

Peer Review File

Article information: <http://dx.doi.org/10.21037/apm-20-1176>

Reviewer Comments

Thank you very much for preparing the manuscript in which you describe your approach to a patient suffering of COVID induced ARDS and heart failure.

Comment 1: I understand your report as a description of a quite new technique in your hospital/country. As such it is worthwhile to describe the details of precautions like you do. Still, I think you should look at international literature and read how they operate the ECMO. How is their approach and what is new in your setting?

The description of the patient's course should be more detailed and not leaving gaps.

The ECMO technique should be presented and explained in the discussion and here

you should compare it to the literature. You should describe the targets of your

strategy and the monitoring. Why did you choose for VA and not VV ECMO?

What were the problems during cannulation (a blood loss of 500 ml is not normal)?

What monitoring device do you use and what do others use?

Although we are all not mother-tongue this text needs urgently a proper English language editing.

Reply: Thank you very much for your review and affirmation of our work, your suggestion is very good, we added the corresponding content of the details and the question you required in the revised manuscript.

Changes in the text: Management of mechanical ventilation section

We described some evidence of the new in our case which was compared with the international literature, see details,

The patient in our case was treated with the APV-CMV, SCMV, and P-SIMV modes when appropriate during ECMO treatment. We set the pressure between 11 ~ 25 cmH₂O, PEEP between 8 ~ 13 cmH₂O, respiratory rate between 12 ~ 20 times/min, and FIO₂ control between 45 ~ 100%. which helps the patient had no pneumothorax or subcutaneous emphysema complications during the treatment. (see Page 9, line 193-197)

Changes in the text: Discussion section

We added some reason of the choose for VA and not VV ECMO?

In the case, as of the patient was specially and is the oldest, so is very difficult to make a step for treatment, of course, our basic goal of ECMO anticoagulation is to maintain the basic balance of anticoagulation, coagulation and fibrinolysis. ECMO assistance can provide hemodynamic support for refractory cardiogenic shock that fails the initial treatment [11-12]. In recent years, venous-arterial extracorporeal membrane oxygenation (veno-arterial extracorporeal membrane oxygenation, VA-ECMO), as an extracorporeal life support technology, has shown important therapeutic value in cardiogenic shock [13-16]. VA-ECMO catheterization paths include femoral vein-femoral artery catheterization and femoral vein-axillary artery catheterization, femoral vein-femoral artery catheterization, and are the most commonly used vascular access. Compared with other paths, the anatomical location of the body surface is simpler, and there is no surrounding Adjacent important blood vessels, nerves and organs can be established by surgical incision or percutaneous puncture (conventional ultrasound guidance) [17]. This path has the advantage of being fast and minimally invasive. We chose femoral vein-femoral artery catheterization. Due to severe edema of the lower limbs, heart failure, and weak femoral artery pulsation, it is difficult to perform blind femoral vein puncture. Therefore, the right femoral vein puncture under the guidance of color Doppler ultrasound, the ultrasound head is applied with conductive paste, Put in a sterile cover, the patient's right lower limb is externally rotated to the external booth, routinely disinfected, draped with perforated towels, local anesthetized with 2% lidocaine, locally disinfected and coated with sterilized conductive paste, and then about 2cm below the midpoint of the right groin is taken. Initial control of the head position, move the probe until the blood vessel is found, enable color Doppler and Doppler to determine the position of the femoral artery and femoral vein, use a deep venous catheter trocar to insert the needle along the puncture point, and see that the needle tip penetrates into the femoral vein cavity under ultrasound. With dark red liquid, insert the guide wire from the guide wire guide hole, exit the puncture needle, expand the skin with a dilator, insert the venous catheter along the guide wire, and remove the guide wire. The infusion and blood return are smooth, confirm that the guide wire is inserted into the blood vessel, withdraw from the deep venous catheter, expand the skin layer by layer, extend the guide wire into the 21# ECMO blood vessel, depth 47cm, suture fixation, sterile 3M tape fixation, procedure Smoothly,

during the VA-ECMO catheterization period, it is necessary to check the speed, flow, oxygen concentration, ACT, APT, heparin dose, etc. Therefore, in the case, we choose for VA but not VV ECMO. (see Page14 , line 304-309;Page15 , line 310-331;Page16, line 332-340)

We added some reasons of the problems during cannulation. (a blood loss of 500 ml is not normal)? What monitoring device do you use and what do others use?

As we known, COVID-19 deteriorating very rapidly. In the case, the patient was specially and is the oldest, so is very difficult to make a step for treatment, of course, our basic goal of ECMO anticoagulation is to maintain the basic balance of anticoagulation, coagulation and fibrinolysis. Generally speaking, little a blood loss is the best, always some people is too special. In the case, during the VA ECMO treatment of the patient, the puncture port slowly oozes blood, the coagulation function is poor, and the blood coagulation function is poor (coagulation four items: plasma prothrombin time 19.8 seconds, activated partial thromboplastin time 148.6 seconds, plasma fibrinogen 5.78g /L), the blood test showed a significant decrease in hemoglobin (blood test combination: hemoglobin 63.00g/L), CRRT heparin sodium anticoagulation should be stopped, the depth of the arterial duct, the local compression of the arterial compressor to stop bleeding, and the application of component blood infusion, etc. After treatment, the patient's right lower limb puncture port oozing blood was significantly reduced, the circulation was stable than before, and the vasoactive drugs were gradually reduced. After treatment, the blood coagulation function was improved after the recheck, and the hemoglobin was higher than before. The treatment effect is good.

