2020 IEEE International Conference on Bioinformatics and Biomedicine (BIBM)

Machine Learning to Predict ICU Admission, ICU Mortality and Survivors' Length of Stay among COVID-19 Patients: Toward Optimal Allocation of ICU Resources

Tingting Dan[1, #], Yang Li[1, #], Ziwei Zhu[1, #], Xijie Chen[1], Wuxiu Quan[1], Yu Hu[1], Guihua Tao[1], Lei Zhu[1], Jijin Zhu[3], Yuyan Jin[1], Longgeng Li[1], Chaokai Liang[2], Hanchun Wen[4,*], Hongmin Cai[1,*]

[1]*School of Computer Science and Engineering, South China University of Technology, Guangzhou, China*

[2]*School of Software Engineering, South China University of Technology, Guangzhou, China*

[3]*Emergency Department, The First Affiliated Hospital of Guangxi Medical University, Guangxi, China*

[4]*Department of Critical Care Medicine, The First Affiliated Hospital of Guangxi Medical University, Guangxi, China*

[#] These authors contributed equally to this work.

* Corresponding authors: hmcai@scut.edu.cn, wenhanchun@gxmu.edu.cn.

2020 IEEE International Conference on Bioinformatics and Biomedicine (BIBM) 978-1-7281-6215-7/20/$31.00 ©2020 IEEE DOI: 10.1109/BIBM49941.2020.9313292

***Abstract*—COVID-19 causes burdens to the ICU. Evidence-based planning and optimal allocation of the scarce ICU resources is urgently needed but remains unaddressed. This study aims to identify variables and test the accuracy to predict the need for ICU admission, death despite ICU care, and among survivors, length of ICU stay, before patients were admitted to ICU. Retrospective data from 733 in-patients confirmed with COVD-19 in Wuhan, China, as of March 18, 2020. Demographic, clinical and laboratory were collected and analyzed using machine learning to build the predictive models. The built machine learning model can accurately assess ICU admission, length of ICU stay, and mortality in COVID-19 patients toward optimal allocation of ICU resources. The prediction can be done by using the clinical data collected within 1-15 days before the actual ICU admission. Lymphocyte absolute value involved in all prediction tasks with a higher AUC. The online predictive system is freely available to the public (http://212.64.70.65:8000/).**

Keywords—Coronavirus Disease 2019 (COVID-19), ICU admission, mortality, machine learning, the turnover rate of ICU.

I. Introduction

Coronavirus Disease 2019 (COVID-19) has rapidly spread around the world [1]. As of November 16th, 54, 906, 130 diagnoses and 1, 325, 621 deaths have been reported globally [2]. The number of people infected with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) increases every day.

A significant challenge of COVID-19 is its threat to scarce medical resources [3]. Of special interest is how to best allocate the intensive care unit (ICU) resources [4]. Toward this goal, some studies model basic reproduction rate hoping to estimate how many ICU beds are needed [5], other studies focus on how to reduce infections [6], while others seek treatments to reduce ICU admissions or shorten ICU stays [7].

We aimed to design a data-driven framework to optimally allocate ICU resources. We attempted to address three open questions. First, who needs to be admitted to ICU, and what risk factors contribute to this? Age is a factor, so are baseline conditions, but exceptions exist [8]. Herein we use machine learning to objectively identify an optimal combination of factors that predicts ICU admissions for individual patients. Second, can we predict who will, unfortunately, die despite being admitted into ICU? At the peak of the outbreak, when ICUs are at a severe shortage, clinicians face a "toughest triage" [9] of having to allocate ICUs or ventilators to those patients with a higher chance of survival or maximum longevity [4]. The decision to withdraw life support is primarily based on a patient's age [4], but with moral controversies and a loose scientific ground. Mining clinical data may suggest evidence-based multifactorial guidance on this unfortunate triage. Conversely, among those admitted into ICU and later discharged alive, can machine learning predict their lengths of ICU stay? This third question is important as the length of ICU stay is related to ICU's turnover rate, and prediction of it can help policy-makers better allocate or prepare ICU resources.

II. Materials and Methods

A. Study Design – Data-powered ICU Model

Fig. 1 outlines our ICU models. Among all inpatients, the model aimed to predict who needs to be admitted into ICU (Task I). Among patients admitted to ICU, the model aimed to predict who would unfortunately die (Task II). And among survivors in ICU, the model aimed to predict the length of stay in the ICU (Task III).

B. Participants

This study was approved by the First Affiliated Hospital of Guangxi Medical University Hospital Ethics Committee, with the informed consent being waived (No. 2020 (KY-E-084)). We retrospectively studied 733 patients diagnosed with COVID-19, who were admitted as inpatients to the Huangpi Hospital of Traditional Chinese Medicine (Wuhan, China) from January to March 2020. Diagnostic methods were consistent with other clinical studies [10], and were based on positive real-time reverse-transcriptase polymerase chain reaction (RT-PCR) assay for nasal and pharyngeal swab specimens, or, the existence of Immunoglobulin M (IgM) and Immunoglobulin G (IgG) antibodies.

