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The fall of conventional mechanical ventilation into the emergence of Veno -Venous Extracorporeal Membrane Oxygenation influenced Extreme Super Super obese patient survival with a COVID-19 ARDS

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ABSTRACT

The COVID-19 pandemic has unfolded and merged across 220 countries, territories worldwide. Recent studies conclude that obesity is an independent significant risk factor for COVID-19 infection. Thus, obesity is an epidemic disease. Any obesity allied with COVID-19 ARDS is life-threatening, heading to respiratory life support associated with several complications and mortality. In this clinical setting, the World health organization (WHO) and Extracorporeal Life Support Organization (ELSO) provide interim guidelines that Veno-Venous extracorporeal membrane oxygenation (VV- ECMO) can be beneficial in selective COVID-19 patients. However, the benefit of extracorporeal membrane oxygenation (ECMO) in Obesity and Severe Obesity remains controversial. Although a few studies favored ECMO in Obesity associated with COVID-19. In contrast, its benefit in extreme super-super obese (class v) is unknown to the present day. Herein we report our successful early VV- ECMO and its retrieval challenges in an extreme super-super obese of Body mass index (BMI >65 kg/m^2). Our report describes our institutional practice, clinical characteristics, and early VV- ECMO induction to enhance patients' speedy recovery and survival. ECMO is a limited resource and must be used selectively, particularly during a pandemic when all resources are scarce.

Keywords: Coronavirus Disease 19 (COVID-19), Veno-Venous Extracorporeal Membrane Oxygenation (VV- ECMO), Blood gas analyses (BGA), Body mass index (BMI), Acute Respiratory Distress Syndrome (ARDS), paO_2/FiO_2 Ratio (P/F Ratio), Fraction of Inspired Oxygen (FiO_2).

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INTRODUCTION

In the year-end of 2019, a highly contagious novel virus began to affect humans in Wuhan, Hubei province, China. According to the United Nations statistical divisional report, this novel virus spread worldwide rapidly across 220 countries and territories. On 11 February 2020, the World health organization (WHO) declared this virus as a severe acute coronavirus -2 (SARS-COV- 2) or coronavirus disease-2019 (COVID-19).As of November 19,2021, 256,534,177 patients have been positive to COVID-19, with 5,151,176 (2%) associated deaths.[1] Like other preceding coronavirus infections, COVID-19 has varying clinical progressions. One in every five COVID-19 patients develops severe symptoms, requires immediate hospitalization, then 8 in 10 hospitalized patients need supplemental oxygen, and one-third of these hospitalized patients on supplemental oxygen may require invasive or noninvasive respiratory life support. Almost all COVID-19 patients in respiratory life support descent into severe acute respiratory distress syndrome (ARDS).[2] ARDS is a progressive pulmonary inflammatory process distinguished by diffuse alveolar injury and rapid, life-threatening clinical deterioration. Early Italian and Chinese studies failed to describe the incidence of obesity in COVID-19.[3] More likely, this paucity may be due to the decreased prevalence of Obesity in Italy,(approximately 19.8%) and China, (approximately 6.3%) compared to other obesity prevalence countries. [4,5]. YouShang et al. stated that most of the COVID-19 have mild symptoms (80.9%), severe symptoms (13.8%), and critical illness (4.7%). The overall mortality rate for critical illness was 49.0% in particular among the old age People with a medical history of underlying diseases such as cardiovascular disease (10.5%), Diabetes mellitus (7.3%), chronic respiratory disease (6.3%), Hypertension (6.0%), cancer (5.6%), and 0.9% for medically free.[6] According to the WHO, an individual with a BMI of over 25kg/m^2 and 30kg/m^2 is considered overweight and obese. Obesity is an epidemic disease, and it is one of the leading causes of preventable deaths globally. The current prevalence of Obesity and Severe Obesity in USA adults is 42.4% and 9.2%, respectively. whereas in Saudi Arabia, obesity prevalence in adults was 33.7%. [7,8] obesity (BMI)>30kg/m2) is a condition of excess or abnormal fat tissue distribution resulting in chronic disease related to chronic inflammation and metabolic dysfunction. [9] The Spanish society for the study of Obesity (SEEDO) classified obesity (kg/m2) in to obesity class Ⅰ (30 to 34.9 kg/m2), obesity class Ⅱ(35-39.9 kg/m2), obesity class Ⅲ(morbidly obese - 40 to 49.9 kg/m^2), obesity class Ⅳ (super obese-50 to 59.9 kg/m^2), obesity class Ⅴ(super super-obese - >60 kg/m2. [10] Recently published data linked obesity as an independent significant risk factor for COVID-19 associated with ARDS, increased hospitalizations, decreased lung compliance, impaired immune function, Lipo-toxicity, and induction of a proinflammatory state, leading to mechanical ventilation.

