Predictive Model of Septic Shock Staging Base on Continuing Invasive Hemodynamic Monitoring

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Abstract: Septic shock is a major public health concern across the world, also is a typical cause for patients being admitted to the intensive care unit. It is easier to be misdiagnosed, yet the situation is getting worse. Septic shock can be classified into three stages: irreversible (early stage), compensated, and decompensated. Sepsis has long been misdiagnosed, but it develops and worsens at an alarming rate, often reaching irreversible levels within hours. This work has expanded the proportion of invasive hemodynamics to septic shock for the development of understanding of the phases of septic shock. This article aims to construct and develop a real-time prediction model of septic shock staging based on continuous invasive hemodynamic monitoring. The ultimate model of the article is a multi-classification prediction model.

In this experiment, the eICU collaborative research database was employed, and four characteristics from the dataset were scored to indicate the stage of septic shock. Need to point out that deep active learning, a new approach that combines deep and active learning, was chosen as the research's major learning approach. Margin sampling is the main query strategy used in the active learning approach, with the random selection strategy serving as a control strategy. There are two groups of query strategies, compare the two groups to see which one is more effective: random selection or active learning. As a result, the query strategy of active learning is considerably most stable than random selection in deep active learning. Although septic shock cannot be diagnosed purely based on hemodynamic characteristics, the model can nevertheless assist clinicians in making an early diagnosis or warning.

1 INTRODUCTION

Septic shock is a common reason for patients to be admitted to the intensive care unit (ICU), and it is also a significant cause of mortality among severely sick patients in the ICU. In 2017, there were 48.9 million instances of sepsis and 11 million fatalities due to sepsis, accounting for roughly 20% of all deaths worldwide (Genga 2017). It is worth noting that COVID-19, from its emergence in 2019 and continues to this day, has been linked to sepsis. Health care personnel pay particular attention to the development of sepsis after a COVID-19 patient is brought to the ICU (Bediako 2021). This was demonstrated in many studies that shock could be divided into three stages: irreversible, compensated, and decompensated shock. Sepsis is very easy to be misdiagnosed, but it deteriorates very quickly in hours. The staging of shock assists medical personnel in determining the severity of the condition and appropriately intervening in treatment and medicines to enhance patient survival rates. There is thereby a need for classification, but it is still a significant challenge to define clearly what stage of shock the patient is at based on the clinical presentation. Thus, to have better knowledge of the phases of septic shock, this research has increased the proportion of invasive hemodynamics in septic shock.

The ultimate objective of this study is to provide some help in using a machine learning approach to determine the stage of shock in patients with sepsis in the ICU, improve efficiency and reduce fatality. There are many excellent reviews in literature dealing with the basic concepts of machine learning and sepsis. Continuing to learn about septic shock using machine learning is also a significant step forward in medicine. Notably, hemodynamic monitoring is critical for the diagnosis and intervention of septic shock patients. The eICU Collaborative Research Database (eICU-CRD) Demo was utilized as a source of clinical study data

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in this study, which comprised 24 hours of continuous vital sign monitoring of systemic circulation (Badawi 2018). The author recruited patients previously diagnosed with sepsis from the eICU-CRD Demo for observation and research. The use of machine learning for invasive continuous hemodynamic monitoring of eICU sepsis patients is expected to further improve the understanding of the shock stage.

2 METHODS

2.1 The eICU-CRD Dataset

Between 2014 and 2015, researchers from the MIT Computational Physiology Laboratory, Philips Healthcare, and PhysioNet's colleagues collected data from over 200,000 ICU patients for the ICU-CRD database (Badawi 2018). It should be pointed out that this database is an electronic version that provides a new model of care in ICU: remote monitoring. The e-recording allows clinicians to instantly retrieve a patient's vital signs, saving time and preventing the loss of paper data. This research utilized the eICU-CRD demo as the experimental database because the researcher intends to see if it can generate predictions with a smaller amount of electronic data. The eICU-CRD demo includes 2,500 patients in the ICU department from 20 large hospitals in the United States. These patients are divided into a training set and test set according to the radio of 8:2. The file in the eICU-CRD called 'vitalPeriodic.csv' is particularly attractive as the main dataset, due to the study is based on the characteristic of hemodynamic to make a prediction model. The VitalPeriodic table includes the continuous invasive hemodynamic monitoring features which are need in this research: heart rate, oxygen saturation (SaO_2), central venous pressure (CVP), systolic blood pressure, and diastolic blood pressure.

