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Mortality and Length of Stay in Patients with COVID-19 on ECMO: A Retrospective Before and After Quality Improvement Study

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MORTALITY AND LENGTH OF STAY IN PATIENTS WITH COVID-19 ON ECMO: A RETROSPECTIVE BEFORE AND AFTER QUALITY IMPROVEMENT STUDY

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Abstract

The use of extracorporeal membrane oxygenation as a supportive modality for patients with COVID-19 pneumonia emerged as the gold standard of care for those who do not respond to traditional therapies. The primary aim of this 10-month, quantitative, retrospective, quality improvement project was to identify if V-V ECMO treatment guidelines, implemented in the treatment of COVID-19 pneumonia, led to decreased mortality rates and lengths of stay. A total of 27 patients met inclusion criteria during queried time frames (n = 14 in Wave 1 and n = 13 in Wave 2). Data collected demonstrated no significant difference (p = .385) in mortality in Wave 1 and Wave 2. Length of stay was significantly longer for Wave 2 (p = .026). Statistically significant differences were identified in four clinical characteristics: inhaled vasodilator utilization (p < .001), remdesivir utilization (p = .004), days to mechanical ventilation (p = .009), and CRRT hours (p = .026). Further research is required to determine if the results of this study are comparable to larger studies with similar treatment guidelines.

Keywords: ECMO, COVID-19, mortality, length of stay

Mortality and Length of Stay in Patients with COVID-19 on ECMO:

A Retrospective Before and After Quality Improvement Study

Extracorporeal membrane oxygenation (ECMO) is a salvage therapy used in the treatment of conditions such as refractory acute respiratory distress syndrome (ARDS), septic shock, pulmonary embolism, and COVID-19. Veno-venous (V-V) ECMO is a well-established therapy for ARDS with a 77% survival rate at 90 days post discharge (Extracorporeal Life Support Organization [ELSO], 2021). Critical care experts decided that V-V ECMO might be a valuable treatment for patients with COVID pneumonia.

In the early stages of the COVID-19 pandemic, a tertiary care hospital in Northeastern United States put many patients on V-V ECMO, utilizing criteria previously outlined for traditional acute respiratory distress syndrome (ARDS) including but not limited to a Murray Score and arterial partial pressure of oxygen divided by the fraction of inspired oxygen or P/F ratio (Patel et al., 2019). The Murray Score grades the degree of lung injury in ARDS. It is calculated using four criteria, respiratory compliance, hypoxemia, level of positive end-expiratory pressure, and chest radiograph findings (Patel et al., 2019).

Despite limited evidence and treatment directions guiding the team, the mortality rates for patients with COVID who required ECMO was very high during the *first wave* at 86%. The first wave refers to any patient placed on V-V ECMO for COVID pneumonia during March 1, 2020, to July 31, 2020. The patients with COVID-19 did not respond well to V-V ECMO as an intervention.

During the first wave, ECMO cases were managed solely by a very large pulmonary critical care physician group. The group operated on a rotating schedule that often resulted in

changes in the plan of care each time a physician changed, leading to a lack of continuity of care. Additionally, not all physicians in the group were considered fully ECMO-trained by organizational standards. The challenges of variations in continuity of care and training frustrated the care team. This scenario presented the opportunity for the ECMO team to evaluate patient selection criteria, among other care delivery models specifically for COVID management. Following the first wave, outcome data was becoming available to guide patient selection, ventilator strategies, sedation recommendations, and anticoagulation therapy.

Problem Statement

The use of ECMO to treat acutely ill patients with COVID-19 is an under-researched intervention. With COVID-19 affecting many people throughout the world, research to determine the best treatments and supportive care continued through the pandemic. Ongoing research on patient selection and treatment criteria for ECMO may benefit patients, providers, and institutions. First, patients will have a defined treatment plan that may result in decreased patient mortality and length of stay. A standard treatment plan and clear patient selection criteria could also decrease complications, additional invasive procedures, ventilator days, vasopressor days, and central line days.

With clear, evidence-based ECMO for COVID-19 guidelines, members of the care team, including providers, nurses, respiratory therapists, perfusion technicians, and physical and occupational therapists, could provide more comprehensive, standardized care to this very complicated patient population (Cho et al., 2020).

Decreasing patients' mortality and complication rates may benefit the institution financially. According to ELSO (2020), the estimated cost of ECMO is $73,122. The high

mortality and cost associated with ECMO during the first wave imposed significant risk to the organization's ECMO program. Establishing standards of care could reduce care variability, therefore improving patient outcomes, decreasing length of stay, and reducing cost of care (Nagaoka et al., 2021).

In consultation with the Chief of Critical Care Medicine at the hospital, the clinical problem was noted as significant. The organization has an excellent reputation for positive outcomes for patients treated with ECMO. The hospital's survival percentages have exceeded international averages for veno-arterial (V-A) and veno-venous (V-V) ECMO since inception of the program over 10 years ago. However, the hospital's survival rate of 14.3% during the first wave of the COVID-19 pandemic was significantly lower than the international average of 62% for patients with COVID who required ECMO (Barbaro et al., 2020). Such disappointing results provide the needs assessment for this project and prompted the ECMO team to make changes and make difficult decisions about whether to offer ECMO for patients with COVID-19 prior to Wave 2.

Purpose

The overall purpose of this retrospective, quality improvement project was to determine if adult patients diagnosed with COVID-19 pneumonia and cannulated with V-V ECMO had lower mortality rates and lengths of stay after ECMO for COVID-19 treatment guidelines were initiated. The project compared mortality rates and lengths of stay in adult patients diagnosed with COVID-19 pneumonia who required ECMO. Patients with COVID-19 pneumonia that were cannulated for V-V ECMO during the first wave, outlined as March 1st, 2020, to July 31st, 2020, will be compared to patients with COVID-19 pneumonia cannulated for V-V ECMO during the second wave, outlined as November 1, 2020, to March 31, 2021.

The primary aim of this 10-month, quantitative, retrospective, quality improvement project was to identify if V-V ECMO treatment guidelines, implemented in the treatment of COVID-19 pneumonia, led to decreased mortality rates and lengths of stay. The data was obtained from the electronic medical record. The results of this before and after project will inform the development of practice standards for adult patients with COVID-19 pneumonia.

Project Question

The project questions were: What is the difference in mortality rates and lengths of stay when comparing first wave and second wave patient outcomes before and after implementing V-V ECMO COVID-19 treatment guidelines for patients with COVID-19 pneumonia?

