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A computational approach to mortality prediction of alcohol use disorder inpatients

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ABSTRACT

Background: Health information technologies can assist clinicians in the Intensive Care Unit (ICU) by providing additional analysis of patient stability. However, because patient diagnoses can be confounded by chronic alcohol use, the predictive value of existing systems is suboptimal. Through the use of Electronic Health Records (EHR), we have developed computer software called *AutoTriage* to generate accurate predictions through multi-dimensional analysis of clinical variables. We analyze the performance of *AutoTriage* on the Alcohol Use Disorder (AUD) subpopulation in this study, and build on results we reported for *AutoTriage* performance on the general population in previous work.
Methods: AUD-related ICD-9 codes were used to obtain a patient population from MIMIC III ICU dataset for a retrospective study. Patient mortality risk score is generated through analysis of eight EHR-based clinical variables. The score is determined by combining weighted subscores, each of which are obtained from singlets, doublets or triplets of one or more of the eight continuous-valued clinical variable inputs. A temporally updating risk score is computed with a continuously revised 12-hour mortality prediction.
Results: Among AUD patients, in a non-overlapping test set, *AutoTriage* outperforms existing systems with an Area Under Receiver Operating Characteristic (AUROC) value of 0.934 for 12-h mortality prediction. At a sensitivity of 90%, *AutoTriage* achieves a specificity of 80%, positive predictive value of 40%, negative predictive value of 89%, and an Odds Ratio of 36.
Conclusions: For mortality prediction, *AutoTriage* demonstrates improvements in both the accuracy and the Odds Ratio over current systems among the AUD patient population.

1. Introduction

Clinical Decision Support Systems (CDSS) can be used to help assess patient conditions and predict patient mortality risk. Accurate predictions in the ICU are needed for timely medical attention and for the allocation of limited ICU resources [1,2]. Several existing prediction models such as Modified Early Warning Score (MEWS) [3], Sepsis-Related Organ Failure Assessment (SOFA) [4], and Simplified Acute Physiology Score (SAPS II) [5], rely on weighted linear combinations of basic patient characteristics such as age, type of admission and vital sign measurements. The high false positive rate of alerts resulting from such classifiers often leads to alarm fatigue in the clinical setting [6]. Desensitization from an overexposure to false alarms has widely been documented to increase response times and decrease receptivity to correct alerts [7]. For the reasons described below, the difficulty of assessing stability is exacerbated in patients suffering from alcohol-use dependence (AUD) and calls for improvement.

AUD patients encompass 1 out of 10 critical care admissions and are up to 8% more likely to experience unplanned re-hospitalization within 30-days of discharge [8,9]. This is because the standard techniques for screening patient stability can be confounded by chronic alcohol use. In particular, signs of acute hypotension, which can be indicative of life-threatening

Abbreviations: ICU, Intensive Care Unit; MICU, Medical Intensive Care Unit; EHR, Electronic Health Records; AUD, Alcohol Use Disorder; ICD-9, International Statistical Classification of Diseases version 9; MIMIC III, Multiparameter Intelligent Monitoring in Intensive Care version III; ROC, Receiver Operating Characteristic; AUROC, Area Under Receiver Operating Characteristic; CDSS, Clinical Decision Support Systems; MEWS, Modified Early Warning Score; SOFA, Sepsis-Related Organ Failure Assessment; SAPS II, Simplified Acute Physiology Score; WBC, White Blood Cell count; HIPAA, Health Insurance Portability and Accountability Act; BIDMC, Beth Israel Deaconess Medical Center; PPV, Positive Predictive Value; NPV, Negative Predictive Value; LR+, Positive Likelihood Ratio; LR-, Negative Likelihood Ratio; OR, Odds Ratio

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homeostatic failures like sepsis, anaphylaxis and renal failure [4,10,11] may be masked among patients in the AUD subpopulation, because AUD patients often suffer from chronic hypertension [12]. Chronic alcohol use can also confound the value of a Leukocyte Differential (WBC) Count, a common lab test used in the diagnosis of a variety of medical conditions [13]. The higher risk of unplanned rehospitalization, in conjunction with poorer diagnostic screening performance, underscore the need for improved risk scoring systems for AUD patients.

