it is often difficult to find reasonable unbiased samples or widely accepted weights.

Anomaly detection (AD) takes the reverse approach: it examines the majority of the data to identify a large population of samples that defines "normal" while marking the remainder small population as "anomalies."[18–20] Widely used to detect spam emails, bank fraud, and internet security breaches, AD identifies those signals that are "abnormal" by measuring how far they deviate from the normal background.[21] Anomalies are generally characterized by being unexpected and having a low probability of occurrence within the overall population. With these factors in mind, injured patients receiving transfusions are relatively uncommon events, and patients with unstable vital signs as a result of their traumatic hemorrhage are rarer still. Accordingly, these scenarios could be considered as anomalies. The purpose of this paper is to demonstrate that AD can effectively identify which patients need life-saving interventions: intensive care admission, transfusion, and massive transfusion. Specifically, we will show that AD is significantly better than standard LR methods at using prehospital vital signs to predict clinically relevant outcomes in a population of acutely injured patients.

METHODS

Population and Data Sources

This retrospective cohort study examined patients evaluated at our trauma center between January 1, 2009, and December 31, 2010. Subjects were included if they were adults who had complete sets of prehospital vital signs (HR, SBP, DBP, RR), were transported directly to our level 1 trauma center from the scene of injury, and survived more than 15 minutes after admission. Patients were excluded if they were under 18 years of age, had incomplete records, or were transferred from another institution. We also excluded those who died shortly after arrival (<15 minutes), because many of these patients are so grievously injured that any intervention is unlikely to help. These patients are readily identified by even untrained bystanders, and the point of this work was to show how AD may identify those patients that may benefit from early interventions, especially those with less-obvious injuries. Patient data were abstracted primarily from our patient registry, which contains prehospital vital signs, demographic and injury severity score (ISS),[22] injury type and mechanism, as well as information on patient care (e.g., intensive care unit [ICU] admission) and outcomes (mortality and length of stay [LOS]). The amount and types of blood products transfused were found through a review of blood bank records and cross-verified with the trauma registry. Registry files were matched to blood bank records using medical record number, time of arrival (within 24 hours), age, sex, and mode of transportation. Protocol approval with a waiver of consent was obtained through the Institutional Review Boards of both the University of Maryland School of Medicine and the U.S. Air Force.

Definitions and Derivation of Study Variables

Shock index (SI) was calculated for each patient by HR divided by SBP. Age-adjusted SI was defined as the subject's age multiplied by SI. The outcomes for prediction included the use of uncrossmatched blood (Group O universal donor) and massive transfusion. Three definitions of massive transfusion (MT) were used and each definition was applied to each case: MT1 ($\geq$5 units pRBCs in the first 4 hours of care), MT2 ($\geq$10 units pRBCs in the first 12 hours of care), and MT3 ($\geq$10 units pRBCs in the first 24 hours of care). These definitions of massive transfusion are not mutually exclusive: MT1 and MT2 are most useful to the clinician who is marshalling resources for an injured patient, while MT3 is the most commonly cited definition.[23] ICU admission and LOS were abstracted from the patient registry, dichotomized into $\geq$3 days and $\geq$7 days, and used as a surrogate measure of the resources needed to treat the patient's injuries. ICU LOS<3 was not considered an endpoint because some patients may be admitted to ICUs for short stays for reasons unrelated to the severity of their illness (e.g., a vent-dependent patient admitted after a fall from standing). Mortality was defined as in-hospital mortality and was taken from the patient registry.

Anomaly Detection and Logistic Regression Analysis

When applying AD methods to the problem of predicting which patient may need a transfusion, we start by construct a vital sign signal (VSS) for each patient. Each of the patient's vital signs is represented as a components of the vector, which is called a VSS vector: $\mathbf{x}_n = (v_{n1}, v_{n2}, \ldots, v_{nL})^T$. This process was repeated for all patients, creating a set of VSS vectors for the entire sample population, $\{\mathbf{x}_n\}_{n=1}^N$, where $\mathbf{x}_n$ is a data sample vector with L-dimensions, each of which describes a particular VSS taken from the nth patient. The kernel Reed-Xiaoli detector (K-RXD) is a commonly used anomaly detector developed by Reed[18] and can be specified by $y = (\mathbf{x} - \boldsymbol{\mu})^T \mathbf{K}^{-1} (\mathbf{x} - \boldsymbol{\mu})$, where$\mathbf{x}$is any VS vector associated with a patient, $\boldsymbol{\mu}$is the sample mean vector, and $\mathbf{K}$ is the sample covariance matrix calculated by:

$$\mathbf{K} = (1/N) \sum\nolimits_{n=1}^{N} (\mathbf{x}_n - \boldsymbol{\mu})(\mathbf{x}_n - \boldsymbol{\mu})^T$$