C. Potential Predictive Variables

We extracted 194 examination indicators (909 variables) from electronic medical records for each inpatient. These 909 variables came from three categories: 1) demographic information (9 indicators, 9 variables), including sex, age, presence or absence of comorbidities (e.g., hypertension, diabetes, cerebral infarction and heart disease); 2) clinical and course examinations (12 indicators, 42 variables), including chest radiographs or CT scan (1-5 scans, average 2.1 scans, presence or absence of ground-glass opacity, consolidation, reversed halo sign, fibrosis and septal thickening, by the consensus of two physicians (HW; JZ)), main symptoms at admission (e.g., fever, dry cough, sputum production and

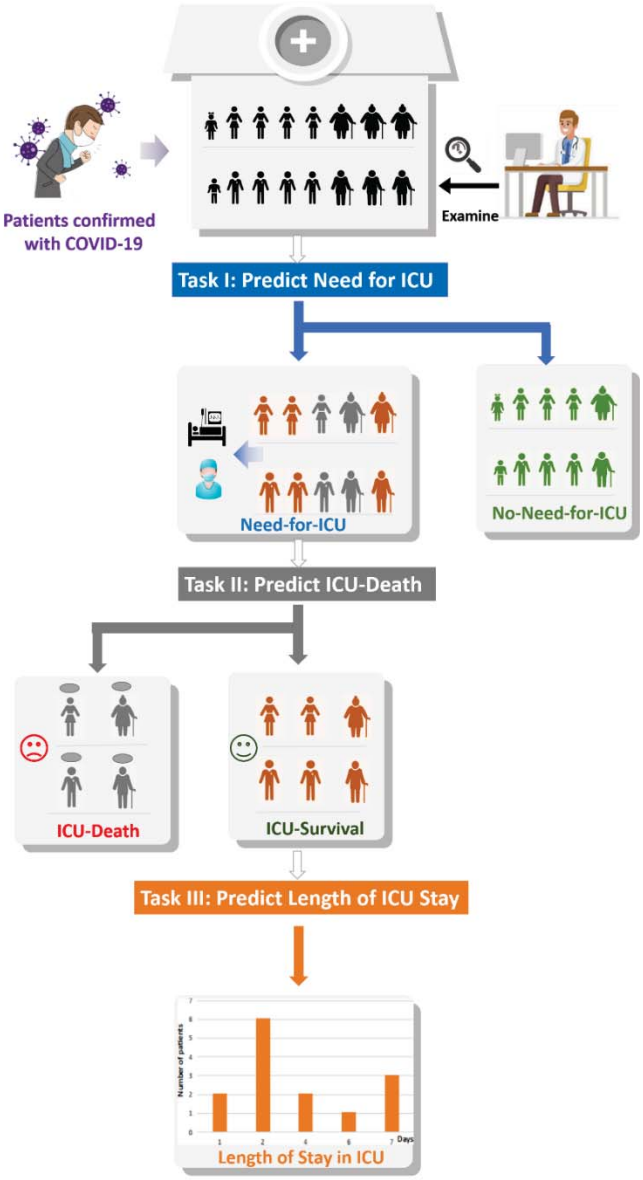


Fig. 1. The chart of our work. **Task I: Predict Need for ICU**, predicting the in-patients who need to be admitted into ICU; **Task II: Predict ICU-Death**, predicting the in-patients who will unfortunately die despite being admitted into ICU**; Task III: Predict Length of ICU Stay**, predicting the length of ICU stay among survivors.

fatigue), and daily routine tests (e.g., pulse, respiration rate, blood pressure, body temperature, oxygen saturation and heart rate); and 3) laboratory indicators (173 indicators, 858 variables), including complete blood count, coagulation profile, serum biochemical tests (including liver function (twelve items), renal function electrolyte (twelve items), blood lipid and blood glucose (three items), procalcitonin detection and fluorescence, glucose determination (various enzymatic methods), six sets of coagulation, five categories of complete blood count + CRP), respiratory tract infection pathogen IgM 9 items and influenza A/B virus antigen detection. All continuous variables were quantified by six statistical measurements, including the mean, median, standard deviation, maximum, minimum, and interquartile range (IQR) [11]. Categorical variables were expressed as binary variables (0,1).

D. Target Variables

I. Need or No Need for ICU. The "Need-for-ICU" group included patients who were actually admitted into ICU and underwent invasive ventilation (N=25), plus patients who died of COVID-19 despite never admitted into ICU due to a shortage of ICU resources (N=8). The "No-Need-for-ICU" group included patients who were not admitted into ICU and were later healed (N=700).

II. ICU Outcome (Death or Survival). Among 25 patients who were actually admitted into ICU, the ICU-Survival group had 17 patients (10 males and 7 females, ages 63±16 years of age), and ICU-Death group had 8 patients (2 males and 6 females, ages 65±15 years of age).