The use of Electronic Health Records (EHR) in hospitals provides an opportunity to improve predictive value from clinical data and provide clinical decision support. Recent studies have used various patient measurements and patient trends to improve mortality predictions, leading to incremental progress [14–16]. To further improve the quality of mortality prediction, we have developed *AutoTriage*, an algorithm which interrogates trends among clinical variables and also analyzes inter-correlations [17]. Using only eight common clinical measurements and analyzing inter-correlations reduces the chances that real-time data unavailability challenges affect algorithm performance. As homeostasis is governed by multi-organ feedback regulation, these variable correlations uncover useful patterns across organ systems. Accurate and early identification of deteriorating patients with assistance from a CDSS tool like *AutoTriage* has the potential to significantly decrease the number of life-threatening situations arising in the critical care wards of the hospital, and in turn lead to reductions in patient mortality rates. In this study, we demonstrate the application of *AutoTriage* on the difficult-to-predict AUD subpopulation to demonstrate the ability of the algorithm to overcome factors that are confounded by traditional diagnostic analysis.

2. Methods

2.1. Data set

Fig. 1 depicts the patient exclusion process used to select 3054 patient records from the Multiparameter Intelligent Monitoring in Intensive Care (MIMIC) III database [18]. The records consist of de-identified clinical information of adults admitted to the Beth Israel Deaconess Medical Center (BIDMC) medical intensive care unit (MICU). Since the study did not impact patient safety and all data were in accordance with the HIPAA Privacy Rule, the requirement for patient consent was waived by the Institutional Review Boards of BIDMC and the Massachusetts Institute of Technology.

Inclusion criteria for this study were:

I. Age of at least 18 years and admission to the MICU.
II. Documented length-of-stay and survival for at least 17 h following admission. A 17-h minimum accounts for a 12-hour advance warning after 5 h of patient monitoring using *AutoTriage*. Documented AUD-related ICD-9 code (291.X, 291.XX, 303.XX, 305.XX, 357.5, 425.5, 535.3X, 571.2, and 571.3, where X denotes a wildcard).

The eight physiological measurements utilized with 1-h resolution were heart rate, pH, pulse pressure, respiration rate, blood oxygen saturation, systolic blood pressure, temperature, and white blood cell count (WBC). With the exception of pH and WBC, these measurements are frequently sampled in the ICU, thus ensuring our predictions are broadly applicable. In addition, MEWS, SAPS II, and SOFA utilize similar measurements for prediction, allowing us to compare performance with these systems.

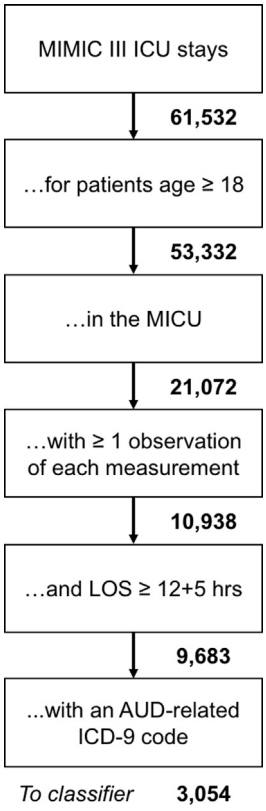

Fig. 1. Patient inclusion flowchart.

2.2. Gold standard

In-hospital mortality was our gold standard. The time of last measurement available was chosen as the time of death of the patient. By this definition, 392 patients were flagged as having in-hospital deaths and 2662 as survivors, resulting in a 12.84% mortality prevalence.

2.3. Binning, feature construction, and score assignment

Our classifiers use a set of four non-linear input features designed to capture empirical risk as a function of the patient measurements. Each individual type of measurement was associated with a non-linear function mapping from value of the measurement to approximate empirical risk of gold standard-defined mortality. These non-linear functions were typically polynomials of degree four or five. The sum of all such functions was taken as the first input to our classifier. Trends for observed patient measurements were also calculated using time-parameterized sequences of measurements. For example, a change in respiratory rate was calculated for each set of two consecutive timestamps with respiratory rate measurements (imputed to the nearest hour) and used as a stand-alone input feature [17]. During hours with no updated entries, the measurement value was approximated as the most recent value available and trends were calculated from this value. In the same fashion as with the measurement values, the empirical risk of mortality as a function of each individual trend was approximated with a polynomial and used as an input feature. The sum of all of these risk approximating functions of the trend values was taken as the second feature input of our classifier. Finally, combinations of two or three trends were related to empirical risk of mortality. In this procedure, the trends were binned by value, where bin edges were assigned heuristically. The empirical risk of mortality for each combination of two or three