

## Rapid Review Report

<b>Review Title:</b>	What are the outcomes of ECMO and COVID, particularly in small centers?
<b>Abbreviated Title:</b>	ECMO for COVID-19
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### Key Findings

- Overall, data are insufficient to recommend for or against the use of ECMO in patients with COVID-19 and refractory hypoxemia.
- The best available evidence points to an overall combined mortality rate of 46% among COVID-19 patients placed on ECMO (n=331). This rate is similar to the overall 40% mortality rate for extracorporeal life support in pulmonary failure. However, mortality rates among COVID-19 patients on ECMO range widely due to patient factors, site specific factors, and small sample sizes in available studies.
- Recommendations for strategies and patient indications/contraindications are available to help guide centres intending to offer ECMO to COVID-19 patients.

### Limitations

- Much of the evidence around the use of ECMO for COVID-19 patients is limited to small trials, mostly retrospective studies, at single centres throughout the world. This makes it difficult to compare patient factors and outcomes across sites.
- There are numerous review papers available on this topic, but all are limited by the same pool of source studies. Thus, recommendations often stem from



expert opinion and/or local experiences using ECMO early on in the pandemic.

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**GRADE of Evidence: C - Low**

A grade of "C" is assigned when further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate. The review may consist of one or more studies with severe limitations.

*For more information about how this rating was determined, visit [https://www.essentialevidenceplus.com/product/ebm\\_loe.cfm?show=grade](https://www.essentialevidenceplus.com/product/ebm_loe.cfm?show=grade)*

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## **Background/Context**

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Extracorporeal membrane oxygenation (ECMO) is a resource-intensive approach to managing severe respiratory failure (1). ECMO can be further subdivided into venovenous (VV-) and veno-arterial (VA-) ECMO, which differ in that the latter is normally used for patients with cardiac/circulatory failure with or without respiratory failure (1). VV-ECMO is indicated for patients with severe hypoxemic respiratory failure which is refractory to mechanical ventilation with optimal positive end expiratory pressure, neuromuscular blockade, and prone positioning (1).

### ***Purpose***

Due to the resource-intensive nature of ECMO, the limited resources and capacity in Saskatchewan's intensive care units, and the looming threat of a surge in COVID-19 cases, questions have been posed regarding whether ECMO has been shown to be beneficial for COVID-19 patients, whether there are specific criteria that should be met for patients to qualify for ECMO, and what other recommendations should be considered in a centre with such limited capacity while facing a surge in cases.

### ***Review Question(s)***

- What are the outcomes associated with use of ECMO in patients with COVID-19?
- Are there patient selection recommendations?
- Are there recommendations or experience with smaller centres using this intervention versus larger centres and are outcomes significantly affected by center size and pre-established ECMO programs/teams?

## **Method**

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For each Rapid Review, the initial question is posed by a decision-maker in the health care system seeking the evidence base for a specific policy decision. According to the subject of the question, the Evidence Task Group Intake Committee allocates this question to the appropriate Working Group. Each Working Group comprises a librarian, researcher, 1-2 clinicians, 1-2 subject matter experts, and a group leader. The Working Group and the decision-maker first discuss the question to ensure it was articulated in a clear, searchable manner. The librarians assigned to your team then conduct a thorough search of the indexed literature, grey literature, news sources, or other sources as agreed upon. Some reference lists for especially pertinent articles are also reviewed. An Evidence Search Report is thereby created. See Appendix for more details on the search strategy. A Rapid Review of the identified literature is then performed by the researcher using the methods of a systematic review, but without a double review or meta-analysis and in a more rapid fashion. Relevant evidence is summarized in both tabular and narrative form, key findings and limitations articulated, and the quality of the body of evidence evaluated using the GRADE hierarchy. The draft Rapid Review is reviewed and edited by the Working Group clinicians, experts, and leader. Once revisions are complete, the Rapid Review is submitted to the requesting decision-maker and placed in the COVID-19 Repository. For certain topics with rapidly changing evidence, after a period of time an updated evidence search is performed, the review process repeated, and an updated Rapid Review released.

## Summary of Evidence

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### *Outcomes of ECMO for COVID-19 Patients:*

In general, evidence regarding the effect of ECMO in managing COVID-19 patients is weak due to a lack of large, multi-centre, controlled trials. The basis for the technology is to provide continued oxygenation of a patient's organs when lung function has deteriorated (2). There is limited evidence associating ECMO with patient survival following infection with influenza and other coronaviruses (1,2); because of this, clinicians have reasoned that it may also be a relevant therapy for COVID-19 patients. Given the nature of viral infection with SARS-CoV-2, it is important to note that ECMO does not provide a treatment for the infection itself, but rather, a mode of life support while the body attempts to eliminate the virus and recover (1). ECMO also does not treat other underlying diseases or comorbid conditions (2). Patients are often on ECMO for 8 days or more (2) and the mortality rate is around 46% (1), although both of these metrics vary widely from study to study. Much of that variation is likely due to small sample sizes in individual studies, differences within patient populations, and the capabilities and initiation practices regarding ECMO at different centres around the world. With that said, many studies report on patient survival associated with an ECMO intervention.

