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Early View

Original research article

A novel model to predict severe COVID-19 and mortality using an artificial intelligence algorithm to interpret chest X-Rays and clinical variables

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Please cite this article as: Munera N, Garcia-Gallo E, Gonzalez Á, *et al*. A novel model to predict severe COVID-19 and mortality using an artificial intelligence algorithm to interpret chest X-Rays and clinical variables. *ERJ Open Res* 2022; in press (https://doi.org/10.1183/23120541.00010-2022).

TITLE: A Novel Model to Predict Severe COVID-19 and Mortality Using an Artificial Intelligence Algorithm to Interpret Chest X-Rays and Clinical Variables.

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Word count: 3511

Abstract word count: 249

Keywords: Artificial intelligence; COVID-19; Machine learning; Mortality prediction; Critical care.

Conflict of interest: All authors have no conflict of interest

TAKE-HOME MESSAGE

In patients with COVID-19, we found that an automated Chest-X-ray interpretation algorithm along with clinical variables is a reliable alternative to identify patients at risk of developing severe COVID-19 that might require admission to the Intensive Care Unit.

ABSTRACT

BACKGROUND: Patients with COVID-19 could develop severe disease requiring admission to the Intensive Care Unit (ICU). This manuscript presents a novel method that predicts whether a patient will need admission to the ICU and assess the risk of in-hospital mortality by training a deep learning model that combines a set of clinical variables and features in the Chest-X-Rays.

METHODS: This was a prospective diagnostic test study. Patients with confirmed SARS-CoV-2 infection between March 2020 and January 2021 were included. This study was designed to build predictive models obtained by training convolutional neural networks for Chest-X-ray images using an artificial intelligence (AI) tool and a Random Forest analysis to identify critical clinical variables. Then, both architectures were connected and fine-tuned to provide combined models.

RESULTS: A total of 2552 patients were included in the clinical cohort. The variables independently associated with ICU admission were age, the fraction of inspired oxygen - FiO2 on admission, dyspnoea on admission, and obesity. Moreover, the variables associated with hospital mortality were age, the fraction of inspired oxygen - FiO2 on admission, and dyspnoea. When implementing the AI model to interpret the Chest-X-rays and the clinical variable identified by random forest, we developed a model that accurately predicts ICU admission (AUC:0.92 ± 0.04) and hospital mortality (AUC:0.81 ± 0.06) in patients with confirmed COVID-19.

CONCLUSIONS: This automated Chest-X-ray interpretation algorithm, along with clinical variables, is a reliable alternative to identify patients at risk of developing severe COVID-19 that might require admission to the ICU.

INTRODUCTION

The disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), better known as COVID-19, has become an international issue due to its social, economic, and health impact [1, 2]. Most patients present a mild disease; however, the infection may evolve to pneumonia and critical infection in some cases [1, 3]. Patients can develop complications such as ventilatory failure, coagulopathies, thrombosis (e.g., disseminated intravascular coagulation), sepsis, multiple organ dysfunction, and death [4, 5]. More than 260 million cases have been confirmed, and more than 4.5 million people have died. Patients at risk of dying due to COVID-19 are male, older adults, and patients with several comorbid conditions [6, 7]. According to the disease's severity and past medical history, the mortality rate associated with the COVID-19 ranges from 2,1% to 55%; therefore, it has become a global public health problem [8-10].

Several stratification strategies have been described to identify patients at higher risk of developing severe COVID-19 and dying afterward. For instance, the CALL score evaluates a patient's comorbidities, age, lymphocyte count, and serum levels of LDH [11, 12]. Another widely used score is the 4C score, which uses a combination of clinical variables and laboratory results to identify patients with severe COVID-19 and a high risk of dying due to COVID-19 [6]. Other studies have assessed Chest X-rays abnormalities, age, comorbidities, and abnormal laboratories to identify patients with severe COVID-19 [13, 14]. However, the predictive capacity of these scores is limited because some of them only include clinical variables or radiological variables but none of them have a combination between these two. Additionally, the scores that include

radiological information require the subjective interpretation of the treating physician, who might not have enough expertise interpreting these images.

The evaluation of diagnostic images is crucial for diagnosing COVID-19 pneumonia regardless of the result of the RT-PCR, especially in patients with high clinical suspicion [15, 16]. A chest x-ray is the most frequently utilized image to diagnose pneumonia and COVID-19; however, the image reading process is highly variable among observers [17]. Features identified in Chest X-rays could be lung consolidations, ground-glass opacity, nodules, and reticular-nodular opacities, leaving the diagnostic capability of the test to the subjective physician interpretation [18]. This limitation is fundamental in areas or hospitals where untrained radiologists are available.

