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Predicting intubation risk among COVID-19 hospitalized patients using artificial neural networks

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Abstract:

BACKGROUND: Accurately predicting the intubation risk in COVID-19 patients at the admission time is critical to optimal use of limited hospital resources, providing customized and evidence-based treatments, and improving the quality of delivered medical care services. This study aimed to design a statistical algorithm to select the best features influencing intubation prediction in coronavirus disease 2019 (COVID-19) hospitalized patients. Then, using selected features, multiple artificial neural network (ANN) configurations were developed to predict intubation risk.

MATERIAL AND METHODS: In this retrospective single-center study, a dataset containing 482 COVID-19 patients who were hospitalized between February 9, 2020 and July 20, 2021 was used. First, the Phi correlation coefficient method was performed for selecting the most important features affecting COVID-19 patients' intubation. Then, the different configurations of ANN were developed. Finally, the performance of ANN configurations was assessed using several evaluation metrics, and the best structure was determined for predicting intubation requirements among hospitalized COVID-19 patients.

RESULTS: The ANN models were developed based on 18 validated features. The results indicated that the best performance belongs to the 18-20-1 ANN configuration with positive predictive value (PPV) = 0.907, negative predictive value (NPV) = 0.941, sensitivity = 0.898, specificity = 0.951, and area under curve (AUC) = 0.906.

CONCLUSIONS: The results demonstrate the effectiveness of the ANN models for timely and reliable prediction of intubation risk in COVID-19 hospitalized patients. Our models can inform clinicians and those involved in policymaking and decision making for prioritizing restricted mechanical ventilation and other related resources for critically COVID-19 patients.

Keywords:

Artificial intelligence, coronavirus, COVID-19, data mining, intubation, machine learning, neural networks

Introduction

Coronavirus disease 2019 (COVID-19) has affected a lot of people globally.[1-3] Most cases experience asymptomatic or mild disease characterized by weakness, muscular pain, sore throat or congestion, an increased body temperature, cough, and chest tightness. Approximately 15–20% of symptomatic patients surge to critical complications such as severe pneumonia, acute respiratory distress syndrome (ARDS), cytokine storm syndrome, and multi-organ failure (MOF), demanding intensive care unit (ICU) services.[4,5] Many health systems face extreme challenges with the surprising number of severe cases, causing many ICU divisions to reach or overpass capacity.[6] The challenges that COVID-19 patients faced were a lack of ICU resources, including mechanical ventilators, personal protective equipment (PPE), ICU beds, and personnel.[7]

Hence, informed decision making is essential, especially where the ICU hospitals are overflowing.[8] In the battle against this

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pandemic, adopting predictive models will be crucial to managing limited ICU resources and informing clinical decision making.[9,10] Clinicians are faced with ambiguities regarding the progression of COVID-19 hospitalized patients, especially in identifying patients who are likely to experience rapid deterioration.[11] This requirement is more focused, especially regarding the mysterious and sophisticated nature of the COVID-19 disease.[11]

The COVID-19 patients who worsen and demand critical care with their breathing require a mechanical ventilator.[12] Thus, there is an immediate request for identifying patients to use respiratory intubation services. This process requires an accurate clinical judgment to decide the need for early or postponing intubation and those who do not necessitate it.[13] So far, many academic organizations have been broadly focused on the application of technology-based solutions such as artificial intelligence (AI) for accurate and timely detection of individuals at high risk of clinical deterioration and severe hypoxia (low SPO2).[14] These solutions can help diagnose deteriorating patients that need supportive oxygen therapy.[15]

Machine learning (ML) is an essential branch of AI that clinicians can use to diagnose critically ill patients and optimal utilization of limited hospital resources.[16,17] Therefore, ML can support the decrease of COVID-19 mortalities and lessen the economic burden on health care systems.[18] Previous studies developed several ML-based predictive models to predict the COVID-19 severity and patient health deterioration,[19,20] the need for ICU hospitalization[20-24] and mechanical ventilation,[25] and mortality.[21,22,26-31]

This paper uses a feature selection method based on the Phi correlation coefficient to select the best features affecting COVID-19 patients' intubation needs. Then, using selected features, multiple ANN configurations were constructed and compared to predict the COVID-19 critically ill patients demanding respiratory intubation.