Conceptual Definitions

The conceptual definitions for the study are as follows:

- Veno-venous extracorporeal membrane oxygenation (V-V ECMO): the placement of a bicaval dual lumen cannula to improve patients' respiratory status that allows efficient drainage from the inferior vena cava and superior vena cava, pumps unoxygenated blood through a membrane oxygenator that removes carbon dioxide and oxygenates the blood, prior to returning it through the right atrium into the tricuspid valve (MacLaren et al., 2012).
- COVID-19: severe respiratory syndrome coronavirus 2 (SARS-CoV-2), a highly contagious pathogenic viral infection diagnosed by polymerase chain reaction (PCR) nasal swab. Symptoms can include fever, cough, fatigue, shortness of breath, muscle aches, chills, sore throat, headache, nausea, vomiting, diarrhea, chest pain, and ground glass opacities seen on computed tomography (Centers for Disease Control and Prevention, 2021).

- Wave 1: period of March 1, 2020, to July 31, 2020
- Wave 2: period of November 1, 2020, to March 31, 2021
- V-V ECMO COVID-19 treatment guidelines: See Appendix B
- Patients with COVID-19: adult patients 18 years of age or greater who are critically ill with SARS-CoV-2 confirmed by PCR nasal swab or bronchoalveolar lavage (Centers for Disease Control and Prevention, 2021).

Review of the Literature

Search Strategy

The search process generated 2,093 articles from five databases: CINAHL, Cochrane Library, La Salle University's Summon, Medline, and PubMed. Keyword search terms included: extracorporeal membrane oxygenation, COVID-19, COVID pneumonia, COVID ARDS with the Boolean connector "AND". Inclusion criteria consisted of articles published between 2019-2022 and full text. Six articles met inclusion criteria (see Table 1). Utilizing the Johns Hopkins Nurse Evidence Level and Quality Guide, all six articles were appraised (See Table 2).

Appraised Studies

Chong et al. (2022) conducted a retrospective cohort study to evaluate the clinical characteristics among COVID-19 survivors and non-survivors requiring ECMO support. Through a systematic search from December 1st, 2019, to June 1St, 2021, sixteen cohort studies involving 706 COVID-19 ECMO patients were selected for assessment of clinical characteristics and complications. Selected studies met the following inclusion criteria: all research study types published in a peer-reviewed journal that compared clinical characteristics between survivors and non-survivors of COVID-19 patients requiring ECMO mechanical support, in which a COVID-19 diagnosis was made in real time utilizing reverse transcription-polymerase chain

reaction from nasopharyngeal or oropharyngeal swabs, or lower respiratory tract specimens of endotracheal secretions or bronchoalveolar lavage, and studies in a peer-reviewed journal publication. Two independent reviewers conducted data collection utilizing the Newcastle-Ottawa Scale (NOS). The longest interval of mortality was identified to determine in-hospital mortality rates at different intervals of 28-day, 30-day, 60-day, 90-day, or 180-day. Comorbidities were identified as preexisting history of coronary artery disease, hypertension, hyperlipidemia, chronic kidney disease, stroke, peripheral arterial disease, malignancy, chronic lung disease, and chronic liver disease. Bleeding was identified as pulmonary hemorrhage, hemorrhagic shock, any bleeding that required intervention or multiple blood transfusions.

The study revealed a pooled mortality rate of 40%. Findings showed that survivors were younger (mean 51 years vs 55 years; p<.001), had fewer comorbidities (23% vs 31%; odds ratio [OR] 0.55; p=.02), used less renal replacement therapy (21% vs 39%; OR 0.41; p=.007), and required less vasopressor support (76% vs 92%; OR 0.35; p=.008) compared to non-survivors. Survivors also had a higher pre-ECMO pH (mean 7.33vs 7.26; p<.001). The rate of bleeding complications was lower in survivors versus non-survivors (32% vs 59%; OR 0.36; p=.001) (Chong et al, 2022). The utilization of broad definitions of comorbidities and bleeding complications helped to address heterogeneity, a study limitation. Results indicated that advanced age, lower pre-ECMO pH, high number of renal replacement therapy hours, multiple comorbidities, vasopressor requirements and bleeding were predictors of mortality in COVID-19 ECMO patients. This conclusion will aid in the risk-benefit evaluation of placing patients with COVID-19 on ECMO.

Bertini et al. (2022) conducted a retrospective cohort study to evaluate the survival rates of patients receiving ECMO for COVID-19 and compared them to patients with influenza. A

systematic search yielded 134 studies including 4,044 patients for review and meta-analysis: 3 prospective investigations, 82 retrospective observational analysis, and 49 case reports. Six of those studies were eligible for comparative meta-analysis of COVID-19 ECMO mortality versus influenza ECMO mortality. Two independent reviewers conducted data collection utilizing the Newcastle-Ottawa Scale (NOS) with discrepancies decided by a third reviewer.

The study revealed an overall in-hospital mortality of 39% (95% CI 0.34-0.43). A secondary analysis revealed patients with COVID-19 supported with ECMO had a higher risk ratio (RR) for mortality in comparison to patients with influenza supported with ECMO: 72/164 (44%) versus 71/186 (38%) RR 1.34; CI 1.05-1.71; p = 0.03 (Bertini et al, 2022). Limitations of this systematic review were the overall heterogeneity in patients and study designs. In addition, outcome definitions for secondary outcome measurements were not described as the primary focus of this study was on mortality. Additionally, there is a risk of duplicate publication bias as it was especially challenging to detect double ECMO runs. Study results will inform the risk-benefit evaluation of placing patients with COVID-19 on ECMO.

Ling et al. (2022) conducted a retrospective cohort study to characterize changes in mortality throughout the COVID-19 pandemic and clarify risk factors for poor outcomes. A systematic search from December 1st, 2019, to January 26th, 2022, yielded 52 studies identifying 18,211 patients with COVID-19 who received ECMO mechanical support. In addition to collecting data on mortality, overall hospital and intensive care unit length of stay, ECMO duration, mechanical ventilation duration, and complications of ECMO data were collected. Three reviewers conducted data collection utilizing a prespecified data extraction form. The Grading of Recommendations, Assessments, Developments, and Evaluations (GRADE) approach was used to evaluate certainty of evidence.