Therefore, there is a need for novel approaches that use easy-to-access clinical data and computer-based image interpretation algorithms that allow untrained clinicians to accurately identify patients at higher risk of developing severe COVID-19 or dying. We hypothesize that using artificial intelligence (AI) and advanced statistical models, we could create an algorithm that detects patients at risk of dying using Chest X-rays and some easy-to-access clinical data. We conducted a study to test this hypothesis, using a previously developed artificial intelligence (AI) algorithm to interpret Chest X-rays and clinical data collected for a prospective multicentre study.

MATERIAL AND METHODS

Study Design

This is a prospective diagnostic test study. Clinical data were collected in the LIVEN COVID-19 study, a voluntary registry created by the Latin American Intensive Care Network (https://www.redliven.org). Variables were compiled by the attending physicians that reviewed medical records and diagnostic testing data for patients admitted to 22 hospitals across eight Latin-American countries, with SARS-CoV-2 infection confirmed by rt-PCR between March 2020 and January 2021. This study aimed to determine the risk factors associated with the development of severe COVID-19 and death. In this sense, three models were trained for the evaluation. The first model assessed predictions using only Chest X-rays; the second model used clinical variables to predict outcomes; finally, the third model used both images and clinical data to identify patients at risk of developing severe COVID-19 or dying during hospital admission. This study was approved by the Institutional Review Board of the Clinica Universidad de La Sabana (TSICCM CUS0012). This study was a secondary analysis of a dataset collected prospectively, so informed consent was waived.

Data collection

Data included sociodemographic variables, comorbid conditions, symptoms, vital signs on hospital admission, and treatments received during the hospitalization. Obesity was determined by treating physicians when the patients had BMI greater than 30. Additionally, Chest X-rays images collected on hospital admission were reported in some patients and were used in our models. Physiological variables and laboratory results were

gathered during the first 24 hours of hospital admission. All data were collected in the Research Electronic Data Capture platform (REDCap, version 8.11.11, Vanderbilt University, Nashville, Tenn.)[19] hosted at the Universidad de La Sabana, Chía, Colombia. Clinical variables were pre-processed before training the proposed classifier. Incomplete clinical information was considered as a general exclusion criterion. Subjects without a chest x-ray were excluded from the image-based model and were included only in the clinical cohort (**Figure 1**).

Model construction

Transfer learning was used to train two hybrid architectures. These architectures were designed to extract features from images and clinical data to predict ICU admission and hospital mortality. A hold-out scheme was used whenever each cohort was assessed (clinical or images), specifically for the images cohort, 70% was reserved for training (this data was used to fit the model), 12% for validation (this data was used to provide an unbiased evaluation of the model fit on the training dataset while tuning model hyperparameters and early stopping the training), finally the remaining 18% was used for testing (this data was used to provide an unbiased evaluation of the final model). Furthermore, to keep all experimentation under the same testing conditions, the subjects selected as validation and testing in the images cohort were also used as such for the clinical one, which due to different sample sizes, results in a differently proportioned split whenever clinical models were assessed to 92.6% for training, 2.9% validation and 4.5% testing.

The images model was a fine-tuned model pre-trained with Imagenet weights (**Figure 2A**). It uses "Hippocrates," a tool that tests for five different backbones (MobileNet, InceptionV3, DenseNet121, Xception) a range of neurons number that goes from 32 to 256 in the last fully connected layer, several values for dropout weights ranging from 0.3 to 0.7, and multiple top layer weights for classification. As a result, one loss optimization was carried out numerous times per backbone and hyperparameters setup, and the model that yields the best performance was selected.

Some preparation and pre-processing for training models with images had to be done before trying backbone learning and convolutional neural network training. Firstly, only frontal views of Posterior-Anterior and Anterior-Posterior chest X-Ray Images with well-defined anatomical structures were selected; as a result, images with strong artifacts or heavily blurred structures were discarded from the study. Secondly, as variations, in contrast, grey-level intensity and capture methods, a pre-processing algorithm was used to take all images to the same dynamic range and remove elements that were not part of the image.

After pre-processing, backbone learning was performed by letting each backbone and parameter configuration learn during a fixed number of iterations. Each network processed the whole dataset five times (5 epochs). Then, the setup that yielded the best performance was used to train over 20 epochs with an early stop to avoid overfitting during the process. The combined model was used to exploit both clinical and image information in the classification process. A custom architecture was proposed for this

model by connecting single sigmoid outputs of both models to a single neuron that predicts the likelihood of any given class (**Figure 2C**). For this case, 002C feature extraction weights for both separate models were frozen since the only weights that can be learned were related to the contribution of clinical and image information for the output prediction and its respective bias. The combined models were trained for 150 epochs with an early stop call-back that prevented the model from overfitting by monitoring validation loss decay. The binary cross-entropy and stochastic gradient descent (SGD) with a learning rate of 0.01 were used as cost function and optimizer.

