Peer Review File

Article information: https://dx.doi.org/10.21037/ccts-21-22.

Reviewer A

Thank you so much for giving me the opportunity to check the article titled "Extracorporeal membrane oxygenation for COVID-19: Lessons learned".

This article described the experience to use VV-ECMO for critical COVID-19 patients.

In current stage, we can find many articles to use VV-ECMO for critical COVID-19 patients. So, we need some novel knowledgement of novel Ingenuity. But, this article is a just critical experience ,not novel discovery and others. So, I think that the article is not acceptable.

I have some questions.

1. Why was the so high frequency of tracheostomy after using VV-ECMO for critical COVID-19 patients (98%)? Do you have any strategies to perform tracheostomy? In general, we should perform tracheostomy for patients who are equipped with a mechanical ventilator or ECMO and whose respiratory condition does not improve even after about 2 weeks. What do you think about it?

As discussed on page 14, lines 270-277, our patients developed severe air

hunger when extubated, and after 4/5 of the initial series required reintubation, we moved to elective tracheostomy within 48hours of ECMO cannulation in order to rapidly wean sedation and mobilize our patients. Our strategy for tracheostomy is outlined on pages 13-14, lines 262-269, including a strictly percutaneous technique to minimize bleeding, performed at the bedside, with the ventilator off and the patient paralyzed to minimize aerosolization.

2. Why was the so high frequency of AKI during VV-ECMO, especially hemodialysis patients? What was the reason of AKI with hemodialysis? I think that the management of VV-ECMO is not so good. Do you have a special team for VV-ECMO? I think you should improve the management of VV-ECMO or reconstruct another special team for VV-ECMO.

Acute kidney injury requiring dialysis is a typically a complication of patient disease, and not the management of these critically ill patients, Indeed, many centers refuse to cannulate patients with evidence of AKI, therefore our accepted risk is actually higher than many centers. Despite this fact, our survival to discharge is markedly higher than the international reported outcomes (see *Lancet* 2020, ELSO dashboard). This reflects better ECMO management, not worse, and is the result of the hard work of our dedicated ECMO team.

3. Why was the high frequency of bleeding complications for VV-ECMO patients? In your article, there are more Hispanic than Arian. In general, Asian tends to get bleeding complications to use heparin as an anticoaglant than European or other races. How did you control APTT strictly between 40 to 60 seconds?

Bleeding complications are well reported in the ECMO population, and higher in the COVID population as has been reported in many other series. Our geographic location resulted in more Hispanic than Asian patients, but our anticoagulation strategy is universal. Heparin was administered at the time of cannulation and titrated by our institutional protocol based on q6hour aPTT levels. Indeed, since the initial submission of this manuscript, based on others' reported data we have moved to a anti-Factor Xa monitoring system, but have not accrued enough patients to definitively comment on a difference.

Reviewer B

Authors submit an experience with venovenous ECMO in Texas during COVID19, highlighting their "adaptive experience" with n=50 patients in 2020 (43 of whom completed their ECMO run), discussing cannulation, anticoagulation and other medications, renal replacement, ventilation, and PT.

This is a large experience compared to other reports, though all such reports have inherent variability from patient acuity and selection criteria. Patients were middle aged, mostly male, and had typical comorbidities, with an average time of ventilation 6 days (0-20) pre cannulation and most had been proned and on neuromuscular blockade. A variety of medications were used in these patients, many of which were only based on anectodal evidence and may not be used now (azithromycin, HCQ, etc)

Here all patients were in cardiothoracic ICU, cannulated in a similar bifemoral manner (variety of circuits and oxygenator), and conversion at 2 weeks to single-site right internal jugular dual lumen cannulation. Mean time on ECMO circuit was 14 days, and 1/3 were given the RIJ cannulation. Conversion to VA ECMO was rare. Almost all patients had tracheostomy ("Ultimately, the pendulum swung from attempting extubation, to avoiding extubation and proceeding with tracheostomy, to immediate early tracheostomy within 48 hours of cannulation"). 3/4 of patients weaned from ECMO, and of these 70% were discharged alive.

This group changed their anticoagulation strategy for VV ECMO from none, to heparin for PTT 55-65 for the pandemic. This is an area of active research.

Complications included AKI, bleeding, thrombocytopenia, Pneumothorax, infection, and VTE.

One important lesson is mobilization - cf "Physical therapy evaluation and treatment was initiated as soon as possible", including with a figure showing "tilt table" - more information on that may be useful. The group also had a template for daily family updates, another need during the pandemic. A separate manuscript dedicated to the physical therapy program initiated is forthcoming.

Table 3 is a reasonable summary. However it is basically a case series and without controlled data.

Agree, however given the complexity of this patient population, it is quite difficult – if not impossible – to provide a control group, hence the descriptive nature of this case series.

Figure 1 does not clearly add to the paper.

The authors feel it conveys the complexity of managing this patient population and requests inclusion.

Reviewer C

The authors describe their experience with 50 VV ECMO patients with

COVID-19 ARDS at a single institution, including strict patient selection guidelines, cannulation methods and long-term cannulation strategies, airway management (all patients not extubatable within 48 hours of cannulation underwent early tracheostomy), anticoagulation, etc. In the end, of the 43 patients who completed an ECMO run, 32 patients (74.4%) were weaned from ECMO and thirty patients (69.8%) were discharged alive from the hospital.

The article includes a large sample of severe COVID-19 patients compared to other reports to and presents a satisfactory result, which is unique and is of great benefit to the readers.

However, there are still some minor questions.

1. CRRT has a relatively high probability of use. Please analyze the reason by comparing with the currently reported literature.

The incidence of acute kidney injury in the population is higher than in other ARDS. Many centers used the presence of AKI as a contraindication to ECMO, and therefore the currently reported literature likely under-reports the true incidence of AKI. Our center has significant experience with simultaneous ECMO and CRRT with high rate of renal recovery (publication pending), and thefore accepted patients for ECMO even with impaired renal function. This naturally led to a higher incidence of

concurrent CRRT utilization.

2. As for the VV ECMO cannulation selection, why did you choose bifemoral VV cannulation at the beginning, and opt to single-site right internal jugular dual lumen cannulation for patients with slow recovery with no evidence of improvement at 14 days and expected prolonged courses? Please clarify the reasons for the cannulation selection.

Our standard approach was bifemoral cannulation at the time of presentation as it is safe, rapid, and reproducible at the bedside in the ICU. Single site dual lumen cannulation is ideally performed in the operating room with increased transport time and potentially exposure time, and therefore was sparingly used early in the pandemic. As it became clear that patients would have prolonged runs with successful therapy and mobilization, it became necessary to revise many patients to an upper body single site. This has been further described in the revised manuscript, pages 7-8, lines 121-128.