Case Report

OPEN ACCESS

Use of venovenous (VV) extracorporeal membrane oxygenation (ECMO) in near-fatal asthma: a case series

Ciro D. Ibarra[1], Saveria Sangiovanni[1], Diego F. Bautista[2,3], Camilo A. Calderón-Miranda[4,3], Gustavo A. Cruz[5,3], Liliana Fernández-Trujillo[6,3]

[1]Clinical Research Center, Fundación Valle del Lili. Cali, Colombia; [2]Department of Critical Care Medicine, Fundación Valle del Lili, Cali, Colombia; [3]Faculty of Health Sciences, Universidad Icesi, Cali, Colombia; [4]Department of Internal Medicine, Cardiology Service, Fundación Valle del Lili, Cali, Colombia; [5]Department of Anesthesiology, Fundación Valle del Lili, Cali, Colombia; [6]Department of Internal Medicine, Pulmonology Service, Fundación Valle del Lili, Cali, Colombia.

ABSTRACT

Introduction: Status asthmaticus (SA) and near-fatal asthma (NFA) are life-threatening conditions that continue to present a management challenge for physicians. Extracorporeal Membrane Oxygenation (ECMO) has been employed as a last resort in treating these patients.

Case presentation: We described six patients who were admitted to the ICU for NFA and received ECMO treatment at a high-complexity institution in Cali, Colombia, between 2015 and 2019. All patients are registered in the ELSO registry. Baseline patient characteristics, arterial blood gases (ABG), ventilatory parameters, and complications were collected as specified in the ELSO registry form. Efficacy was analyzed in terms of the improvement in respiratory acidosis, the number of ventilator-free days (VFD), and a reduction in mechanical power (MP). MP, which refers to the energy associated with the mechanical forces involved in breathing and the functioning of the respiratory system, was calculated using a mathematical formula. Safety was evaluated based on the incidence of complications. After 12 hours of ECMO, we achieved a correction of respiratory acidosis, a significant decrease in all ventilatory parameters, and a reduction in MP ranging from 52.8% to 89%. There was one mortality. Among the five surviving patients, all except one, who required a tracheostomy, had a high VFD score, with a mode of 26 days, demonstrating a reduction in ventilation time.

Conclusion: Further randomized controlled trials are needed to fully understand the efficacy and safety profiles of ECMO in SA/NFA. MP is being widely used to achieve safer ventilation, and although more data is required, it appears to be a promising option for evaluating the risk of developing VILI and the success of the therapy.

Key words: Status asthmaticus, Near-Fatal Asthma, Extracorporeal Membrane Oxygenation, Mechanical Power, Case Series.

Correspondence: Liliana Fernández-Trujillo MD. Department of Internal Medicine, Pulmonology Service, Interventional Pulmonology. Avenida Simón Bolívar. Cra. 98 No.18-49, Fundación Valle del Lili. Tower 6, 4th Floor. Cali, Colombia. Zip code 760032, telephone number: + (57) 3155006300. E-mail: liliana.fernandez@fvl.org.co, lilianafernandeztrujillo@gmail.com

Contributions: All authors have read and approved the manuscript, and significantly contributed to this paper. CDI: Literature review, manuscript writing and correction, final approval of manuscript. SS: Literature review, manuscript writing and correction, final approval of manuscript. DFB: Conception and design, literature review, manuscript writing and correction, final approval of manuscript. CAC: Conception and design, literature review, manuscript writing and correction, final approval of manuscript. GAC: literature review, manuscript writing and correction, final approval of manuscript. LFT: Conception and design, literature review, manuscript writing and correction, final approval of manuscript.

Ethics approval: This manuscript was written in compliance with the ethical standards of the institutional ethics committee and with the 1964 Helsinki Declaration. We have approval from the Ethics Committee in Biomedical Research from Fundación Valle del Lili. This is supported in letter No. 143 of 2020, record No. 11, which is available if needed with the Corresponding Author.

Availability of data and material: All data and material are available for sharing if needed.

Conflict of interest: The authors declare that they have no competing interests. This manuscript has not been published and is not under consideration for publication elsewhere. Additionally, all of the authors have approved the contents of this paper and have agreed to the journal´s submission policies.