Statistical analysis

To predict the probability of ICU admission or hospital mortality, a random forest (RF) model was used. The RF model is an ensemble-learning model that uses multiple decision trees as its base models. In the end, a majority voting system is implemented to synthesize the results of all the base models. Also, a logistic regression model was designed to select the clinical variables and laboratory results that best predicted the outcomes. Sociodemographic and physiological data selected by the RF model were included as independent variables in the multivariate analysis. Some variables were included for biological plausibility. Odds ratios (ORs) were obtained based on the exponentials of the final logistic regression model coefficients.

A predictive clinical model was built as a simple perceptron model for the AI prototype (**Figure 2B**). All the selected clinical variables in the logistic regression model were connected to a single neuron output layer with a sigmoid activation function. Then, the

model was trained for 150 epochs with an early stop call-back that prevents it from overfitting by monitoring validation loss decay. For this training, the binary cross-entropy was defined as the cost function, and SGD with a learning rate of 0.001 was used as the optimizer.

A statistical analysis using bootstrapping was performed to validate each model. First, the testing set was sampled with replacement to obtain 250 samples, each with a sample size equal to the 50% of the original' 'set's size. Then, each sample was assessed by using the area under the receiver-operating curve (AUC-ROC), obtaining a metric population (AUC population). Finally, statistics such as mean, standard deviation, and 95% confidence intervals were also computed for the AUC population. As a result, the bootstrapped test of the AUC population calculated per model was used to compare the performance of the proposed models. Then, a distribution comparison of the three AUC populations under a t-test to establish statistically significant differences across the proposed models were performed. Additional evaluation measurements like sensitivity, specificity, and accuracy metrics were also computed over all the testing sets for each model. All statistical analyses were performed using SciPy 1.7.1 in Python 3.8 and R Studio Version 1.3.1056.

RESULTS

A total of 3007 patients were registered in the LIVEN COVID-19 study. After excluding patients with no ICU hospital mortality data or the clinical variables needed on clinical admission, 2550 patients were included in the clinical cohort for the ICU admission

predictive model and 2552 for the hospital mortality analysis. A total of 59.5% (1517/2550) of the patients required ICU admission and were distributed as follows in the models: 92.6% (1404/1517) underwent training, 4.5% (68/1517) underwent testing, and 2.9% (45/1517) underwent validation. Of all the patients included in the clinical cohort, 23.7% (604/2552) died during hospital admission. **Figure 1** presents how these patients were distributed in the models.

A total of 23.9% (720/3007) of the overall cohort had chest x-ray images available; however, 80.8% had clear frontal images (582/720). Of the image's cohort, 31.3% (182/582) of patients died, and of these, 69.2% (126/182) underwent training, 18.7% (34/182) underwent testing and 12.1% (22/182) underwent validation. 63.7% (371/582) required ICU admission and were distributed as presented in **Figure 1.**

The variables independently associated with ICU admission were, age (OR: 1.62; 95%CI: 1.43-1.83, *p<0.001*), fraction of inspired oxygen - FiO2 on admission (OR: 4.10; 95%CI: 3.55-4.73, *p<0.001*), systolic pressure on admission (OR: 1.20; 95%CI: 1.05-1.38, *p=0.007*), diastolic pressure on admission (OR: 0.80; 95%CI: 0.70-0.93, *p=0.003*), SatO2 (OR: 0.84; 95%CI: 0.76-0.94, *p=0.002)*, Glasgow on admission (OR: 0.60; 95%CI: 0.53-0.69, *p=0.007*), male (OR: 1.42; 95%CI: 1.28-1.59, *p<0.001*), dyspnoea on admission (OR: 1.42; 95%CI: 1.28-1.58, *p<0.001*), obesity (OR: 1.42; 95%CI: 1.28-1.58, *p<0.001*), arterial hypertension (OR: 1.17; 95%CI: 1.05-1.32, *p=0.005*) and diabetes mellitus (OR: 1.22; 95%CI: 1.10-1.36, *p<0.001*). Vomit/nausea, CKD, conjunctivitis, and skin ulcers were no relevant for this final model (**Table 1**).