According to public health surveillance. California, USA. Declared that obesity (BMI ≥30 kg/m^2) and extreme Obesity (BMI ≥40 kg/m^2) were independent risk factors for those greater than ≥ 20 years old hospitalized with pandemic 2009 Influenza Swine Flu (H1N1). Of 1008 patients, 268 patients, 58% had a BMI ≥of 30 kg/m^2, and 43% had a BMI ≥of 40 kg/m^2. [11] In a systematic review of 637 Middle East respiratory syndrome coronavirus (MERS-CoV) patients, 16% were obese. [12] A meta-analysis study of 266 H1N1 patients with severe ARDS retrieved by VV- ECMO generated a survival rate of 72.5% with prolonged hospitalization. Similarly, the ECMO group had significantly lowered the in-hospital mortality of 65% versus 100% of the control group of MERS-CoV patients.[13,14] These promising outcomes executed the WHO and ELSO to provide interim guidelines to consider ECMO in selective covid-19 patients.[15]

Adding these prior experiences from H1N1 influenza, MERS CoV, and its impact on obesity had progressed the physicians currently into vigilance strategy, aggressive, and early care for COVID-19 patients. Although a few published data exist on ECMO benefits in obesity. Its effectiveness in severe obesity COVID-19 is unclear, particularly in extreme super-super obese patients (B.M.I.> 60 kg/m^2). Preferring VV-ECMO in such a group of patients is rare and challenging. This Case report (VV-ECMO - Extreme super-super obese) describes our first-ever success retrieval in our center, Asser central hospital, Saudi Arabia. Additionally, this report emphasizes that early VV ECMO application can influence the patient's survival and the feasibility of its use in extreme super-super obese individuals virtually in the intensive care unit (ICU) in the future.

Table 1 Selected lab values of 39 old male (BMI-65Kg/m^2) with covid-19 infection from admission to VV-ECMO decannulation (16 days)

Lab values		Day1	Day2	Day3	Day4	Day 7	Day10	Day13	Day15	Day16
Haemoglobin (g/dL)		13	13.6	11.6	10.3	8.6	10.3	9	8.3	8.0
White blood cell (10^3mcl)		5.67	7.0	8.0	6.6	15.0	15.5	10.0	6.7	7.6
Platlets (10^3mcl)		212	251	313	243	415	231	104	73	69
Creatine (mg/dL)		0.7	0.9	0.6	1.0	1.1	0.8	1.0	0.6	0.9
APTT (s)		30.0	25.7	31.0	52.3	24.1	22.0	27.3	29.6	34.0
Fibronogen (gm/dl)		2.06	2.69	1.43	1.67	0.56	0.47	1.13	2.17	2.32
Pre- ECMO				**Blood gases**				**Trial 2hrs**	**Off Trial 24hrs**	**Off Post ECMO**
pH	7.20	7.43	7.36	7.48	7.54	7.55	7.44	7.43	7.44	7.41
Pco2 (mmhg)	59.9	34.1	46.8	37	33.4	32.1	44.9	44.5	32.2	34.8
Po2 (mmhg)	49	70.3	78.7	92.1	101	78.4	80.5	78.2	114	98.7
Hco3 (mmol/L)	22.1	23.6	25.3	28.3	30.3	29.7	29.9	28.8	23	23.1
sO2	80.1	95.9	95.4	97.4	98.4	97.4	97.6	96.6	98.9	98.2
PaO2/fiO2 Ratio	49	175	196	230	252	196	201	196	285	247