Introduction

Status asthmaticus (SA) and near-fatal asthma (NFA) are life-threatening conditions that continue to present a treatment challenge for physicians. SA represents an acute, severe asthma exacerbation that does not respond to initial therapy, while NFA refers to SA that progresses to respiratory failure [1]. Data from around the world suggests that the frequency of patients requiring intensive care unit (ICU) admission for asthma exacerbations has decreased from 10% to approximately 2-4% [2]. However, among patients in the ICU, the need for mechanical ventilation (MV) has remained consistent at around 36%, with a hospital mortality rate of up to 9.8% [2–4].

In certain circumstances, conventional treatments for asthma, such as bronchodilators, corticosteroids, and mechanical ventilation (MV), may prove insufficient. In such cases, several adjunct therapies must be initiated, such as ketamine, general anesthesia, and, as a last resort, extracorporeal membrane oxygenation (ECMO) [1,5]. The guidelines from the Extracorporeal Life Support Organization (ELSO) for adult respiratory failure specify the indications for ECMO therapy, including conditions like CO_2 retention syndromes [6], such as asthma.

The primary goal of ECMO therapy is to correct tissue hypoxia, but evidence suggests that one of its significant benefits is reducing the frequency of ventilator-induced lung injury (VILI), a common complication of MV. Mechanical power (MP), defined as the amount of energy delivered to the respiratory system by a mechanical ventilator per tidal cycle and ventilating frequency, determined by volume, pressure, flow, and respiratory rate [7,8] (Figure 1), is a novel concept intrinsically related to the development of VILI. We believe that by reducing MP, we can contribute to the prevention of VILI.

The objective of this article is to describe a series of six patients with NFA who received ECMO as a last resort, with a particular emphasis on monitoring and preventing VILI using MP.

Materials and methods

We conducted a retrospective search of patients admitted to the ICU for NFA who received ECMO at a high-complexity institution in Cali, Colombia, between 2015 and 2019. All patients had a history of poorly controlled asthma and were experiencing an episode of SA/NFA. They all received standard treatment consisting on beta-2 agonist and anticholinergic inhalers, intravenous (IV) steroids, and magnesium sulfate, in addition to adjunct therapies such as ketamine or inhalational anesthetics like sevoflurane. Moreover, they met the criteria outlined in the ELSO guidelines for managing hypercapnic respiratory failure in adults: CO_2 retention despite MV and high Plateau Pressure (Pplat > 30 cm H_2O), PaO_2/FiO_2 < 80 for at least 3 hours, or pH < 7.25 for at least 3 hours, when conventional medical management strategies had been exhausted [6]. All patients are included in the ELSO registry.

Patients underwent cannulation in the operating room. All but one patient were cannulated using the internal jugular vein with a double-lumen cannula (AVALON® #27, the smallest available). The remaining patient was cannulated via the right femoral vein using a BIOMEDICUS® #21 cannula, after unsuccessful attempts to cannulate the internal jugular vein, despite performing a venodisection. All patients were successfully placed on venovenous (VV) ECMO.

Baseline patient characteristics, arterial blood gases (ABG), and ventilatory parameters were collected as per the ELSO registry form [9]. Pre-ECMO ABG and ventilatory parameters were recorded as close as possible to ECMO initiation, within a 6-hour window prior to starting ECMO. Post-ECMO ABG and post-ECMO ventilatory parameters were collected around 24 hours after ECMO initiation, with measurements not taken prior to 18 hours or after 30 hours. Additional data included parameters related to ECMO gas flow, ECMO time, the need for blood products, inotropic and vasoactive support, complications, ICU duration, and mortality. Complications were documented according to the ELSO guidelines [6,9].

$$\text{Mechanical Power} = \frac{\text{VE X (Peak Pressure + PEEP + F/6)}}{20}$$

VE, minute ventilation; PEEP, Positive end-expiratory pressure; F, inspiratory flow

Figure 1. Mechanical Power Formula Proposed by Giosa *et al.*

Case series presentation

Case 1

A 29-year-old female, who had experienced her last severe asthma attack three years earlier, requiring intubation and MV, was a regular user of beta-2 inhalers, using them approximately twice a week. She initially presented at another healthcare facility with a severe asthma exacerbation, where standard treatment for her acute asthma attack was initiated but showed a poor response, leading to intubation with oxygen administered through Bag-Valve-Mask (BVM) ventilation. She was then transferred to our emergency department. Her vital signs at admission were as follows: blood pressure 152/120 mmHg, heart rate 149 beats per minute, respiratory rate 12 breaths per minute, oxygen saturation (SO_2) at 97%, and a temperature of 37 degrees Celsius. Physical examination revealed the use of accessory muscles, universal wheezing, and rhonchi in both pulmonary fields. The patient was then connected to a ventilator in pressure control mode, with settings detailed in Table 1. A chest X-ray indicated signs of hyperinflation without other abnormal findings. Initial ABG documentation revealed severe respiratory acidosis. She was subsequently transferred to the ICU for hypercapnic respiratory failure in the context of SA/NFA, with a poor response to standard care.