Like all medical procedures, ECMO is not without associated risks, which include mechanical malfunction of the devices leading to thrombosis, intubation problems, oxygenator dysfunction, and air embolisms, and patient-related complications like bleeding, renal insufficiency, infection, hemolysis, hyperbilirubinemia, and other complications of the circulatory, respiratory, and nervous system (2). Some specific issues related to COVID-19 patients include being uniquely predisposed to bleeding and/or thrombotic complications (1). Often, individual studies will highlight the prevalence of specific adverse events related to their specific patient cohort, for example, hypercoagulability and oxygenator failure (3), intracranial hemorrhage (4), etc.

### *Patient Selection Criteria:*

Due to the resource-intensive nature of ECMO and recognizing the limited resource availability many centres face during a pandemic, multiple organizations and many authors have published guidelines (locally, regionally, nationally, and internationally) to help centres determine appropriate criteria for patients to be selected for ECMO. The Extracorporeal Life Support Organization (ELSO) has developed commonly cited guidelines for ECMO use with COVID-19 patients (5). These guidelines were developed as a consensus document by an international group of interdisciplinary ECMO providers. Criteria for selection include both indications and contraindications and the authors highlight that these criteria may change rapidly as new evidence is accrued (5). Please refer to the source document for an in-depth understanding of these criteria. In addition, the authors recommend that centres alter the stringency of their selection criteria as resource demand increases in a pandemic situation (5). This recommendation is repeated often in the literature and further discussed below.

### *Recommendations for Implementation:*

Much of the literature appears to come from large centres who have well established and resourced, interdisciplinary ECMO teams in place. This may limit the applicability of their recommendations to smaller centres.

The first recommendation is to define the criteria for how patients will be selected for ECMO. Of note, most authors recommend that these criteria become more stringent as resources become strained. This is particularly relevant given that the data are not clear on the precise benefits of using ECMO for COVID-19 patients and, therefore, the resources used by this therapy may be better put to use in other ways, especially during a pandemic surge.

Ramanathan et al. (6) provide general recommendations for planning and providing ECMO during a pandemic. In general, it is not recommended to initiate or attempt to scale up an ECMO program if one wasn't already in place prior to the pandemic, although some authors have provided commentaries on their success in these types of endeavours (7,8).

Many articles also highlight the ethical issues that are inherent to such a topic. Most authors recommend that an interdisciplinary team be involved in all decisions regarding which patients should be offered ECMO. Additionally, it is recommended to have conversations as early as possible with patients and/or their decision-makers about end of life care. When discussing ECMO specifically, practitioners are reminded that this therapy mustn't be used as a "bridge to nowhere" (1). That is to say, conversations should be had with patients and/or their decision-makers about desired outcomes and therapeutic endpoints. These conversations are important given the resource-intensive nature of ECMO, including not just personnel, but the length of time these patients remain in the intensive care unit and the need for appropriate resource distribution during a surge. Murugappan et al. (1) provide an outline of different approaches to resource distribution, none of which have an evidence base to indicate preference over any others.

## Conclusions

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While there is optimism surrounding the use of ECMO as a therapy for COVID-19 patients, the current data are insufficient to recommend for or against this modality. The best evidence available indicates a 46% mortality rate among COVID-19 patients receiving ECMO and a host of potential adverse events to consider. Additionally, initiation of this therapy must be carefully considered by an interdisciplinary team to ensure that patients are appropriately selected and limited resources are used wisely, especially when facing pandemic-related patient surges.

A more comprehensive perspective of the content of this rapid review can be found in the review articles by Murugappan et al. (1), Ma et al. (2), and the guidelines published by the ELSO (5).

## Glossary

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COVID-19 – Coronavirus Disease 2019

ECMO – extracorporeal membrane oxygenation

ELSO – extracorporeal life support organization

SARS-CoV-2 – severe acute respiratory syndrome coronavirus 2

VA-ECMO – veno-arterial extracorporeal membrane oxygenation

VV-ECMO – venovenous extracorporeal membrane oxygenation

## References Included in Summary

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## Appendix: Evidence Search Details

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### ***Search Strategies***

(Copy from the evidence search report, or refer to the evidence search report with the same number.)

### ***Search Strategies***

#### **Keywords Used in Varying Combinations:**

AGMP | AGM | “Aerosol Generating Procedures” | “Aerosol Generating Medical Procedures”

COVID | Coronavirus

Transmission | Infectivity | Infectiousness | Communicability | Occupational Risk | Occupational Exposure

#### ***Sources***

- (Particular databases, was grey literature included, etc.)
- Refer to the evidence search report for extensive sources. Be sure to include any additional resources not referenced in the evidence search report.
- This field is mandatory.



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