Moreover, the variables associated with hospital mortality were age (OR: 1.68; 95%CI: 1.51-1.87, *p<0.001*), fraction of inspired oxygen - FiO2 on admission (OR: 4.32; 95%CI: 3.75-4.97, *p<0.001*), systolic pressure on admission (OR: 1.20; 95%CI: 1.05-1.38, *p=0.007*), diastolic pressure on admission (OR: 0.80; 95%CI: 0.70-0.93, *p=0.003*), SatO2 (OR: 0.82; 95%CI: 0.74-0.91, *p<0.001)*, Glasgow on admission (OR: 0.61; 95%CI: 0.54-0.69, *p<0.001*), male (OR: 1.44; 95%CI: 1.29-1.60, *p<0.001*), dyspnoea on admission (OR: 1.50; 95%CI: 1.35-1.66, *p<0.001*), obesity (OR: 1.43; 95%CI: 1.28-1.59, *p<0.001*), chronic kidney disease (OR: 1.20; 95%CI: 1.08-1.33, *p<0.001*) and arterial hypertension (OR: 1.21; 95%CI: 1.08-1.35 *p=0.001*). Diabetes mellitus on admission was no relevant for this final model **(Table 1).**

ICU admission models

ROC curves for ICU admission are presented in **Figures 3A, 3C, 3E**. This assessment yielded a performance of 0.88 ± 0.05 for the images-based model, 0.90 ± 0.04 for the clinical model, and 0.92 ± 0.04 for the combined model. Furthermore, additional metrics such as sensitivity and specificity are provided for each model in **Table 2**. All possible combinations of each AUC for the three models showed statistical differences (*p*< 0.0001). Visualization of ROC populations and mean curves for each model is displayed in **Figures 4A 4B.**

Hospital Mortality

The ROC curves for hospital mortality are presented in **Figures 3B, 3D, 3F**. Additionally, metrics like sensitivity and specificity are provided for each model in **Table 2**. This assessment yielded performances of 0.75 ± 0.07 for the images-based model, 0.81 ± 0.06 for the clinical model, and 0.81 ± 0.06 for the combined model. Sensitivity performance was 71%, 75%, and 75% for images, clinical and combined models. Similarly, specificity metrics were 76%, 71%,74% for the three proposed models. Additionally, positive predictive values (PPV) were 59%, 57%, 58% and negative predictive values (NPV) 84%, 84% 85%. No statistically significant differences were found in the AUC comparison between clinical and combined models (p=0.13). However, when the AUC of the imaging model was compared with the combined model (p< 0.0001) and the AUC of the clinical model with the images-based model (p< 0.0001), statistically significant differences were found **(Figures 4C, 4D).**

DISCUSSION

This study presents algorithms for predicting whether COVID-19 patients may require ICU admission or are likely to die within hospitalization by using an automatised method to interpret chest x-rays, clinical variables, and a combination of both. We found that models constructed with Chest x-ray images (interpreted by an AI algorithm) and clinical data presented good discriminatory performance regarding ICU admission and hospital mortality. Notably, the models using clinical data and the AI algorithm combined had an excellent discriminatory power to identify patients at risk of developing severe COVID-

19. Nevertheless, predicting hospital mortality by combining Chest x-ray features and clinical information did not perform significantly. Finally, the Chest x-ray images model alone had the lower predictive potential for both outcomes.

Different predictive models for the COVID-19 illness progression have been developed throughout the pandemic. Routinely measured clinical variables have been used as essential predictors of severity. Zhao Z. *et al.*,[20], in a retrospective study of 4997 COVID-19 patients, showed that the presence of shortness of breath, elevated heart rate, elevated respiratory rate, and decreased pulse oxygen saturation was significantly associated with a higher proportion of patients admitted to the ICU. Additionally, other authors have described that diagnostic image analysis provides consistent information of pulmonary involvement and complements clinical prediction in COVID-19 patients. In another study, Jiao Z. *et al*.[21] developed a multicentre retrospective study of 1834 patients with COVID-19, reporting that when Chest X-rays were added to clinical data, the receiver operating characteristic curve increased from 0.82 (95% CI 0.79-0.82) to 0.84 (0.81-0.85) with a p-value <0.0001 for severity prediction. On top of that, Soda P. *et al.*[22] designed a hybrid approach model using clinical data associated with Chest x-ray images of 820 COVID-19 patients finding the best performance for critical infection prediction when using both inputs. Our combined model also demonstrated that the clinical information provides consistent performance that improves the classification metrics when complemented with an AI image features extraction algorithm. These results suggest a complementary role between imaging, demographics, routine

laboratories involving lung function, and others to determine whether a patient is likely to require ICU admission.

