A Quantitative Model for Sepsis Stratification

Jing Xia[1], Min Zhu[1], Shengyu Zhang[1], Molei Yan[2], Guolong Cai[2], Jing Yan[2], and Gangmin Ning[1]

[1] Department of Biomedical Engineering, Zhejiang University, Hangzhou, China
[2] Zhejiang Hospital, Hangzhou, China

Abstract— **Sepsis is a kind of systemic inflammatory response syndrome caused by infection and it endangers the life of patients seriously due to its rapid development progression and high mortality rate. In clinic it is highly demanded to quantitatively stratify the severity of sepsis for individual management. This work aimed to build a quantitative model for sepsis patients which can stratify the disease severity in three levels. For this purpose, clinical data were collected and preprocessed, i.e. screening, normalization and data replenishing. Afterwards, sepsis sensitive parameters were tested and selected, which were utilized as the input of the stratification model. For the model, the algorithm of Support Vector Machine was applied. Eventually, the model was tested in total of 522 clinical cases and an accuracy of 67.5% in stratification was achieved. The performance of the established model is superior to the conventional APACHE scoring method. Preliminary results exhibited that the established model is potential to help improve the patients' management by quickly stratifying the sepsis severity.**

Keywords— **sepsis, stratification model, support vector machine, APACHE scoring**

I. Introduction

Sepsis is a kind of systemic inflammatory response syndrome caused by infection[1]. It has become one of the worldwide healthcare problems due to its rapid development progression and high mortality rate, which is reported as 28.7-49.7%[2,3].

Sepsis is a highly dynamic illness and to quickly assess individuals' sepsis severity is critical for reducing the mortality. Thus, it is of great significance to develop a quantitative approach to identify high risk patients[3,4] and make a quick stratification of sepsis severity. Presently, several severity scoring systems have been used in clinic, such as Acute Physiology and Chronic Health Evaluation II (APACHEII). However, these methods are complicated and impractical[4].

This work aims to build a physiological parameters based quantitative model for sepsis patients that can stratify the severity in three levels.

II. Materials and Methods

The severity stratification process includes three steps. Firstly, statistical analysis of clinical parameters is conducted to screen severity level related features. Secondly, data normalization and replenishing is introduced. Finally, two-layer stratification model is built[5].

A. Data source

Totally 522 sepsis patients were recruited between June 2012 and January 2013. All patients were informed consent to participate in the study.

The patients enrolled had sepsis syndrome with at least one organ dysfunction or hypoperfusion and were divided into three severity levels. The definitions of the three levels are as follows: level one is sepsis plus sepsis-induced organ dysfunction or tissue hypoperfusion; level two is sepsis-induced persisting hypotension despite adequate fluid resuscitation; level three is multi organ dysfunction. The cohort sizes of three levels are 131, 240 and 151, respectively.

Clinical data contain personal information (age, gender, height, weight, etc.), history of disease (diabetes, hypertension, chronic lung disease, blood disease, cancer, cerebrovascular accident, etc.), physical symptoms and examinations (fever, chills, temperature, heart rate, respiratory rate, mean arterial pressure, etc.) and laboratory tests.

B. Data preprocess

First, clinical parameters were statistically tested and screened. Kolmogorov-Smirnov method was carried out to test the normality of continuous data. For attributes in normal distribution, independent Student's t test was applied to analyze the differences among the groups, otherwise, Wilcoxon rank sum test was used. Besides, the inter-group differences of categorical data were analyzed using Chi-square test. For all statistical tests, a p-value of <0.05 was considered significant.

Selected attributes were then scaled through the min-max normalization so that they fell in the identical range [0, 1]. In order to retain the most information of data, attributes

J. Goh and C.T. Lim (eds.), *7th World Congress on Bioengineering 2015*,
IFMBE Proceedings 52, DOI: 10.1007/978-3-319-19452-3_46

with missing data were replenished using the mean imputation method.

C. Model development

Support Vector Machine (SVM) was used to construct the model. As one of machine learning algorithms, SVM is based on statistical learning theory and uses the principle of structural risk minimization[6,7]. Based on LIBSVM[8], parameters are adjusted to build the most satisfied models.

Multi-layer stratification model is applied in the study as shown in Fig. 1. In the first layer, the samples are distinguished into cohorts of severity level one and none one. In the second layer, the none one subgroup is identified as severity level two or three. Consequently, as output, patients are stratified into severity level one, two and three.