Upon ICU admission, the patient required high airway pressures, resulting in barotrauma, hemodynamic decompensation, and cardiopulmonary arrest. She responded to cardiorespiratory resuscitation, and vasoactive support with norepinephrine was initiated, requiring high doses, leading to the initiation of vasopressin. Despite continuous nebulization with salbutamol, she persisted with severe bronchospasm, prompting the administration of ketamine infusion and general anesthesia with sevoflurane. A chest X-ray revealed a right pneumothorax, which was treated with thoracostomy, resulting in a secondary bronchopleural fistula of 50% (Figure 2). Additionally, ABG results indicated further respiratory acidosis, requiring high ventilatory parameters with a MP of 14 joules/min. VV ECMO was initiated. Blood gases and ventilatory parameters slightly improved during the first 12 hours of ECMO, with a decrease in MP of 61.5% (Table 1). The patient was on ECMO for a total of 11 days (Table 2). However, she experienced several pulmonary, hematologic, renal, and infectious complications and

Table 1. Patient's overview, pre and post ECMO ABG's and ventilatory settings.

	Patient 1		**Patient 2**		**Patient 3**		**Patient 4**		**Patient 5**		**Patient 6**	
Gender	Female		Female		Female		Female		Female		Male	
Age	29		33		53		55		17		49	
Weight	65		60		45		70		90		60	
ECMO ABG	**Pre**	**Post**	**Pre**	**Post**	**Pre**	**Post**	**Pre**	**Post**	**Pre**	**Post**	**Pre**	**Post**
pH	6.99	7.47	6.8	7.3	6.97	7.41	7.01	7.5	7.01	7.36	6.90	7.49
$PaCO_2$ (mmHg)	121	37	183.4	33.2	148.2	35	124	42.8	100	42	125	32
PaO_2 (mmHg)	112	158	74.2	65.1	167	134	83	65.9	191	42	206	63
HCO_3 (mmol/L)	28	26.4	28.3	18.1	-*	24	35	29.9	22	23	-*	24
SaO_2 (%)	95	99	71.2	91	100	99	90	94.8	95	90	99	94
Pre ECMO Ventilatory settings	**Pre**	**Post**	**Pre**	**Post**	**Pre**	**Post**	**Pre**	**Post**	**Pre**	**Post**	**Pre**	**Post**
Respiratory rate (rpm)	14	14	10	18	14	10	8	18	22	10	18	10
FiO_2 (%)	52	24	90	21	80	40	70	32	100	30	65	30
PIP (cm H_2O)	39	23	57	24	30	10	49	22	49	18	40	22
PEEP (cm H_2O)	7	8	2	10	5	5	9	8	8	8	8	8
Paw (cm H_2O)	10	11	17	14	16	7	19	10	18	12	11	14
Mechanical Power (Joules/min)	14	5.4	7.2	3.4	9.5	2	11	1.9	20.2	2.2	15.6	4

*Undetectable HCO_3 values.

died 13 days after her ICU admission (Table 3). Her ventilator-free days (VFD) score was 0.

Case 2

A 33-year-old woman, who had experienced her last acute asthma attack a month earlier, sought medical attention at a primary health center due to a progressive shortness of breath and wheezing that did not improve with inhalation therapy with beta-2 agonist and anticholinergic inhalers at home. Initially, she was prescribed an IV steroid regimen and inhalation therapy with short-acting beta-2 agonist for an acute asthmatic episode, along with non-invasive mechanical ventilation (NIMV), with a poor response. Consequently, she was referred to our institution as a life-threatening emergency. Upon admission, her vital signs were as follows: blood pressure 146/81 mmHg, heart rate 130 beats per minute, respiratory rate 32 breaths per minute, SO_2 at 96%, and a temperature of 36 degrees Celsius. Physical examination revealed the use of accessory muscles, decreased breath sounds, and universal expiratory wheezing. Standard therapy was initiated, and a chest X-ray indicated air trapping without other abnormal findings. Initial ABG analysis showed respiratory acidosis. However, the patient's