Material and Methods

This retrospective study aimed to develop an intelligent predictive model based on ANN for predicting the need for intubation among hospitalized COVID-19 patients. The methodology of the proposed method is shown in Figure 1.

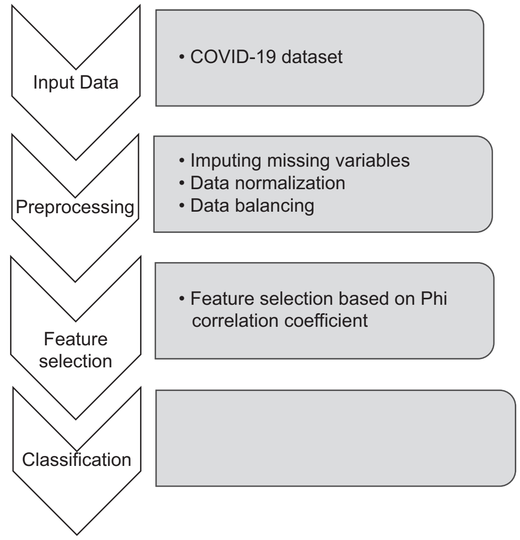

Figure 1: An overview of the methodology of the proposed method for COVID-19 intubation prediction

Providing an associated dataset

This study was extracted from the research project performed in Abadan city with the ethical code of IR.ABADANUMS.REC.1401.033. Our purpose in performing this research was to investigate different factors associated with the need for intubation among hospitalized COVID-19 patients. In a retrospective study, the data of COVID-19 hospitalized patients were extracted from Ayatollah Talleghani Hospital, Abadan city, southwest of Khuzestan, Iran, from February 9, 2020 to July 20, 2021. During this time, 6854 suspected people with COVID-19 had been referred to this treatment center, of whom 853 were known as hospitalized COVID-19 with positive diagnostic results, and their clinical data were entered into the registry database using six classifications of 57 features. The 57 features existed in the registry database including laboratory tests such as red cell count, white cell count, hemoglobin rate, hematocrit, absolute lymphocytic count, absolute neutrophil count, platelet count, blood creatinine, blood calcium, blood sodium, blood potassium, blood magnesium, blood phosphor, blood urea nitrogen (BUN), total bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (ASP), serum albumin, lactate dehydrogenase, activated partial thromboplastin time, blood glucose, erythrocyte sedimentation rate (ESR), prothrombin time, C-reactive protein (CRP), alkaline phosphatase, and hyper-sensitive troponin; clinical manifestations such as cough, contusion, nausea, muscular pain, fever, chill, body temperature, gastro-intestinal symptoms, loss of taste, loss of smell, sore throat, headache, vomit, rhinorrhea, dyspnea, and pneumonia; epidemiological factors such as smoking and alcohol consumption; demographical factors such as age, weight, height, sex, and blood type; radiological findings such as lung consolidation and pleural fluid; and history of diseases such as blood pressure, diabetes, and cardiac and other underline diseases as independent variables (input) associated with intubation among hospitalized COVID-19 patients.

The dependent (output) variable was intubation prediction among these patients as a two-valued variable (Intubation yes & no).

Normalizing the associated dataset

In this study, first, two health information experts (R-N and M-SH) investigated all registry case records by consulting two infectious and internal disease specialists regarding existing noisy, outlier, duplicates, and missing data. Then, these data were omitted or replaced with suitable values. Generally, the data with more than 70% missing values were omitted from the study. For the records which encompassed less than 70% missing values, the series mean method and discrete missing value replacement were used for embedding the quantitative and qualitative variables, respectively.

