Prediction of Septic Shock for ICU patients with Chronic Diseases

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Abstract

We predicted the probability of onset of sepsis, severe sepsis and septic shock for patient in Intensive Care Unit (ICU). The 1,640 subjects are selected from the public database MIMIC-II. Specifically, the population of this study is patients with diabetes, kidney and lung related chronic disease. We used ensembling machine learning methods to predict outcome, and compared different algorithms for sepsis prediction.

1. Introduction

Sepsis is the body's extreme response to an infection. It is defined as a combination of Systemic Inflammatory Response Syndrome (SIRS), and a confirmed or suspected infection, usually caused by bacteria[1]. Untreated or inadequately treated cases of sepsis can lead to condition known as severe sepsis or septic shock. Septic shock is defined as a subset of sepsis in which particularly profound circulatory, cellular, and metabolic abnormalities are associated with a greater risk of mortality than with sepsis alone. Therefore, early diagnosis of sepsis is essential for successful treatment.

In adults, Systemic Inflammatory Response Syndrome (SIRS) is defined as the presence of two or more of the following[2]:

1. Body temperature below 36C (96.8F) or above 38C (100.4F)
2. Tachycardia, with heart rate above 90 beats per minute
3. Tachypea (increased respiratory rate), with respiratory rate above 20 per minute
4. White blood cell (WBC) count less than 4,000/mm3(cubic millimeter) or above 12,000/mm3

Many automated sepsis screening tools described in the literature are primarily based on SIRS criteria, with additional specifications that are tailored to individual hospital systems[3]. A recently developed risk stratification tool that was presented along with the new sepsis definitions is termed the quick sepsis-related organ failure assessment (qSOFA). It uses three criteria, assigning one point for low blood pressure (SBP $<$ 100 mmHg), high respiratory rate ($\geq$ breaths per min), or altered mentation (Glasgow coma scale $<$ 15). The score ranges from 0 to 3 points. The presence of 2 or more qSOFA points near the onset of infection was associated with a greater risk of death or prolonged intensive care unit stay.

Recent advances in early detection of sepsis have resulted in substantial progress in predicting the onset of sepsis for ICU patients. However, many studies focus on the general ICU patient without considering their medical histories. According to Centers for Disease Control and Prevention, though anyone can get an infection, certain people are at higher risk:

- Adults 65 or older
- People with chronic medical conditions, such as diabetes, lung disease, cancer, and kidney disease
- People with weakened immune systems
- Children younger than one

Our goal was to detect the presence of sepsis for ICU patient with chronic diseases such as diabetes, lung disease and kidney disease. By identifying patients with these medical conditions, we hope to provide a powerful prediction for the risk of sepsis, severe sepsis, and septic shock so that hospitals can better initiate prevention strategies for these patients.

2. Experimental Setup

2.1 Cohort Selection

The dataset used in this study is from MIMIC II (Multiparameter Intelligent Monitoring in Intensive Care), which is the clinical data collected from Beth Israel Deaconess Medical-Center. Since our study focuses on patients with chronic diseases, the cohort is comprised of ICU patients with diabetes, chronic kidney diseases, and chronic lung diseases.

	Diabetes(%)	Kidney(%)	Lung(%)
Sepsis (n=40)	80	25	15
Severe Sepsis (n=217)	73.3	29.9	10.1
Septic Shock (n=109)	72.5	24.8	11.9

Table 1: Chronic Disease(%) for each Syndrome

	Mean	Median
Blood Pressure	76.01	74.87
Heart Rate	85.18	84.02
Respiratory Rate	19.98	19.52
Oxygen Saturation	96.75	97.24
Temperature	98.05	98.10

Table 2: Vital Signs Statistics of Chronic Disease Patients (n=1,640)

