Outcomes after extracorporeal life support for COVID-19 myocarditis: an analysis of the Extracorporeal Life Support Organization Registry

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First described early in the pandemic, coronavirus disease 2019 (COVID-19)-associated fulminant myocarditis can present with arrhythmias and cardiogenic shock, but may be treatable with mechanical circulatory support, such as venoarterial (VA) extracorporeal life support (ECLS) [1]. To better characterize severe myocarditis during the COVID-19 pandemic, we analyzed adult patients with severe COVID-19 who received ECLS for cardiac, pulmonary, or combined failure using an international registry.

We calculated the rate of mechanical circulatory support use among patients receiving ECLS for COVID-19, describing patient characteristics and risk factors for mortality. We utilized the Extracorporeal Life Support Organization (ELSO) Registry and extracted data on patients ≥ 18 years old, diagnosed with COVID-19 from January 1, 2020, through March 31, 2021. Data released from ELSO are de-identified, do not meet the definition of Human Subjects Research, and therefore do not require repeat human subjects review.

Among 4792 patients receiving ECLS for COVID-19 (Table 1), 4.9% (234) were supported with VA-ECMO, and 88 patients (1.8%) had acute myocarditis during the study period. Among those with myocarditis, 35% were women ($p = 0.092$). COVID-19 patients receiving ECLS who were diagnosed with myocarditis ($n = 88$) were more likely to be managed with cardiac support versus pulmonary support (53% vs. 42%, $p < 0.001$). Among all patients supported for a cardiac indication, patients with myocarditis had less hypercarbia (PaCO$_2$: 45 mmHg vs. 66 mmHg; $p < 0.001$), less hypoxemia (PaO$_2$: 94 mmHg vs. 80 mmHg; $p = 0.078$), greater metabolic acidosis (serum bicarbonate 22 mEq/L vs. 28 mEq/L; $p < 0.001$), lower blood pressure (systolic: 101 mmHg vs. 119 mmHg; $p < 0.001$), and lower pulse pressure (43 mmHg vs. 55 mmHg; $p < 0.001$) compared with patients without myocarditis. Death percentages were similar between those with and without myocarditis.

We acknowledge limitations to this analysis. The Registry did not require myocardial biopsy to prove myocarditis, and hence, patients may have had myocarditis diagnosed as acutely decreased myocardial function on echocardiography accompanied by elevated cardiac enzymes and/or electrocardiographic changes. To account for potential overdiagnosis of myocarditis, we performed a sensitivity analysis excluding patients coded for acute myocardial infarction (AMI). The results were unchanged.

