Original Article
http://mjiri.iums.ac.ir
Medical Journal of the Islamic Republic of Iran (MJIRI)

Med J Islam Repub Iran. 2022 (29 Nov);36.144. https://doi.org/10.47176/mjiri.36.144

Prediction of COVID-19 Patients' Survival by Deep Learning Approaches

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Received: 22 Feb 2022 Published: 29 Nov 2022

Abstract

Background: Despite many studies done to predict severe coronavirus 2019 (COVID-19) patients, there is no applicable clinical prediction model to predict and distinguish severe patients early. Based on laboratory and demographic data, we have developed and validated a deep learning model to predict survival and assist in the triage of COVID-19 patients in the early stages.

Methods: This retrospective study developed a survival prediction model based on the deep learning method using demographic and laboratory data. The database consisted of data from 487 patients with COVID-19 diagnosed by the reverse transcription-polymerase chain reaction test and admitted to Imam Khomeini hospital affiliated to Tehran University of Medical Sciences from February 21, 2020, to June 24, 2020.

Results: The developed model achieved an area under the curve (AUC) of 0.96 for survival prediction. The results demonstrated the developed model provided high precision (0.95, 0.93), recall (0.90,0.97), and F1-score (0.93,0.95) for low- and high-risk groups.

Conclusion: The developed model is a deep learning-based, data-driven prediction tool that can predict the survival of COVID-19 patients with an AUC of 0.96. This model helps classify admitted patients into low-risk and high-risk groups and helps triage patients in the early stages.

Keywords: COVID-19, Prediction, Survival Analysis, Triage, Deep Learning

Conflicts of Interest: None declared
Funding: This study was funded and supported by Tehran University of Medical Sciences (TUMS), grant No. 99-1-102-47532.

Cite this article as: Taheriyan M, Ayyoubzadeh SM, Ebrahimi M, R. Niakan Kalhor Sh, Abooei AH, Gholamzadeh M, Ayyoubzadeh SM. Prediction of COVID-19 Patients' Survival by Deep Learning Approaches. *Med J Islam Repub Iran.* 2022 (29 Nov);36:144. https://doi.org/10.47176/mjiri.36.144

Introduction

In December 2019, several cases of pneumonia were reported in Wuhan, China. The new SARS-Cov-2 virus caused that type of pneumonia, and the disease caused by the virus was called coronavirus 2019 (COVID-19). The disease quickly spread to other areas, and on January 30, 2020, the World Health Organization (WHO) declared the outbreak a pandemic (1). Since then, based on the official statistics, until February 2022, more than 380 million people have been infected with COVID-19 disease, and more than 5 million have died because of this disease (2, 3).

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↑What is "already known" in this topic:
Many studies have been performed to predict survival in patients with coronavirus disease 2019 (COVID-19). In most studies, the survival prediction models were based on a radiological images dataset. Some studies predicted survival by using vital signs, comorbidities, treatment, and laboratory data.

→What this article adds:
In this study, survival in patients was predicted using only laboratory and demographic data. Because of the fewer side effects and the lower cost of repeated lab tests compared with imaging, this dataset was focused. The prediction model was created based on the deep learning technique and had a good performance with an area under the curve (AUC) of 0.96.

Early diagnosis and timely treatment are critical to preventing the disease's progression. Disease severity prediction models are one of the solutions used for this purpose. These models are used to triage and prioritize patients and assist in clinical decision-making (4-6). Predictive models can identify high-risk patients early by predicting disease severity and estimating the probability of death. By allocating more time and resources to high-risk patients, the mortality rate of COVID-19 disease can be reduced (7). Usually, the developed mortality prediction models utilize medical images and/or clinical and laboratory data (8, 9). As computerized tomography (CT) scans are expensive and increase the risk of radiation exposure, especially in children, there is a need to focus on more available data for prognosis model development. According to the WHO guidelines for COVID-19 management, imaging is only recommended if the test is unavailable. However, the COVID test results are time-consuming, or the test results might be negative despite the disease symptoms (10). Therefore, prediction models based on other patient-related data are necessary for model development and assist clinical decision-making. When a patient is referred to a health center with reasonable fees, laboratory results are more readily available to them. This data source plays a vital role in predicting the severity of the disease. It is an accessible data source, without too much cost and adverse consequences, with fewer side effects than other data sources such as lung CT scans or images (11).