The study revealed an overall in-hospital mortality of 48.8% (95% CI 44.8-52.9%). In addition, results showed that pooled P/F ratio at ECMO canulation was 72.4 (95% CI 68.8-76.0) and the pooled sequential organ failure assessment (SOFA) score was 9.24 (95% CI 8.27-10.23); the time of clinical symptoms or hospitalization to invasive mechanical ventilation initiation was 7.3 days (95% CI 4.1-10.5), and ECMO cannulation occurred after an additional 4.89 days (95% CI 4.26-5.53) of invasive mechanical ventilation (Ling et al, 2022). The utilization of the GRADE approach, the I-squared and Chi-squared test, and forest plot visual inspection were included to address potential study limitations, including heterogeneity (Ling et al, 2022). Study results will inform the risk-benefit evaluation of placing patients with COVID-19 on ECMO.

Zhu et al. (2020) conducted a retrospective cohort study to determine 90-day mortality rates for adult patients with COVID-19 who received ECMO support compared to invasive mechanical ventilation therapy alone. A systematic search yielded two randomized controlled trials (RCTs) and five observational studies for analysis totaling 867 patients. The random effects model was utilized for outcome calculation and the GRADE Guideline Development tool was utilized to assess the quality of each outcome. Two independent researchers extracted and evaluated data with discrepancies reviewed by all researchers. The quality assessments of the two RCTs were conducted using Jadad scores and the Cochrane Risk of Bias tool. The five observational studies were assessed for bias using the Newcastle-Ottawa Scale.

The study revealed that when compared with invasive mechanical ventilation alone, ECMO support significantly reduced mortality in patients with COVID-19 at 30, 60, and 90 days (based on RCT studies, RR 0.74, 95% CI 0.59-0.93, p=.01, I^2=0%, moderate quality; based on observational studies, RR 0.61 95% CI 0.46-0.81, p<.001, I^2=0%, low quality) (Zhu et al, 2020). Limitations included significant variations in criteria for initiating ECMO potentially impacting

outcomes. This limitation was mitigated by performing multiple sensitivity analysis utilizing the Sidik-Jonkman method, Biggerstaff-Tweedie method, or a fixed-effect model. Overall results were validated across various methods. The study conclusion will aid the healthcare team in the risk-benefit evaluation of placing patients with COVID-19 on ECMO.

Ramanathan et al. (2021) conducted a retrospective cohort study to provide a guide for future clinical decision-making and research for COVID-19 patients who develop severe acute respiratory syndrome (ARDS) and are mechanically supported by ECMO. In-hospital mortality was the primary outcome. Secondary outcomes consisted of duration of ECMO therapy and mechanical ventilation, weaning rate from ECMO, and complications while supported by ECMO. Complications were identified broadly as defined by ELSO guidelines. A systematic search yielded 22 observational studies with 1896 adult patients with COVID-19 mechanically supported with ECMO from December 1st, 2019, to January 10th, 2021. The random effects model was utilized for outcome calculation and the GRADE Guideline Development tool was utilized to assess the certainty of each outcome. Bias risk assessment was completed utilizing the Joanna Briggs Institute checklist. Two independent reviewers conducted data collection with discrepancies resolved by a third reviewer.

The study revealed overall in-hospital mortality for patients with COVID-19 mechanically supported by ECMO was 37.1% (95% CI 32.3-42.0%, high certainty). ECMO support duration was 15.1 days (95% CI 13.4-18.7). Weaning from ECMO was accomplished in 67.6% (95% CI 50.5-82.7%) of patients. A total of 1583 ECMO complications were reported (18 studies, 1721 patients) and renal complications were the most common (Ramanathan, 2021). Longer ECMO duration was associated with increased mortality. Limitations included significant variations in criteria for the initiation and maintenance of ECMO potentially

impacting outcomes. Despite these limitations, the study concluded that V-V ECMO appears to be an effective intervention for carefully selected patients with COVID-19 (Ramanathan, 2021).

Smith et al. (2022) conducted a single-center retrospective cohort study to evaluate COVID-19 V-V ECMO survival to discharge and 1-year-follow-up data for patients who were successfully discharged from the hospital. The study reviewed all patients with severe COVID-19 infections who were mechanically supported by VV ECMO from March 10th, 2020, to May 1st, 2020. Thirty patients were evaluated, selected, and managed by a multidisciplinary ECMO team. Management strategies included frequent bronchoscopy, early tracheostomy, and the use of prone positioning during ECMO. Survival to discharge was the primary outcome of this study and 1-year follow up data were also reported.

This review revealed that of the 30 patients with COVID-19 supported with V-V ECMO, 27 survived to discharge (90% survival rate). All living patients were discharged home or to an acute rehabilitation facility on room air except for one patient (3.7%). Median follow-up of 10.8 months (interquartile range [IQR], 8.9-14.4 months since ECMO cannulation showed survival of 86.7% (includes one patient who underwent lung transplant). Forty-four percent (12/27) had pulmonary function testing with a median percent predicted forced expiratory volume of 100% (IQR, 91-110%). Six-minute walk test was performed in 59.3% (16/27), median value of 350 m (IQR, 286-379 m) (Smith et al, 2022). Limitations of this study include the lack of randomization to ECMO versus traditional medical therapy among patients with severe COVID-19. The study concluded that with proper patient selection and aggressive management strategies, the use of VV ECMO mechanical support can result in increased survival rates. The results of this study will not only aid in the patient selection process but also the management of patients with severe COVID-19.

Supady et al. (2021) conducted a retrospective non-interventional international multicenter registry study of patients with COVID-19 treated with V-V ECMO to evaluate the performance of several clinical scores to predict 30-day survival. The study reviewed 127 patients treated with V-V ECMO across 15 hospitals across Switzerland, Italy, Germany, Belgium, and the United States. Calculated clinical predictor scores included the Sequential Organ Failure Assessment (SOFA) score, Simplified Acute Physiology Score II (SAPS II), Acute Physiology and Chronic Health Evaluation II (APACHE II) Score, Respiratory Extracorporeal Membrane Oxygenation Survival Prediction (RESP) Score, Predicting Death for Severe ARDS on V-V ECMO (PRESERVE) Score, and 30-day survival. Data was analyzed using GraphPad Prism 8 (GraphPad Software, San Diego, CA, USA). A limitation to this study design is that it was a single-arm retrospective multicenter registry so there was no way to compare results to a control group. Additionally, the overall number of patients included in the study was rather low which could limit the power of the results (Supady et al.,2021)

This study revealed that overall 30-day survival was 54%. Median age was 59 years, 21.3% (27/127) of the sample was female, and median body mass index (BMI) was 29 kg/m². Median SOFA, SAPS II, APACHE II, RESP, and PRESERVE Scores were 9, 36, 17, 1, and 4, respectively (Supady et al., 2021). The area under the receiver operating characteristic (AUROC) was used to determine prognostic accuracy with scores ranging from 0.548 and 0.605. The researcher concluded that although these scores are excellent additional tools to be used in the evaluation of prognosis, the scores themselves cannot independently utilized to guide treatment decisions for patients with severe COVID-19 ARDS undergoing V-V ECMO (Supady et al., 2021).