In summary, among patients with COVID-19 supported with ECLS, a diagnosis of myocarditis was
| Variable, n (%)                      | Alla (n = 4792) | Myocarditisa (n = 88) | No myocarditisa (n = 4704) | P-value |
|-------------------------------------|-----------------|-----------------------|-----------------------------|---------|
| Age (years)b                        | 49.2 (11.5)     | 47.6 (13.7)           | 49.2 (11.4)                 | 0.187   |
| Sex                                 |                 |                       |                             |         |
| Female                              | 1305 (27.2)     | 31 (35.2)             | 1274 (27.1)                 | 0.092   |
| Male                                | 3487 (72.8)     | 57 (64.8)             | 3430 (72.9)                 |         |
| Charlson comorbidity index (CCI)b   | 0.4 (0.8)       | 0.6 (0.8)             | 0.4 (0.8)                   | 0.024   |
| SAVE scoreb                         | −6.7 (3.2)      | −5.2 (3.3)            | −6.7 (3.2)                  | 0.001   |
| Inotropes prior to ECLS             |                 |                       |                             | <0.001  |
| No                                  | 4643 (96.9)     | 62 (70.5)             | 4581 (97.4)                 |         |
| Yes                                 | 149 (3.1)       | 26 (29.5)             | 123 (2.6)                   |         |
| Vasopressors prior to ECLS          |                 |                       |                             | <0.001  |
| No                                  | 1975 (41.2)     | 15 (17)               | 1960 (41.7)                 |         |
| Yes                                 | 2817 (58.8)     | 73 (83)               | 2744 (58.3)                 |         |
| Medical conditions                  |                 |                       |                             |         |
| Asthma                              |                 |                       |                             |         |
| No                                  | 4279 (89.3)     | 79 (89.8)             | 4200 (89.3)                 | 1       |
| Yes                                 | 513 (10.7)      | 9 (10.2)              | 504 (10.7)                  |         |
| Obesity (BMI > 30 kg/m²)            |                 |                       |                             |         |
| No                                  | 2309 (48.2)     | 57 (64.8)             | 2252 (47.9)                 | 0.002   |
| Yes                                 | 2483 (51.8)     | 31 (35.2)             | 2452 (52.1)                 |         |
| Diabetes                            |                 |                       |                             |         |
| No                                  | 3349 (69.9)     | 67 (76.1)             | 3282 (69.8)                 | 0.241   |
| Yes                                 | 1443 (30.1)     | 21 (23.9)             | 1422 (30.2)                 |         |
| Chronic lung disease                |                 |                       |                             |         |
| No                                  | 4596 (95.9)     | 82 (93.2)             | 4514 (96)                   | 0.174   |
| Yes                                 | 196 (4.1)       | 6 (6.8)               | 190 (4)                     |         |
| Immunocompromised                   |                 |                       |                             |         |
| No                                  | 4598 (96)       | 81 (92)               | 4517 (96)                   | 0.09    |
| Yes                                 | 194 (4)         | 7 (8)                 | 187 (4)                     |         |
| Cancer                              |                 |                       |                             |         |
| No                                  | 4705 (98.2)     | 84 (95.5)             | 4621 (98.2)                 | 0.075   |
| Yes                                 | 87 (1.8)        | 4 (4.5)               | 83 (1.8)                    |         |
| Chronic heart disease               |                 |                       |                             |         |
| No                                  | 4588 (95.7)     | 79 (89.8)             | 4509 (95.9)                 | 0.012   |
| Yes                                 | 204 (4.3)       | 9 (10.2)              | 195 (4.1)                   |         |
| Chronic renal insufficiency         |                 |                       |                             |         |
| No                                  | 4640 (96.8)     | 84 (95.5)             | 4556 (96.9)                 | 0.362   |
| Yes                                 | 152 (3.2)       | 4 (4.5)               | 148 (3.1)                   |         |
| Pregnancy                           |                 |                       |                             |         |
| No                                  | 4683 (97.7)     | 87 (98.9)             | 4596 (97.7)                 | 0.724   |
| Yes                                 | 109 (2.3)       | 1 (1.1)               | 108 (2.3)                   |         |
| Frailty                             |                 |                       |                             |         |
| No                                  | 4759 (99.3)     | 87 (98.9)             | 4672 (99.3)                 | 0.459   |
| Yes                                 | 33 (0.7)        | 1 (1.1)               | 32 (0.7)                    |         |
| Physiologic values prior to ECLSb   |                 |                       |                             |         |
| C-reactive protein                  | 124.4 (139)     | 107.2 (129.3)         | 124.7 (139.2)               | 0.414   |
| pH                                  | 7.3 (1.1)       | 7.3 (1.1)             | 7.3 (1.1)                   | 0.588   |
| PaCO₂ (mmHg)                        | 65.5 (26.4)     | 45.2 (15.8)           | 65.9 (26.5)                 | <0.001  |
| PaO₂ (mmHg)                         | 79.9 (66.4)     | 94.1 (63.7)           | 79.7 (66.5)                 | 0.078   |
| Serum bicarbonate                   | 28.3 (7.1)      | 21.5 (8.2)            | 28.4 (7.1)                  | <0.001  |
| Arterial saturation (%)             | 88.4 (9.6)      | 90.9 (9.1)            | 88.4 (9.6)                  | 0.04    |
| Systolic blood pressure (mmHg)      | 118.6 (24.7)    | 101 (28.7)            | 118.9 (24.5)                | <0.001  |
| Diastolic blood pressure (mmHg)     | 63.7 (13.2)     | 58.4 (12.6)           | 63.7 (13.2)                 | 0.001   |
| Arterial pulse pressure (SBP-DBP)   | 54.9 (19.3)     | 42.5 (20.8)           | 55.2 (19.2)                 | <0.001  |
| Administered medications            |                 |                       |                             |         |
| Systemic steroids                   | No              | 1398 (29.2)           | 31 (35.2)                   | 0.236   |
|                                    | Yes             | 3394 (70.8)           | 57 (64.8)                   | 3337 (70.9) |
| Remdesivir                          | No              | 2555 (53.3)           | 58 (65.9)                   | 2497 (53.1) |
|                                    | Yes             | 2237 (46.7)           | 30 (34.1)                   | 2207 (46.9) |
| Convalescent plasma                 | No              | 3362 (70.2)           | 74 (84.1)                   | 3288 (69.9) |
|                                    | Yes             | 1430 (29.8)           | 14 (15.9)                   | 1416 (30.1) |
| Chloroquine/hydroxychloroquine      | No              | 4028 (84.1)           | 70 (79.5)                   | 3958 (84.1) |
|                                    | Yes             | 764 (15.9)            | 18 (20.5)                   | 746 (15.9) |
uncommon (1.8%) and mortality was 51%. In context, mortality among ECLS patients in the ELSO Registry for COVID-19 was 37% early in the pandemic, and 52% later [2]. This is compared to 25–42% mortality for critically ill COVID-19 patients without ECLS [3]. Risk factors for death among patients with myocarditis receiving ECLS were increasing age and preexisting diabetes mellitus. These findings are consistent with previously identified mortality risk factors in non-ECLS patients with severe COVID-19 [3].