Although COVID-19 is still a new debate, many studies have been conducted in various areas of screening (12-15), predicting and forecasting (16-18), and contact tracing (19) using machine learning algorithms and deep learning techniques (20). In addition, studies regarding mortality prediction of COVID-19 patients have been performed using 3 or more types of patient data from images, demographics, vital signs, symptoms, comorbidities, treatment, and laboratory data (21).

Instead of using images, we used only laboratory data to predict the patient's condition in this study. This study helps identify patients whose status will be more critical, and an early understanding of this situation is beneficial for managing and providing appropriate care. We aim to use machine learning methods, especially deep learning to predict patient death. We also aim to identify patients who need more medical care and intervention from the beginning with early diagnosis. This prediction method makes use of laboratory data from patients and can identify high-risk individuals to provide them with specialized treatment and interventions. In this study, by creating a predictive model based on laboratory data, we classify patients into low-risk and high-risk groups who identify as patients needing more care and earlier medical interventions. The prediction results produced by the developed model can be presented to the specialist simultaneously with the patient's laboratory findings. They can assist the specialist in clinical decision-making.

Methods

Study Participants

This was a retrospective study. Diagnosis of patients was made based on the guidelines of the WHO for COVID-19 patients (10). The primary diagnosis of the disease in the Imam Khomeini Hospital Complex (IKHC) of Tehran, Iran, has been made and verified by reverse transcription-polymerase chain reaction (RT-PCR) testing. The study participants were all patients admitted to the IKHC from February 21, 2020, and discharged or died until June 24, 2020. We collected data from the health information system (HIS) Dataset of IKHC. The HIS of the IKHC includes demographic, laboratory, and clinical data such as signs, symptoms, comorbidities, and prescribed drugs.

Moreover, the admission, discharge, and death-related data are also recorded in the HIS. We extracted the demographic and laboratory data of patients infected with COVID-19. We collected 487 patients' data with positive RT-PCR tests. Data analysis was performed on laboratory findings of patients' blood, urine, and venous blood gas (VBG) tests. This study was permitted and approved by the local ethics committee of IKHC (IR.TUMS.SPH.REC.1399.048).

Laboratory Data

The laboratory tests were performed for each patient with COVID-19 infection in 4 main categories: VBG, complete blood count (CBC), urine analysis (U/A), and other laboratory tests. The venous blood gas or VBG estimates patients' acid-base status, oxygenation, and carbon dioxide concentration (22). A complete blood count (CBC) is a practical diagnostic test that counts blood cells, including red blood cells, white blood cells, and platelets (23). Finally, the U/A or urinalysis is a urine test used for detecting and managing a wide range of disorders, such as urinary tract infections, kidney disease, and diabetes (24). The factors measured in each category of tests and their descriptions are presented in Table 1.

Data Preparation

Laboratory data related to 487 patients infected with COVID-19 were collected from the HIS system of the IKHC. Then, the results of 22,6879 experiments related to these patients were extracted from the HIS. The data belonged to 285 patients who died and 202 patients discharged due to covid infection. These data were converted from row data (each experiment in a row) to column data (each experiment in one column) by a program developed in Python 3.6. The extracted dataset included 535 experiments for each patient, and most of the time, only the value of 78 experiments was recorded. As a result, we reduced the number of laboratory-related dataset columns from 535 to 78 columns. These 78 experiments for each patient are listed in Table 1. In the next phase, experiments with high uniformity of values were excluded in which more than 90% of records had the same values. These omitted experiments were U/A-Ketone, U/A-Bilirubin, U/A-Urobilinogen, and U/A-Nitrite. Then, the One-hot encoding method converted qualitative values to quantitative ones.

Model Development

After data collection and preparation, we designed a mortality prediction model as a classification task with a binary

[DOI: 10.47176/mjiri.36.144]