A retrospective, multicenter study was conducted by Saeed et al. (2022) to determine if cannulation method for V-V ECMO is related to patient outcome. The study included patients 18 years of age or older who required V-V ECMO for severe respiratory failure due to COVID-19 pneumonia between March 1, 2020, to April 30th, 2021. A total of 435 patients were included in the cohort from 17 centers. Patients were divided into three groups based on initial method of cannulation: (1) single, dual-lumen cannula in internal jugular vein with tip positioned in the inferior vena cava (C-IVC), (2) single, dual-lumen cannula in internal jugular vein with tip positioned int eh pulmonary artery (C-PA), and (3) femoral vein-femoral vein or femoral vein-internal jugular vein (dual-site, C-DS). Data was collected using REDCap. Study limitations included a lack of standardized criteria for patient selection, cannulation method, and/or clinical management among the participating centers (Saeed et al., 2022).

Study results included that C-DS was performed in 247 cases (57%, age: 49, IQR: 39-57 years; 30% female), C-PA was performed in 99 cases (23%, age: 53, IQR: 42-59 years; 26% female), and 89 patients (20%) received C-IVC (age 46, IQR: 35-54; 33% female) (Saeed et al., 2022). Additional results included 90-day, in-hospital mortality was 60% (C-DS), 41% (C-PA), and 61% (C-IVC), $p = 0.06$. With an adjustment for clinical characteristics, the in-hospital mortality likelihood in comparison to C-DS was lower with C-PA (aHR:0.52, 95% CI 0.32-0.85, $p = 0.009$) and similar with C-IVC (aHR: 0.96, 95% CI 0.63-1.47, $p = 0.86$) (Saeed et al., 2022). This retrospective, multicenter study concluded the utilization of catheter directed flow into the pulmonary artery bypassing the right ventricle with a single dual-lumen cannula is associated with reduced mortality in patients with COVID-19 undergoing V-V ECMO.

Related Literature

Puslecki et al. (2021) conducted a narrative literature search on nursing care of patients with COVID-19 who were supported mechanically by ECMO. The purpose of this evaluation was to develop a Standard Operating Procedure (SOP) for clinicians caring for patients with COVID-19 on ECMO. A translational simulation was conducted to assist in identifying challenges and opportunities in the care of ECMO patients. The simulation was developed and facilitated by two trainers, in an isolated intensive care room in the Centre of Medical Simulation, Poznan University of Medical Sciences. Two intensive care nurses, one perfusionist, an intensivist, and a cardiac surgeon conducted the simulation utilizing a high-fidelity Laerdal 3G SimMan with an artificial vessel loop. Supplementary equipment included an invasive mechanical ventilator, a vital sign monitor, infusion pumps, an ECMO pump and ECMO circuit setup. The attendees were provided with a series of various clinical scenario simulations that occurred over nine hours. Following the simulation, three hours were spent debriefing on the various scenarios.

Based on author clinical experience, expert consultations, and the translational simulation, the team identified three areas requiring improvements, and developed innovations for those areas. Those areas were (1) work organization, (2) daily nursing care and management of COVID-19 ECMO patients, and (3) ECMO cannulation and related procedures (Puslecki et al, 2021). The researchers determined the most impactful aspects of nursing care and management of COVID-19 ECMO patients were non-technical in nature and consisted of effective communication, trust within team members, checklist usage, and dedicated training. Limitations of this study included the challenges associated with duplicating the simulation and SOP. This would only be possible in similar centers with similar organizational structures. Formal

evaluation of the SOP proposals did not occur due to constraints created by the COVID-19 pandemic itself. The conclusions and recommendations of this study could impact patient selection, competency training, and organizational preparedness in providing ECMO support.

A case study presented by Voicu et al. (2021) describes the clinical course of a 39-year-old patient diagnosed with severe COVID-19 ARDS pneumonia causing complete alveolar consolidation and airway closure for several weeks. In addition to the standard treatment of immunomodulatory drugs and dexamethasone, V-V ECMO was utilized. Special attention was given to compliance, plateau pressure, and ventilatory management of this patient given the complete alveolar consolidation. Utilizing computed tomography imagining and a ventilator airway pressure curve analysis, the patient's ventilatory pattern was monitored very closely. Ventilator changes were made frequently to support the rapid changes in lung function and compliance. The patient exhibited extremely low compliance of 2.5ml/cm H_2O for approximately 35 of the 71 days of V-V ECMO.

After multiple complications, the patient was weaned from V-V ECMO on hospital day 75, liberated from mechanical ventilation on hospital day 95, and weaned from oxygen on hospital day 99. The patient was discharged from the hospital on day 113. This case study shows the importance of closely monitoring lung compliance and plateau pressure, as well as adapting ventilator settings to the physiologic status of the lung. Prolonged treatment with V-V ECMO may be associated with survival and complete pulmonary recovery.

Summary

Systematic reviews and meta-analyses were most prevalent in the review of literature. Due to the ever changing and challenging climate of the COVID-19 pandemic, most studies were retrospective cohort studies with a heavy focus on ELSO registry data. Study researchers

commonly expressed the premature nature of making detailed definitive recommendations for ECMO support in the COVID-19 patient population. Researchers identified the following common factors contributing to higher mortality rates in the COVID ECMO patients: increased age, multiple comorbidities, increased ECMO duration, and increased duration of renal replacement therapy while on ECMO support. The literature highlighted factors which contributed to higher mortality but ultimately, did not support specific patient selection criteria or standard practices for clinical management of patients with COVID-19 who required ECMO. The research studies reviewed by this researcher concluded that more research is needed to validate early recommendations for clinical management of COVID-19 ECMO patients.

The major gap in the literature is due to the extremely short amount of time ECMO support has been utilized for COVID-19. Being that COVID-19 appeared globally less than three years ago, little is understood about the virus itself and its subvariants. The primary research focus has been on pharmacological interventions and vaccination development. ECMO support for patients with COVID-19 requires dedicated research to develop foundational clinical guidelines.

Conceptual Model

Donabedian's Health Care Quality Model (2005) was developed by Avedis Donabedian, a professor of medical care organization at the University of Michigan School of Public Health, in 1966 (Ayanian & Markel, 2016). The Donabedian Model consists of three main constructs: structure, process, and outcome (Ayanian & Markel, 2016). These three constructs are utilized to evaluate the quality of health care provided by health care institutions.