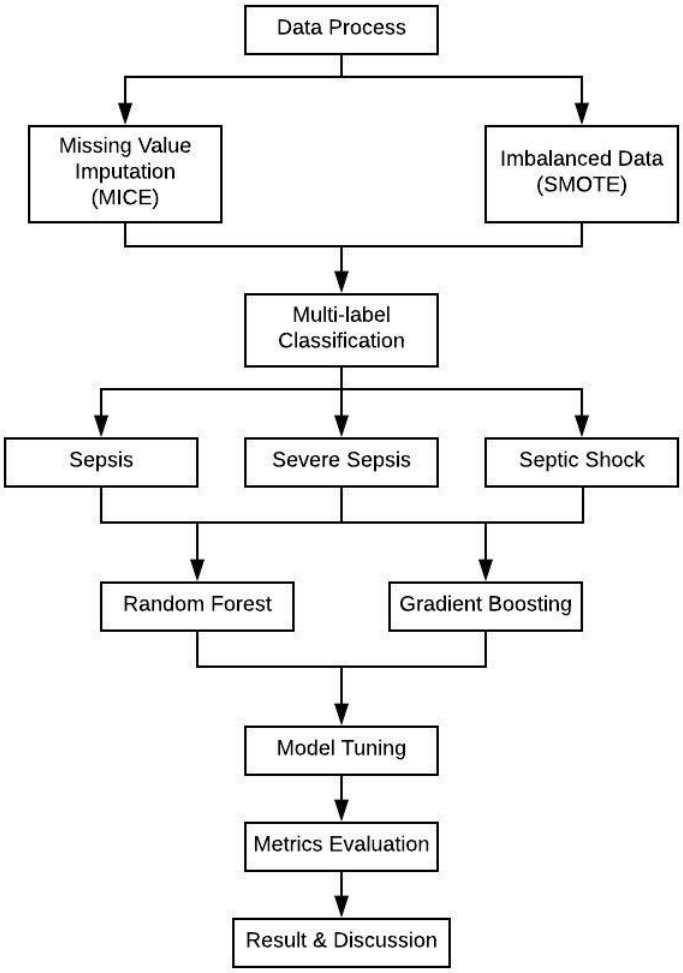


Figure 1: Pipeline

2.2 Data Extraction

Extracted from the MIMIC II dataset, we utilized the tables containing hospitalization information, vital signs measurement, patient demographics, and medical diagnosis. Regarding the data preprocessing, we first identify the code of our interested chronic diseases (diabetes, kidney, and lung) and the targets (sepsis, severe sepsis, and septic shock). We then filter the hospitalization (hadm_id) with the identified chronic disease. For these selected hospitalizations, we used one-hot encoding to transform the three diseases into the binary representation. As for the outcome variables, we also conducted the binary transformation and joined the two wide-format tables using column "hadm_id", resulting in a table with each row representing a unique hospitalization. For the next step, we added other features such as the vital signs and demographic information to the wide-format table by hadm_id. In the original data from MIMIC II, each instance represents a unique ICU stay. Therefore, one hospitalization can have several records of the same vital sign since a patient can be admitted to ICU more than one time per hospitalization. To address the multiple records issue, we averaged the vital sign measurements among the ICU stays to represent the unique hospitalization. After the data preprocessing, the final table contains 1,640 rows with 20 features. For our analysis, we assumed each hospitalization is independent and treated each hospitalization as one instance.

Before running the model, we handled the problems of missing values and imbalanced data in our dataset. Regarding the missing values, the issue primarily comes from the vital sign features with blood pressure containing the highest percentage (7.99%) of missing values. We adopted MICE (Multivariate Imputation by Chained Equations) as our imputation method with the assumption that the values are missing at random. As for the imbalanced data, we implemented SMOTE (Synthetic Minority Over-Sampling Technique) to overcome the skewed dataset. SMOTE incorporates the k nearest neighbor as the underlying method to over-sample the minority class and under-sample the majority class.

	Missing Value(%)
Sex	0.366
Age	0.122
Blood Pressure	7.99
Heart Rate	4.82
Respiratory Rate	5.06
Oxygen Rate	5.06
Temperature	6.52

Table 3: Missing value(%) of predictors

	Sepsis(%)	Severe Sepsis(%)	Septic Shock(%)
Original	2.44	13.2	6.65
SMOTE	26.8	42.9	27.6

Table 4: Imbalanced data(%) with SMOTE

2.3 Feature Choices

The features in this study is composed of 4 categories: demographics, vital signs, chronic disease indicator, and the outcome variables. The original variables including race and diagnosis were converted to dummy variables with the binary representation since we want to assess the importance of each variable in terms of the 3 syndromes. To implement random forest and gradient boosting algorithms, we then transformed the outcome variables (sepsis, severe sepsis, and septic shock) into categorical variables.

	Feature
Demographic	age, sex, white, asian, black, hispanic, others, unknown
Vital Signs	blood.pressure, heart.rate, respiratory.rate, oxygen.saturation, temperature
Chronic Disease	diabetes, kidney, lung
Outcome	Sepsis, SeverSepsis, SepticShock

Table 5: Feature Selection

2.4 Comparison Methods

Our analysis used the similar approach with the study from BMJ Journal[4], which implemented ensemble machine learning techniques to evaluated the existing sepsis prediction algorithm (InSight). Compared to the study which adopted 10-fold cross validation on gradient boosting method to predict the onset of sepsis, severe sepsis, and septic shock, we used only 5-fold cross validation yet incorporated the tuning process on the max depth of each tree and the number of boosting iterations.