Table 1. Collected laboratory data

Category	Laboratory Test	Description
VBG	PH	The clinical evaluation of acid-base problems (25)
	PCO_2	Evaluates the measure of CO2 and alveolar ventilation (26)
	PO_2	The partial pressure of oxygen in venous blood (27)
	Hct	Indicates the proportion of red blood cells in the blood (28)
	BEecf	Base excess in the extracellular fluid is an indicator of metabolic acidosis (29)
	HCO_3	A significant form of CO2 in blood, Indicates acidosis and alkalosis (30)
	TCO_2	Precise means to evaluate a total measure of Co2 found in blood (31)
CBC	RBC	Red blood cell count, low levels imply anemia and bleeding (28)
	WBC	White cell count (28)
	Hb	Shows the amount of hemoglobin, responsible mainly for o2 transmission (28)
	HCT	indicates the proportion of red blood cells in the blood (28)
	MCV	Mean cell volume of RBCs or erythrocytes (28)
	MCH	the average amount of hemoglobin in RBCs (28)
	MCHC	Average hemoglobin concentration in RBC indicates anemia type (28)
	PLT	Platelet count in blood, These cells cause coagulation formation (28)
	RDW-SD	The index shows disturbance of red cells width and anemia (32)
	RDW-CV	shows both disturbance of RBCs width and mean cell size (33)
	PDW	The index indicates platelet size divergence (34)
	MPV	The average volume of platelets (34)
	P-LCR	Platelet large cell ratio indicates the ratio of significant platelets presence (35)
	Neutrophils	WBCs can eliminate infections, especially bacterial ones (28)
	Lymphocytes	WBCs with anti-infection ability more common in viral ones (28)
	Mix Cell	Count of WBCs rather than neutrophil and lymphocyte (28)
	CBC diff-RBC	Red blood cell count, low levels imply anemia and bleeding (28)
	CBC diff-Hb	Shows the amount of hemoglobin, responsible mainly for o2 transmission (28)
	CBC diff-HCT	indicates the proportion of red blood cells in the blood (28)
	CBC diff-MCV	Mean cell volume of RBCs or erythrocytes (28)
	CBC diff-MCH	the average amount of hemoglobin in RBCs (28)
	CBC diff-MCHC	Average hemoglobin concentration in RBC indicates anemia type (28)
	CBC diff-PLT	Platelet count in blood, These cells cause coagulation formation (28)
	CBC diff-RDW-SD	The index shows disturbance of red cells width and anemia (32)
	CBC diff-RDW-CV	shows both disturbance of RBCs width and mean cell size (33)
	CBC diff-PDW	The index indicates platelet size divergence (34)
	CBC diff-MPV	The average volume of platelets (34)
	CBC diff-P-LCR	Platelet large cell ratio indicates the ratio of significant platelets presence (35)
	CBC diff-Neutrophils	WBCs can eliminate infections, especially bacterial ones (28)
	CBC diff-Lymphocytes	WBCs with anti-infection ability more common in viral ones (28)
	CBC diff-Mix Cell	Count of WBCs rather than neutrophil and lymphocyte (28)
U/A	Color	Color: Indicates the color of the urine sample, including yellow, dark yellow, red, and blue (36)
	Appearance	Appearance: indicates the transparency of the sample (36)
	SG.gravity	Compares the density of urine to water indicates kidney function (36)
	pH	Shows acidity or basic quality of the sample that helps tubules evaluation (36)
	Protein	Indicates the presence of protein in the urine, which is called proteinuria (36)
	Glucose	The presence of glucose in the urine, Positive values may indicate diabetes (36)
	Ketone	A metabolite is produced in fat burning when glucose is insufficient (36)
	Blood	Shows presence of blood, Positive values may show kidney injury (36)
	Bilirubin	A substance produced during hemolysis indicates liver disease (36)
	Urobilinogen	A product during the bilirubin cycle, High levels show liver disease (36)
	Nitrite	A substance produced from nitrate by bacteria (36)
	WBC	The presence of WBCs in urine indicates infection (pyuria) (36)
	RBC	The presence of WBCs in urine indicates hematuria (36)
	Ep-Cell	Indicates presence of epithelial cells, may show infection or UTI (36)
	Bacteria	Presence of bacteria, infection in a urinary tract called bacteriuria (36)
	Mucus	presence in high values suggests infection, dysfunction, or stones (37)
	Yeast	Yeast: yeast infection index, most typical form is candida infection (38)
	Cast	Structures formed in tubular cells made up of protein, RBCs or so on (36)
	Crystal	Solid substances are made up of chemicals present in urine (36)

outcome of discharge or death. Based on the outcome, we categorized patients into 2 groups: the high-risk category, which displays patients who have passed away, and the low-risk group, which shows patients who were discharged. As additional criteria for low-risk group patients, we also took into account a doctor's discharge, a patient's general state of health, follow-up, and personal satisfaction. A prediction model based on the deep learning technique was developed. The deep learning technique is a category of machine learning algorithms. The concept of “deep” in the deep learning technique refers to using multiple layers in the network. The deep learning method is based on artificial neural networks with feature learning. In fact, by utilizing multilayers neural networks, this technique extracts high-level features from raw data.