Structure is identified as the setting in which the care is provided, provider qualifications, material resources, organizational structure, and administrative systems. Process is identified as

the components of care provided including but not limited to diagnosis, diagnostic testing, treatment, and how patients move through the continuum of care to discharge. Outcome consists of the effects of structure and process on patients and specific patient populations. Examples of outcomes are mortality and morbidity statistics, surgical site infection rates, patient satisfaction scores, and social restoration to baseline health (Ayanian & Markel, 2016). This theory's foundation is rooted in asking the question *What goes on here?* (Ayanian & Markel, 2016). Understanding the constructs of how care is provided is vital to understanding how care can be streamlined and improved. Within Donabedian's Model, the assumption is made that given the proper settings and instrumentalities, good medical care will follow.

Donabedian's Health Care Quality Model is applicable to this scholarly project because this model provides a framework to evaluate quality of care with the intent of improving mortality and morbidity. Based on limited clinical management guidelines available prior to wave one, V-V ECMO for COVID pneumonia should have yielded better patient outcomes. The survival rate of 9% requires a thorough evaluation of current process and care guidelines. Therefore, Donabedian's Health Care Quality Model was utilized as the conceptual model for this scholarly project.

Design

According to Polit and Beck (2017), a retrospective design begins with the manifestation of the outcome in the present, followed by a search for a presumed cause occurring in the past. This quantitative, retrospective, before and after quality improvement project compares mortality rates and lengths of stay in critically ill adult patients treated with ECMO during the first wave (March 1, 2020, to July 31, 2020) and second wave (November 1, 2020, to March 31, 2021)

periods. The data sources are the mortality rates and lengths of stay obtained during a review of the tertiary care hospital's electronic medical record (EMR).

Sample and Setting

The sample included the EMRs of adult patients diagnosed with COVID-19 and who required ECMO mechanical support admitted to a single tertiary-care intensive care unit in Northeast Pennsylvania. Patients' records were extracted from the inpatient EMR based on a principle International Classification of Disease, tenth edition (ICD-10) code of U07.1, COVID-19. Data was then filtered by adult participants with ICD-10 code Z92.81, ECMO. Additional filters were utilized to include only participants with COVID-19 on ECMO during Wave 1 and Wave 2. ECMO during these two timeframes were included in the study. Incarcerated persons and pregnant patients were excluded from this study.

Ethical Considerations

The Institutional Review Boards (IRBs) of Lehigh Valley Health Network and La Salle University were asked to review the study. Lehigh Valley Health Network will be the primary IRB, and La Salle University's IRB will be the secondary. There is no immediate risk to patients as this is a retrospective study. The Research Department at Lehigh Valley Health Network determined this project did not meet the regulatory requirements for human subject research as defined by 45 CFR 26.102(d). As such, IRB review and approval is not required (see Appendix A).

Data was known to the project director (PD), the Chair of the project team, project committee members at La Salle University, an external statistician, and the preceptor at Lehigh Valley Health Network. Upon completion of data interpretation, data files were destroyed as

outlined by Lehigh Valley Health Network's IRB. This study abided by all legal and ethical requirements, with special consideration for study participant privacy, as outlined by the Health Insurance Portability and Accountability Act (HIPAA) of 1996. The potential benefits of this research outweigh the risks, as the risk associated with this retrospective chart review are minimal. A potential benefit of this research is the development of comprehensive V-V ECMO treatment guidelines for patients with COVID-19 pneumonia which could reduce in-hospital mortality.

Instrumentation

A data collection form was created to document patients' data (see Appendix C). Wave one and wave two data have been differentiated. Demographic data included age, gender, diagnosis, days to invasive mechanical ventilations, number of hours on neuromuscular blockade (NMBA), number of hours on vasopressors, number of hours in the prone position, use of inhaled vasodilators, days to ECMO cannulation, pre-ECMO pH and P/F ratio, number of days requiring ECMO support, complications, and survival to discharge. Complications have been recorded following the broad guidelines of Extracorporeal Life Support Organization (ELSO). These included renal failure, bleeding that required blood transfusion or procedural intervention, and hospital acquired infections (ELSO, 2021).

Procedures for Data Collection

Following the determination from Lehigh Valley Health System's Research Department (see Appendix A), data was collected from the EMR. The data collection form (see Appendix C) was used to record demographic, ECMO, mortality rates, and lengths of stay for patients treated during Wave 1 and Wave 2. The PD retrieved data through inpatient EMRs by selecting medical

record numbers (MRN). REDCap, a password-protected survey tool was utilized to collect deidentified data and downloaded to Microsoft Excel and IBM Statistical Package for the Social Sciences (SPSS) version 28 licensed by La Salle University. The data file and results were stored on the organization's password-protected computer system in the event of data loss within the REDCap system.

Data Analysis Methods

IBM SPSS version 28 software was utilized for statistical analysis. Descriptive statistics were calculated on demographic data and ECMO data for Wave 1 and Wave 2 and displayed in a table. The inferential statistical test, Chi Square, was utilized to compare Wave 1 and Wave 2 (independent variable) by mortality (dependent variable) frequencies. The inferential test, T-test, was used to compare Wave 1 and Wave 2 (independent variable) lengths of stay (dependent variable). A chi-square test was conducted when comparing differences in categorical variables and a T-test was utilized to compare a categorical variable (Wave 1 or Wave 2) with a continuous variable. The T-test results were displayed in a table**.** The significance levels for the Chi Square and T-Test were set at 0.05 and confidence interval for the T-Test was set at 0.95.

Results

A total of 28 patients were identified as receiving ECMO for COVID-19 during Wave 1 and Wave 2. Of the 28 patients, one patient was excluded due to incarceration status. Ultimately, there were 27 patients total who met inclusion criteria during queried time frames (n = 14 in Wave 1 and n = 13 in Wave 2). Table 1 offers a summary of the descriptive statistics. In both Wave 1 and Wave 2, most patients were male. Inhaled vasodilator use and remdesivir use were significantly different between Wave 1 and Wave 2 with higher use of remdesivir in Wave 2 ($p = .004$) and higher use of inhaled vasodilators in Wave 1 ($p < .001$). Days to mechanical ventilation

was significantly shorter for Wave 1 than Wave 2 (p = .009). CRRT hours was another variable with a significant difference between groups (p = .026).