III. Length of ICU Stay among Survivors. Survivors (N=17) stayed in ICU for 6 ± 2 days (range: 1-21 days). Of them, 3 (17.6%) patients stayed in the ICU for over two standard deviations away from the mean value, thus they were considered as outliers and excluded.

E. Prediction and Variable Selection

We first examined the predictive value of every variable by the receiver operating characteristic curve (ROC) and the area under the curve (AUC). Variables were ranked by their AUC values for predicting the need for ICU (target variable I) and death/survival in ICU (target variable II).

In multivariate prediction, we used the top ten variables with the highest AUC values to build binary classifiers for predicting the need for ICU (target variable I) and death/survival in ICU (target variable II). We used a support vector machine (SVM) [12] with the kernel of poly for the binary classification. We employed the ensemble learning strategy [13] to balance the sample size between the Need-for-ICU and No-Need-for-ICU groups. For the death and survival groups, we further conducted the recursive feature elimination [14] to select the significant features. Using target variable I as an example, our training set contained 586 patients (560 patients in the No-Need-for-ICU group and 26 in the Need-for-ICU group), and our testing set contained 147 patients (140 No-Need-for-ICU and 7 Need-for-ICU). We divided 560 No-Need-for-ICU patients into 22 groups, each coupled with 26 Need-for-ICU patients. Thus, the 22 groups of balanced training subset were used to train 22 SVM models and to be applied on the test samples, where the final predicted class was obtained by majority voting. In the multivariate prediction of the length of ICU stay for survivors, we used the least absolute shrinkage and selection operator (LASSO) regression model. We used the L1-norm regularizer to encourage only a few variables being selected (i.e., the sparsity of the LASSO model). The variables ranked within the top ten largest absolute value of regression coefficients were selected and analyzed individually.

III. Results

A. Characteristics of Patients

Demographic and clinical characteristics are analyzed. The median age of the collected 733 patients was 50 years (IQR 39-61). There were 406 (55.4%) males. The numbers of male and female patients in each age interval (0-17, 18-24, 25-49, 50-64, >65 years) are ([7, 6], [14, 6], [184, 147], [130, 99], [70, 65]). Most patients in the Need-for-ICU were above 50 years of age. Of the patients admitted into ICU, death happened in 5% patients in the 25-49 years age group, 14% of

patients in the 50-64 years age group, and 18% of patients in the >65 years age group. Comorbidities existed in 222 patients [30.3%], including diabetes (48 [6.5%]), hypertension (108 [14.7%]), hyperlipidemia (5 [0.7%]), cerebral infarction (11 [1.5%]) hepatorenal insufficiency (17 [2.3%]) and heart disease (33 [4.5 %]). The most comm symptoms at onset of illness were fever, dry cough or fatigue ((595 [81.2%] patients); common symptoms were sputum production (578 [78.9%]), food refusal or feeding difficulties (29 [4.0%]) and CT scan for double lung infection (499 [68.1%]).

B. Prediction of ICU Admission

When considered alone, ten clinical variables achieved the highest AUC predicting a patient's need for ICU admission (Table I). They were: the mean of oxygen saturation (SaO2_mean, AUC=0.95), the mean of high sensitivity troponin I (hs-cTnI_mean, AUC=0.94), the mean of myoglobin (Mb_mean, AUC=0.92), the mean of albumin (Albumin_mean, AUC=0.87), the mean of lactate dehydrogenase (LDH_mean, AUC=0.87), the variance of high sensitivity troponin I (hs-cTnI_var, AUC=0.85), the variance of myoglobin (Mb_var, AUC=0.85), the mean of D-Dimer (D-Dimer_mean, AUC=0.84), the mean of lymphocyte percentage (LP_mean, AUC=0.83), and the mean of lymphocyte absolute value (LAV_mean, AUC=0.83). The Need-for-ICU and No-Need-for-ICU groups had significantly different values in these variables (p-value < 0.001, their box-plots are shown in Fig. 2).

Multivariate analysis found that jointly considering these top ten factors had an accuracy superior to most single variate. Its accuracy and AUC were 0.83 and 0.84 for predicting whether inpatients will need ICU care (Fig. 3A).

C. Prediction of ICU-Death

Table II lists the top ten clinical variables that, when considered alone, best predicted death in ICU. They were: the mean of lymphocyte percentage (LP_mean, AUC=0.97), the mean of lymphocyte absolute value (LAV_mean, AUC=0.96), the mean of lactate dehydrogenase (LDH_mean, AUC=0.89), the mean of D-Dimer (D-Dimer_mean, AUC=0.88), the mean of Albumin (Albumin_mean, AUC=0.83), the mean of adenosine deaminase (ADA_mean, AUC=0.78), the variance of lactate dehydrogenase (LDH_var, AUC=0.76), the variance of direct bilirubin (DBIL_var, AUC=0.62), the variance of respiratory rate (RR_var, AUC=0.58) and the variance of the pulse (Pulse_var, AUC=0.52). Their corresponding boxplots with respect to the two types of patients were also visualized in Fig. 4. LP, LAV and D-Dimer were indicated to be statistically different (p-value $\leqslant$ 0.001). A patient admitted into ICU was more likely to die with a lower LP, lower LAV, lower Albumin, higher LDH, higher D-Dimer, larger fluctuation (variance) of ADA, larger fluctuation (variance) of RR, larger fluctuation (variance) of DBIL, and larger fluctuation (variance) of the pulse.