Like other approaches to AD, the K-RXD method calculates a distance between a given point of data and the nearest neighboring data points (the Mahalanobis distance). Compared to Euclidean distance based methods, the K-RXD method calculates this distance in proportion to the inverse of the covariance of the neighboring dataset, which allows the distance to be interpreted as the number of standard deviations from the observation to the centroid of the dataset. This property allows for correlation between model variables, which cannot be done using Euclidean-based methods. The K-XRD approach does require normally distributed data, but this assumption is often satisfied when working with large data sets.

Due to the scarcity of abnormal cases, the sample covariance matrix $\mathbf{K}$ was estimated for this study without separating normal cases from abnormal ones (an unsupervised approach). This allows the method to detect abnormal cases without assigning *a priori* class labels. In this case, we can calculate a response variable$y$for each case [20] and find the optimal area under the receiver operating characteristic curve (AUROC).[24,25]

For LR, the analysis was completed using all of the patient's prehospital vitals (HR, SBP, DBP, RR).[14,15] Stepwise logistic regression was used to avoid overfitting. Forward steps used the Wald Chi-squared test to determine whether a variable should be retained (p-value < 0.2) or excluded (p-value > 0.3) for each of the model end-points.

Model Validation and Comparison

Both models were internally validated by randomly dividing the study sample into 10 equal-sized and non-overlapping data subsets. A stratified sampling strategy was used to preserve the prevalence of positive outcomes from the original data set. Nine of the deciles were used to generate the coefficients of the LR and AD equations, which were validated against the remaining 10%. This process was repeated for a total of 10 training and testing cycles. The average AUROC from all training and testing cycles was calculated for each end point used to evaluate the models' performance in predicting mortality, ICU admission, and blood product use.[26,27] The optimal sensitivity and specificity was reported for each outcome and model and compared using student t-tests. Cut-offs were determined using the point with the highest Youden Index.

RESULTS

In total, 5,464 of the 8,912 total patients seen at our trauma center during the study period were eligible for inclusion in the study (61.3%, Figure 1). 3,798 were male (69.5%), and the majority of our patients were either Caucasian (64.3%) or African-American (27.4%, Table 1). The majority of patients had normal SI (SI $<$ 0.9), sustained minor injuries (ISS $\leq$ 9, 62.8%) with a blunt mechanism (88.6%), and had a 3-day LOS.

Table 2 shows the incidence of the 7 study outcomes used to test the AD and LR models: how many patients received uncrossmatched blood, how many received MTs, how many were admitted to the ICU, or died. A total of 212 patients received (3.9%) uncrossmatched blood. Depending on the definition used, between 91 and 124 (1.7–2.3%) patients underwent MT. Five hundred fifteen of the 5,464 patients included in this study were admitted to the ICU (9.4%) and 170 (3.1%) died.

Table 3 shows the sensitivity, specificity, and AUROCs from both AD and LR across all 100 testing and training cycles in stratified 10 fold by 10 times cross-validation for the 7 patient-centered outcomes. The sensitivity of LR was somewhat greater than AD across the different outcomes, but the specificity of predictions was significantly enhanced when using AD. With AD, the AUROC predicting the administration of uncrossmatched blood, 3- and 7-day ICU stays, and mortality, were significantly better using AD compared to LR. The variances of the AUROCs generated using AD are significantly smaller than those of LR for MT1, 3- and 7-day ICU stays, and mortality.

DISCUSSION

In this retrospective study, we used a convenience cohort of acutely injured patients to show that AD methods could be used to successfully determine which patients would require blood transfusions or ICU care or would die. In our data set, AD provides increased AUROC and decreased variability compared