Feature selection

For acquiring the most relevant variables for predicting the need for intubation among hospitalized COVID-19 patients, we used the feature selection (FS) process. FS selects the best subset of the high-dimensional databases to get the most relevant features concerning the research subject.[32] There are three FS types for gaining the most important features including 1 - filtering, 2 - wrapper, and 3 - embedded methods. The variables are associated with the output class in filtering methods such as Chi-square. They are independent of the primary data mining algorithm and determine the relationship between one input and one output in high speed and simple computational methods.[33] In this study, we used the filter type because of the high speed in calculations, especially in large-dimensional datasets such as health care data and the generality of using this method in many recent works. For this purpose, the Phi correlation coefficient (Φ) was considered for determining the most critical factors influencing the need for intubation among hospitalized COVID-19 patients. Also, $P < 0.01$ was regarded as a statistically meaningful level. Generally, some essential advantages of this method can be enumerated as easier investigation of the dataset for research aims through diminishing the dataset's dimension, increasing the performance of data mining algorithms using the selected research's features, reducing the time for building data models, and precluding from data mining algorithms via leveraging appropriate records belonging to selected data subsets.[33]

Modeling of artificial neural networks

An ANN is a computational structure consisting of processing units called neurons, and a connection mechanism between them called coefficients or weights can imitate humans' thinking processes.[34] There are two different types of ANN architectures, including feed-forward and feedback networks. In the feed-forward type, the connection between one neuron and the next is one-directional, and therefore, no loops can be built on this configuration. There are connections between one neuron and adjacent neurons two-directionally in one loop.[35] Generally, the ANN's structure includes three layers: input, hidden or processing, and output. The input layer gets attributes, data, or signals through the ANN training process. It changes them into standardized elements using mathematical functions with more accurate numerical values of the processing feeds suitable for mathematical analysis. The hidden layers include processing neurons responsible for the analytic process using the connections between neurons. The primary ANN's analytical process occurs in these layers. The output layer, similar to the hidden layer, encompasses the neurons but gives the analytic results obtained by hidden layer neurons.[36,37] Because of managing high amounts of data, using ANNs as natural human neural networks has the common ability in various applications such as prediction and data classification.[38] In this study, the feed-forward backpropagation (FFBP) algorithm was the best characteristic for configuring the ANN as parallel processing, popularity, and impressiveness, and quickly training the most sophisticated multi-layered networks.[39] Also, in this study, the levenberg–Marquardt (LM) algorithm has been utilized as a data training function because of its high calculation speed and reputation in reducing the mean squared error (MSE) when fitting the ANN using the training data.[39,40] As a connection mechanism between neurons, the tansig function or hyperbolic tangent transfer function was used in this study. This sigmoid function type of ANN activation is fast in performance, although it is not accurate.[41] The number of ANN training epochs in this study was adjusted to 1000, and the learning time was unlimited considering the high-speed performance of the LM data training type.

Selecting the artificial neural network configuration

The numbers of ANNs' input and output were equal to the input and output variables. To select the best structure of the ANN, we investigated the performance of the ANN configurations using different evaluation criteria such as positive predictive values (PPVs), negative predictive values (NPVs), sensitivity, specificity, and area under the receiver operating characteristic (ROC) curve (AUC ROC) with one hidden layer and one neuron existing in it when training the ANN. Then, we added one neuron in the hidden layer by 100 neurons or added one hidden layer when needed and measured the ANN performance. The best configuration of the ANN was obtained via the most satisfactory amount of these performance criteria. Moreover, in the data training process of ANN, 70% of data were used for the training algorithm. Also, 15% and 15% were used to validate and test the ANN algorithm, respectively. At last, the performance of the final configuration of the ANN was investigated in more detail by measuring the MSE, analyzing the ANN's regression, and examining the error histogram of the developed algorithm.