CASE REPORT

The 39-year-old male, known hypothyroidism on regular treatment, no history of Diabetes mellitus, Hypertension, Chronic respiratory diseases, or Smoking, tested positive for the COVID-19 RT-PCR. On the 7th day of his home quarantine (this case timeline starts from day 1), he arrived at our emergency room with fever symptoms on and off, chest tightness, generalized myalgia, and productive cough. Vitals at the emergency room were as follows: Glasgow coma scale (GCS) 15/15, Respiratory rate (RR), 20 breaths/min, Heart rate (HR), 87 beats/min, Blood pressure (BP) 113/64 mmHg. On room air, oxygen saturation measured by pulse oximeter (SpO_2) was 64% treated with O_2 15 L/min, and then spO_2 rose to 89%–90%. Initial Blood gas analyses (BGA) were pH 7.39, pCO2 38.9 mmHg, pO2 39.3 mmHg, HCO3 23.3mmol/L. On physical examination, A weight of 183 kg, a height of 168 cm, and BMI of 65 kg/m^2 (class v - Extreme super- super obese) with a neck circumference of 55 cm, mild jugular distension, and higher central fat distribution. Laboratory test results on admission shown in Table - 1. Bilateral wheezes on auscultation, Anteroposterior chest X-ray revealed bilateral patchy and confluent opacities with ground glass opacification prevalent more in the right than the left lung field. [Figure-1(a)]. He was diagnosed with acute hypoxic respiratory failure associated with COVID-19 ARDS. Hence, patient shifted to the intensive care unit for close observations after obtaining written informed consent. Oxygen therapy was tailored to 15 L/min via a non-rebreathing mask in ICU Since there was a drop in SpO^2 of 80%. In the following next 2 hours, his respiratory status deteriorated progressively, driving SpO^2 to 76%. Repeated BGA showed hypoxia and respiratory acidosis: pH:7.20, pCO2:57.9 mmHg, pO2:44.7 mmHg, HCO3: 22.3 mmol/L. A trial of hi-flow nasal cannula 60 Liter per minute (Lpm) via heated circuit with 100% Fraction of inspired oxygen (FiO_2) and Noninvasive ventilation (NIV) via BIPAP started to reduce breathing effort. Nevertheless, he could not maintain his oxygenation at the 8th hour of ICU admission. He was intubated electively in a rapid sequence manner with full personal protective equipment (PPE) measures.We placed him in a prone position and initiated a pressure-regulated volume control ventilation (PRVC) at a FiO_2 of 1.0, respiratory rate (RR) of 18 breath/min, Tidal volume (VT) 4 ml/per kg, I: E ratio of 1:2, and positive end-expiratory pressure (PEEP) 16 cmH_2O. Furthermore, to facilitate a synchrony between patient and ventilator, sedation of Propofol 70 mg/hr, Midazolam 7 mg/hr, Fentanyl 100 mcg/hr, Ketamine 50 mg/hr, and Neuromuscular agent rocuronium bromide 50 mg/hr were maintained and infused continuously through the central venous line (internal jugular access). In addition, inhaled bronchodilators (salbutamol 2.5 mg/hr, ipratropium 0.5 mg/hr) for every 6 hours were included.