In the case of prediction of hospital mortality, Balbi M. et. al.[23] found that PaO2/FiO2 ratio was associated with higher mortality rate (OR [95% CI] 0.99 [0.98 - 1], p= 0.002), as well as the presence of cardiovascular disease (3.21 [1.28-8.39], p<0.014), and age (1.16 [1.11-1.22], p< 0.001), with statistical differences despite had only 340 COVID-19 patients in their retrospective study. Similarly, Ryan L et al.[24] developed a model by a methodology of "boosted" decision trees including variables like age, heart rate, respiratory rate, peripheral oxygen saturation, temperature, systolic blood pressure, diastolic blood pressure, white blood cell counts, platelets, lactate, creatinine, and bilirubin levels, reporting an area under the ROC (AUROC) of 0.86 to predict 48h-mortality on COVID-19 patients. Moreover, the model showed a better performance compared with the AUROC of current 48h-mortality scores (qSOFA= 0.792, MEWS= 0.724, and CURB-65= 0.802) [24]. Nevertheless, this study had a community hospital dataset of only 114 COVID-19 patients and did not include information about diagnostic images. Our clinical model included similar variables and had better discriminatory power than previous studies. Importantly, in our study, we used the Random Forest analysis that is more robust to identify the variables associated with the outcomes. However, our model using automatized chest X-ray interpretation and clinical data had a modest prediction power for mortality.

Different images findings have been associated with COVID-19 disease. Balbi M. et al.[23] described that ground-glass opacities with consolidation (69%) were the most common Chest x-ray finding evaluated in COVID-19 patients, with an almost perfect inter-rater agreement related with the parenchymal opacity (Kappa = 0.90), Brixia score (ICC = 0.91), and percentage of lung involvement (ICC = 0.95). Nevertheless, the Chest x-ray characteristics and the risk of mortality or risk for ICU admission were not assessed in the multivariate analysis. Likewise, Au-Yong. I. et al.,[25], in their retrospective cohort study of 751 patients with COVID-19, demonstrated that a higher percentage of Chest x-ray opacity is related to lower survival (50-75% opacity had 7.6 median escalation free survival days [95% CI 5.4-23.7 days] and 76-100% opacity had 2.6 days [95% CI 1.5-16.6 days] with p value<0.001. Despite this, our results suggest that an automatized model of interpretation of Chest x-ray characteristics alone did not achieve the best performance for predicting COVID-19 severity or in-hospital mortality compared to models that combined clinical data. Thus, we believe that using our automated algorithm to interpret chest X-rays and some clinical characteristics might be extremely useful to identify patients at risk of developing severe COVID-19 and those at risk of dying due to this infection. Determining these high-risk patients might be critical when untrained personnel interprets the chest-x-rays.

There are some limitations of this study that are important to consider. First, a few Chest X-ray images had inconsistent quality and noisy data that may affect the performance of the automatized algorithm for reading the images in clinical practice. However, the images could be pre-processed and fixed to mitigate this issue. Second, the number of

patients with images available was small. Therefore, the sample size of both images and combined cohorts was less than the clinical information sample. The algorithm's performance might have been affected, causing it to fail to make robust predictions. However, this is one of the few studies that have included radiological findings in predictor models, which is a strength of our algorithms and allows us to generate new hypotheses about using artificial intelligence in medical practice. Indeed, the model's performance with a chest X-ray could improve the prediction capacity when combined with clinical variables. Third, although deep neural networks have exhibited superior performance in various tasks, interpretability is always the Achilles' heel of deep neural networks. At present, deep neural networks obtain high discrimination power at the cost of low interpretability of their black-box representations. We believe that high model interpretability may help people break several bottlenecks of deep learning, e.g., learning from very few annotations, learning via human-computer communications at the semantic level, and semantically debugging network representations. Likewise, the applicability of the models will depend to a great extent on the local health systems and the willingness of the clinicians to request the images and the corresponding laboratories. Future follow-up studies will add tremendous value to the current evidence by testing this model, specifically those based on X-ray images.

To sum up, our study presents evidence that our automatized algorithm to interpret Chest-x-rays along with some clinical data might be an instrumental tool to identify patients at higher risk of developing severe COVID-19. Notably, our model does not require the physician's interpretation of the images; it only requires an image, and the IA system

interprets the variables and makes an automated analysis. Predicting ICU admission using images, clinical information, or a combination of both yielded consistent results across all three experiments. The combined model is the best to identify patients at risk of severe COVID-19. Also, Chest X-ray images demonstrated better predictive power in the case of ICU admission compared with mortality prediction, and their utility is improved when it is complemented with clinical information. Future work involves clinical trials with ICU admission predictors that evaluate our models' external validation and improve clinical outcomes of COVID-19 patients.

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TABLES

Table 1: Clinical variables selected by logistic regression models to assess ICU admission and Hospital Mortality prediction.