Multivariate analysis found that the performance of the top ten factors was superior to all single variate (Fig. 3B). Its accuracy and AUC were 0.92 and 0.98 using 3-fold cross-validation for predicting whether inpatients will unfortunately die despite being admitted into ICU.

D. Prediction of Length of ICU Stay among Survivors

Table III shows that the top ten clinical variables most predictive of length of ICU stay among survivors were: the mean of lymphocyte absolute value (LAV_mean, MAE=1.91 days), the mean of erythrocyte count (RBC_mean, MAE=1.68 days), the mean of total cholesterol (TCHO_mean, MAE=2.22 days), adenovirus IgM antibody (ADV-IgM_mean, MAE=2.25 days), the mean of hypersensitive C-reactive protein (hs-CRP_mean, MAE=2.04 days), the variance of high sensitivity troponin I (hs-cTnI_var, MAE=1.92 days), the variance of total cholesterol (TCHO_var, MAE=2.12 days), Q fever Rickettsia IgM antibody (Q-fever IgM, MAE=2.01 days), heart disease (MAE=1.34 days) and age (MAE=1.72 days). If the patient was older and suffered from heart disease, the longer they stayed in the ICU. As well as the abnormal values for LAV, RBC, TCHO, hs-cTnI, hs-CRP, Q-fever IgM and ADV-IgM affected the length of stay in the ICU.

Multivariate analysis found that the performance of the top ten factors was superior to all single variate (Fig. 3C). The mean absolute error (MAE) was obtained using 3-fold cross-validation, it yields the results of 0.723 on the data set and implies that we achieved an error of less than one day predicting the length of ICU stay among survivors before the patients were admitted to ICU.

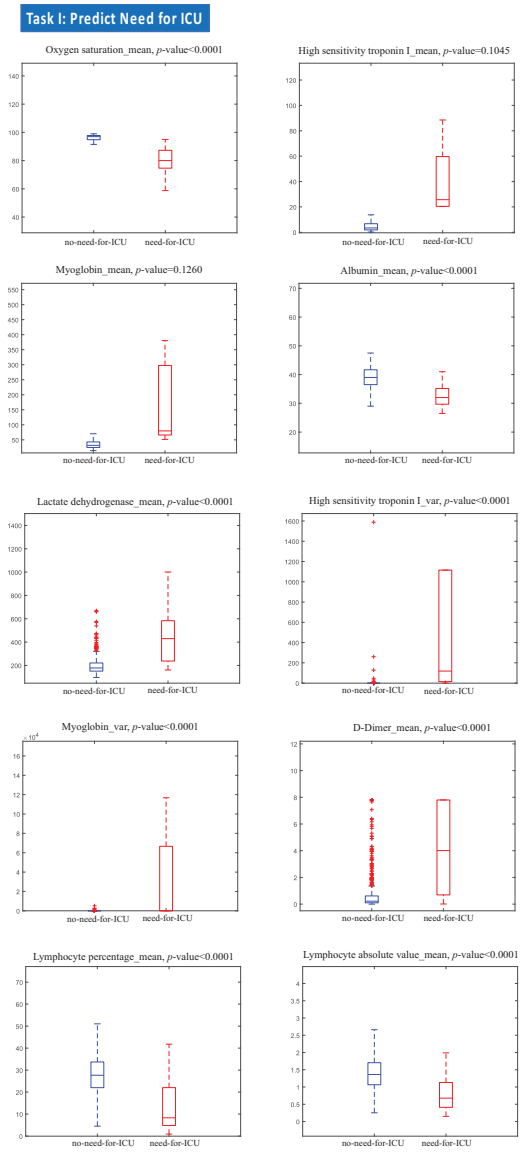


Fig. 2. The boxplots of the distributions of top ten factors in the need-for-ICU group versus no-need-for-ICU groups.

