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

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Clinical Research Informatics

- Clinical problem
- Real world data
- Machine learning predictive analytics
COVID-19 models

**ARTIFICIAL INTELLIGENCE**

_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”
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
THE most resource intensive ICU therapy

Local ECMO initiation schematic

- Parent
- Ventilator
- MD 1/PICU Attending
- Echo machine
- Imaging cardiologist
- Zoll
- IV pole
- ECMO circuit
- Interventionalists
- Advanced ECMO specialist
- Redside RN
- MD 2/ PICU or Hospitalist
- Charge RN
- Computer
- RT
- Cell phone
ECMO during the COVID-19 pandemic: when is it unjustified?

Darryl Abrams¹,², Roberto Lorusso³, Jean-Louis Vincent⁴ and Daniel Brodie¹,²*

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*

Conventional Capacity

- System is running within capacity, judicious ECMO case selection
  - Capacity exists
  - Judicious patient selection
  - Offer VV, VA ECMO in selected COVID-19 patients based on usual criteria
  - Offer ECMO for non COVID-19 indications
  - ECMO only in expert centres

Confinement Capacity Tier 1

- System is running within expanded capacity; triage to maximize ECMO capacity to outcome
  - Expanded capacity
  - Triage to maximise resource:benefit ratio
  - VV, VA ECMO in younger COVID-19 patients with single organ failure
  - Judicious ECMO use for non COVID-19 indications
  - ECMO not offered

Confinement Capacity Tier 2

- Expanded capacity close to saturation, restrictive ECMO selection criteria
  - Capacity saturated
  - Restrictive ECMO criteria for all indications
  - Prioritise non COVID-19 indications with better chance of survival
  - VV ECMO in younger, single organ failure COVID-19 patients
  - VA ECMO and ECMO not offered

Crisis Capacity

- System is overwhelmed, ECMO may no longer be appropriate, concentrate resources to usual care
  - Capacity overwhelmed
  - ECMO not feasible in both COVID-19 and non-COVID-19 patients
  - Triage ICU admissions
  - Consider ceasing all futile care to create capacity in the system

Washington University Physicians
Department of Pediatrics
Division of Pediatric Critical Care Medicine
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

<table>
<thead>
<tr>
<th>All ELSO</th>
<th>Still on ECMO</th>
<th>Still Hospitalized at ELSO Center</th>
<th>Total (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>North America</td>
<td>103</td>
<td>190</td>
<td>10,972</td>
</tr>
<tr>
<td>Europe</td>
<td>144</td>
<td>201</td>
<td>3,480</td>
</tr>
<tr>
<td>Asia Pacific</td>
<td>36</td>
<td>81</td>
<td>501</td>
</tr>
<tr>
<td>Latin America</td>
<td>76</td>
<td>192</td>
<td>1,264</td>
</tr>
<tr>
<td>SWAAC</td>
<td>25</td>
<td>50</td>
<td>1,152</td>
</tr>
</tbody>
</table>

Reports counts of ECMO-supported suspected or confirmed COVID-19 cases by ELSO Chapter

COVID-19 cases on ECMO in the ELSO Registry

Total COVID-19 Cases
COVID-19 Confirmed Cases
17,274

Total counts of COVID-19 confirmed patients.
**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?
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

Data processing

- Labs: 73
- Flowsheet: 124

Modelling

- Time series variables
  - Data processing
  - Data with static variables
    - Log. Reg
    - ML GBT
Multi-horizon approach “ForecastECMO” – predict ECMO use at 2 hour intervals from admission

