SuperLearner versus Clinicians to Prioritise Trauma Patients (working title)

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Abstract

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Author Summary

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Introduction

Trauma is a major threat to population health globally [1, 2]. Every year about 4.6 million people die because of trauma - a number that exceeds the total number of yearly deaths from HIV/AIDS, malaria and tuberculosis combined. The most common cause of trauma is road traffic injuries (RTIs); in 2016 an estimated 1.3 million people died from RTIs alone [2]. Global actors have vowed to try to halve the number of deaths from road trauma by 2020, but this sustainable development goal is far from being realized [3]. This situation calls for not only more interventions, but also strengthened research on effective trauma care delivery.

Trauma care is highly time sensitive and delays to treatment has been associated with increased mortality across settings [4–6]. Early identification and management of potentially life threatening injuries is crucial for survival. A key component of trauma care is therefore the process of prioritizing patients to match level of care with clinical acuity [7, 8]. The existing literature on how to prioritise trauma patients focuses largely on two issues. First, in the prehospital setting the main focus has been to idenfity patients who merit transfer to a trauma centre [9]. Second, in the hospital setting a substantial body of research has focused on the appropriate criteria for trauma team activation [10, 11].

Although both these issues are important, clinicians all over the world are on a daily basis faced with the more complex problem of how to decide in what order to assess and treat trauma patients that arrive to the emergency department (ED). In health systems with formalised criteria for prioritizing ED patients, all patients are assigned a priority coupled with a target time to treat. These priorities are may be coded using colors, for example red, orange, yellow and green, with red being assigned to the most urgent patients and green to the least urgent [12], or numbers [13].

In health systems without formalized criteria, for example in many low resource settings, clinician gestalt is used informally to prioritize among trauma patients arriving to the ED [14]. As there is commonly no formal prehospital care systems in such settings, trauma patients often arrive to the ED without warning and without any form of previous prioritisation to guide the appropriate level of care in hospital [15]. Also, mass casualties may occur frequently, especially in RTIs. Identifying ways to quickly prioritize the patients in need of more immediate care would therefore be very valuable in a many low resource settings.

In contrast to trauma centre transfer or trauma team activation, the approach to prioritization among trauma patients arriving to the ED has received little attention from the research community. Framed as a classification problem this challenge can be addressed using a statistical learner. Logistic or proportional hazards models are common classification learners whereas more modern alternatives include random forests or convolutional neural networks. These learners all exist along the machine learning spectrum governed by their relative "human-to-machine decision-making-effort", with regression learners in the more-human-than-machine (MHTM) end and networks at the other, more machine than human (MMTH), end of the spectrum [16].

The application of MMTH learners to solve classification problems in medicine is not new [17], but the uptake and use of such learners in trauma research has been slow [18]. Some studies have approached the trauma centre transfer and trauma team activation issues using MMTH learners, and the results are conflicting with regards to the superiority of such learners over MHTM learners or standard criteria [19–22]. One very recent study used a random forest learner to assign priority to patients in a general ED population, and found a slight performance improvement using this MMTH learner compared to the standard criteria [23].

Thus, there seems to be a paucity of reseach on how to leverage machine learning to prioritise among trauma patients in the ED. Therefore, we set out to conduct a benchmark study, in which we attempted to improve on what we considered the two most important limitations of previous related research, namely the use of retrospective data and the focus on one specific MHTM or MMTH learner. We aimed to compare the performance of an ensemble machine learning methodology called SuperLearner to that of clinician gestalt based on patients' presentation. Our hypothesis was that the performance of the SuperLearner would be non-inferior to that of clinician gestalt.

Materials and Methods

Study Design

We used data from an ongoing prospective cohort at three publichospitals in urban India. Our analysis is an adjunct to a registered observational study to compare the performance of clinical prediction models with clinicians (ClinicalTrials.gov identifier NCT02838459).

Study Setting

Data anlysed for this study came from patients enrolled between 28 July 2016 and XX YYYY ZZZZ at the three hospitals Khershedji Behramji Bhabha hospital (KBBH) in Mumbai, Lok Nayak Hospital of Maulana Azad Medical College (MAMC) in Delhi, and the Institute of Post-Graduate Medical Education and Research and Seth Sukhlal Karnani Memorial Hospital (SSKM) in Kolkata. KBBH is a community hospital with XX inpatient beds. There are departments of surgery, orthopedics and anesthesia. It has a general ED where all patients are seen. Most patients present directly and are not transferred from another health centre. Plain X-rays and ultrasonography are available around the clock but computed tomography (CT) is only available in-house during day-time. During evenings and nights patients in need of a CT are referred elsewhere. MAMC and SSKM are both university and tertiary referral hospitals. This means that all specialities and imaging facilities relevant to trauma care, except emergency medicine, is available in-house around the clock. MAMC has approximately 2200 inpatient beds and SSKM has around XX inpatient beds. MAMC has a general ED whereas SSKM has two EDs, one where patients with suspected or confirmed neurosurgical