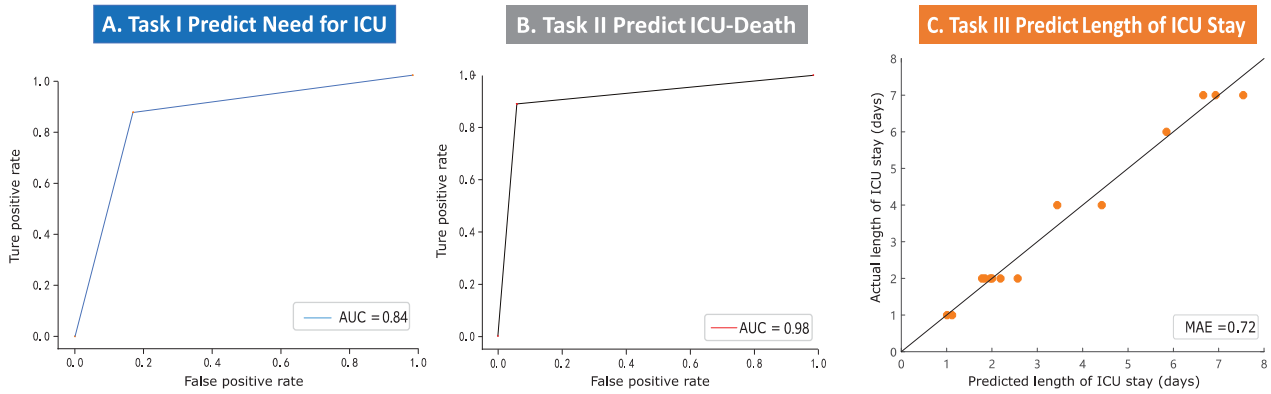


Fig. 3. Multivariate analysis for three tasks. Left: ROC for predicting need for ICU admission, on the testing set based on SVM of the selected 10 features. Middle: ROC for predicting ICU-Death using 3-fold cross-validation, on the whole set based on SVM of the selected 10 features. Right: predicted versus actual length of ICU stay in leave-one-out cross validation.

TABLE I.

SINGLE-VARIATE ANALYSIS FOR TASK I. '_MEAN' AND '_VAR' DENOTES THE MEAN AND VARIANCE OF CONTINUOUS VARIABLES, RESPECTIVELY.

Task I-Predict need for ICU	Optimal threshold (unit)	Under the optimal threshold Sensitivity	Under the optimal threshold Specificity	AUC
Clinical and course examinations				
Oxygen saturation (SaO2_mean)	< 88.0 (%)	0.800	0.966	0.948
Laboratory indicators				
High sensitivity troponin I (hs-cTnI_mean)	> 20.3 (pg/ml)	1.00	0.909	0.936
Myoglobin (Mb_myouean)	> 51.55 (ng/ml)	1.00	0.806	0.924
Albumin (Albumin_mean)	< 33.125 (g/L)	0.688	0.940	0.867
Lactate dehydrogenase (LDH_mean)	> 227.33 (u/l)	0.833	0.771	0.866
High sensitivity troponin I (hs-cTnI_var)	> 19.36 (pg/ml^2)	0.80	0.970	0.850
Myoglobin (Mb_var)	> 27.56 (ng/ml^2)	0.80	0.897	0.850
D-Dimer (D-Dimer_mean)	> 1.71 (ug/ml)	0.667	0.895	0.841
Lymphocyte percentage (LP_mean)	< 16.48 (%)	0.742	0.897	0.830
Lymphocyte absolute value (LAV_mean)	< 0.8875 (10^9/L)	0.710	0.867	0.830