After 120 minutes of post-intubation and prone position, a respiratory index such as peak airway pressure (Ppeak) and plateau pressure (Pplat) are 57 and 37 cmH_2O, are at high risk of promoting barotrauma. Hence, the TV and PEEP were reduced to 3.0ml/kg and 12 cmH2O, respectively. Repeated BGA was pH 7.188, pCO_2 96.7 mmHg, pO2 49.0 mmHg, HCO3 22.4 mmol/L. Therefore, pressure control ventilation (PCV)was initiated with FiO2 1.0, RR 24 breath/min, PEEP 12, PC 30 cmH2O.Therefore, peak airway pressure is reduced and the risk of barotrauma minimized. However, the patient reverted to the supine position due to hemodynamic instability, severe hypoxia, and respiratory acidosis persisted in the serials of BGA results with no improvement of a respiratory index, specifically Pplat >34cmH_2O and PaO_2/FiO_2 (P/F Ratio) is 49mmHg. After 16 hours from ICU admission, the team decided for VV-ECMO cannulation (day 1) based on the following relevant factors 1. pre- ECMO lab blood counts and coagulation profiles. (Table-1) 2. Clinical presentation such as P/F Ratio <100 mmHg persistently for more than 6 hours of mechanical ventilation, with persistent respiratory acidosis with a pH <7.2, pCO2 86 mmHg, high plateau pressure ≥35 cmH2O with tidal volumes of 3.0 ml/kg, and Murray lung injury score was 3.5 (patient Murray lung injury scoring: Hypoxemia ≤100 mmHg, score-4, peep ≥12cmH2O, score-3, Respiratory system compliance 19 ml/cm H_2O, score-4, Alveolar consolidation confined to quadrants, score - 3).

As per our institutional policy, the standards of personal protective equipment (PPE) have been maintained in the context of COVID-19 infections; this constitutes WHO recommended Medical Devices, specifically: two layers of gloves, helmet, goggles, face shields, gowns, and N95 masks worn before VV-ECMO cannulation. The original cannulation plan is to approach the right femoral vein as a drainage cannula and the right internal jugular (IJ) vein as a return cannula. Surprisingly, the right femoral vein is unattainable due to prior thrombosis. So, alternate left femoral vein access was secured. Two intensivists with vast ECMO experience simultaneously cannulated the right jugular vein (figure- 1 (b)) with size 19 fr and left femoral vein with size 25 fr by Ultrasound guidance to decrease overall exposure and procedure time out. There was no complication associated with VV ECMO cannulation. A centrifugal pump used was Getinge/Maquet®, Rastatt, Germany, with an initial flow of 4.5 L/min, sweep gas of 4L/m, Heparin 5000 IU given at cannulation time. Then 1200 IU per hour heparin infusion was initiated to keep the target APTT within 60-70s. We decide to maintain the pressure control ventilation and not to alter the ventilator settings beyond these limitations of peak inspiratory pressure (PIP) of more than 28 mm Hg, PEEP of 12 to 16cmH_2O, RR of 14 to 16 breaths/min or less, and FiO_2 of 0.40 or less till VV-ECMO decannulation. VV-ECMO circuit flow was titrated based on oxygenation, and we did not exceed revolutions per minute thresholds for possible hemolysis. Conversely, to avoid thrombus formation in the oxygenator, the flow was maintained above 3 L/min, and the time course of VV-ECMO running vs. fibrinogen level is shown in figure-2(a).