2.2 Features and Score Setting

Four features were collected to determine the stage of septic shock: heart rate, CVP, mean arterial pressure (MAP), SaO2.

2.2.1 Heart Rate

When cardiovascular decomposition occurs, the heart is the first compensation mechanism. At this time, the heart rate will increase to ensure sufficient cardiac output. According to the definition and diagnostic criteria of sepsis and septic shock, a heart rate of more than 90 beats per minute or two standard deviations greater than the normal value of the same age can be confirmed or suspected of infection(CCM1993).

2.2.2 CVP

It is generally believed that CVP at 8 to 12mmHg is a treatment target for severe infections and septic shock. In recent years, CVP has been challenged as a pressure indicator to evaluate volume load. It is now believed that CVP can be used to determine the type of shock. However, unless in the extreme range of the variables, such as in the case of a history of bleeding, and the CVP value is 0mmHg, it should always be interpreted together with other variables (Antonelli 2014).

2.2.3 MAP

Invasive blood pressure (IBP) is a commonly used technique in the ICU. Continuous monitoring as one of the advantages of IBP could provide patients status in real-time. In our research, MAP is selected as a variable shown the IBP's feedback of patients.

2.2.4 SaO2

As an important monitoring indicator of severe infection and septic shock recovery, SaO2, also selected as one of the scoring indicators in this article. SaO2 value is from 60% to 80% in patients with severe infection and septic shock in normal circumstances. It must also be mentioned that a significant increase in mortality when the SaO2 value is less than 70%.

2.2.5 Scoring Design

The designer created a simplified score sheet based on the given information and the MAP data in the APACHE II score, as shown in table 1.

Table 1: Criteria for scores calculated based on invasive hemodynamic data patients.

Parameters	Points			
	+4	+3	+2	+1
Heart Rate (BPM)	-	-	-	≥90
CVP (mmHg)	-	-	-	<8 & >12
MAP (mmHg)	≥160 or ≤49	130~159	≥110 or ≤ 69	-
SaO2 (%)	60~70	70~80	-	-

In addition, the scores are divided as follows based on the aforementioned features and scores to identify the phases of septic shock: 1) a score of 0 to 4 is judged to be a non-septic patient. The patient's septic shock phase is assessed to be more severe as the score rises. 2) with the score of 4, it is in irreversible stage, 3) it is belonging to a compensated stage when the score is 5 to 7, 4) and the patient will be classified as in the decompensated phase with the score of 8 to 10. This shown as below figure. This is the multi-classification standard of this experiment.

Table 2: Stratification criteria for multi-classification scores.

Score	**Non-sepsis**	**Irreversible**	**Compensated**	**Decompensated**
0				
1				
2				
3				
4				
5				
6				
7				
8				
9				
10				

2.3 Model Development

The eICU-CRD is collected patients'physiological data every few minutes. As mentioned previously, the patients are randomly separated into two parts: 80% for model training (2000 patients), 20% as the test set. Convolution neural networks (CNN) also is a multi-layer neural network, were utilized in this research to create a prediction model of which phase of the septic shock the patient will be in. CNN has the ability to extract features automatically, the convolution layer is in charge of extracting features and convolution is used to extract the needed information (Asafuddoula 2016).

One of our goals is to develop a prediction model with as minimal data as feasible; the model also uses deep active learning (DAL), a hybrid of deep and active learning(Chang 2020). The flow of the model is shown in Figure 1 below. DAL framework can be roughly divided into two parts: the active learning query strategy on the unlabeled data set and the training method of the deep learning model(Chang 2020). There are hundreds, if not thousands, of records for each of the 2,500 patients. Unlike most traditional active learning algorithms, which query one by one, batch model deep active learning (BMDAL) picks an entire batch of unlabeled data based on certain selection criteria (Agarwal 2019). The amount of information and diversity of the samples are considered at the same time as the batch selection of samples (Agarwal 2019). The DAL code is built on a Github library called "deep active learning" and is publicly available. It is worth pointing is that the optimizer of the DAL used Adam. The benefit of DAL code is that it has a rapid gradient to huge data, which is ideal for our needs in eICU-CRD, where we need to analyze enormous volumes of data. Another significant advantage of the DAL is that it does not boost the budget of recognition and classification (Chang 2014).