conditions are seen and one where patients with other acute conditions are seen. The rationale for this setup is that SSKM is the only referral centre for neurosurgical care in the Kolkata metropolitan area, which has a population of close to 15 million people. Because both MAMC and SSKM are tertiary referral hospitals a majority of patients arriving at their EDs are transferred from other health facilities, with almost no transfer protocols in place. Prehospital care is rudimentary in all three cities, with no organised emergency medical services. Ambulances are predominatly used for inter-hospital transfers and most patients who arrive directly from the scene of the incident are brought by the police or in private vehicles. Patients arriving to the ED are at all centres first seen by a casualty medical officer on a largely first come first served basis. There is no formalised system for prioritising ED patients at any of the centres.

Data Collection

Data was collected by one dedicated project officer at each site. The project officers all had a masters degree in life sciences. They worked five eight hour shifts per week so that mornings, evenings and nights were covered according to a rotating schedule. In each shift, project officers spent approximately six hours collecting data in the ED and the remaining two following up patients. The collected dat awas then transferred this data to a digital database. The rationale for this setup was to ensure collection of high-quality data from a representative sample of trauma patients arriving to the EDs at participating centres, while keeping to the projects budget constraints.

Participants

Eligibility criteria

Any person aged $\geq$ 18 years or older and who presented alive to the emergency department (ED) of participating sites with history of trauma was included. The age cutoff was chosen to align with Indian laws on research ethics and informed consent. We defined history of trauma as having any of the external causes of morbidity and mortality listed in block V01-Y36, chapter XX of the International Classification of Disease version 10 (ICD-10) codebook as primary complaint, with some exclusions (Supplementary material). These causes were excluded because they are not considered trauma at the participating centres.

Source and methods of selection of participants and follow up

The project officers enrolled the first ten consecutive patients who presented to the ED during each shift. The number of patients to enrol was set to ten to make follow up feasible. A follow-up was completed by the project officer 30 days after participant arrived at participating hospital. The follow-up was completed in person or on phone, depending on whether the patient was still hospitalised or if the patient had been discharged. Phone numbers of one or more contact persons, e.g. relatives, were collected on enrollment and contacted if the participant did not reply on follow up. Only if neither the participant nor the contact person answered any of three repeated phone calls was the outcome recorded as missing.

Variables, Data Sources and Measurement

Patient characteristics and SuperLearner variables

The dependent variable, or label, used to train the SuperLearner was all-cause 30 day mortality, defined as death from any cause within 30 days of arrival to a participating centre. These data were extracted from patient records if the patient was still in hospital 30 days after arrival, or collected by calling the patient or a patient representative if the patient was not in hospital.

The independent variables, or features, included patient age in years, sex, mechanism of injury, type of injury, mode of transport, transfer status, time from injury to arrival in hours. The project officers collected data on these features by asking the patient, a patient representative, or by

extracting the data from the patient's file. Sex was coded as male or female. Mechanism of injury was coded by the project officers using ICD-10 after completing the World Health Organization's (WHO) electronic ICD-10-training tool [24]. The levels of mechanism of injury was collapsed for analysis into transport accident (codes V00-V99), falls (W00-W19), burns (X00-X19), intentional self harm (X60-X84), assault (X85-X99 and Y00-Y09), and other mechanism (W20-99, X20-59 and Y10-36). Type of injury was coded as blunt, penetrating, or both blunt and penetrating. Mode of transport was coded as ambulance, police, private vehicle, or arrived walking. Transfer status was a binary feature indicating if the patient was transferred from another health facility or not.

The features also included vital signs measured on arrival to the ED at participating centres. The project officers recorded all vital signs using hand held equipment, i.e. these were not extracted from patient records, after receiving two days of training and yearly refreshers. Only if the hand held equipment failed to record a value did the project officers extract data from other attached monitoring equipment, if available. Systolic and diastolic blood pressure (SBP and DBP) were measured using an automatic blood pressure monitor (OMRON HEM-7130-L). Heart rate (HR) and peripheral capillary oxygen saturation (SpO^2) were measured using a portable non-invasive fingertip pulse oximeter (ChoiceMMed MD300 C2D). Respiratory rate (RR) was measured manually by counting the number of breaths during one minute. Level of consciousness was measured using both the Glasgow coma scale (GCS) and the Alert, Voice, Pain, and Unresponsive scale (AVPU). GCS has three components, called the eye, verbal, and motor components. Each component indicates the response of the patient to no, voice or painful stimuli. The eye component ranges from one to four, where four indicates that the patient opens his or her eyes spontaneously (best response) whereas one indicates that the patient does not open eyes regardless of stimuli (worst response). The verbal and motor responses are graded similarly, but ranges between one to five and one to six respectively. All components also include a non-testable level. In assigning GCS the project officers used the official Glasgow Coma Scale Assessment Aid [25]. AVPU simply indicates whether the patient is alert, responds to voice stimuli, painful stimuli, or does not respond at all.