The deep learning model was created in Python using the Keras application programming interface (API) of TensorFlow Version 2.3. The deep network architecture of the designed model is shown in Figure 1. The dataset was randomly divided into 3 categories in the developing model

[DOI: 10.47176/mjiri.36.144]

Table 1. Continued

Category	Laboratory Test	Description
another laboratory test	AST	A good indicator of liver diseases like cirrhosis (39)
	ALT	More specific marker of liver diseases and infection than AST (39)
	ALP	Alkaline phosphatase determines liver and bone diseases (39)
	Na	Sodium levels may indicate kidney or heart function (40)
	K	This electrolyte is measured to evaluate heart and kidney function (41)
	Albumin (Alb)	The most abundant protein in the blood (42)
	Calcium (Ca)	Mineral indicator of liver, muscle, kidney, and bone status (43)
	Phosphorus	High values show kidney diseases or hypoparathyroidism (44)
	Mg	An electrolyte that plays a role in different body functions
	NT-PRO-BNP	BNP is a hormone secreted by the heart in heart failure (45) NT-PRO-BNP: It is a pro hormone released by the same cells (45)
	LDH	hemolysis, necrosis, pneumonia, and acidosis increases enzyme levels (46)
	CPK	CPK: Damages to muscles, brain, and heart would increase it (47)
	PTT-APTT	Evaluate the internal coagulation pathway (48)
	PCT-Pro-calcitonin	The protein indicates bacterial infection and sepsis (49)
	Cr-Creatinine	A byproduct of creatine, Kidney function indicator (50)
	Urea	Primary metabolite derived from dietary protein and tissue protein (50)
	PT-Control	A fixed value that does not change according to patients
	PT-I.N.R	Measures the function of the external coagulation pathway (51)
	CRP	C reactive protein is an indicator of infection (52)
	Bill T&D-Bill.T	Evaluates bilirubin which is produced in RBC hemolysis (53)
	Bill T&D-Bill.D	The amount of bilirubin that is conjugated by the liver (53)