Results

After segregating the samples that owned 70% or higher missing values in their attributes and applying other exclusion criteria such as noisy and abnormal values, lower than 18 years old, and discharged or died from emergency departments, finally, 371 records were excluded from the study. Therefore, 482 records remained for analysis. Among them, 176 cases belonged to hospitalized COVID-19 patients who needed the intubation during hospitalization, and 306 were associated with those who did not use the intubation. Among the first group, 91 and 85 cases were related to men and women, respectively, with an average age of 55.23± 6.662, and in the second group, 160 and 146 cases have appertained to men and women, respectively, with an average age of 53.41±4.228. The results of getting the most essential predicting factors for intubation requirement among hospitalized COVID-19 patients using the Phi coefficient correlation (Φ) at $P < 0.01$ have been represented in Table 1.

According to the information provided in Table 1, 18 variables acquired the statistically meaningful correlation related to the output class at $P < 0.01$. Therefore, the factors affecting intubation prediction among hospitalized COVID-19 patients were statistically significant. The five laboratory attributes including white cell count (Φ = 0.643) (P < 0.01), BUN (Φ = 0.617) (P < 0.01), activated partial thromboplastin time (Φ = 0.514) (P < 0.01), absolute neutrophil count (Φ = 0.452) (P < 0.01), and absolute lymphocyte count (Φ = 0.418) (P < 0.01) gained the higher correlation with output class. Generally, in this research, the laboratory data were recognized as the essential features in predicting intubation requirements among hospitalized COVID-19 patients. Some results of comparing different ANN architectures up to ten sigmoid nodes in the hidden layer using the best data training epochs per neuron have been demonstrated in Table 2.

In Figure 1, the ANN with 18 sigmoid nodes in the input layer equaled the number of the factors affecting intubation requirements among hospitalized COVID-19 patients, 20 neurons in the hidden layer, and one node in the output layer considering the output variable. The results showed that this configuration had the best capability for predicting intubation requirements among hospitalized COVID-19 patients compared to other ANN structures using the different performance criteria described in Table 2. Also, to investigate the ANN structure performance of classifying the research samples in the three states of training, validating, and testing, the confusion matrix of this configuration has been depicted in Figure 2.

According to Figure 2, the validation of the ANN with True Positive (TP) = 23 (31.9%) and True Negative (TN) = 46 (63.9%), as a whole, correctly classified cases of 95.8% and False Negative (FN) = 2 (2.8%) and False Positive (FP) = 1 (1.4%), and in total, incorrectly classified cases of 4.2% had the best capability compared to other situations of the ANN's configurations. Also, the testing mode of the ANN with TP = 17 (23.6%), TN = 48 (66.7%), T = 90.3%, FN = 3 (42.%), FP = 4 (5.6%), and F = 9.7% attained the lowest performance in this regard. Generally, using the total confusion matrix (TCM) as the primary performance evaluation criteria, the selected ANN had acquired TP = 159 (33%), TN = 290 (6.2%), FN = 15 (3.1%), and FP = 18 (3.7%) for classifying both hospitalized COVID-19 patients who required the intubation and those who did not. The mean squared error (MSE) diagram of the selected ANN configuration for measuring the considered ANN error during the training time has been shown in Figure 3.

As shown in Figure 3, by considering the ANN's MSE as the squared difference between the predicted and actual values and the best criteria during the fitting ANN, we observed that during the five epochs used for training the selected ANN. Also, at the second epoch, the ANN error had reached the minimum amount (validation's MSE < 0.1). Also, the training and testing modes of the ANN with MSE < 0.1 gained a pleasant performance during the ANN's fitting time. Based on the selected configuration, in Figure 4, the user interface of the determined ANN as the Clinical Decision Support