The rationale for including these specific features were that they can be reasonably exptected to be available when a trauma patient arrives to the ED. They, or some variation thereof, represent standard variables collected in more or less all health systems. They are also included in the most well know clinical prediction models designed to predict trauma mortality [26].

Clinicians' priorities

For the purpose of this study, clinicians were instructed by the project officers to assign a priority to each patient. The priority levels were color coded. Red was assigned to the most serious patients that should be treated first. Green was assigned to the least serious patients that should be treated last. Orange and yellow were intermediate levels, where orange patients were less serious than red but more serious than yellow and green whereas yellow patients were less serious than red and orange patients but more serious than green patients. The clinicians were allowed to use all information available at the time when they assigned these variables, which was as soon as they had first seen the patient. The priorities were not used to guide further patient care and no interventions were implemented as part of the study for patients assigned to the more urgent priority levels.

Bias

Remains to be written.

Quantitative Variables

All quantitative features (age, SBP, DBP, HR, SpO^2, and RR) were treated as continuous.

Qualitative Variables

The levels of all qualitative variables (sex, mechanism of injury, type of injury, mode of transport, transfer status, and GCS components) were treated as buckets (dummy variables).

Statistical Methods

We used R for all analyses [27]. We first made a non-random temporal split of the complete data set into a training and test set. The split was made to achieve an adequate sample size in each set as detailed in the study size section below. We then calculated descriptive statistics of all variables, using medians and interquartile ranges (IQR) for continuous variables and counts and percentages for qualitative variables.

Development of the SuperLearner

We then developed our SuperLearner in the training set using the SuperLearner R package [28]. SuperLearner is an ensemble machine learning algorithm, meaning that it uses a library of techniques or specific learners, in principle any technique or learner that the analyst wants, to come up with an "optimal learner". Our library included techniques suitable for predicting a binary outcome such as all cause 30-day mortality (Table To Be Defined). The SuperLearner was trained using ten fold cross validation. This procedure is implemented by default in the SuperLearner package and entails splitting the development data in ten mutually exclusive parts of approximately the same size. All learners included in the library are then fitted using the combined data of nine of these parts and evaluated in the tenth. This procedure is then repeated ten times, i.e. each part is used once as the evaluation data, and is intended to limit overfitting and reduce optimism.

Assigning Priority Levels using the SuperLearner Prediction

The SuperLearner was then used to assign levels of priority to the patients in the training set. This was done by bucketing the SuperLearner prediction into four buckets by its values at the 25^{th}, 50^{th}, and 75^{th} percentiles. These buckets corresponded to the green, yellow, orange, and red levels of priority assigned by the clinicians'. The performance of both the continuous and bucketed SuperLearner predictions in the training set was then evaluated using the area under the receiver operating characteristics curve (AUROCC). We then used the SuperLearner to predict the outcomes of the patients in the test set and used the cutoff values from the training set to assign a level of priority to each patient in this set.

Comparing the SuperLearner and Clinicians

The perfomance of the continous and bucketed SuperLearner predictions, as well as the clinicians, was then evaluated by estimating their AUROCC. The levels of priority assigned by the SuperLearner and clinicians respectively were then compared by estimating the net reclassification, in events (patient with the outcome, i.e. who died within 30-days from arrival) and non-events (patient without the outcome) respectively. The net reclassification in events was defined as the difference between the proportion of events assigned a higher priority by the SuperLearner than the clinicians and the proportion of events assigned a lower priority by the SuperLearner than the clinicians. Conversely, the net reclassification in non-events was defined as the difference between the proportion of non-events assigned to a lower priority by the SuperLearner than the clinicians and the proportion of non-events assigned a higher priority by the SuperLearner than the clinicians.

We used an emperical bootstrap with 1000 draws of the same size as the original set to estimate 95% confidence interval (CI) around point estimates and differences. We concluded that the SuperLearner was non-inferior to clinicians if the 95% CI of the net reclassification in events did not exceed a pre-specified level of -0.05, indicating that clinicians correctly classified 5 in 100 events more than the SuperLearner.

Handling of missing data

Observations with missing data on all cause 30-day mortality or priority level assigned by clinicians were excluded. Missing data in features was treated as informative. For each feature with missing data we created a missingness indicator, a variable that took the value of 1 if the feature value was missing and 0 otherwise. Missing feature values were then replaced with the median of observed data for quantitative features and the most common level for qualitative features. We included the missingness indicators as features in the SuperLearner.

Study Size

Remains to be written.

Results

Remains to be written.

Discussion

Remains to be written.

Limitations

How do we account for the dynamic changes that the patient undergoes? The data variables used to train the superlearner are point estimates. But the patient clinical condition would keep changing. How do we account for this?

Are all the data variables considered for the super learners training? Is the super learners training limited by the data variables we use and enter for the study?

Handling of missing data. Exluding observations with missing outcome.

Conclusion

Remains to be written.

Acknowledgments

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