Multi-horizon predictive modeling for ECMO resource allocation in COVID-19 pandemic

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“The development of storage, analytic, and interpretive methods to optimize the transformation of increasingly voluminous biomedical data, and genomic data, into proactive, predictive, preventive, and participatory health”
COVID-19 models

Hundreds of AI tools have been built to catch covid. None of them helped.

Some have been used in hospitals, despite not being properly tested. But the pandemic could help make medical AI better.

By Will Douglas Heaven
July 30, 2021

Prediction models for diagnosis and prognosis of covid-19: systematic review and critical appraisal

BMJ 2020;369 doi:https://doi.org/10.1136/bmj.m1328 (Published 07 April 2020)

“The pandemic has made it clear to many researchers that the way AI tools are built needs to change”

“Frankenstein data sets”

Seventy nine models identified patients at risk in the general population (using proxy outcomes for covid-19)

Thirty three diagnostic models were identified for detecting covid-19, in addition to 75 diagnostic models based on medical images, 10 diagnostic models for severity classification, and 107 prognostic models for predicting, among others, mortality risk, progression to severe disease

Proposed models are poorly reported and at high risk of bias, raising concern that their predictions could be unreliable when applied in daily practice

Two prediction models (one for diagnosis and one for prognosis) were identified as being of higher quality than others and efforts should be made to validate these in other datasets
SARS-CoV2 “COVID-19” pandemic

• Unforeseen strains on global healthcare systems
• ECMO – life sustaining therapy in cardiopulmonary failure
  • Extensive expertise and resources
  • Significant risks and morbidities
• Guidelines discourage commissioning new ECMO centers

THE most resource intensive ICU therapy
Extracorporeal Membrane Oxygenation (ECMO)

- The most complex, highest-risk and resource-intensive modality in intensive care units (ICU)
  - 1 – 5 year mortality rates 45% - 57%
  - Inpatient costs US$22,305 - 334,608/day (2019)

- ECMO mortality prediction scores, neither designed nor validated for patient triage or resource allocation
THE most resource intensive ICU therapy

Local ECMO initiation schematic
ECMO during the COVID-19 pandemic: when is it unjustified?

Darryl Abrams¹², Roberto Lorusso³, Jean-Louis Vincent⁴ and Daniel Brodie¹²

Extracorporeal Membrane Oxygenation for Critically Ill Patients with COVID-19–related Acute Respiratory Distress Syndrome: Worth the Effort?

Planning and provision of ECMO services for severe ARDS during the COVID-19 pandemic and other outbreaks of emerging infectious diseases

Kollengode Ramanathan, David Antognini, Alain Combes, Matthew Paden, Bishoy Zakhary, Mark Ogino, Graeme MacLaren, Daniel Brodie*, Kiran Shekar*
COVID-19 Cases on ECMO in the ELSO Registry:

Total COVID-19 Cases: 17,674

Total counts of COVID-19 confirmed patients.

Patients who initiated ECMO at least 90 days ago:

COVID-19 Confirmed: 16,255
COVID-19 In-hospital Mortality: 48%

COVID-19 ECMO counts by ELSO Chapter:

- North America: 11,211
- Europe: 3,529
- Asia Pacific: 571
- Latin America: 1,271
- SWAAC: 1,185

Reports counts of ECMO-supported suspected or confirmed COVID-19 cases by ELSO Chapter (provided the chapter has at least 5 cases reported)

Extracorporeal membrane oxygenation for coronavirus disease 2019-related acute respiratory distress syndrome

Short, Briana\textsuperscript{a,b}; Abrams, Darryl\textsuperscript{a,b}; Brodie, Daniel\textsuperscript{a,b}

Author Information


Resource allocation, patient triage, unexpected volumes

Regional experience
Gaps in current knowledge

No tools to early identify patients at risk of needing ECMO
Current recommendations limited to criteria to initiate ECMO based on immediately pre-ECMO labs and therapeutic requirements

Tools available for resource allocation limited to:
- Scores of severity of ICU illness
- Immediate pre-ECMO markers of respiratory failure

Big data approach?
Machine learning?
Translational Biomedical Informatics?
Hypothesis

Machine Learning Predictive algorithm

ICU Admission  Therapy initiation

Failure to respond

Maximum Conventional therapies

Transfer to ECMO Center

Resource reallocation

Unstable For Transfer Poor outcome

ECMO initiation
Methods

- Institutional data registry:
  - All COVID-19 patients
  - 15 hospitals – BJC
  - March 3rd 2020 – October 1st 2021