Our findings are important for a number of reasons. While within many high-income nations, high rates of vaccination have greatly reduced mortality, across the world vaccination rates remain only 60% and the pandemic is not over. Our results are the largest COVID-19 myocarditis case series using ECLS and may inform future outbreaks. Finally, we identified that risk factors for mortality among patients with myocarditis on ECLS are not different than among patients without myocarditis. In conclusion, within the largest international Registry of patients requiring ECLS circulatory support for COVID-19, mortality appears higher than for patients with COVID-19 without ECLS, but no different than those on ECLS with only acute respiratory failure.

**Abbreviations**

COVID-19: Coronavirus disease 2019; ECLS: Extracorporeal life support; ELSO: Extracorporeal Life Support Organization; AMI: Acute myocardial infarction.

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**Author contributions**

JT, RB, GM, and DB designed the study; JT, CST, KH, RB, GM, and DB conducted the study; JT and CST contributed to data acquisition and analysis; JT was involved in drafting of the manuscript; and all authors revised the article for important intellectual content and had approved the final manuscript for publication. JT had full access to the study data and takes responsibility for the data integrity, accuracy, and integrity of the submission as a whole. All authors read and approved the final manuscript.

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**Availability of data and materials**

Data were analyzed under contract from ELSO and can be requested from ELSO directly.
Declarations

Ethics approval and consent to participate
This was an analysis of fully de-identified data, which is not human subjects research and therefore did not require Institutional Review Board approval.

Consent for publication
Not applicable.

Competing interests
Dr. Tonna is the Chair-elect of the Registry Committee of the Extracorporeal Life Support Organization (ELSO). Dr. Barbaro is the ELSO Registry Chair. Dr. MacLaren serves on the board of directors for ELSO. Dr. Brodie receives research support from ALung Technologies. He has been on the medical advisory boards for Abiomed, Xenios, Medtronic, Inspira, and Cellenkos. He is the President-elect of ELSO and the Chair of the Executive Committee of the International ECMO Network (ECMONet).

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