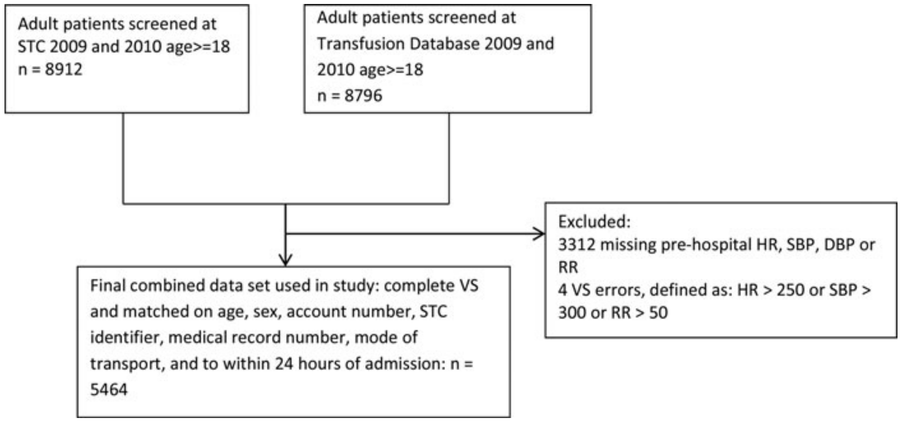

FIGURE 1. Study consort diagram.

to standard LR methods. These results may have an impact on prehospital triage decisions and resource allocation. We have shown that advanced computational methods can find slight differences in the standard prehospital vital signs that predict the need for life-saving interventions with accuracy (AUROC = 0.709–0.876). Other authors have attempted to create automated tools or heuristics to assist with prehospital triage decisions, but many of these rely on physician evaluation, advanced imaging, or laboratory testing, none of which is available prehospital.[14] In this paper, we show that AD provides significantly better predictions than LR for the use of uncrossmatched blood, ICU admission, and in-hospital mortality.

In addition to enhanced outcome prediction power measured by AUROC, AD provides several mathematical advantages over LR. A fundamental disadvantage of the LR approach is that it becomes considerably underpowered when the item of interest is rare. Since rare samples do not contribute much statistics, the parameters used by LR analysis to predict these rare cases are therefore underestimated. This is particularly true for very biased and skewed data. By contrast, AD is specifically designed to highlight rare non-normal events (e.g., transfusions and deaths in our trauma population). To create clinical predictions, the coefficients for the terms in an LR are calculated by training the LR equation on a given population. Adding characteristics usually increases the accuracy of a model's predictions, but these coefficients must be recalculated over again[28] and adding terms generally increases the variance of the results in LR. It is possible to create efficient regression algorithms, but the algorithm has to be uniquely fit to the patient population of interest by hand and by an experienced statistician. AD does not need to create these coefficients, and so it is computationally easy. Moreover, AD can also add as many

TABLE 1. Demographics of study population

Demographic	Value
Total, *N*	5,464
Age, mean (SD)	42.6 (19)
Sex, male *n* (%)	3798 (69.5)
Race, *n* (%)	
American Indian	27 (0.5)
Black	1499 (27.4)
Hispanic	237 (4.3)
White	3513 (64.3)
Other	188 (3.5)
Admission GCS, mean (SD)	14.1 (2.5)
Prehospital vital signs, mean (SD)	
HR	92.2 (20.5)
SBP	138.2 (26.6)
RR	18.7 (4.4)
SI	0.74 (0.73)
MOI, *n* (%)	
Blunt	4839 (88.6)
Penetrating	493 (9)
Other	132 (2.4)
ISS, *n* (%)	
≤9	3434 (62.8)
10–15	715 (13.1)
16–24	698 (12.8)
≥25	617 (11.3)
LOS (days)	3 (6.3)
ICU stay (days)	1.3 (5)

GCS: Glasgow Coma Scale; HR: heart rate; SBP: systolic blood pressure; DBP: diastolic blood pressure; RR: respiratory rate; SI: shock index; MOI: mechanism of injury; ISS: injury severity score; LOS: length of stay; ICU: intensive care unit.

TABLE 2. Incidence of clinical outcomes in study population

Outcome	*N* (%)
Uncrossmatched blood	212 (3.9)
MT1*	124 (2.3)
MT2	91 (1.7)
MT3	100 (1.8)
ICU Admission	
3 days	515 (9.4)
7days	335 (6.1)
Mortality	170 (3.1)

*MT: massive transfusion; MT1: ≥5 units packed red blood cells [pRBCs] in the first 4 hours of care; MT2: ≥10 units pRBCs in the first 12 hours of care;, and MT3: ≥10 units pRBCs in the first 24 hours of care; intensive care unit admission is ICU.