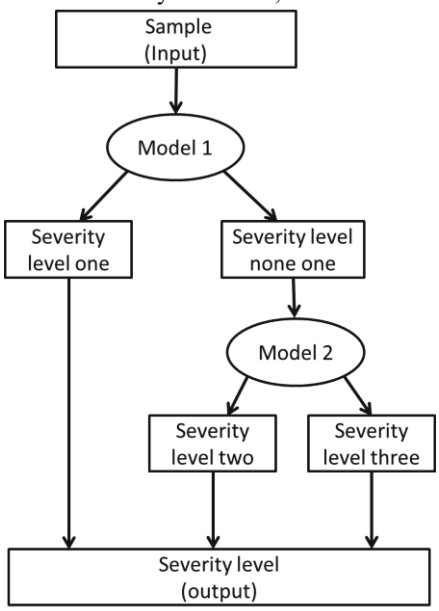

Fig.1 Schematic diagram of the two-layer stratification model for sepsis severity

D. Model Evaluation

The validity of the model is tested by the accuracy in predicting patients with different severity levels. Also, the results are compared with the APACHE scoring system[9].

III. Results

A. Dataset Characteristics

Table 1 gives the characteristics of the study cohort. The average age of the patients was 63.5 years. The percentages of male and female were 64.0% is and 36.0%, respectively. For the patients, hypertension was the most common disease (63.4%) followed by cerebrovascular accident (15.9%) and diabetes (15.5%).

Table 1 Characteristics of the study cohort

	N(%)
Age(mean±sd)	63.5±19.0
Gender	
Male	334(64.0%)
Female	188(36.0%)
History of disease	
Diabetes	81(15.5%)
Hypertension	190(36.4%)
Chronic lung	72(13.8%)
Blood disease	9(1.7%)
Cancer	41(7.9%)
Cerebrovascular accident	83(15.9%)

B. Selected Attributes

For the model 1, 32 attributes were selected, including personal information (age, height), history of disease (cerebrovascular accident), physical symptoms and examinations (fever, dyspnea, obnubilation, cough, hemoptysis, cyanosis, temperature, heart rate, respiratory rate, mean arterial pressure, urine volume) and laboratory tests (triglycerides, arterial PH, direct bilirubin, intravenous PH, albumin, PaO_2, BUN, BE, Cr, SaO_2, Na^+, FiO_2, Cl^-, $PaCO_2$, Plt, PCO_2, PCT, blood lactate). These attributes showed significant difference between severity level one and else group.

For the model 2, 26 attributes were chosen, including personal information (age), history of disease (connective tissue disease), physical symptoms and examinations (chills, anorexia, obnubilation, clammy skin, cough, wheeze, bloating, mean arterial pressure, urine volume) and laboratory tests (direct bilirubin, intravenous PH, ALT, SaO_2, AST, PaO_2, albumin, BE, BUN, blood lactate, CTNI, WBC, Plt, PCT). These attributes showed significance between severity level two and level three group.

C. Model Prediction

In all, 371 samples were chosen as training set, and the rest 151 samples as testing set. In the testing set, the sample sizes of severity level one, two and three were 35, 76 and 40, respectively.

The prediction results of model 1 are listed in Table 2. The accuracy, sensitivity and specificity of model 1 were 67.5%, 60.0% and 89.7%, respectively.

The prediction results of model 2 are given in Table 3. The accuracy, sensitivity and specificity of the model 2 were 79.3%, 81.6% and 75.0%, respectively.

Generally, the accuracy of the overall model was 67.5%. And the accuracy of severity level one, two and three was 60.0%, 71.1% and 67.5%, respectively.

As for misclassified samples, there are six different types of misclassification, which are summarized in Table 4.

Table 2 Prediction result of model1

	True (level one)	False (level none one)
Predicted true (level one)	21	12
Predicted false (level none one)	14	104

Table 3 Prediction results of model 2

	True (level two)	False (level three)
Predicted true (level two)	62	10
Predicted false (level three)	14	30

Table 4 Misclassifications of the stratification model

Type of misclassification	Sample size (proportion)
Level 1(real)→Level 2(predicted)	9(6.0%)
Level 1(real)→Level 3(predicted)	5(3.3%)
Level 2(real)→Level 1(predicted)	8(5.3%)
Level 2(real)→Level 3(predicted)	14(9.3%)
Level 3(real)→Level 1(predicted)	4(2.6%)
Level 3(real)→Level 2(predicted)	9(6.0%)

D. Comparison with the APACHE model

Considering the APACHE scores, 19.5 and 24.5 were set as cutoff for classifying the patients into severity level one, two and three. Namely, patients with APACHE score lower than 19.5 points, between 19.5 and 24.5 points, higher than 24.5 points were identified as severity level 1, 2 and 3, respectively.