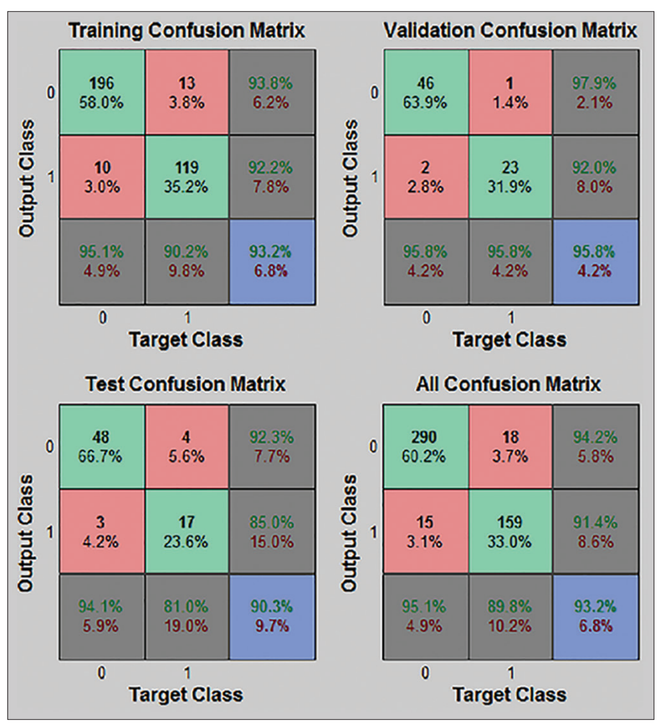

Figure 2: The selected ANN's confusion matrix

Table 1: The important intubation indicators at *P*<0.01

Variable	Type	Frequency or Mean±SD	Φ	*P*
Cough	Binominal	Yes (352) No (130)	0.195	<0.01
Length of hospitalization	Numeric	5.03±2.188	0.244	<0.01
Contusion	Binominal	Yes (180) No (302)	0.129	<0.01
Dyapnea	Binominal	Yes (442) No (40)	0.121	<0.01
Hypertension	Binominal	Yes (189) No (293)	0.166	<0.01
Loss of taste	Binominal	Yes (124) No (358)	0.135	<0.01
Absolute lymphocyte count	Numeric	21.702±12.01	0.418	<0.01
BUN	Numeric	56.759±12.785	0.617	<0.01
Runny nose	Binominal	Yes (202) No (280)	0.146	<0.01
CRP	Numeric	138.27±3.447	0.295	<0.01
Pleural fluid	Binominal	Yes (107) No (375)	0.294	<0.01
Cardiac disease	Binominal	Yes (157) No (325)	0.161	<0.01
White cell count	Numeric	9684.878±124.17	0.643	<0.01
Hypersensitive throponin	Binominal	Yes (38) No (444)	0.174	<0.01
Loss of smell	Binominal	Yes (137) No (345)	0.167	<0.01
Activated partial thromboplastin time	Numeric	35.453±9.23	0.514	<0.01
Oxygen therapy	Binominal	Yes (437) No (45)	0.129	<0.01
Absolute neutrophil count	Numeric	76.71±12.865	0.452	<0.01

Table 2: Performance of different ANN architectures

ANN architecture	Best training epochs	PPV	NPV	Sensitivity	Specificity	AUC
18-1-1	10	0.442	0.676	0.482	0.621	0.577
18-2-1	13	0.44	0.683	0.471	0.656	0.586
18-3-1	8	0.454	0.723	0.573	0.64	0.61
18-4-1	16	0.564	0.736	0.522	0.767	0.692
18-5-1	12	0.617	0.772	0.596	0.787	0.721
18-6-1	20	0.672	0.794	0.63	0.823	0.785
18-7-1	12	0.675	0.833	0.721	0.8	0.755
18-8-1	6	0.757	0.839	0.71	0.869	0.821
18-9-1	13	0.727	0.864	0.772	0.833	0.806
18-10-1	15	0.758	0.881	0.8	0.852	0.835

System (CDSS) has been implemented in the MATLAB V 2013a environment.