2.5 Evaluation Criteria

Besides the accuracy rate, we assessed our models with ROC curve and AUC to ensure the result is not biased by the skewness of the dataset even though we handled the imbalanced data using SMOTE in the earlier step.

3. Method: Gradient Boosting and Random Forest

Since sepsis, severe sepsis and septic shock could happen sequentially to a patient in a single hospitalization, our task is a multi-label classification task. Our approach is to take binary relevance method, independently training one binary classifier for each label.

We choose Naive Bayes method as our baseline, and use two ensemble learning methods as our classifiers: random forest and gradient boosting method. The reason we chose these algorithms is that we believe that the accuracy of our prediction is of great significance. Compared to decision tree whose advantage is its interpretability, and logistic regression whose advantage is that it could also inform us the coefficients of features, we put more emphasis on the accuracy.

For each syndrome, we fit gradient boosting and random forest models, tuned the hyperparameters of each models, predicted the test data with optimal parameters chosen through cross-validation.

3.1 Gradient Boosting

For gradient boosting, we tuned two hyperparameters: number of boosting iterations and maximum of tree depth. For example, after cross validation for the sepsis prediction, we found that the optimal number of iteration is 3,600 and optimal tree depth is 15, given the shrinkage rate is 0.001 and minimum terminated node size is 30.

3.2 Random Forest

For random forest, we tuned two hyperparameters: number of trees and number of nodes at each split. The node impurity is measured by Gini index. In the result section, we also presented the variable importance for the prediction.

4. Results

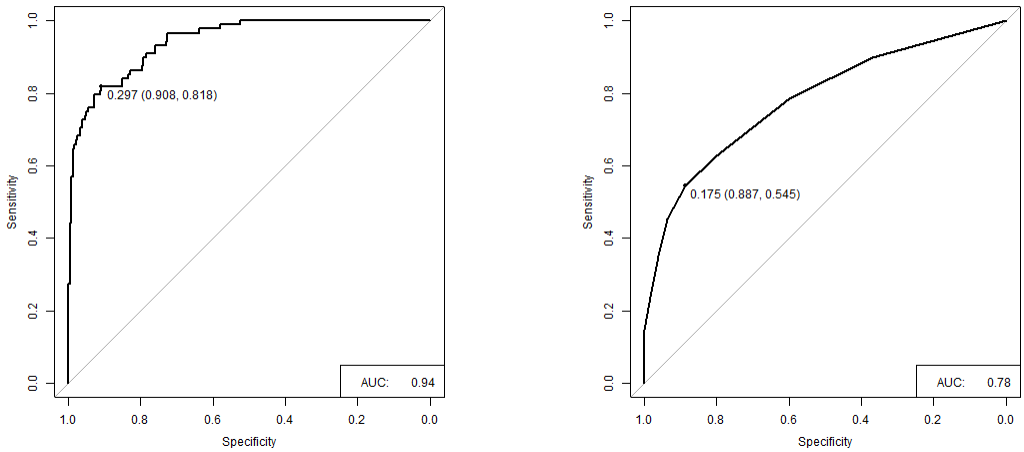
Resulted are presented by comparing two different algorithms for each syndromes (Sepsis, severe sepsis,septic shock).

4.1 Results on Sepsis

Gradient Boosting outperforms the other two methods in terms of AUC and accuracy rate.

Method	Accuracy(%)	AUC(%)
Naive Bayes	78	84
Random Forest	77	84
Gradient Boosting	89	93

Table 6: Sepsis Prediction Outcome



(a) Gradient Boosting (b) Random Forest

Figure 2: ROC curve

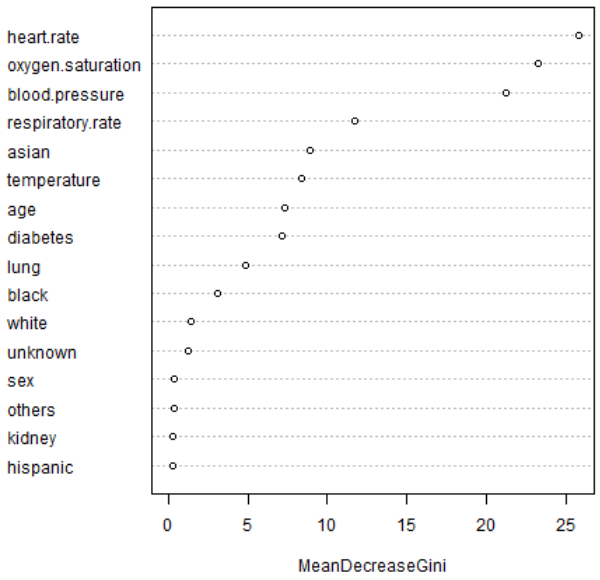


Figure 3: Variable Importance

4.2 Results on Severe Sepsis

Same results apply to severe sepsis and septic shock. (see page 8)