Only 68 samples were involved in the APACHE scoring for comparison as it requires strict completeness of data.

The accuracy of APACHE classification in severity level one, two and three was 62%,61% and 33%, respectively. In contrast, the corresponding accuracy resulted from the two-layer stratification model was 71%,68% and 78%, respectively.

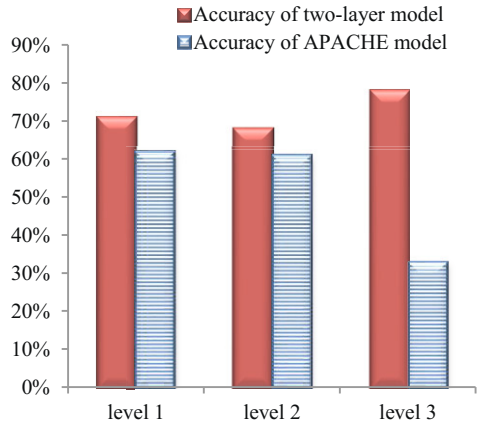

Fig.2 Comparison of the accuracy of APACHE model and two-layer stratification model

IV. Discussion

The prediction results of model 1 and model 2 showed that the first layer model is less sensitive and more specific, while the sensitivity and specificity of the second layer model are almost equal.

From Table 4, it can be seen that the largest proportion of misclassification was the type that level two cases were falsely predicted as level three, followed by level one being falsely predicted as level two and level three being falsely predicted as level two. It indicates that misclassifications are more likely to occur in neighbor levels. It can be interpreted as that these samples have similar clinical symptoms which make it difficult to distinguish them.

As shown in Fig. 2, the two-layer stratification model has a better discrimination than the APACHE model. The APACHE scoring system was designed for various kinds of severe diseases in clinic, while the stratification model was established upon sensitive parameters to sepsis severity. In this aspect, it is not surprised that the stratification model is superior to the APACHE model.

V. Conclusions

The present work proposed an SVM based two-layer stratification model for sepsis. The patients are identified as severity one, two and three with a general accuracy of 67.5%. Compared to the conventional method of APACHE, it has the advantages of better discrimination, more objective and lower requirement for data completeness. In conclusion, the established model has the potency to provide a computational tool for sepsis stratification and help improve the patients' management.

Acknowledgment

This work is supported by the National Nature Science Foundation of China (Grant 81271662), the Department of Science and Technology of Zhejiang Province (Grant 2011R50018), and the Ministry of Health of China (Grant 201202011).

Conflict of Interest

The authors declare that they have no conflict of interest.

References

1. Levy M M, Fink M P, Marshall J C, et al. 2001 SCCM/ESICM/ACCP/ATS/SIS International sepsis definitions conference. Intensive care medicine. 2003; 29: 530-538.
2. Dellinger R P, Levy M M, Rhodes A, et al. Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock, 2012. Intensive care medicine. 2013; 39: 165-228.
3. Vorwerk C, Loryman B, Coats T J, et al. Prediction of mortality in adult emergency department patients with sepsis. Emergency Medicine Journal. 2009; 26.4: 254-258.
4. Chen C, Chong C, Liu Y, et al. Risk stratification of severe sepsis patients in the emergency department. Emergency medicine journal. 2006; 23.4: 281-285.
5. Fu X, Ren Y, Yang G, et al. A computational model for heart failure stratification. proceedings of the Computing in Cardiology, 2011.IEEE:2011;385-388.
6. Cortes C, Vapnik V.Support-vector networks. Machine Learning. 1995; 20.3: 273-297.
7. Burges C J C. A tutorial on support vector machines for pattern recognition. Data Mining and Knowledge Discovery. 1998; 2.2: 121-167.
8. Chang CC, Lin CJ. LIBSVM: a library for support vector machines. ACM Transactions on Intelligent Systems and Technology. 2011; 2.3: 1-27.
9. Knaus W A, Draper E A, Wagner D P, et al. APACHE II: a severity of disease classification system. Critical care medicine. 1985; 13.10: 818-829.

Author: GangminNing
Institute: Department of Biomedical Engineering, Zhejiang University
Street: Zheda Road 38, Yuquan Campus, Hangzhou,P.R.China
City: Hangzhou
Country: China
Email: gmning@zju.edu.cn