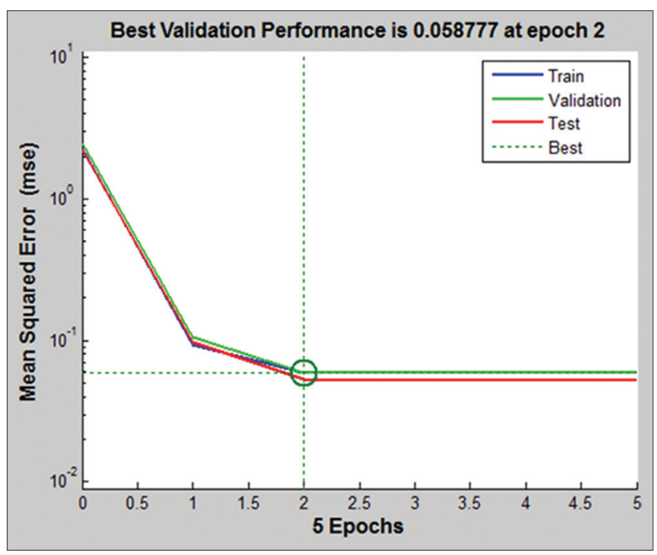

Figure 3: The MSE of the selected ANN

Discussion

Early and accurate prognosis of COVID-19 severity can help drop the enormous burden on hospitals by aiding to triage critically ill patients and projecting future requirements for optimal management of scarce ICU resources.[42] In our study, the Phi correlation coefficient techniques first determined the most important and clinically relevant features affecting intubation. Second, multiple FFBP ANN configurations were developed and evaluated to predict MV's need in hospitalized COVID-19 patients.