Variable	ICU admission		Hospital Mortality	
	Logistic regression variables OR (95% CI)	**p-value**	**Logistic regression variables** OR (95% CI)	**p-value**
Age	1.62 (1.43-1.83)	<0.001	1.68 (1.51-1.87)	<0.001
FiO2 on admission	4.10 (3.55-4.73)	<0.001	4.32 (3.75-4.97)	<0.001
SP on admission	1.20 (1.05-1.38)	0.007	1.20 (1.05-1.38)	0.007
DP on admission	0.80 (0.70-0.93)	0.003	0.80 (0.70-0.93)	0.003
SatO2 on admission	0.84 (0.76-0.94)	0.002	0.82 (0.74-0.91)	<0.001
Glasgow on admission	0.60 (0.53-0.69)	<0.001	0.61 (0.54-0.69)	<0.001
Sex	1.42 (1.28-1.59)	<0.001	1.44 (1.29-1.60)	<0.001
Dyspnoea on admission	1.42 (1.28-1.58)	<0.001	1.50 (1.35-1.66)	<0.001
Obesity	1.42 (1.28-1.58)	<0.001	1.43 (1.28-1.59)	<0.001
Vomit/Nausea on admission			1.00 (0.90-1.11)	0.88
Abdominal pain on admission	1.08 (0.98-1.20)	0.11	1.05 (0.94-1.16)	0.34
CKD on admission			1.20 (1.08-1.33)	<0.001
Conjunctivitis on admission			1.00 (0.90-1.12)	0.91
HBP on admission	1.17 (1.05-1.32)	0.005	1.21 (1.08-1.35)	0.001

Skin ulcers on admission			0.95 (0.86-1.06)	0.43
DM on admission	1.22 (1.10-1.36)	<0.001		

Abbreviation: FiO2: Fraction of inspired oxygen; SP: Systolic pressure; DP: Diastolic pressure; SatO2: Saturation of oxygen; HBP: Arterial hypertension; CKD: Chronic kidney disease; DM: Non-complicated diabetes. **Note:** The missing values on the table were variables not selected for the predictive model analysis due to statistical significance or biological plausibility.

Table 2: Performance metrics for ICU admission and hospital mortality model assessment.

Model	Sensitivity	Specificity	PPV	NPV	AUC	Mean AUC CI
ICU admission						
Images	0.85	0.81	0.89	0.75	0.88 ± 0.05	0.8788 – 0.8911
Clinical	0.87	0.78	0.88	0.76	0.90 ± 0.04	0.8956 – 0.9059
Combined	0.91	0.78	0.89	0.83	0.92 ± 0.04	0.9113 – 0.9218
Hospital mortality						
Images	0.71	0.76	0.59	0.84	0.75 ± 0.07	0.7368 - 0.7546
Clinical	0.71	0.75	0.57	0.84	0.81 ± 0.06	0.7981 – 0.8132
Combined	0.74	0.75	0.58	0.85	0.81 ± 0.06	0.8066 – 0.8205

FIGURE LEGENDS

Figure 1: Cohorts for outcome assessments for the LIVEN COVID dataset. On the left side, exclusion criteria are presented, and on the right side of the figure, splits for clinical cohort and images cohort are specified.

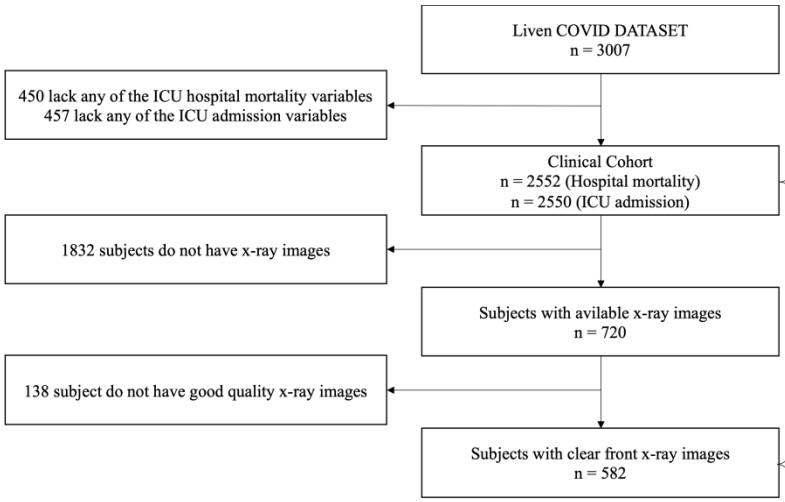
Figure 2: Convolutional neural network (CNN) models construction, panel A displays the proposed approach for obtaining a model from images by backbone learning. Panel B shows the proposed perceptron model to use clinical data for outcome assessment, and panel C displays the proposed combination of A and B.

Figure 3: ROC curves of Intensive Care Unit (ICU) admission and hospital mortality assessment and statistical comparison of models per outcome assessment.

Figure 4: ROC curves of Intensive Care Unit (ICU) admission and hospital mortality assessment using proposed models.