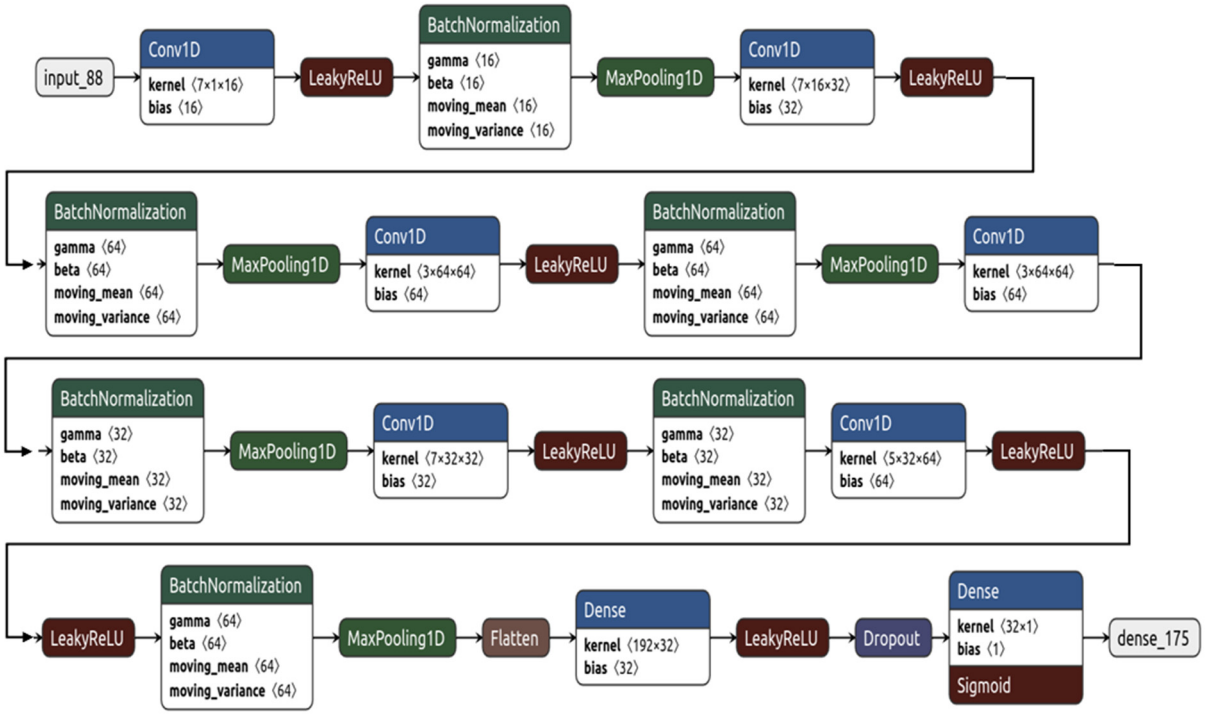

Fig. 1. The proposed deep learning model architecture

process, including 340 records for training, 97 for validation, and 50 for testing. Validation data optimized the model's parameters.

Model Performance Evaluation

The prediction model's performance in this study is assessed by the following measures: accuracy, recall, precision, F-measure, and area under the curve (AUC). The accuracy measure is the proportion of correct predictions in all cases. It denotes the proportion of cases out of all cases for which a discharge or death was accurately anticipated. The precision indicates the relevant cases among the retrieved cases, and the recall measurement refers to the relevant cases retrieved. The formula of metrics is as follows in Table 2 (54).

The receiver operating characteristic (ROC) curve is a plot of the true positive rate/sensitivity (y-axis) versus the false positive rate/1-specificity (x-axis) for candidate threshold values between 0 and 1. The area under the ROC curve is known as the AUC and is a valuable separability performance metric. It shows the capability of distinguishing between classes. The higher AUC indicates a better prediction model performance (55).

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Table 2. Standard metrics for predictive analysis

Metric	Formula
Accuracy	(TP+TN) / (P+N)
Precision	TP / (TP+FP)
Recall	TP / (TP+FN)
F- measure (F1- score)	2TP / (2TP+FP+FN)

False Positives (FP), False Negatives (FN), True Positives (TP), and True Negatives (TN)

Results

Dataset Characteristics

The study included 487 patient-related data, separated into a training dataset with 340 records, a validation dataset with 97 records, and a test dataset with 50 records. The dataset target is a binomial variable with "'1' and "'0' values which indicate high-risk and low-risk patients.

Model Evaluation

We evaluated the performance of the developed model using predictive analysis measures. The performance of the models is presented in Table 3 and Figure 2.

Discussion

This study is devoted to applying a deep learning model to classify infected patients with COVID-19 using laboratory data. Although most studies have predicted the severity of COVID-19 disease using data from radiographic images (56-60), we have tried to use laboratory data to predict the severity of the disease in patients with COVID-19. This research was conducted considering that laboratory tests have fewer side effects than X-rays. In addition, laboratory tests are often part of a routine checkup during illness. Also, laboratory tests are not expensive, and most people can afford them.

According to the model's performance, deep learning techniques based on demographic and lab tests can efficiently predict an individual's severity of COVID-19 illness. Hence, it can be utilized in treatment management and resource allocation based on the patient's condition (60) right before referring to the hospital. Similarly, Singh et al developed a model to provide a severity risk score with a deep learning approach using laboratory data. However, our developed model has higher accuracy compared with Singh's model (61).

The applied data for this experiment has included 487 patients diagnosed with COVID-19 who referred to the IKHC. In these situations, the patient spent some time in the hospital before either recovering or passing away. With a small sample size, other investigations may identify people with severe COVID-19. For instance, Gao et al (62) conducted their experiment using just 43 records. Another benefit of the model is the speedier referral of patients to the hospital. Most developed models concerning COVID-19 were related to critical cases and severe symptoms,

Table 3. Performance metrics of the proposed model

Metric	Low-Risk Group	High-Risk Group	Weighted Average
Precision	0.95	0.93	0.94
Recall	0.90	0.97	0.94
F1-Score	0.93	0.95	0.94
Accuracy		0.94	
AUC		0.94	