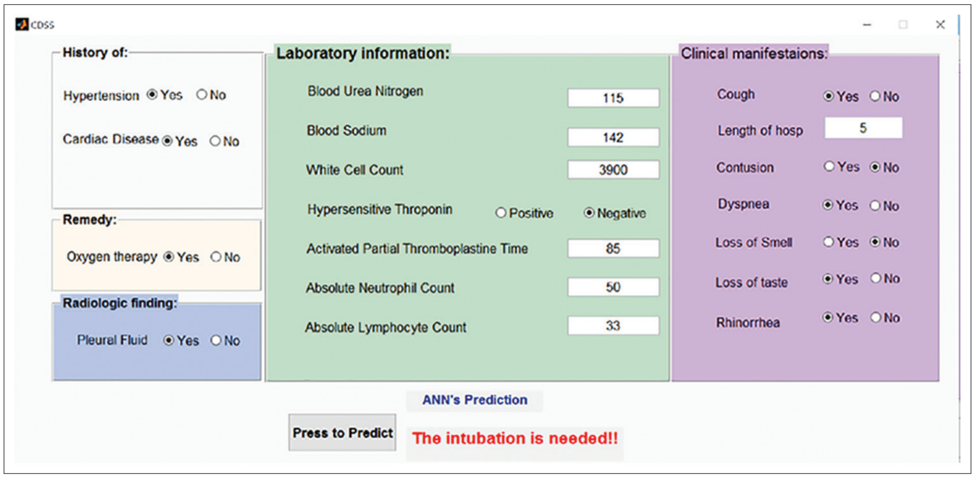

Figure 4: The designed CDSS user interface

In the present study, 18 features were identified as critical contributions to predicting intubation in COVID-19 patients. So far, most research has performed feature selection to select clinically significant variables (predictors) on COVID-19 patient deterioration and intubation risk. The determined features are used as input for the construction of ML-based predictive models. Domínguez-Olmedo JL *et al*. developed an ML-based CDSS to predict intubation risk among COVID-19 hospitalized patients. Their study selected the four top features of lactate dehydrogenase activity, CRP levels, neutrophil counts, and urea levels. Aljouie AF *et al*.[43] specified age, body mass index (BMI), length of stay (LOS), oxygen saturation, D-dimer, and cardiovascular diseases as best subset features. Varun Arvind *et al*.[25] selected laboratory variables such as CRP, D-dimer, ALT, ASP, and leuko/lymphocyte counts as essential for COVID-19 intubation risk prediction. Hoyt Burdicka *et al*.[44] selected age, BMI, fever and chill, CRP, BUN, SPO2, lung lesion, and underlining diseases as the best features to predict the need for ventilation in COVID-19 patients. Our study introduced the absolute lymphocyte/neutrophil count, BUN, white cell count, and activated partial thromboplastin time as the best predictive features for COVID-19 intubation prediction.

After performing feature selection, we developed several FFBP ANN configurations to predict the risk of intubation in COVID-19 patients at the onset of hospitalization. Thus far, some efforts have been performed on using ANN methods to predict COVID-19 poor outcomes and patient deterioration. Zhao *et al*.[22] analyzed 1087 patients' data to construct an ML-based prediction model to predict intubation. The ANN-based model obtained the best performance in their study, with an AUC of 0.74. Using the ANN technique, Vaid *et al*. and Gao *et al*. predicted the risk of patient deterioration and MV with ROCs of 0.822% and 0.976%, respectively, outperformed all other models.[26,29] In another study performed by Assaf *et al*.,[19] they attempted to predict the intubation risk for COVID-19 patients. Finally, the ANN gained the best result with a sensitivity of 88.0%, a specificity of 92.0%, and an accuracy of 92.0%. Foenini *et al*.[45] also compared three ML techniques for predicting ICU admission. The best performance was reported with the backpropagation neural network with a sensitivity of 91%, a specificity of 91%, and an AUC of 0.93. Similarly, in the current study, the results portrayed the effectiveness of the proposed ANNs, especially in the configuration of 18 sigmoid nodes in the input layer, 20 neurons in the hidden layer, and one node in the output layer with a PPV of 0.907, an NPV of 0.941, a sensitivity of 0.898, a specificity of 0.951, and an AUC-ROC of 0.906 for intubation risk prediction in COVID-19 hospitalized patients. The developed ANN model, especially in the configuration of 18-20-1, performed well.

Our study developed a scientific and non-invasive evidence-based technique based on the ANN technique. The ANN is very appropriate for modeling multi-faceted non-linear relationships in health care. It can be applied even for analyzing noisy, imbalanced, and incomplete datasets. The proposed configuration showed the best performance compared to the conventional statistical methods. The developed models in our study can help frontline clinicians for performing timely and reliable diagnosis of the disease deterioration and consequently decrease the severe complications and mortalities from this pandemic. This model can inform physicians' decision making because of its simplicity, user-friendliness, and easy-to-use features.

Limitations and reconsecrations

This study had some limitations that must be considered. First, we retrospectively used a single-center dataset that may contain missing, duplicate, imbalanced, noisy, and meaningless data. Second, the limited sample size certainly limits the generalizability of the developed models. Finally, the used dataset lacks some important paraclinical features. The performance accuracy of our model and its generalizability will be enhanced if we test more ML techniques in the larger, multi-center, and prospective dataset, which is equipped with more qualitative and validated data.

Conclusions

This study has developed and evaluated several ANN configurations to predict the intubation among COVID-19 patients using baseline and selected clinical variables (18 risk factors). The results revealed that the ANN model, especially in the configuration of 18-20-1, performed the best. Given the significant challenges to ICU hospital resources during the COVID-19 pandemic, the accurate prediction of patients requiring tracheal intubation can provide objective, measurable, and evidence-based guidance to predict the disease progression of hospitalized patients with COVID-19 and use of limited ICU resources.

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Conflicts of interest
There are no conflicts of interest.

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