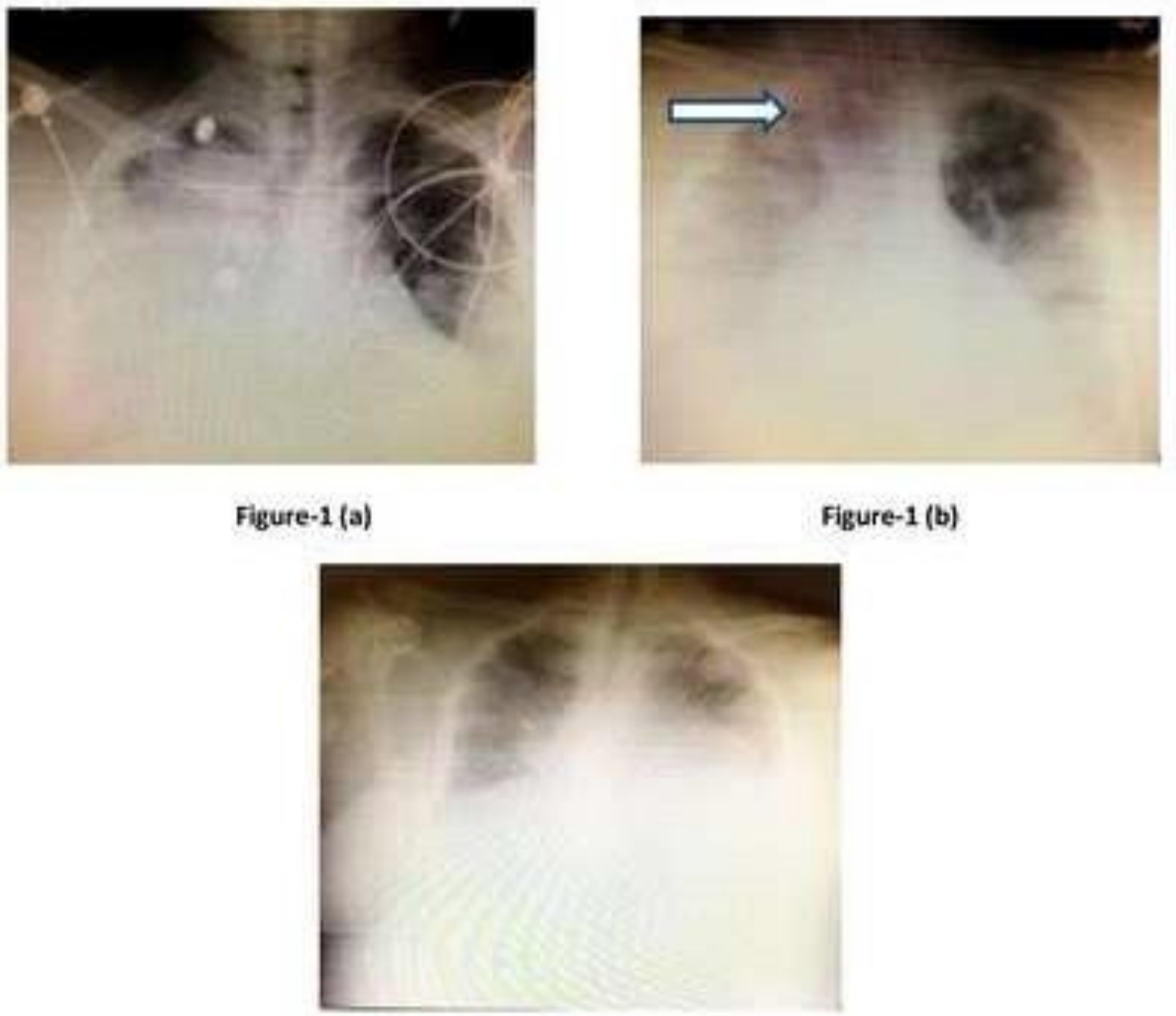
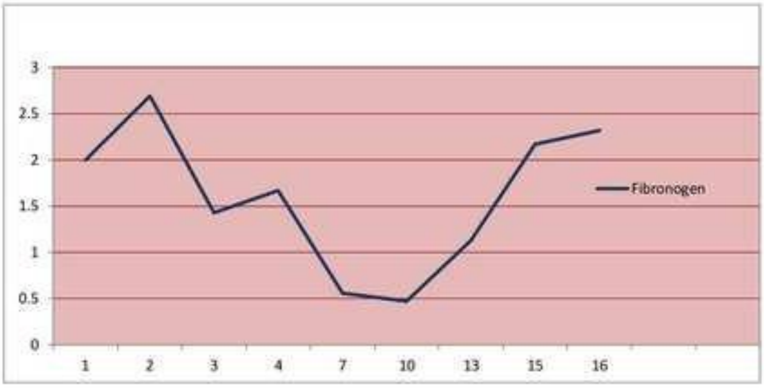


Figure-1 (a)

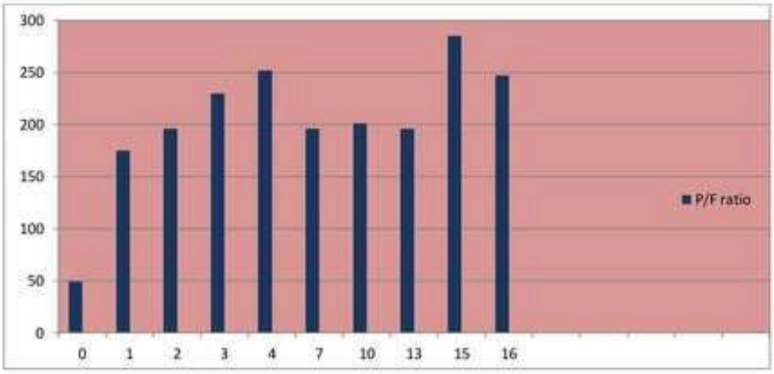
Figure-1 (b)