- Inclusion criteria:
  - SARS-CoV-2 viral PCR positive
  - Admitted to ICU ≥ 24 hours

- Exclusion criteria:
  - Age < 3 years
  - Institutional ECMO exclusion criteria:
    - Age > 70 years
    - BMI > 45 Kg/m²

- Outcome:
  - ECMO during hospitalization
  - ECMO confirmed to be directly related to COVID-19 infection - detailed chart review

- Comparatives:
  - Logistic regression (LR) models of all considered variables
  - Severity of illness score: SOFA
  - ECMO decision making variable: PF ratio
  - ECMO mortality prediction score: PREdiction of Survival on ECMO Therapy (PRESET)
Variables

- Demographics
- Comorbidities
- Labs
- Medications
- Flowsheet

Flow diagram:

1. **Data processing**
   - 73 Labs
   - 124 Flowsheet
   - Time series variables
   - Data processing

2. **Modelling**
   - Log. Reg
   - ML GBT

Additional notes:
- Normal
Multi-horizon approach “ForecastECMO” – predict ECMO use at 2 hour intervals from admission

Modeling

Prediction horizons 0- 96 hours prior to ECMO initiation
Modeling

GBT models: Prediction horizons 0-96 hours prior to ECMO initiation
Training and evaluation: 10 random shuffles of 10-fold stratified cross validation

ForecastECMO

XGBoost: 212 included variables

Clinical GBT

XGBoost 30 a priori clinical variables; relevance to ECMO decision making
<table>
<thead>
<tr>
<th>Features</th>
<th>Total cohort, (n = 6247)</th>
<th>Development cohort</th>
<th>Holdout cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ECMO, (n = 67)</td>
<td>Non-ECMO, (n = 2251)</td>
<td>ECMO, (n = 68)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>54 [26, 64]</td>
<td>54 [44, 59]*</td>
<td>58 [45, 65]*</td>
</tr>
<tr>
<td>Male sex, (n (%))</td>
<td>3550 [57]</td>
<td>46 (69)</td>
<td>1255 (56)*</td>
</tr>
<tr>
<td>Caucasian, (n (%))</td>
<td>3965 [64]</td>
<td>38 (57)*</td>
<td>1348 (60)*</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>76 [56, 95]</td>
<td>85 [79, 105]*</td>
<td>84 [67, 100]*</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26 [20, 32]</td>
<td>30 [26, 33]*</td>
<td>28 [24, 34]*</td>
</tr>
<tr>
<td>Tobacco use, (n (%))</td>
<td>1207 [19]</td>
<td>5 (7)*</td>
<td>500 (22)*</td>
</tr>
<tr>
<td>SOFA*</td>
<td>9 [6, 13]</td>
<td>12 [10, 13]*</td>
<td>11 [7, 14]*</td>
</tr>
<tr>
<td>Lowest PF ratio*</td>
<td>112 [66, 204]</td>
<td>56 [48, 69]*</td>
<td>107 [65, 201]*</td>
</tr>
<tr>
<td>Hospital mortality, (n (%))</td>
<td>1079 [17]</td>
<td>32 (48)*</td>
<td>391 (17)*</td>
</tr>
<tr>
<td>CCI</td>
<td>4 [1, 7]</td>
<td>2 [1, 4.5]*</td>
<td>4 [2, 8]*</td>
</tr>
<tr>
<td>Chronic pulmonary disease, (n (%))</td>
<td>2305 [37]</td>
<td>18 (27)*</td>
<td>899 (40)*</td>
</tr>
<tr>
<td>Diabetes, (n (%))</td>
<td>2994 [48]</td>
<td>36 (54)</td>
<td>1388 (62)</td>
</tr>
<tr>
<td>Malignancy, (n (%))</td>
<td>1537 [25]</td>
<td>6 (9)*</td>
<td>594 (26)*</td>
</tr>
<tr>
<td>Renal disease, (n (%))</td>
<td>1369 [22]</td>
<td>13 (19)</td>
<td>568 (25)</td>
</tr>
<tr>
<td>Hospital length of stay (days)</td>
<td>8 [4, 18]</td>
<td>24 [13, 42]*</td>
<td>8 [4, 17]*</td>
</tr>
<tr>
<td>Mechanical ventilation (days)*</td>
<td>2 [0, 7]</td>
<td>10 [2, 22]*</td>
<td>3 [1, 10]*</td>
</tr>
<tr>
<td>CRRT, (n (%))</td>
<td>386 (6)</td>
<td>16 (24)*</td>
<td>145 (6)*</td>
</tr>
<tr>
<td>Remdesivir, (n (%))</td>
<td>764 (12)</td>
<td>27 (40)*</td>
<td>372 (17)*</td>
</tr>
<tr>
<td>Neuromuscular blockade, (n (%))</td>
<td>631 (10)</td>
<td>45 (67)*</td>
<td>188 (8)*</td>
</tr>
<tr>
<td>Nitric oxide/Iloprost, (n (%))</td>
<td>511 (8)</td>
<td>41 (61)*</td>
<td>196 (9)*</td>
</tr>
<tr>
<td>Dopamine &lt;5 (\mu g/kg/min, Dobut., milrinone or levosimendan, (n (%))*</td>
<td>592 (10)</td>
<td>15 (22)*</td>
<td>145 (6)*</td>
</tr>
<tr>
<td>Dopamine 5–15 (\mu g/kg/min, Epi/EpsilonNorEpi &lt;0.1 (\mu g/kg/min, Vaso, Phenyl, (n (%))*</td>
<td>3219 (52)</td>
<td>67 (100)*</td>
<td>1138 (51)*</td>
</tr>
<tr>
<td>Dopamine &gt;15 (\mu g/kg/min, Epi/EpsilonNorEpi &gt;0.1 (\mu g/kg/min, (n (%))*</td>
<td>2154 (35)</td>
<td>63 (94)*</td>
<td>726 (32)*</td>
</tr>
</tbody>
</table>
Model performance