Table 1

Patient Demographics and Clinical Characteristics

Variable	Wave 1 (n = 14)		Wave 2 (n = 13)	
	n	*%*	*n*	*%*
Gender				
Male	12	85.71%	11	84.62%
Female	2	14.29%	2	15.38%
Unvaccinated	14	100%	13	100%
Use of remdesivir*	5	35.71%	12	92.31%
Use of immune modulators	2	14.29%	6	46.15%
Inhaled vasodilator use**	12	85.71%	2	15.38%
Renal failure	7	50%	6	46.15%
Bleeding that required blood transfusion	13	92.86%	12	92.31%
Hospital acquired infection	7	50%	10	76.92%
	M	*SD*	*M*	*SD*
Age (years)	52.7	8.9	54.5	7.9
Body Mass Index	33.1	7.3	32.4	6.3
Days to mechanical ventilation (hospital day)***	6.1	4.0	10.6	4.3
Pre-ECMO pH	7.3	0.1	7.3	0.2
Days to ECMO cannulation (hospital day)	10.0	3.6	13.2	5.1
Days to ECMO de-cannulation (hospital day)	20.7	6.0	34.8	10.9
Days to liberation from mechanical ventilation (hospital day)	48.5	0.7	52.3	18.0
Paralytic use (hours)	300.6	185.5	356.0	380.1
Vasopressor use (hours)	479.2	242.7	591.0	479.8
Prone positioning (hours)	133.6	258.4	50.2	53.8
Inhaled vasodilator use (hours)	221.8	172.7	197.5	37.5
CRRT (hours)****	141.3	155.0	688.3	542.4
Blood transfusion (number of units transfused)	10.3	16.4	22.8	15.5

Note. ECMO = extracorporeal membrane oxygenation; CRRT = continuous renal replacement therapy. * $p = .004$. ** $p < .001$. *** $p = .009$. **** $p = .026$.

To examine mortality, a chi-square test was conducted comparing Wave 1 and Wave 2 mortality rates in the hospital. The results show no significant difference in the mortality in hospital in Wave 1 (n = 12, 85.7%) and Wave 2 (n = 9, 69.2%), X2 (1, N = 27) = 1.06, p = .385. All six patients that were alive at discharge were also alive at 6 months post discharge. An independent samples t-test was conducted to compare length of stay for Wave 1 and Wave 2 patients. Length of stay was significantly longer for Wave 2 with an average of 54.2 days (SD = 22.3) compared to 33.6 (SD = 22.7) in Wave 1, p = .026.

Discussion

Length of stay was significantly longer for Wave 2 with an average of 54.2 days (SD = 22.3) compared to 33.6 (SD = 22.7) in Wave 1, p = .026. Although clinical data suggests patients in Wave 2 were more acutely ill than patients in Wave 1 with more hours requiring vasopressors and CRRT, and requiring more blood transfusions, the length of stay was significantly longer. This could be attributed to providers having a better understanding of how to medically manage patients with COVID-19 who required ECMO. New guidelines and recommendations were being released more frequently in the Wave 2 timeframe and in the few weeks prior to the start of Wave 2. Although the difference in mortality was not statistically significant from Wave 1 (n = 12, 85.7%) to Wave 2, (n = 9, 69.2%), the decrease suggests guidelines implemented in Wave 2 could have had a positive impact on mortality as the reviewed literature suggests.

Significant differences were observed in four clinical characteristics between Wave 1 and Wave 2. Remdesivir and immunomodulators were not widely available during Wave 1. The Emergency Use Authorization (EAU) and recommendation to utilize remdesivir was not issued until May 1st, 2020, with full approval from the Federal Drug Administration (FDA) on October 22nd, 2020 (FDA.gov, 2020); this most likely accounts for its increased use in Wave 2. In

addition, days to mechanical ventilation were significantly less in Wave 1 when compared to Wave 2. Early in the pandemic providers had less knowledge of appropriate ventilator management for patients with COVID-19. In Wave 1, providers had a lower tolerance for low oxygen saturation; intubating quickly when patients had a sustained oxygen saturation of 88% or less, therefore, contributing to the shorter duration to mechanical ventilation. In Wave 2, non-invasive ventilation was utilized more aggressively and pre-ECMO oxygen saturations as low as 75% were tolerated if the patient exhibited appropriate mentation. This resulted in mean of a 4.5-day difference to initiation of mechanical ventilation between Wave 1 and Wave 2.

Another statically significant difference was noted in the utilization of inhaled vasodilators (n = 12 in Wave 1 and n = 2 in Wave 2). This could be an indication of more selective and consistent use of inhaled vasodilators in Wave 2. In Wave 1, five of twelve patients (41.6%) that received inhaled vasodilators had multiple initiations and discontinuations of the medication, and only one patient (8.3%) whose inhaled vasodilator was discontinued within 24 hours of ECMO cannulation. Per Wave 2 guidelines, inhaled vasodilators were to be administered until ECMO was initiated, and then weaned off within 24 hours of ECMO cannulation. Of the two patients who received inhaled vasodilators in Wave 2, both only had one initiation and one discontinuation and, with both discontinuations occurring within 24 hours of ECMO cannulation. Another factor that could have impacted inhaled vasodilator utilization is the consistent ventilator management strategy implemented in Wave 2. Per Wave 2 guidelines, ventilator management included: wean current settings down to either pressure control, 10cm H_2O positive end-expiratory pressure (PEEP), 10mL tidal volume (V_t), respiratory rate (RR) of 10 breaths per minute, and 0.4 fraction of inspired oxygen (FIO_2) or assist control ventilation with plateau pressure ≤ 25mLs per cm H_2O, 10 cm H_2O PEEP, RR of 10 breaths per minute.

Patients with a conservative, lung-protective ventilation strategy may have improved oxygenation, thus reducing the need to initiate inhaled vasodilators (Cho et al., 2022).

The fourth clinical characteristic with a statistically significant difference was number of CRRT hours. Although the number of patients who required CRRT were similar in Wave 1 (n = 7, 50%) and Wave 2 (n = 6, 46%), the number of CRRT hours was 4.87 times greater in Wave 2 than Wave 1. This could be attributed to the overall longer length of stay for patients in Wave 2 versus Wave 1.

