Development and Validation of Prediction Models for Mechanical Ventilation, Renal Replacement Therapy, and Readmission in Hospitalized Patients with COVID-19

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Abstract
We construct prognostic models for Covid-19 patients targeting three important inpatient outcomes: mechanical ventilation, renal replacement therapy (RRT), and hospital readmission. We develop and validate our models using electronic health record data from a major medical center in New York City which has been formatted according to the OMOP standard. Our models are performant, interpretable, and produce well-calibrated likelihoods for each target outcome.
Research Category: patient-level prediction

Background
Clinical prediction models can be used effectively to assess patient prognosis, aiding in triage decisions and providing potential intervention targets to improve outcomes. Nevertheless, most published Covid-19 prediction models have focused on disease diagnosis while the few prognostic models have largely targeted mortality risk estimation[1]. Covid-19 patients are at risk for several major complications during an inpatient hospital course. Roughly 12-33% of these patients suffer respiratory failure and require mechanical ventilation[2–5]. 14% of all hospitalized Covid-19 suffer acute kidney injury and require RRT. This proportion rises to 35% for intensive care patients. In addition, roughly 4.5% of Covid-19 patients receiving emergency or inpatient care are readmitted within 7 days of discharge[6]. Each of these outcomes carries significant implications for patient outcomes, long term sequelae, and resource utilization, as hospitals face limited access to ventilators, RRT machines, and beds.

In this work, we aim to build interpretable prognostic models for Covid-19 patients which estimate the risk of respiratory failure requiring mechanical ventilation, acute renal failure requiring RRT, and hospital readmission. We develop our models using OMOP-formatted electronic health record (EHR) data from Columbia University Irving Medical Center (CUIMC).

Methods
Cohorts and Clinical Observations Our datasets are comprised of demographics, clinical lab measurements, vital signs, and conditions for patients with active SARS-CoV-2 infection confirmed by a positive PCR-based test. For RRT and ventilation models, we use data gathered during the first 12-hours of a hospital course, including data from patients' historical records if available. We do the same for readmission models, but include all data for the full hospital course.
Our validation cohort contains patients receive care at the Allen Hospital, a community hospital member of CUIMC. The development cohort includes patients from all other CUIMC care sites.

Outcome Definitions Mechanical ventilation was defined according to the placement of an endotracheal tube (ETT) as recorded in nursing flowsheets. A patient is considered positive for mechanical ventilation if an ETT is placed at least 12 hours after the start of their hospital course. RRT is defined similarly using variables related to RRT in nursing flowsheets.
Readmission was defined as an emergency room visit or inpatient admission occurring within 2-7 days of previous discharge.

Statistical Analysis We experiment with three model classes to predict each outcome: L1-penalized logistic regression (Logistic L1), elastic-net logistic regression (Logistic EN), and gradient boosted trees (XG Boost). For each model class and outcome, we use 5-fold cross validation on the development cohort to tune hyperparameters using the area under the curve (AUC) for the receiver operating characteristic (ROC) curve as the selection metric. Next, for a given outcome, we identify the best performing model, retrain on the full training set, and evaluate on the validation cohort. We report the ROC and the precision-recall (PR) curves and their AUCs

for both the development and validation cohorts. We obtain 95% confidence intervals for all statistics using the reverse percentile bootstrap.

For our final models we evaluate feature importance using SHAP[7], a method of estimating instance-wise Shapley values. We also visualize the calibration of each model's predicted outcome likelihood.

Results

Table 1 summarizes the predictive performance for the best models within each outcome. Due to space constraints we visualize the SHAP feature importance and calibration for our ventilation models only in Figure 1.

		Development		Validation	
Outcome	**Model**	**AUROC**	**AUPRC**	**AUROC**	**AUPRC**
Ventilation	XG Boost	.869 [.847, .892]	.613 [.557, .666]	.743 [.679, .811]	.137 [.047, .175]
RRT	Logistic L1	.847 [.813, .882]	.381 [.291, .451]	.847 [.768, .934]	.325 [.114, .497]
Readmission	Logistic EN	.830 [.803, .856]	.307 [.244, .353]	.871 [.830, .919]	.504 [.386, .599]

Table 1. Predictive performance of best model for each target outcome on development and validation cohorts. Cells contain point estimates with 95% confidence intervals.

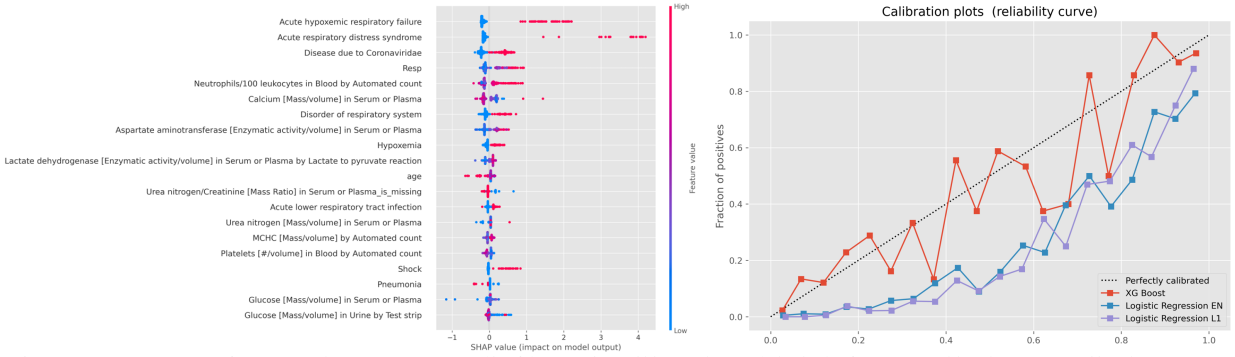

Figure 1. SHAP feature importance (left) and calibration (right) for ventilation prediction. SHAP: Feature with 20 highest SHAP values are shown. Red (blue) points are instances with high (low) values for the corresponding feature. Calibration for all ventilation models are shown.

Discussion/Conclusions

Our results demonstrate that interpretable, performant, prognostic models targeting resource-intensive outcomes important to the management of Covid-19 may be trained using routinely recorded clinical variables. Moreover, we have shown these models can be trained so their predictions may be used to guide care. For ventilation and RRT, our models use only the data available within the first 12 hours of a patient's hospital course. Thus, their predictions may be made available to clinicians actively managing Covid-19 patients. Meanwhile, for readmission, our model utilizes data gathered throughout the current stay, making predictions available by the end of a hospital course when they would have the largest impact. As our models are trained and validated with data from CUIMC's care sites, additional external validation studies are needed to further verify the generalizability of our results.

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