TABLE 3 Mean and standard deviation (SD) for the area under the receiver operating curve (AUROC) for each the 7 study outcomes, as generated using anomaly detection (AD) and logistic regression (LR)

	AD			LR			Comparisons	
Endpoint*	Sens†	Spec‡	AUROC	Sens†	Spec‡	AUROC	Delong, p§	Test for AUROC Variance, p‖
Uncross-matched	0.688	0.769	0.786 ± 0.006	0.891	0.500	0.734 ± 0.007	0.019	0.053
MT								
MT1	0.813	0.694	0.807 ± 0.006	0.860	0.653	0.801 ± 0.009	0.816	0.003
MT2	0.830	0.703	0.790 ± 0.009	0.888	0.615	0.810 ± 0.008	0.562	0.779
MT3	0.830	0.690	0.789 ± 0.007	0.804	0.710	0.813 ± 0.008	0.475	0.259
ICU Admission								
3 days	0.695	0.645	0.709 ± 0.004	0.767	0.466	0.609 ± 0.005	<0.0001	0.0001
7 days	0.686	0.701	0.734 ± 0.004	0.853	0.397	0.614 ± 0.007	<0.0001	<0.0001
Mortality	0.817	0.806	0.876 ± 0.004	0.803	0.682	0.767 ± 0.009	<0.0001	<0.0001

*Uncross-matched refers to the transfusion of uncross-matched blood. MT1 (≥5 units packed red blood cells [pRBCs] in the first 4 hours of care), MT2 (≥10 units pRBCs in the first 12 hours of care), and MT3 (≥10 units pRBCs in the first 24 hours of care). ICU admission and LOS were abstracted from the patient registry, dichotomized into ≥3 days and ≥7 days. Mortality was defined as in-hospital mortality. All endpoints were taken from the patient registry. Cut-offs were determined by the value with the highest Youden Index.

†All sensitivities are significantly different (t-test, $p < 0.0001$), except for the endpoint of mortality ($p = 0.43$).

‡All specificities are significantly different (t-test, $p < 0.0001$).

§AUROCs are considered significantly different when Delong's $p < 0.05$.

‖The variances of the AUROCs are considered significantly different when their p-value < 0.05.

characteristics or vital signs as one needs to gain further model precision. Most importantly, the AUROCs generated by AD were less variable in this data set than those generated by LR for predicting the use of uncross matched blood, MT1, ICU admission, and in-hospital mortality. This implies that the predictions are more stable and generalizable across multiple patient populations.

These results have several immediate applications to the field of prehospital medicine. The AD method is computationally inexpensive; hence, the models could be incorporated into a website or smartphone app, providing prehospital decision support and allowing providers to initiate interventions in the field.[29] This is most important in the current era of hypotensive resuscitation and balanced transfusion ratios, where the appropriate and early administration of blood products improves outcomes.[4,30,31] These results are an improvement over our previous work, where we were able to use LR methods to identify which trauma patients would receive MT with an accuracy similar to that of in-person physician examination.[32] These results suggest that it may be possible to answer a call for devices that provide rapid and automated transfusion and clinical predictions, based on non-invasive prehospital vital signs, without the need for ISS estimation or additional provider input.[33]

There are many more software packages supporting LR approaches, and LR is a more commonly used approach to multivariate analysis than AD. AD is used in some fields such as information security and fraud detection, but it is infrequently used in medicine. This study shows that AD could be a promising alternative to LR in building predictive models for clinical outcomes. Importantly, AD operates well using rare-events data. Many valuable observations with negative outcomes could be kept in the training set as background. Moreover, AD could be used when the outcome labels are missing. This is ideal when handling a large unlabeled data set, a situation where LR often fails.

As a single-center retrospective study, this work is subject to unmeasured biases. The decision whether or not to transfuse a patient is based on many factors that may not be contained in the registry and therefore not included in our AD algorithm. These results should be replicated in a separate center. By eliminating those patients who died early (within 15 minutes of arrival to the trauma center,) we have biased our results towards less severe injuries. In addition, by eliminating those patients without complete vitals, we may have further biased our study population towards minor injuries, as those with incomplete vitals are generally sicker and have more grievous injuries. These results are most likely to have an impact in a coordinated trauma system, with the resources to train and allow prehospital providers to initiate transfusions at the scene of injury.

CONCLUSIONS

Mortality outcomes in patients with traumatic injuries improve the earlier appropriate interventions are started. This method of using AD and prehospital vital signs to predict clinical outcomes could assist prehospital providers in identifying which patients would most benefit from early interventions, right at the scene of injury. With inexpensive, automated computing power, a coordinated trauma system could use AD methods to enhance their triage algorithms and increase their effectiveness through the rapid and appropriate deployment of resources.

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