Figure-1 (c)

Figure 1. Chest X-ray of 39-year-old male (BMI>65 Kg/m2) with covid -19 infection. a: chest x-ray on admission, b: on VV-ECMO- Right jugular catheter (white arrow), c: post VV-ECMO(after 36 days)



Characteristics of fibrinogen level vs VV-ECMO (16 days)- Figure: 2 (a)



Characteristics of PaO_2/ FiO_2 ratio vs VV-ECMO (16 days)- figure: 2 (b)

Figure 2. a: Characteristics of fibrinogen level vs VV-ECMO (16 days); b: Characteristics of PaO_2/FiO^2 ratio vs VV-ECMO (16 days)

The paCO2 was maintained within the standard limit by altering the sweep gas flow rate. On day 14th, lab values, chest x-ray, and lung dynamics improved. BGA was pH 7.41, pCO2 46mmHg, pO2 85.2mmHg, HCO3 28.1mmol/L. Hence, the team decides to reduce the sweep gas flow rate to 0.5 L/ min. Subsequently, the gas flow disconnected for 2 hours, repeated BGA revealed PaCO2 was less than 45 mm Hg, and a P/F Ratio is 196mmHg. On day 15th, the first 12 hours of trial-off initiated, and the trial-off was extended for another 12 hours since the P/F Ratio-285 mmHg and the total 24 hours trial-off P/F Ratio was 247mmHg shown in figure-2(b). Accordingly, on day 16th, VV-ECMO was decannulated, and simultaneously patient underwent tracheostomy with size 9 ID for fast-track weaning from the mechanical ventilator. On day 20, we weaned the patient from the mechanical ventilator with the tracheal mask of 6 Lpm followed by intensive pulmonary rehabilitation. On day 26, tracheostomy was decannulated, switched to nasal prongs of 4 Lpm with satisfactory chest X-ray shown in figure 1(c), and shifted to ward on day 38 with stable hemodynamics, lab, and BGA shown in table-1. At earlier, on ICU admission, the patient received a loading dose of Favipiravir 1800 mg BID for one day followed by 800mg BID for 10 days and Dexamethasone 8mg for 10 days were given intravenously through central venous line (internal jugular access). He turned to MRSA and Acinetobacter infections from blood and sputum culture, exacerbating his covid-19 infection during ECMO treatment, and treated successfully with a Colistin loading dose of 9 million followed by 4.5 million for 14 days and vancomycin 15mg/kg BID for 14 days. No vascular injuries or significant bleeding, or thrombosis were reported during ECMO running.

DISCUSSION

To our experience, this is the first-ever successful VV-ECMO retrieval in extreme super-super obese (BMI 65 kg/m2) associated with severe COVID-19 in our center (Aseer Central Hospital , Saudi Arabia). The ECMO is a promising rescue therapy in acute cardiac and respiratory failure clinical settings. In context, its supremacy over conventional treatments of COVID-19 is debatable. Our manuscript demonstrates that VV-ECMO can influence class v obesity's survival. Our successful retrieval suggests that obesity can be an independent risk factor