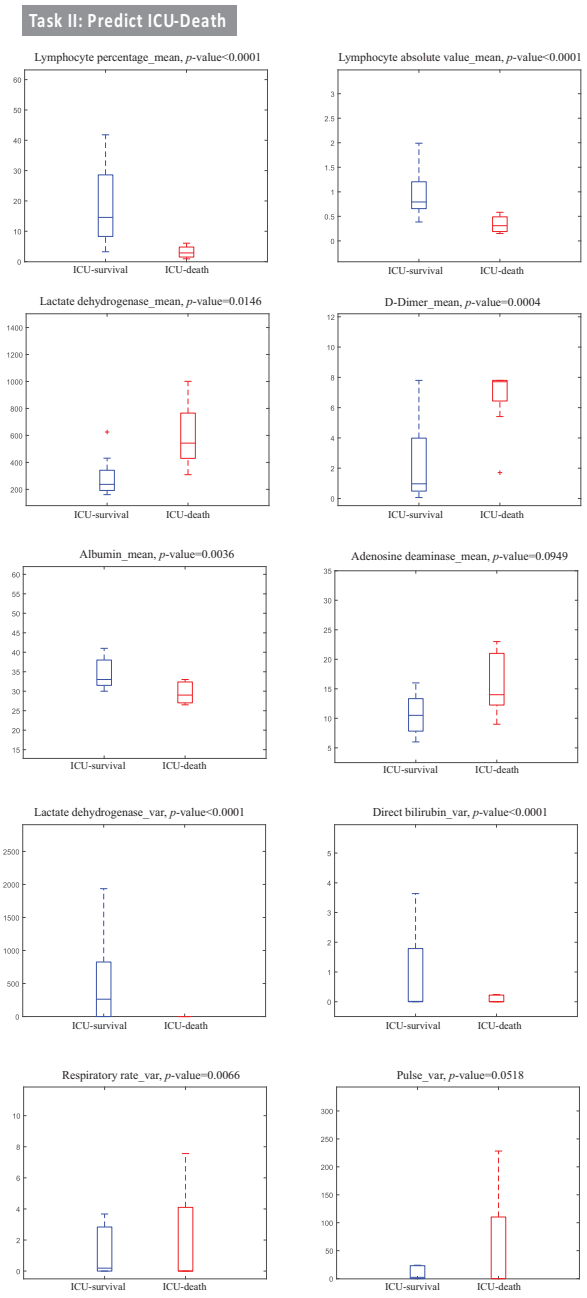


Fig. 4. The boxplots of the distributions of top ten factors in the ICU-survival versus ICU-death groups.

IV. Discussion

Our study aimed to use machine learning to provide early, quantitative and objective suggestions for the optimal planning and allocation of the scarce ICU resources during the COVID-19 outbreak (Fig. 1, study design).

We started from whether it is possible to use clinical information before a patient was admitted into ICU to predict the patient's future need for ICU admission. There is increasing interest in predicting the severity of COVID-19, but "severity" is not always clearly defined – some defined it as death or needing ventilators [15], others defined it based on lesion volumes in lung images [16] or based on guidelines from Health Commission of specific nations [10]. Ours is the first that specifically focuses on the need for ICU admission (Fig. 1, Task I). The perspective is to tie the severity of COVID-19 to the actual ICU load [17], [18]. We conducted the first study to show that admission to ICU could be predicted, 1-15 days before the patient was admitted into ICU. This would give hospitals and policymakers precious time window to potentially allocate patients into hospitals with ICU capacities or to estimate ICU shortages [4].

We showed that jointly considering our selected top ten clinical variables achieved a higher accuracy (AUC=0.8429, Fig. 3A) than most individual variables alone (Table I). Noteworthy, we found that three single variables with higher AUC, Sensitivity and Specificity on the whole set, which are oxygen saturation (SaO2, AUC=0.948, Sensitivity=0.800, Specificity=0.966), high sensitivity troponin I (hs-cTnI, AUC=0.936, Sensitivity=1.000, Specificity=0.909) and myoglobin (Mb, AUC=0.924, Sensitivity=1.000, Specificity=0.806). A patient was more likely to need ICU admission if the oxygen saturation (SaO2) was lower than88% (AUC=0.95), the high sensitivity troponin I (hs-cTnI) was higher than 20.3 pg/ml, or myoglobin (Mb) was lower than 51.55 ng/ml. The latter two indicated cardiac muscle abnormalities. In previous perceptions, the value of SaO2 is 95%-98% in normal people, yet the value of SaO2 was lower than 88% in the patients with COVID-19. It indicated that the patient was in a hypoxic state and needed to be treated with ventilators (invasive or non-invasive). Furthermore, oxygen is stored in muscle tissue, which is the energy supply generation system when energy is needed for muscle exercise. Myocardium is slightly damaged. In other words, it enters the blood circulation directly from myocardial cells.

The second contribution of the paper is that we showed the possibility to predict who would, unfortunately, die despite being admitted into ICU. When Wuhan, China, and Lombardy, Italy experienced their peaks of the COVID-19 outbreak, an unfortunate reality was that clinicians had to decide, among many patients who urgently needed ICU admissions, who were the lucky few that could be admitted into ICU [19]. A major consideration in this sad decision was the chance to survive if admitted into ICU, or the expected longevity [4]. Elderly or diabetic patients, among others, were often sacrificed [20].

In the first such study, we found that the somewhat "inevitable death" among patients admitted into ICU was best predicted by lymphocyte percentage (LP), lymphocyte absolute value (LAV), lactate dehydrogenase (LDH), D-Dimer, albumin, adenosine deaminase (ADA), direct bilirubin (DB), respiratory rate (RR) and pulse. D-Dimer proved to be a risk factor in previous work [21], the value is higher than 5.41 ug/ml, it indicated that the circulatory system is in a state of high coagulation, and can easily lead to pulmonary embolism. LDH and DB were also identified as risk factors [15]. Lymphocyte, albumin and adenosine deaminase all heralded by virus infection and damaged the human immune system. Large fluctuations in RR and pulse in the clinical courses indicated that the patients were extremely unstable. These factors were not closely related to the age and diabetes in the aforementioned research to a certain extent, they all directly reflected the manifestation of COVID-19.

In the third piece of the paper, we showed that the length of ICU stay could be predicted among those discharged alive from ICU. Herein we focused on the length of ICU stay among survivors, because the survivors can objectively respond to the progress of the course of the disease. Predicting the length of ICU stay can also help quantify the turnover rate of ICU. We found that, older age (>60 years) and with heart disease together best predicted a longer stay at ICU among survivors.