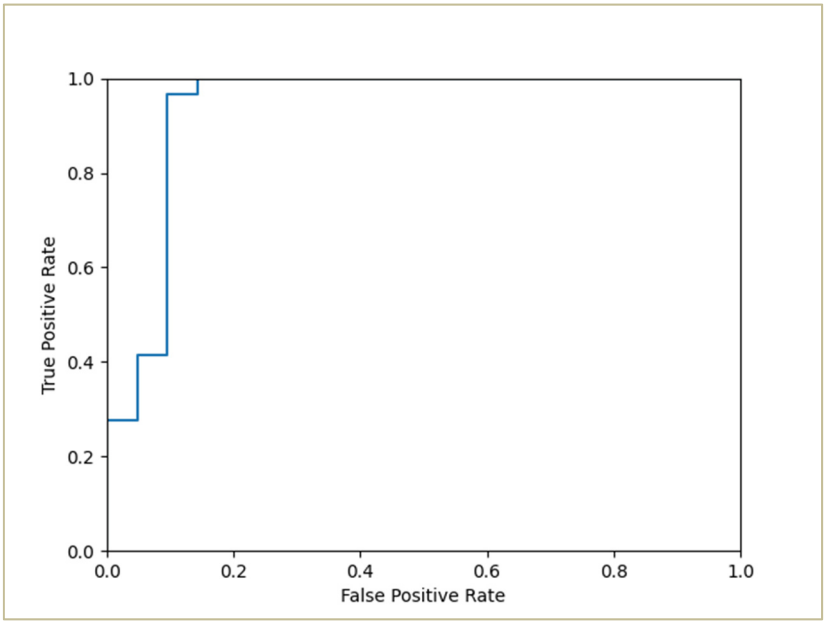

Fig. 2. ROC curve of the proposed model

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while our model could be applied for patient triage in routine clinical practice and better clinical decision-making. In addition, our proposed model could aid clinicians regarding resource allocation to eligible patients (16) by using only laboratory data. The rest of the developed models used a combination of different patients' data to create their own models. For example, in addition to laboratory data, Snider used demographic and comorbidities data (62) and Yan used demographic and COVID-19 symptom data (16). Alaska (59) investigated the prediction of COVID-19 infection with the demographic, vital sign, and laboratory data that make up 142 variables. Moreover, Tezza (63) and Bertsimas (64) applied demographic, comorbidities, and vital signs in addition to laboratory data.

Moreover, Guan (65) created a risk prediction model with demographic, comorbidities, symptoms, and laboratory data. In 2 studies, 5 categories of patient data were considered. Demographic, comorbidities, symptoms, vital signs, and laboratory were used in a study conducted by Hu (66). While demographic, comorbidities, vital signs, treatment, and laboratory were utilized by Subudhi (67).

Deep learning can deal with data with bigger sizes and dimensionality without feature analysis (68). This has an impact on the model's quality, and a greater model quality ensures that health care professionals will use it in practice. That is, by using this tool, we identify cases at the onset of critical status in the hospital and provide the proper care. Without cost and invasive intervention, the patient would be categorized into low- and high-risk classes. Figure 2 presents how the validated developed model can be used in the hospital care process for the new cases and at which stage this analysis will be done in the care process, starting from the reception point. This can be decided based on the point of care from which patients' data have been collected. For instance, data from patients in the same stage of the intensive care unit (ICU) inpatient outcome prediction model has been gathered (69, 70); however, it is too late to make a decision in this regard as the patient has already gone through the severe stage. However, the forecast must be made early enough for caregivers to prepare appropriate responses, such as reserving ICU beds or relocating to another facility for intensive care.

Although this model can be useful for identifying patients with a high risk, it can still be enhanced by development using more data from multicenter settings. Further work for