Method	Accuracy(%)	AUC(%)
Naive Bayes	68	72
Random Forest	73	83
Gradient Boosting	80	88

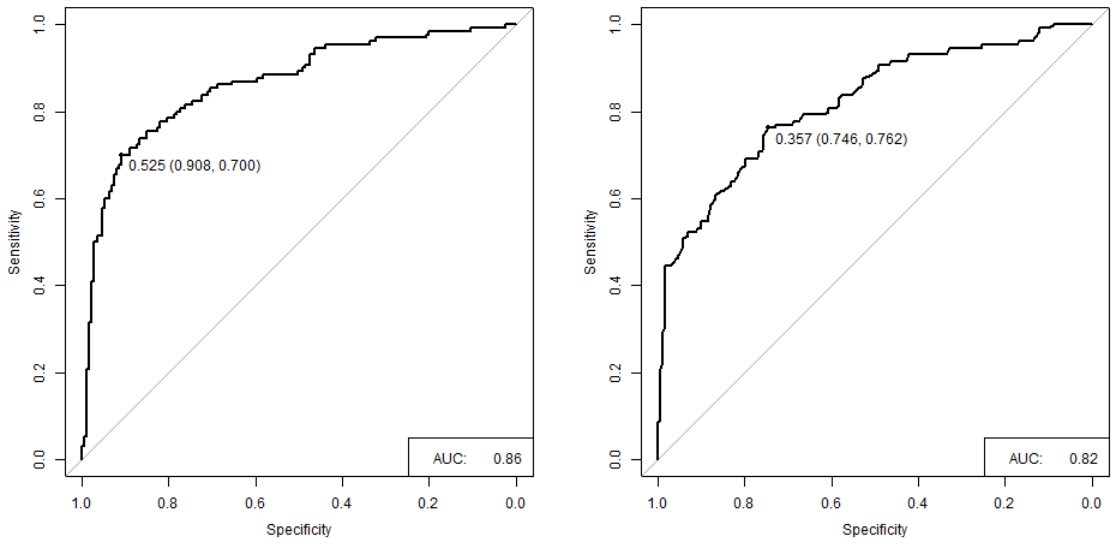
Table 7: Severe Sepsis Prediction Outcome

4.3 Results on Septic Shock

(see page 9)

Method	Accuracy(%)	AUC(%)
Naive Bayes	82	80
Random Forest	82	85
Gradient Boosting	89	91

Table 8: Septic Shock Prediction Outcome



(a) Gradient Boosting (b) Random Forest

Figure 4: ROC curve

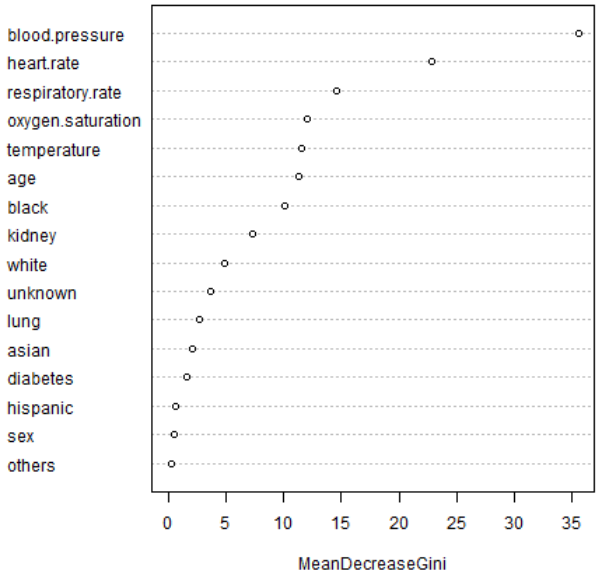
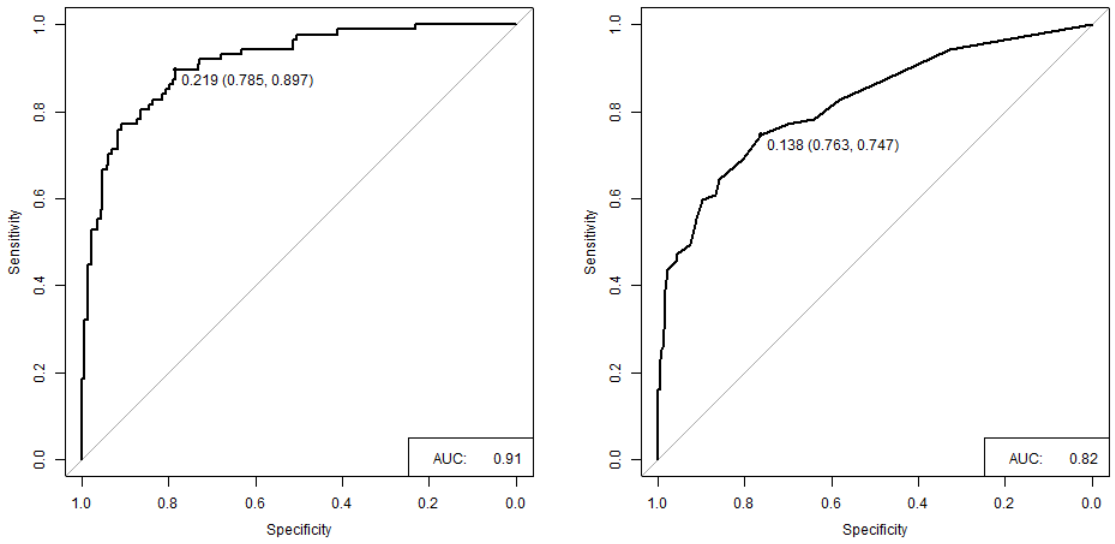