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
## Results

| Features                                      | Total cohort,  
|                                             | Development cohort | Holdout cohort | Non-ECMO,  
| n = 6247                                     | ECMO,  
|                                             | n = 67             | Non-ECMO,  
|                                             | n = 2251           | ECMO,  
|                                             | n = 68             | Non-ECMO,  
|                                             | n = 3861           |
| Age (years)                                  | 54 [26, 64]        | 54 [44, 59]*    | 55 [43, 61]*    | 48 [13, 63]*    |
| Male sex, n (%)                              | 3550 (57)         | 46 (69)        | 1255 (56)*      | 45 (66)          | 2204 (57)         | 42 (62)          | 2537 (66)        |
| Caucasian, n (%)                             | 3965 (64)         | 38 (57)*       | 1348 (60)*      | 42 (62)          | 2537 (66)         |
| Weight (kg)                                  | 76 [56, 95]       | 85 [79, 105]*  | 84 [67, 100]*   | 29 [26, 34]*    | 25 [19, 31]*      | 5 [7]*           | 697 (18)*       |
| BMI (kg/m²)                                  | 26 [20, 32]       | 30 [26, 33]*   | 28 [24, 34]*    | 9 [6, 12]*      | 12 [9, 14]*       | 55 [50, 63]*     | 126 [71, 218]*  |
| Tobacco use, n (%)                           | 1207 (19)         | 5 (7)*         | 500 (22)*       | 5 (7)*           | 697 (18)*         | 630 (16)*        |
| SOFAa                                        | 9 [6, 13]         | 12 [10, 13]*   | 11 [7, 14]*     | 9 [6, 12]*      | 12 [9, 14]*       | 55 [50, 63]*     | 126 [71, 218]*  |
| Lowest PF ratioa                             | 112 [66, 204]     | 56 [48, 69]*   | 107 [65, 201]*  | 55 [50, 63]*     | 126 [71, 218]*    |
| Hospital mortality, n (%)                   | 1079 (17)         | 32 (48)*       | 391 (17)*       | 26 (38)*         | 630 (16)*         |
| CCI                                          | 4 [1, 7]          | 2 [1, 4.5]*    | 4 [2, 8]*       | 3 [1, 4]        | 3 [1, 7]          |
| Chronic pulmonary disease, n (%)            | 2305 (37)         | 18 (27)*       | 899 (40)*       | 13 (19)*         | 1375 (36)*        |
| Diabetes, n (%)                              | 2994 (48)         | 36 (54)        | 1388 (62)       | 30 (44)          | 1540 (40)         |
| Malignancy, n (%)                            | 1537 (25)         | 6 (9)*         | 594 (26)*       | 10 (15)          | 927 (24)          |
| Renal disease, n (%)                         | 1369 (22)         | 13 (19)        | 568 (25)        | 9 (13)           | 779 (20)          |
| Hospital length of stay (days)              | 8 [4, 18]         | 24 [13, 42]*   | 8 [4, 17]*      | 38 [27, 53]*    | 8 [4, 18]*        |
| Mechanical ventilation (days)a              | 2 [0, 7]          | 10 [2, 22]*    | 3 [1, 10]*      | 21 [6, 37]*     | 4 [1, 15]*        |
| CRRT, n (%)                                  | 386 (6)           | 16 (24)*       | 145 (6)*        | 14 (21)*         | 211 (5)*          |
| Remdesivir, n (%)                            | 764 (12)          | 27 (40)*       | 372 (17)*       | 26 (38)*         | 339 (9)           |
| Neuromuscular blockade, n (%)                | 631 (10)          | 45 (67)*       | 188 (8)*        | 56 (83)*         | 342 (9)           |
| Nitric oxide/Iloprost, n (%)                | 511 (8)           | 41 (61)*       | 196 (9)*        | 45 (67)*         | 229 (6)*          |
| Dopa. <5 µg/kg/min, Dobut., milrinone or    | 592 (10)          | 15 (22)*       | 145 (6)*        | 11 (16)*         | 421 (11)*         |
| levosimendan, n (%)                          | Dopa. 5–15 µg/kg/min, Epi/NorEpi  |
| <0.1 µg/kg/min, Vaso, Pheny, n (%)#         | 3219 (52)         | 67 (100)*      | 1138 (51)*      | 68 (100)*        | 1946 (49)*        |
| Dopa >15 µg/kg/min, Epi/NorEpi >0.1 µg/kg/min, n (%)# | 2154 (35)        | 63 (94)*       | 726 (32)*       | 65 (96)*         | 1300 (33)*        |
Model performance

Development

Holdout

Precision
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)

High

Feature value

Low
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

Risk of Unplanned Readmission

Score calculated about an hour ago

<table>
<thead>
<tr>
<th>Range</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>23%</td>
<td>High Risk</td>
</tr>
<tr>
<td>11%</td>
<td>Mod Risk</td>
</tr>
<tr>
<td>0%</td>
<td>Low Risk</td>
</tr>
</tbody>
</table>

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 1</td>
<td></td>
</tr>
<tr>
<td>14% Number of active Rx orders 6</td>
<td></td>
</tr>
<tr>
<td>12% Current length of stay 3.951 days</td>
<td></td>
</tr>
<tr>
<td>6% Future appointment scheduled</td>
<td></td>
</tr>
<tr>
<td>&lt;1% Age 1</td>
<td></td>
</tr>
</tbody>
</table>

Factors Not Contributing to Score

Description

View model formula and coefficients

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

Bing Xue
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Philip Payne, PhD
Chenyang Lu, PhD