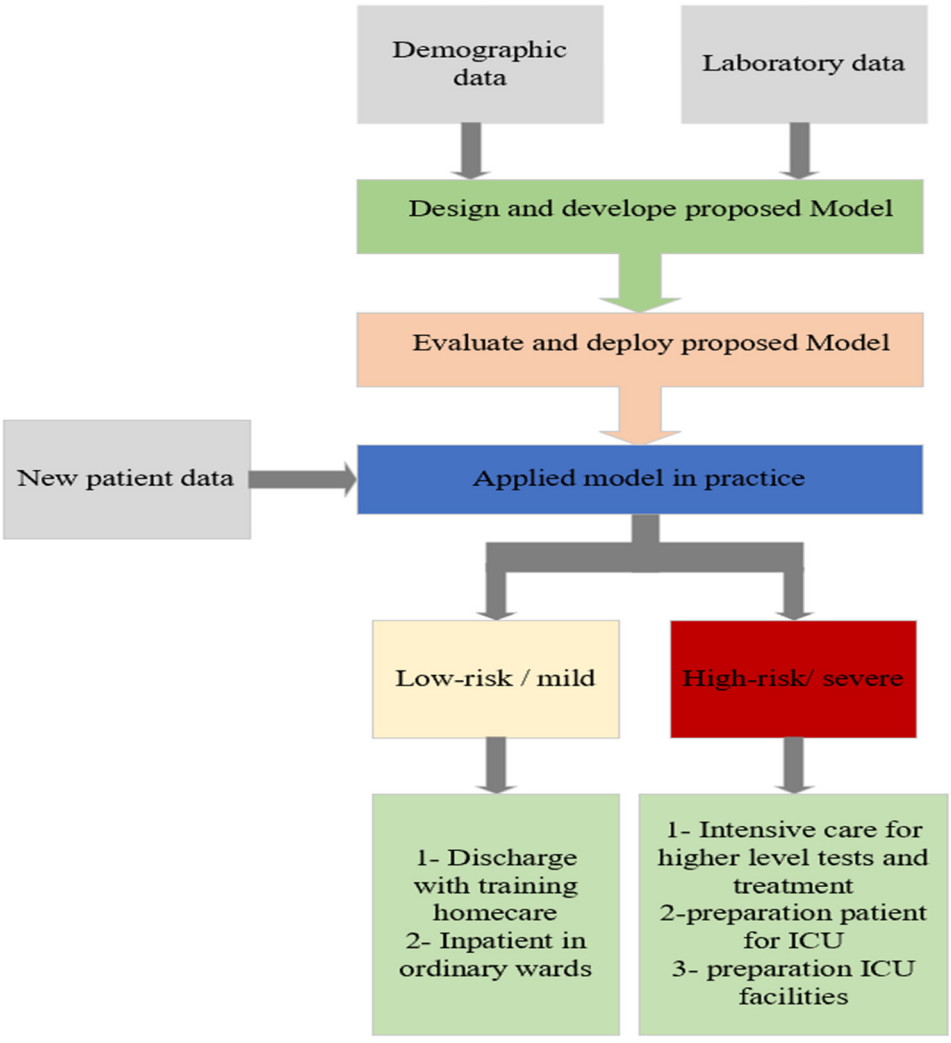

Fig. 3. Application of the developed model in the hospital care process

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system development using the available model is suggested. The developed model can be applied in the decision support system development to ease its usage by clinicians with no need to manually check the value of each variable. More automated ways for data entries and synchronization make it even easier to be used in practice.

The study has some limitations. The volume of data has a significant role in the deep learning model. For a more comprehensive result, a higher volume of data is needed. Further research can lower the features needed to predict by analyzing the impact of the variables and feature selection. Despite these limitations, creating a prediction model based on laboratory data with good performance is the advantage of the study. This model, along with other developed models, can give a more comprehensive view to clinicians. This model can be used in practice and is helpful in clinical decision support systems.

Conclusion

To sum up, emergent pandemic and viral disease outbreaks may create a situation requiring the support of technology-based methods in clinical decision-making. The support may be encompassed in different areas, and the triage of cases and the need for intensive care is one of them. This study applied a deep learning-based model. The model obtained valid results with an of AUC 0.94 to predict the survival of COVID-19 patients by laboratory data. Therefore, it may be used for further application for decision support system development.

Acknowledgment

We would like to express our gratitude to Tehran University of Medical Sciences for funding this research.

Authors' Contributions

S.R.N.K, M.E, S.M.A, and M.G. contributed to the conception and design of the work; A.H.A. and S.M.A. contributed to the data acquisition. S.M.A. contributed to analysis and data modeling. M.T., A.H.A, and M.G. contributed to drafting and revising the manuscript. S.R.N.K contributed to the supervision of the work.

Ethical Approval

This study has acknowledged the ethical standards, governmental norms, and criteria for performing medical research in Iran. The approval Id for this research is IR.TUMS.SPH.REC.1399.048 issued from Tehran University of Medical Sciences.

Conflict of Interests

The authors declare that they have no competing interests.

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[DOI: 10.47176/mjiri.36.144]