Figure 5: Variable Importance



(a) Gradient Boosting (b) Random Forest

Figure 6: ROC curve

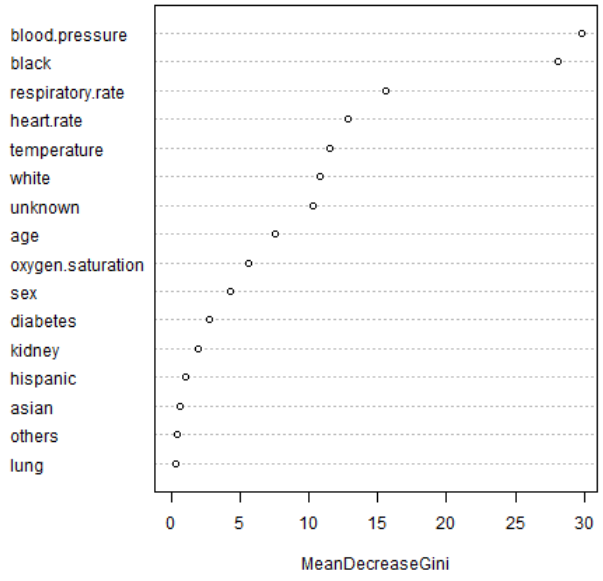


Figure 7: Variable Importance

5. Discussion and Related Work

Based on the result of our study, we can conclude that vital signs are important indicators for predicting the onset of sepsis, severe sepsis, and septic shock, which is in line with the findings from the paper by BMJ Journal[4]. Also, for different levels of sepsis condition, certain race exhibits different level of importance for the prediction. For instance, race black is an important variable while predicting septic shock. Therefore, by taking race into consideration, doctors can be more informed of the risk of sepsis condition for the patients with chronic diseases. However, there are some limitations for the study. We only focused on the ICU patients with certain type of chronic diseases (diabetes, kidney diseases, and lung disease). Hence, the result only applies to patients with the specific medical condition. The other limitation is derived from the small sample size of the analysis. Our models were constructed upon 1,640 instances, which may generate different results with larger sample size. In addition, MIMIC II is not the most updated dataset. The clinical data only ranges from 2001 to 2008. To generalize our study, we will need to use a more recent dataset from MIMIC III.

6. Conclusion

In sum, the study focuses on the prediction of the onset of sepsis-related condition for ICU patients with diabetes, chronic kidney disease, or chronic lung disease. We divided the original multi-label classification problem into 3 binary classification tasks and leveraged the ensemble machine learning method with Nave Bayes as our baseline. For future extension on the study, we will include other types of chronic diseases such as cancer and cardiovascular disease. Additionally, using a more up-to-date database such as MIMIC III to analyze sepsis-related syndromes will also be our focus.

References

[1] Mervyn Singer, Clifford S. Deutschman, and Christopher Warren Seymour. The third international consensus definitions for sepsis and septic shock (sepsis-3). 2016.

[2] Poushali Bhattacharjee, Dana P. Edelson, and Matthew M. Churpek. Identifying patients with sepsis on the hospital wards. 2017.

[3] Senthil K. Nachimuthu and Peter J. Haug. Early detection of sepsis in the emergency department using dynamic bayesian networks. 2012.

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