Additionally, a patient stayed longer in ICU before discharged alive if the patient had higher total cholesterol (possibly hyperlipidemia).

Noteworthy, lymphocyte absolute value involved in all predictive tasks, its abnormality verified that COVID-19 patients were viral infectious diseases.

These contributions came with certain limitations. First, like in other pilot machine learning studies of COVID-19 [15], there is need for a larger sample size (like us, they used hundreds of patients), need for more balanced data (like us, they had more patients with favorable outcomes and patients with adverse outcomes), need for multi-site verification (like us, two of three COVID-19 machine learning studies were on single-site data), and need to generalize to multi-national data (like us, they used data from Wuhan, China). Second, our high prediction accuracy only provided scientific evidence to assist patient triage and allocation of ICU resources. Moral and legal issues are considered beyond the scope of this study.

Despite limitations, our study objectively analyzed and predicted the patients who will enter the ICU, mortality and the length of stay in ICU. With the epidemic continuing to spread in many countries, maybe there will be a new round of outbreaks, our strategy provides quantitative evidence and method to calculate the turnover rate of the ICU, thus facilitating the optimal allocation of ICU resources.

V. Conclusion

This pilot study shows that machine learning could predict which patient with COVID-19 needs ICU admission and which patients would, unfortunately, still die even admitted to ICU, and among survivors, the length of ICU stay. All predictions were achieved 1-15 days before the patients were actually admitted to ICU. The high predictive power provides a quantitative reference to better plan and allocates ICU resources.

Acknowledgment

This work was partially supported by the National Natural Science Foundation of China (61771007). The authors thank the volunteers from the South China University of Technology for manually tiding the clinical course data.

TABLE II.
SINGLE-VARIATE ANALYSIS FOR TASK II. '_MEAN' AND '_VAR' DENOTES THE MEAN AND VARIANCE OF CONTINUOUS VARIABLES, RESPECTIVELY.

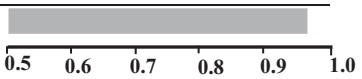
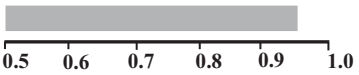
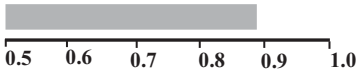
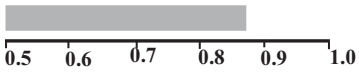
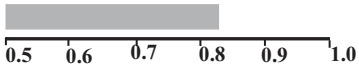
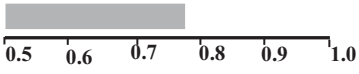
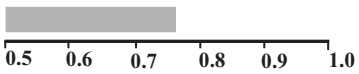
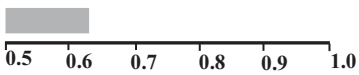
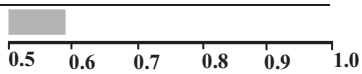
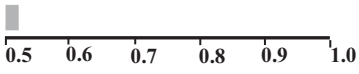
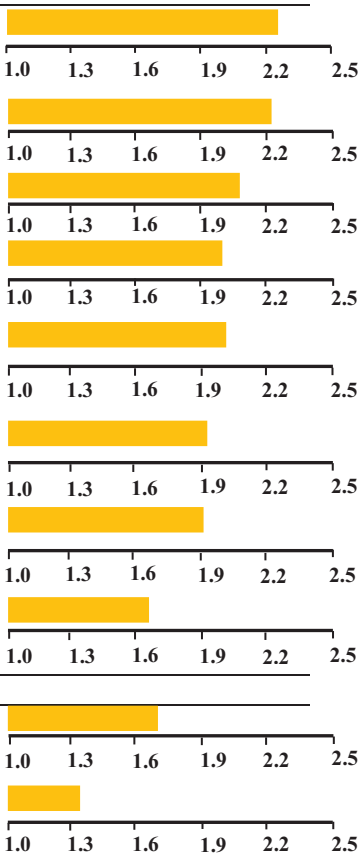
Task II-Predict ICU-Death	Optimal threshold (unit)	Under the optimal threshold Sensitivity	Under the optimal threshold Specificity	AUC	
Laboratory indicators					
Lymphocyte percentage (LP_mean)	< 6.6 (%)	1.0	0.941	0.971	
Lymphocyte absolute value (LAV_mean)	< 0.645 (10^9/L)	1.0	0.824	0.961	
Lactate dehydrogenase (LDH_mean)	> 428.0 (u/l)	0.857	0.833	0.893	
D-Dimer (D-Dimer_mean)	> 5.41 (ug/ml)	0.875	0.882	0.876	
Albumin (Albumin_mean)	< 30.0 (g/L)	0.571	1.0	0.832	
Adenosine deaminase (ADA_mean)	> 12.0 (U/L)	0.857	0.647	0.777	
Lactate dehydrogenase (LDH_var)	< 144.89 (u/l^2)	1.0	0.583	0.762	
Direct bilirubin (DBIL_var)	< 1.58 ($umol/L^2$)	1.0	0.353	0.622	
Clinical and course examinations					
Respiratory rate (RR_var)	< 0.1875 ($Times^2$ / min^2)	0.625	0.588	0.577	
Pulse (Pulse_var)	< 0.24 ($Times^2$ / min^2)	0.625	0.588	0.518	

TABLE III.
SINGLE-VARIATE ANALYSIS FOR TASK III. '_MEAN' AND '_VAR' DENOTES THE MEAN AND VARIANCE OF CONTINUOUS VARIABLES.