Accuracy

Development

Holdout
Model performance

Precision

Development

Holdout
Model performance – 18 hours

AUROC

Development

Holdout
Model performance – 18 hours

AUPRC

Development

Holdout
What is a good alert tool?

<table>
<thead>
<tr>
<th></th>
<th>Development Incidence: 2.89%</th>
<th>Holdout Incidence: 1.73%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AUROC</td>
<td>AUPRC</td>
</tr>
<tr>
<td>ForecastECMO</td>
<td>0.94 [0.93–0.95]</td>
<td>0.546 [0.51–0.582]</td>
</tr>
<tr>
<td>PF ratio</td>
<td>0.52</td>
<td>0.032</td>
</tr>
<tr>
<td>SOFA score</td>
<td>0.56</td>
<td>0.032</td>
</tr>
<tr>
<td>PRESET score</td>
<td>0.66</td>
<td>0.077</td>
</tr>
<tr>
<td>LR</td>
<td>0.92 [0.91–0.93]</td>
<td>0.474 [0.435–0.512]</td>
</tr>
<tr>
<td>Clinical GBT</td>
<td>0.82 [0.8–0.83]</td>
<td>0.248 [0.218–0.277]</td>
</tr>
</tbody>
</table>
SHAP (SHapley Additive exPlanations)

How features effect model performance

- LSTAT
- RM
- DIS
- AGE
- CRIM
- NOX
- PTRATIO
- TAX
- B
- Sum of 4 other features

SHAP value (impact on model output)
Positive cohort – patients supported on ECMO
Negative cohort – patients not supported on ECMO
Machine learning models have the potential to serve as clinical decision support tools in **resource allocation** and **patient triage** in healthcare system stress.
Real time EHR example

**Factors Contributing to Score**

<table>
<thead>
<tr>
<th>Contribution Factor</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>30% ECG/EKG order present in last 6 months</td>
<td></td>
</tr>
<tr>
<td>22% Imaging order present in last 6 months</td>
<td></td>
</tr>
<tr>
<td>16% Number of hospitalizations in last year</td>
<td>1</td>
</tr>
<tr>
<td>14% Number of active Rx orders</td>
<td>6</td>
</tr>
<tr>
<td>12% Current length of stay</td>
<td>3.951 days</td>
</tr>
<tr>
<td>6% Future appointment</td>
<td>scheduled</td>
</tr>
<tr>
<td>&lt;1% Age</td>
<td>1</td>
</tr>
</tbody>
</table>

**Factors Not Contributing to Score**

- Predicted risk of an unplanned readmission in the next 30 days.

This score is available for currently admitted patients.
Thank you

Washington University in St Louis Institute of Informatics
BJC Healthcare Innovations lab
Big Ideas Competition

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