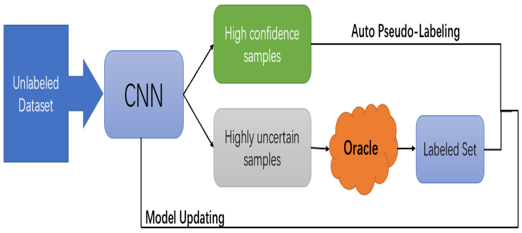

Figure1: The framework of the deep active learning process.

2.4 Query Strategy

The most important things in active learning are how to select samples for labeling and the selection of query strategy. There are two main principles for how to select samples for labeling: uncertainty principle and difference principle. Margin sampling as one of the uncertainty samplings was chosen in the active learning. The concept of active labeling by margin sampling is to give the sample the smallest separation between the top two class predictions, as seen in the equation:

$$x_i^{MS} = \underset{x_i}{\operatorname{argmin}}(p(y_1|x_i) - p(y_2|x_i)) \quad (1)$$

where y 1 and y 2 are the deep learning network's first and second most probable class labels, respectively (Agarwal 2019). The Random sampling strategy, is mainly as a control strategy. This strategy randomly select a certain proportion of samples from the unlabeled samples and submit them to the labeler for labeling. It also has been used in this article. In the processing, there are two groups:

One uses a combination of margin sampling and the Random sampling, referred to as active learning by learning strategy. Another does not use a margin sampling strategy.

To determine which strategy is more successful, the two groups will be compared in the next and the more effective strategy will be found between random selection and active learning.

3 RESULTS AND ANALYSIS

According to information derived from the eICU-CRD sub-database 'diagnose', the proportion of people diagnosed with septic shock during their ICU stay was 7.33 percent of the total number of people in the database. The percentage of positive to negative occurrences was 3:38. These are patients who were diagnosed with sepsis and shock by clinicians, but who were not classified as being in the septic shock phases by the doctors.

After 15 rounds with 1000 batch sizes and 1000 queries per round, the ultimate accuracy of the active learning by learning approach is 55.017 percentage, whereas the accuracy of random selection is 51.958 percent. Regardless of the fact that there may not be much of a difference in the accuracy, Figure 2 illustrates that the accuracy of random selection outperforms that of active learning initially. As shown in the diagram, the initial random selection approach has significantly higher accuracy and stability than the active learning technique. However, when additional input data and data are labeled, the stability of random selection tends to deteriorate, compared to active learning.

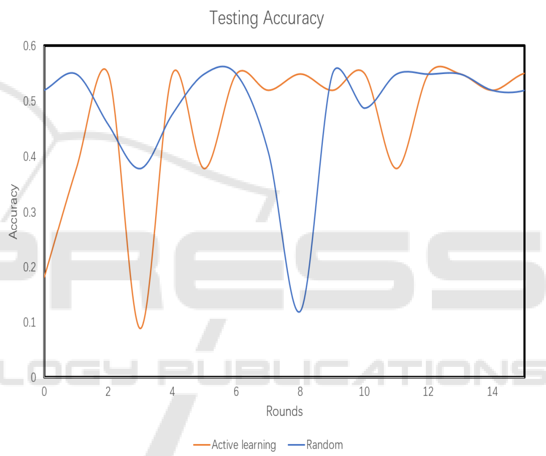

Figure 2: Active accuracy of two query strategies.

Conversely, since more data is added to the model, the accuracy of active learning gradually overcomes the measurement rate of random selection, and the active learning model is more stable than random selection. This article also makes use of deep learning. Deep neural networks (DNN) were constructed, and the batch-based sample query approach was used. The following graphs of accuracy and loss are obtained using the case of a batch size of 64. Deep learning is better than active learning if readers look objectively at the accuracy and loss of the final model in this experiment, as is demonstrated in figures 3 and 4.