for covid-19. A US report acknowledges that among 5700 covid-19 hospitalized patients, Obesity incidence is 41.7%. Two studies mentioned that in obese individuals, COVID-19 increases by 30%, in which morbid-obesity individuals' admission to ICU. increases by 74%.[16] Likewise, our patient had a higher BMI with a huge neck circumference, and higher central fat distribution resulted in airway obstruction and hypoxia. These features worsened more in lying and supine positions due to the diaphragm's cephalic displacement. Hence, a high Fowler's position continued during the HFNC and NIV administration.[17] However, increased intraabdominal pressure, restrictive chest wall, decreased lung volumes, diaphragm contractility, and increased breathing promotes severe refractory hypoxia heading to mechanical ventilation. Similarly, the US and Mexico's combined data showed a necessity of mechanical ventilation in Obesity increases by 66%, and it is identical to Simonett et al.'s narrative that the relationship of covid-19 patients requiring mechanical ventilation increases with BMI. [18] While initial hours of our proning improved alveolar ventilation, oxygenation, and this improvement are probably due to open lung approach by keeping external positive end-expiratory pressure of at least 12 to 16 cm H_2O and easing the diaphragm's pressure and unloading the abdominal contents, thereby opening small airways and dependent lung parts by prone position. [19] However, this maneuver resulted in low tidal volume, low oxygenation, high plateau pressure, hypoxia, respiratory acidosis, and hemodynamic instability within few hours of the prone position. In this setting, VV-ECMO provided us comprehensive guaranteed respiratory support. Adjunct with an organized treatment algorithm, resource allocation, ECMO inflow, and outflow configuration plan to our selected young adult patient with no previous health ailments to whom all the conventional respiratory measures failed. An initial report from China observed that ECMO in six COVID-19 patients resulted in only one survived to discharge. Another study reported that in 8 patients only 4 survived ECMO decannulation. Similarly, thirty-two US patients from various ECMO centers showed a mortality of 31% and 53% still on ECMO for three weeks.[20] In our case, VV- ECMO started early within 24 hours of ICU admission and continued for the next 16 days as a supportive treatment to improve lung compliance and gas exchange to resolve hypoxemia and hypercapnia. thereby permitting lower plateau pressures and decreased pulmonary vascular resistance through which the respiratory, circulatory and other vital organs functional indexes are well maintained for safe retrieval.[21] As well, antibiotics were adjusted accordingly to achieve an excellent therapeutic effect. As reported in previous studies, our ECMO running time, cannulation, and decannulation duration were not significantly longer than the usual time. In our case, the right femoral vein thrombosis (pre-ECMO) and abdominal thrombosis (post-ECMO) were managed successfully without any invasive interventions. Likewise, the recent study addressed the incidence of vascular thrombosis in pre-ECMO and thrombotic events on post-ECMO as 31.5% and 47.4%[21]. Generally, ECMO cannulation, running time, and weaning in class v obesity are complex, challenging, and time-consuming. Besides, general precautious measures by wearing and working under full PPE for a more extended time proved extraordinarily strenuous but still viable. We followed the ELSO and WHO current guidelines in selecting our patient with ARDS and a Murray lung injury Score of 3.5. Generally, Murray Score is used to assess the severity of acute lung injury, and it combines four criteria: hypoxemia, lungs compliance, chest radiographic findings, and positive end-expiratory pressure, respectively. Each criterion earns a score from 0 to 4 according to its severity. The definitive score is obtained by dividing the combined score by the number of components used. A zero scoring signifies no lung injury, a scoring of 1 – 2.5 signifies mild to moderate lung injury, and a final score of more than 2.5 signifies the presence of ARDS, and a Murray Score of 3-4 may be considered for ECMO cannulation in the suitable clinical setting or referral to the ECMO center. Furthermore, this Murray score benefits our team in selecting our patient for successful VV-ECMO treatment. In addition, we followed ELSO guidelines and strategies to reduce infection risk to our health care associates involved in our patient care. [22,23] Our study emphasizes that following a reasonable trial period if maximum conventional ventilation support fails, consideration of providing early VV-ECMO in this group of patients is promising in the absence of any comorbidities.

CONCLUSION

The Early VV-ECMO induction, running, and weaning are achievable in the institution with high resources. However, obesity is a complex disease. Infinite clinical knowledge and a comprehensive skilled clinical team are needed to determine the benefit-risk Ratio by choosing the patients to whom VV-ECMO will be the savior.

CONFLICT OF INTEREST

None to declare.

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ETHICAL APPROVAL

The Research Ethical Committee of our institution approved this Case Study. We secured written informed consent obtained from the patient for publication of this case and any accompanying images.

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