The treatment guidelines implemented in Wave 2 were controversial amongst the large health care team who cared for patients during Wave 1, although developed from the recommendations of the Extracorporeal Life Support Organization. The change in ventilator management caused considerable controversy amongst respiratory leadership and pulmonary critical care leadership. It took just over six weeks to come to an agreement on the new guidelines. Despite unconventional ventilator and sedation management, mortality did in fact decrease. The decrease in mortality, although not statistically significant, is consistent with the literature suggesting a clearly defined management strategy of V-V ECMO support in patients with severe COVID-19 can result in increased survival (Smith et al., 2022). The literature also suggests early initiation of V-V ECMO is associated with improved outcomes in patients with COVID-19 (Kuriahra et al., 2021). This study supports this as the average time from initiation of mechanical ventilation to initiation of V-V ECMO was 4.07 days in Wave 1 compared to 2.54 days in Wave 2, potentially contributing to a lower mortality in Wave 2.

Limitations

A limitation of this study is the small sample size. This limitation was anticipated due to the strict inclusion criteria of patients with COVID-19 who required ECMO during a 10-month

time frame. Furthermore, not all treatment options such as Remdesivir and immune modulators were readily available during Wave 1 when compared to Wave 2. Additionally, the study was conducted in a small single unit at one research site, limiting the ability to generalize the recommendations to other health systems who perform ECMO.

Conclusion

The primary aim of this 10-month, quantitative, retrospective, quality improvement project was to identify if V-V ECMO treatment guidelines, implemented in the treatment of COVID-19 pneumonia, led to decreased mortality rates and lengths of stay. Although not statistically significant, mortality decreased from 85.7% to 69.2% with the implementation of standard treatment guidelines. Length of stay was significantly longer for Wave 2 with an average of 54.2 days (SD = 22.3) compared to 33.6 (SD = 22.7) in Wave 1, $p = .026$. This could have been attributed to providers having a better understanding of how to medically manage patients with COVID-19 who required ECMO, and therefore stabilizing them for longer periods of time.

The results of this study could potentially set the foundation for a treatment standard for patients with COVID-19 who require ECMO. Further research is required to determine if the results of this study are comparable to larger studies with similar treatment guidelines. ECMO is a salvage therapy that is typically only utilized in those patients with a high risk of mortality; therefore, careful patient selection and high standards of care should be the priority of the care team (Nagaoko et al., 2021). The results of this study will be shared with ECMO team to further prepare for additional patients with COVID-19 who require ECMO.

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Appendix A

Lehigh Valley Health Network

IRB/RPPO
1255 S. Cedar Crest Blvd.
Suite 3200
Allentown, PA 18103

NOT HUMAN RESEARCH DETERMINATION

November 18, 2022

IRB00001409 (IRB1) registered under FWA #00000624

Chantal Branco
X1923@lvh.com

Dear Chantal Branco:

On 11/18/2022, the IRB reviewed the following submission:

Type of Review:	Initial Study
Title of Study:	HSRD: Mortality and Length of Stay in Patients with COVID-19 on ECMO: A Retrospective Before and After Quality Improvement Study
Investigator:	Chantal Branco
IRB ID:	STUDY00001199
Funding:	None
Grant ID:	None
IND, IDE, or HDE:	None
Documents Reviewed:	• HSRD-COVID ECMO, Category: IRB Protocol

The IRB determined that, as submitted, the project referenced above does not meet the regulatory requirements for human subject research as defined by 45 CFR 26.102(d). As such, IRB review and approval is not required.

This determination applies only to the activities described in the IRB submission and does not apply should any changes be made. If changes are being considered and there are questions about whether IRB review is needed, please submit a study modification to the IRB for a determination. You can create a modification by clicking Create Modification / CR within the study.

Sincerely,

Karla Cressman, BS, CCRP
Manager, Office of Research Integrity

Appendix B

COVID-19 ECMO Guidelines

(Adapted from ELSO guidelines for ECMO in COVID-19)

(ECMO Working Group, personal communication, October 2020)

Respiratory

- Ventilator plan: Wean current settings down to either pressure control, 10cm H_2O positive end-expiratory pressure (PEEP), 10mL tidal volume (V_t), respiratory rate (RR) of 10 breaths per minute, and 0.4 fraction of inspired oxygen (FIO_2) or assist control ventilation with plateau pressure ≤ 25mLs per cm H_2O, 10 cm H_2O PEEP, RR of 10 breaths per minute
- Decrease partial pressure of carbon dioxide (pCO_2) by ~ 10mm of mercury per hour if pCO_2 was ≥ 90mm of mercury via sweep gas settings on ECMO circuit
- Wean off inhaled vasodilators within first 24 hours or less of ECMO cannulation
- Goal oxygen saturation ≥ 85%
- Perform tracheostomy within 3 days of ECMO cannulation

Sedation

- Discontinue paralytic infusion within 12 hours of ECMO cannulation
- First line: propofol
- Second line: dexmedetomidine hydrochloride
- Avoid the use of benzodiazepines
- Avoid the use of narcotics with the exception to assist with decreasing work of breathing
- If work of breathing is high, goal pH 7.45-7.50)
- Using Richmond Agitation Sedation Score (RASS), wean sedation to RASS 0 to -1

- Start quetiapine within 48 hours of cannulation

Perfusion

- start ECMO flow 50-80ml/kg/min of ideal body weight
- Cannulation Strategy – single, dual lumen cannula in internal jugular vein with tip positioned in the pulmonary artery
- Initiate pressure monitoring at drainage cannula
- Calculate oxygen uptake using pre-oxygenator saturation, post-oxygenator saturation and hemoglobin

Anticoagulation

- Target partial thromboplastin time (PTT) 50-90 seconds, if there is no need for anticoagulation for another reason such as pulmonary embolism or atrial fibrillation

Continuous Renal Replacement Therapy (CRRT)

- Run independently from the ECMO circuit
- Only use ECMO circuit if unable to obtain hemodialysis access

Appendix C

Data Collection Tool

1. MRN:
2. Participant Identifier:
3. Gender: Male Female Non-binary
4. Age:
5. Date/Time of Admission:
6. Length of Stay:
7. BMI:
8. Vaccine Status (if yes, date of vaccine):
9. Use of Remdesivir: Yes No
10. Use of Immune Modulators (Barcitinib, Tocilizumab): Yes No
11. Date of/Days to Invasive Mechanical Ventilation:
12. Pre-ECMO pH:
13. Pre-ECMO P/F ratio:
14. Date of/Days to ECMO Cannulation:
15. Date of/Days to ECMO De-Cannulation:
16. Date of/Days to Liberation from Invasive Mechanical Ventilation:
17. Number of Hours on Paralytic:
18. Number of Hours on Vasopressors:
19. Number of Hours in the Prone Position:
20. Use of Inhaled Vasodilators: Yes No
    a. If yes, for how long? (# of hours)