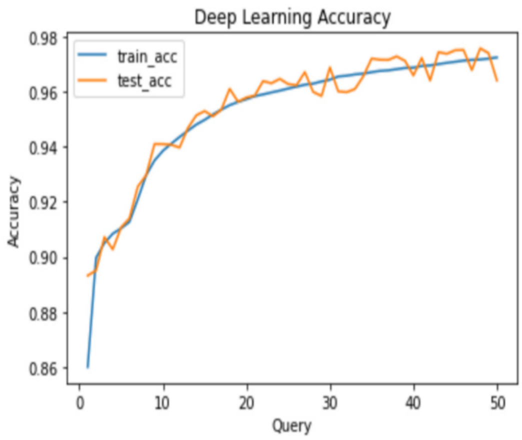

Figure 3. Deep learning accuracy.

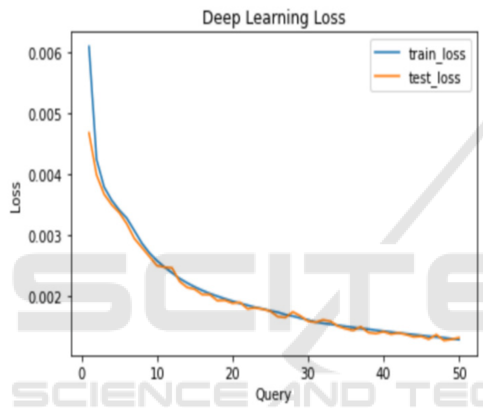

Figure 4. Deep learning loss.

4 DISCUSSION

The most direct charm of active learning is that it can significantly reduce the cost of labeling samples. Researchers have discovered that accuracy is quite low and about 0.55 based on of Figure 2, which represents accuracy in both query techniques, random selection and active learning. for this, the authors have come up with the following hypothesis. Firstly, it can no longer learn from the data, although it is an active learning model. Our deep learning model, on the other hand, appears to contradict this notion. Furthermore, the authors discovered that the percentage of individuals with septic shock in the eICU-CRD demo is extremely tiny. The percentage of scores below 4 that indicate a non-sepsis state is approximately 0.99, and the distribution is extremely unbalanced. As a result, it's thought that this data set isn't appropriate for the test model, and the accuracy rate is poor. Even though the testing accuracy is indeed very high for this type of database, it really has no effect on the model. A further option is that a deep active learning library setting was not properly debugged in the experiment, preventing the DAL model from learning anything.

Another thing worth mentioning is that because of the interdependence of the sympathetic and parasympathetic nervous systems, shock should not be judged simply based on "normal" hemodynamic measurements. Regardless of the fact that the model can predict a patient's sepsis stage based on current eICU datasets, it still has to be validated and adjusted before it can be utilized in real life. Since this complex septic shock phase is solely assessed by invasive hemodynamics, the model is still immature. Nevertheless, most ICU patients who underwent intubation medication are adept at gathering invasive hemodynamics parameters. As a consequence, the model can still be used as a guide to assist clinicians in promptly diagnosing or warning of the onset of more severe shock.

5 CONCLUSIONS

Based on hemodynamic data and the features of most intubation treatments in ICU patients, this paper provides a technique for predicting and staging septic shock in the article. For multi-class prediction, deep active learning and deep learning active learning are used to study. Deep learning validates the model's feasibility and correctness. The query strategy of active learning is considerably most stable than random selection in deep active learning. The fraction of patients with sepsis is too small since the data is concentrated, resulting in the low accuracy of the active learning model. The low accuracy and instability of the DAL model are caused.

However, this paper also has the deficiency that the author's knowledge of the DAL source code is incomplete and inaccurate, a representative database should be chosen to debug the model and code. And even though it cannot fully diagnose and forecast septic shock with invasive and continuous hemodynamic monitoring of patients, this experiment is likely to increase the understanding of the shock stage and aid clinicians in quick diagnosis and real-time prediction. Even if invasive hemodynamics cannot properly detect and discriminate the stages of septic shock after successful debugging of the future model, it will offer a new research avenue for the study of the stages of septic shock. Septic shock may be immediately interfered with and the mortality incidence of septic shock can be reduced by accurately evaluating the stage of septic shock and offering assistance to medical personnel.

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