Task III-Predict length of ICU Stay	Correlation	*p*_value	Lasso Coefficient	Prediction MAE
Laboratory indicators				
Adenovirus IgM antibody (ADV-IgM)	-0.351	0.218	0.757	2.254
Total cholesterol (TCHO_mean)	0.231	0.424	0.340	2.219
Total cholesterol (TCHO_var)	-0.419	0.134	0.867	2.121
Hypersensitive C-reactive protein (hs-CRP_mean)	-0.311	0.278	0.538	2.035
Q fever Rickettsia IgM antibody (Q-fever IgM)	-0.234	0.420	1.821	2.015
High sensitivity troponin I (hs-cTnI_var)	-0.50	0.069	0.671	1.924
Lymphocyte absolute value (LAV_mean)	0.40	0.156	4.246	1.912
Erythrocyte Count (RBC_mean)	0.669	0.009	2.477	1.678
Demographic information				
Age	-0.614	0.019	0.081	1.721
Heart disease	0.641	0.013	3.036	1.343



REFERENCES

[1] Wu JT, Leung K, Leung GM. Nowcasting and forecasting the potential domestic and international spread of the 2019-nCoV outbreak originating in Wuhan, China: a modelling study. Lancet 2020;395(10225):689-697.

[2] Dong E, Du H, Gardner L. An interactive web-based dashboard to track COVID-19 in real time. Lancet Infect Dis 2020;20(5):533-534.

[3] Fauci AS, Lane HC, Redfield RR. Covid-19 — navigating the uncharted. N Engl J Med 2020;382(13):1268-1269.

[4] Emanuel EJ, Persad G, Upshur R, et al. Fair allocation of scarce medical resources in the time of Covid-19. N Engl J Med 2020;382(21):2049-2055.

[5] Li Q, Guan X, Wu P, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus–infected pneumonia. N Engl J Med 2020;382(13):1199-1207.

[6] Pan A, Liu L, Wang C, et al. Association of Public Health Interventions With the Epidemiology of the COVID-19 Outbreak in Wuhan, China. JAMA 2020;323(19):1915-1923.

[7] Grein J, Ohmagari N, Shin D, et al. Compassionate use of Remdesivir for patients with severe Covid-19. N Engl J Med 2020;382:2327-2336.

[8] Jordan RE, Adab P, Cheng KK. Covid-19: risk factors for severe disease and death. BMJ 2020;368:m1198.

[9] Truog RD, Mitchell C, Daley GQ. The toughest triage-allocating ventilators in a pandemic. N Engl J Med 2020;382(21):1973-1975.

[10] Commission CNH. Diagnostic and treatment protocol for Novel Coronavirus Pneumonia: Trial version 7. In; 2020.

[11] Guan W, Ni Z, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020;382(18):1708-1720.

[12] Cortes C, Vapnik V. Support-vector networks. Mach Learn 1995;20:273-297.

[13] Haixiang G, Yijing L, Shang J, et al. Learning from class-imbalanced data: Review of methods and applications. Expert Syst Appl 2017;73:220-239.

[14] Guyon I, Wston J, Barnhill S. Gene selection for cancer classification using support vector machines. Mach Learn 2002;46(1/2/3):389-422.

[15] Liang W, Liang H, Ou L, et al. Development and validation of a clinical risk score to predict the occurrence of critical illness in hospitalized patients with COVID-19. JAMA Intern Med 2020; e202033.

[16] Zhang K, Liu X, Shen J, et al. Clinically applicable AI system for accurate diagnosis, quantitative measurements, and prognosis of COVID-19 pneumonia using computed tomography. Cell 2020;181(6):1423-1433.

[17] Bhatraju PK, Ghassemieh BJ, Nichols M, et al. Covid-19 in critically ill patients in the Seattle region — case series. N Engl J Med 2020;382(21):2012-2022.

[18] Grasselli G, Pesenti A, Cecconi M. Critical care utilization for the COVID-19 outbreak in Lombardy, Italy: Early experience and forecast during an emergency response. JAMA 2020;323(16):1545-1546.

[19] Vincent J, Taccone FS. Understanding pathways to death in patients with COVID-19. Lancet Respir Med 2020;8(5):430-432.

[20] Grasselli G, Zangrillo A, Zanella A, et al. Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy region, Italy. JAMA 2020;323(16):1574-1581.

[21] Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020;395(10229):1054-1062.