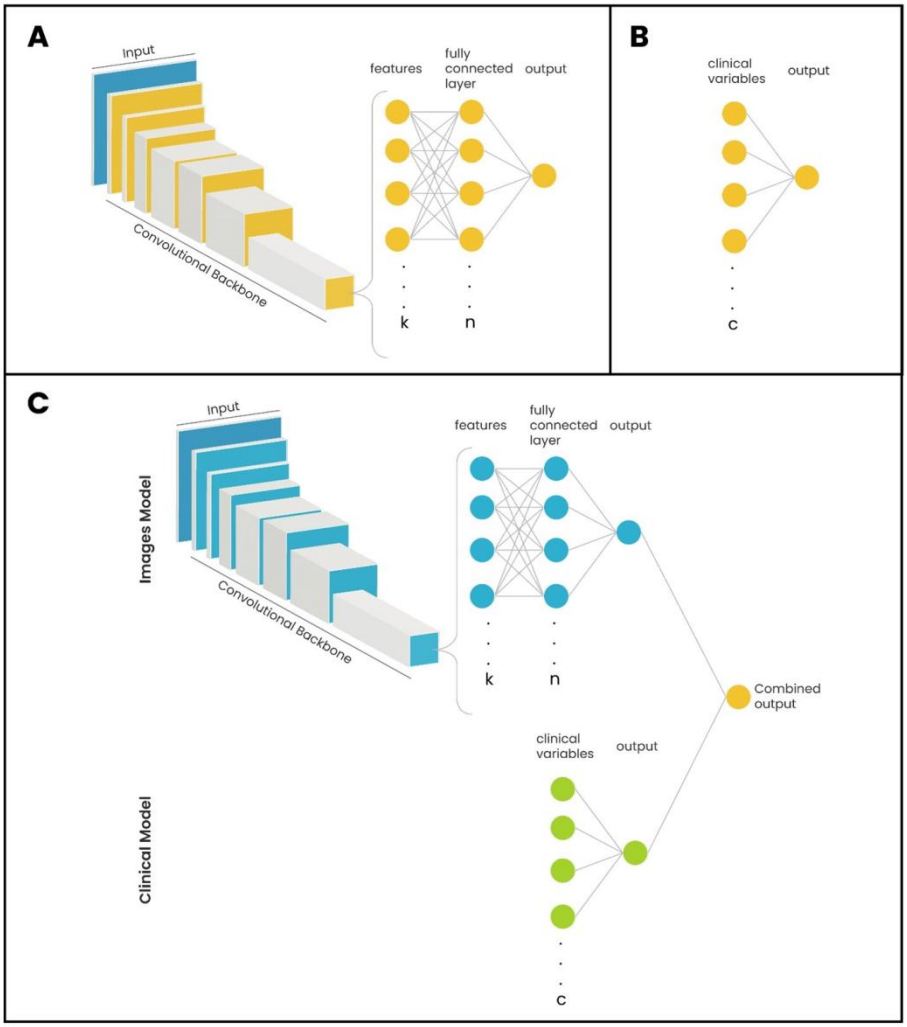
SUPPORTING INFORMATION

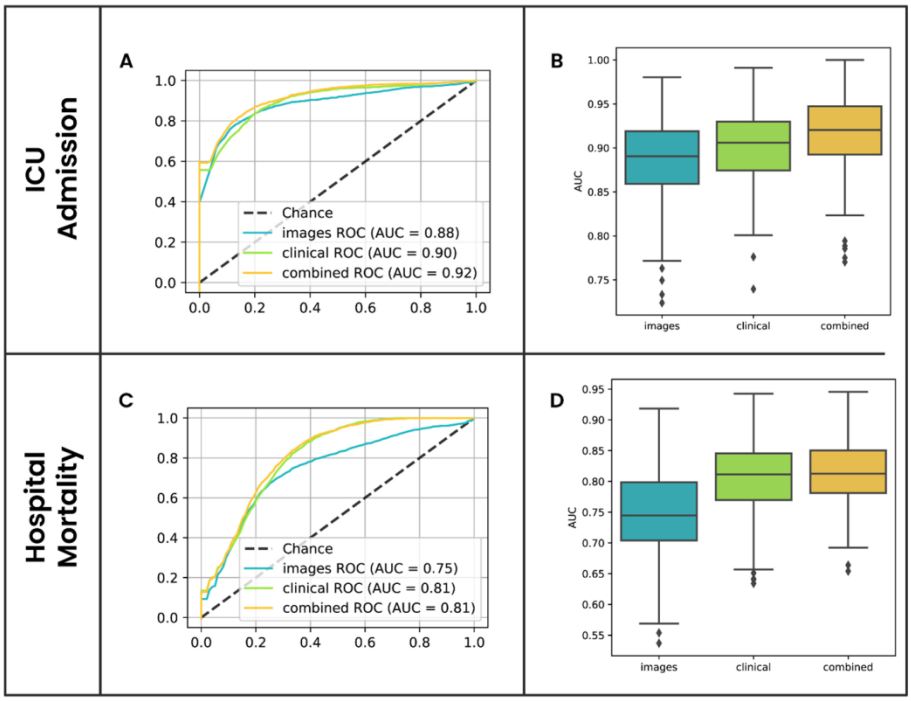
S1 File. Data set with information recollected for this study.