21. Complications

    a. Renal failure: Yes No

        i. If yes, did the patient require dialysis and for how long?

    b. Bleeding that required blood transfusion or procedural intervention: Yes No

        i. If yes, how many units of blood did the patient receive?

    c. Hospital acquired infections: Yes No

22. Survival to Discharge from hospital (primary measure of mortality): Yes No

23. Survival to 6 months post discharge: Yes No

Table 2

Search Process Review of Literature

N					
Database	Total Articles	Articles Remaining After Title Review	Articles Remaining After Abstract Review	Articles Retrieved and Examined	Articles that fit Inclusion Criteria
Cochrane Library	0				
Summon	694	80	24	16	4
CINAHL	277	94	61	29	1
Medline	810	0			
PubMed	312	50	47	20	1

Table 3

Review of Literature Matrix Systematized Review

Database # Article First Author, Year (full citation in References)	**Purpose of Study** **Major Variables (IV, DV) or Phenomenon**	**Theory or Conceptual Framework**	**Design**	**Measurement Major Variables (Instrument)**	**Data Analysis (Name of Statistics, descriptive, Inferential and Results)**	**Findings**	**Evidence Level of Research & Quality Johns Hopkins Nursing Evidence-Based Practice**
Summon #1 Chong, 2022	Compare the clinical characteristics between COVID-19 survivors and non-survivors requiring ECMO support	None	Retrospective Cohort study	Data was retrieved from multiple databases (Pubmed, Cochrane, Embase, Scopus, & Web of Science)	Dichotomous variables were assessed using the Mantel-Haenszel statistical method and measured in odds ratios (ORs). Difference in continuous variables was evaluated by the inverse variance (IV) statistical method and measured in standard mean difference	16 cohorts involving 706 COVID-19 patients requiring ECMO support with a pooled mortality rate of 40% included. Younger age (mean 51 years vs 55 years; p<.001), fewer comorbidities (23% vs 31%; odds ratio [OR] 0.55; p=.02), less renal replacement	III-A

					(SMDs). Using DerSimonian and Laird's random-effects model, pooled ORs, SMDs, and 95% confidence intervals (CIs) were calculated, and extracted outcomes were pooled by weighted averages.	therapy (21% vs 39%; OR 0.41; p=.007), & vasopressor support (76% vs 92%; OR 0.35; p=.008) were demonstrated in survivors vs. non-survivors. Survivors also had a higher pre-ECMO pH (mean 7.33vs 7.26; p<.001). Rate of bleeding complications was lower in survivors vs non-survivors (32% vs 59%; OR 0.36; p=.001).	
Summon #2 Bertini, 2022	To analyze survival rates of COVID ECMO patients & compare with survival rates of influenza ECMO patients	None	Retrospective cohort study	Data was retrieved from multiple databases (Cochrane, MEDLINE/PubMed, EMBASE)	Inverse variance method (95% CI) was utilized to examine the rates of primary & secondary outcomes in VV ECMO for COVID-19. Random effects model (meta, metafor, demtar	ECMO was used in 4,044 patients with an in-hospital mortality of 39% (95% CI 0.34-0.43). COVID ECMO patients had higher risk ratio (RR) for mortality than influenza COVID patients: 72/164	III-A

					packages for R and R-Studio Version 1.3 for macOS) to reduce type II errors.	(44%) vs 71/186 (38%) RR 1.34; 95% CI 1.05-1.71; p=0.03. ECMO could be beneficial for COVID-19	
Summon #3 Ling, 2022	To provide updated mortality rates in patients with COVID-19 mechanically supported with ECMO and clarify risk factors for poor outcomes	None	Retrospective cohort study	Data was retrieved from multiple databases (MEDLINE, Embase, Cochrane, Scopus)	Random-effects meta-analyses (DerSimonian & Laird) based on logit transformation, computed confidence intervals (CI) suing Clopper-Pearson method	52 studies comprising of 18,211 patients with a pooled mortality rate of 48.8% (95% CI 44.8-52.9%, high certainty)	III-A
Summon #4 Zhu, 2021	To provide 90-day mortality patients with COVID-19 mechanically supported by ECMO	None	Retrospective cohort study	Data was retrieved from multiple databases (EMBASE, Medline, Cochrane Library, Web of Science, Wanfang databases, & CNKI)	Random-effects model used for outcome calculation. Mantel-Haenszel model was used to assess heterogeneity. GRADE Guideline Development tool was utilized to assess quality of each outcome.	Compared with mechanical ventilation alone, ECMO therapy significantly reduced the mortality at 90 days (based on RCT studies, RR 0.74, 95% CI 0.59-0.93, p=.01, I^2=0%, moderate quality; based on observational studies, RR 0.61 95% CI 0.46-0.81,	III-A

						p<.001, I^2=0%, low quality) & at 30 & 60 days	
PubMed #1 Ramanathan, 2021	To provide a guide for future clinical decision-making and research for COVID-19 patients mechanically supported by ECMO	None	Retrospective cohort study	Data was retrieved from multiple databases (Medline, EMBASE, Cochrane, Scopus)	Inverse-variance weighted random-effects analysis (DerSimonian & Laird) and 95% CI were computed using Clopper-Pearson method	22 observational studies with 1896 patients. Pooled in-hospital mortality was 37.1% (95% CI 32.3-42.0%, high certainty). Age and ECMO duration were associated with increased mortality. ECMO support duration was 15.1 days (95% CI 13.4-18.7). Weaning from ECMO was accomplished in 67.6% (95% CI 50.5-82.7%) of patients. A total of 1583 ECMO complications were reported (18 studies, 1721 patients) & renal complications were the most common.	III-A

CINAHL #1 Smith, 2022	To provide data to show COVID-19 ECMO survival to discharge and 1-year-follow-up data for patients who were successfully discharged from the hospital	None	Single-center retrospective cohort study	Retrospective review of all patients with severe COVID-19 who were cannulated for V-V ECMO between March10th, 2020 and May 1st, 2020.		30 patients with COVID-19 were supported with V-V ECMO, 27 of whom survived to discharge. All were discharged home or to acute rehab on room air with the exception of 1 patient (3.7%). Median follow-up of 10.8 months (interquartile range [IQR], 8.9-14.4 months since ECMO cannulation showed survival of 86.7% (includes 1 patient who underwent lung transplant). 44.4% (12/27) had pulmonary function testing with a median percent predicted forced expiratory volume of 100% (IQR, 91-110%). 6-minute walk test	III-A

						was performed in 59.3% (16/27), median value of 350 m (IQR, 286-379 m)	