Comment 2: The report interestingly describes in through detail the treatment of an elderly person suffering from COVID-19. Though interesting and reported in much detail, the manuscript lacks of particular relevance and novelty, since only well-established standard are described. with respect to specifics of COVID-19, the specific therapy mentioned is no longer recommended and recommended therapy according to recent evidence is not considered. therefore, the relevance of this historic report is very limited.

Reply: Thank you for your comments. All of your opinions are very precious, although the ECMO is a universal method for the treatment of COVID-19, it is indeed lacks of particular relevance and novelty. However, the situation of elderly patients is

particularly complicated. Due to the large gap in the level of medical care in various regions, elderly patients in some regions have not received adequate treatment, so we want to share some successful experiences of treatment for others reference and learn.

Comment 3: Your diagnostic was cardiogenic shock.

1. Could you provide some data about Echocardiographic findings? Was there a cardiogenic shock, Covid-19 related myocarditis or septic shock with cardiac damage because of Burkholderia infections during clinical course?
2. Were Interleukin-6, Ferritin, D-dimer or lymphocyte measured during the patient's clinical course?
3. In your discussion, you say that "the successful cases of ECMO treatment for children or young people infected with COVID-19 are worth further exploration". There are reports and case series published of infected children or young patients showing successful cases of ECMO in fully recovered.
4. In your discussion "There is still a lack of clinical management experience to guide the treatment of the disease". Currently, some organizations such as the Spanish Society of Intensive Medicine have published recommendations on clinical management of Covid-19 disease.

Reply: Thank for your advice, your suggestions are very important, and they will be of great guiding significance for my future scientific research. We added the corresponding content about your questions:

We added some data about the case was diagnostic cardiogenic shock, Was there a cardiogenic shock, Covid-19 related myocarditis or septic shock with cardiac damage because of Burkholderia infections during clinical course? see details,

During treatment in the isolated ICU, the patient developed unstable breathing and circulation, oliguria, cold limbs, increased BNP, ECG indicated atrial fibrillation, sinus bradycardia, and cardiac color doppler ultrasound indicated cardiac insufficiency.

On February 2, the patient had unstable circulation, cold limbs, low hemoglobin, increased BNP, and cardiac insufficiency. ECG showed atrial fibrillation and sinus bradycardia. He was given appropriate fluids and continued to give dobutamine to strengthen the blood pressure after cardiac treatment. The fluctuation is 89-141/48-83mmHg. When the blood oxygen drops, the high-flow humidification oxygen therapy device assisted breathing (flow rate 45-50L/min, FiO2 60%), the

blood oxygen saturation fluctuates at about 76%, and the tracheal intubation ventilator assists breathing. On February 6, the patient's blood pressure was as low as 77/44 mmHg, hemoglobin was 75g/L, limbs were cold, and the body was edema. CRRT was suspended, appropriate fluid supplementation, albumin supplementation, infusion of concentrated red blood cells, plasma, and increased vascular activity Treatment with drugs, the patient's blood pressure fluctuates at 95/53mmHg, and the patient's heart rate drops to 31bpm at 0:55 on 2020/2/7, blood pressure: 61/36mmHg, blood oxygen cannot be detected, and repeated intravenous injections of epinephrine and adrenaline to maintain blood pressure , Pre-return blood to stop CRRT, adjust ventilator parameters, appropriate fluid supplementation, continue red blood cell and plasma infusion, and other active rescue treatments. After 1 minute, the patient's heart rate fluctuated at 115 beats/min. After 10 minutes, the blood pressure gradually rose to 109/58mmHg, and the patient respired Unstable, considering that it is difficult to correct cardiogenic shock, immediately start VA-ECMO for circulation and supportive treatment.

We added some data about the patient Interleukin-6, Ferritin, D-dimer or lymphocyte measured during the patient's clinical course?

During clinical treatment, no interleukin-6 was detected, ferritin was not measured, but C-reactive protein, hemoglobin D-dimer and lymphocytes were detected. See details,

| Measure | Jan. 3 1 | Feb . 2 | Feb. 5 | Feb. 7 | Feb. 10 | Feb. 15 | Feb. 19 | Feb. 21 | Feb. 25 |
|---|-------------|------------|-----------|-----------|------------|------------|------------|---------|---------|
| haemoglobin (g/L) | 79.00 | 73.00 | 68.00 | 75.00 | 78.00 | 92.00 | 79.00 | 111.00 | 114.00 |
| d-dimer assay (µg/L) | 1.1 | 2400 | 6020 | 2910 | 10690 | 29760 | 50040 | 46640 | 5880 |
| Absolute lymphocyte value (x10 ⁹ /L) | 0.78 | 0.48 | 0.16 | 0.37 | 0.69 | 0.60 | 0.63 | 0.52 | 0.92 |
| C-reactive protein (mg/L) | 13.74 | 77.44 | 112.44 | 99.48 | 98.5 | 59.84 | 91.46 | - | 53.8 |

We answered the questions about "the successful cases of ECMO treatment for children or young people infected with COVID-19 are worth further exploration". There are reports and case series published of infected children or young patients showing successful cases of ECMO in fully recovered.

Although there are successful cases, there are individualized differences that require multi-center research and exploration. Moreover, COVID-19 is still spreading and may become more and more serious. More and more people need ECMO treatment.

We added the response of the last advice,

Thank you very much for your valuable comments, I will carefully study the Spanish Society of Intensive Medicine and other organizations have issued recommendations on the clinical management of Covid-19 disease.

In addition, I asked my colleagues improved the language and fixed the grammar issues of my manuscript. we revised according to the editorial requests, corrected the existing issues, and modified our text as advised.

Thanks again for the suggestions, and I hope I can learn more from you.