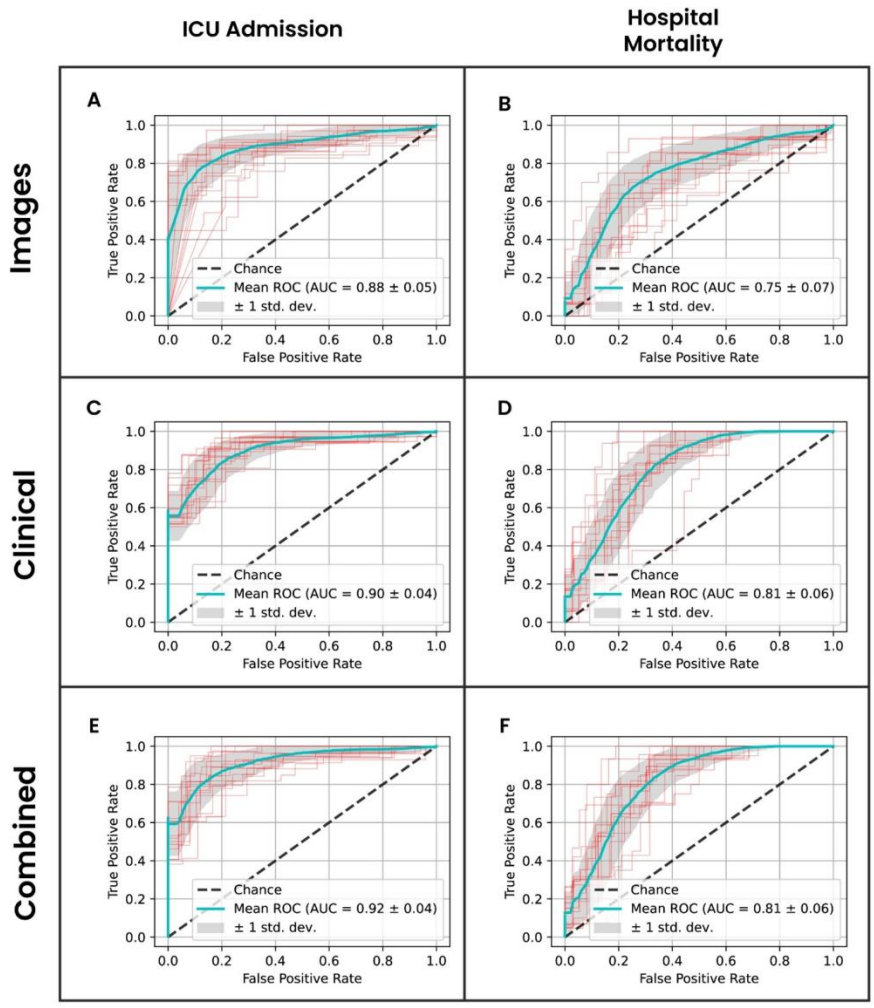


		Train	Test	Validation
ICU Admisión	**Yes**	1404	68	45
	No	972	37	24
Hospital Mortality	**Yes**	548	34	22
	No	1830	71	47

		Train	Test	Validation
ICU Admisión	**Yes**	258	68	45
	No	150	37	24
Hospital Mortality	**Yes**	126	34	22
	No	282	71	47


A
Input
Convolutional Backbone
features
fully connected layer
output
k
n
B
clinical variables
output
c
C
Images Model
Input
Convolutional Backbone
features
fully connected layer
output
k
n
Combined output
Clinical Model
clinical variables
output
c


ICU Admission
Hospital Mortality
A
B
C
D
Chance
images ROC (AUC = 0.88)
clinical ROC (AUC = 0.90)
combined ROC (AUC = 0.92)
Chance
images ROC (AUC = 0.75)
clinical ROC (AUC = 0.81)
combined ROC (AUC = 0.81)
AUC
images
clinical
combined


ICU Admission
Hospital Mortality
Images
Clinical
Combined
A
B
C
D
E
F
True Positive Rate
False Positive Rate
Chance
Mean ROC (AUC = 0.88 ± 0.05)
Mean ROC (AUC = 0.75 ± 0.07)
Mean ROC (AUC = 0.90 ± 0.04)
Mean ROC (AUC = 0.81 ± 0.06)
Mean ROC (AUC = 0.92 ± 0.04)
Mean ROC (AUC = 0.81 ± 0.06)
± 1 std. dev.