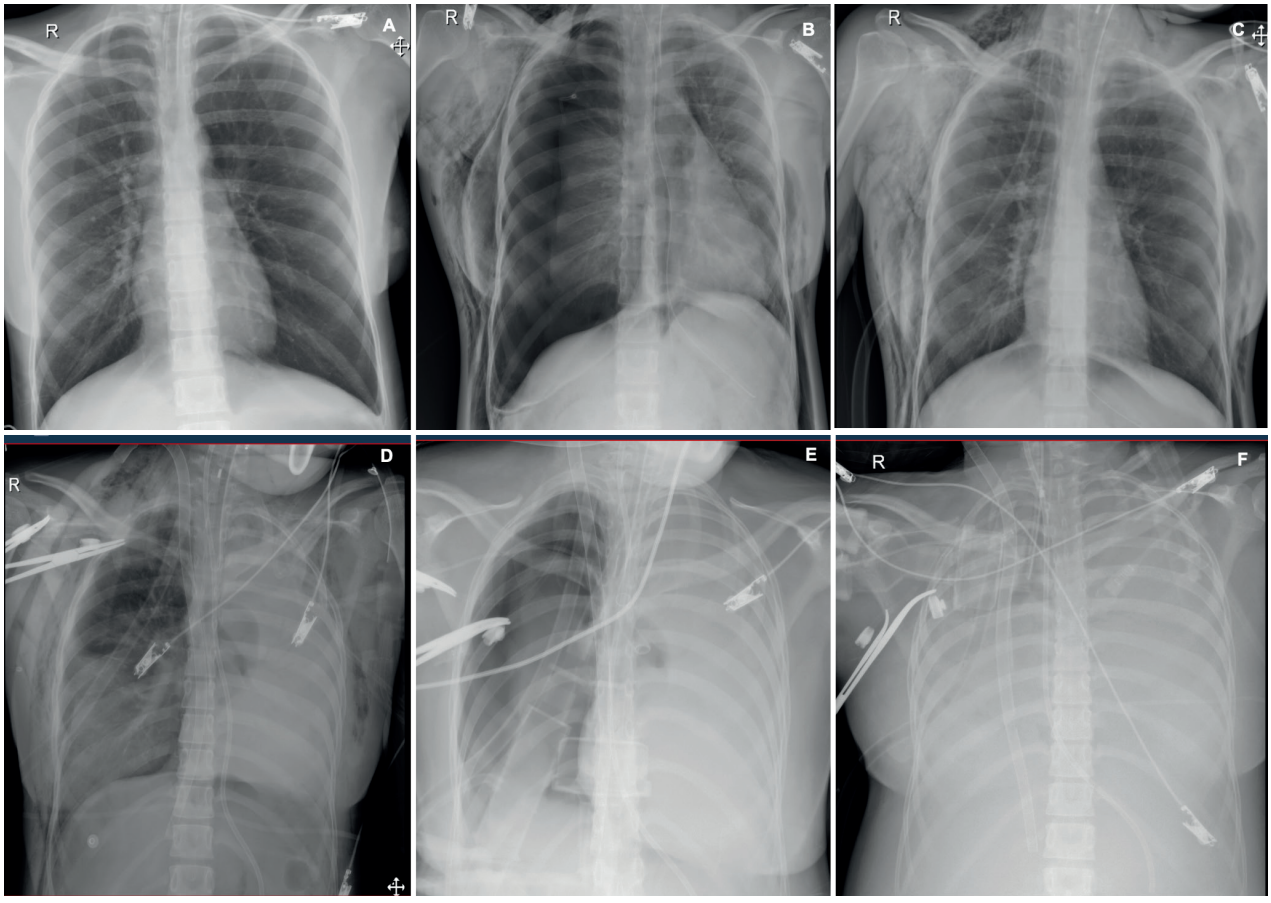

Figure 2. Sequential chest X-ray of case 1. A. Signs of pulmonary hyperinflation with diaphragmatic flattening. Orotracheal tube in proper position, there are no consolidations and pleural angles are free. B. Severe right pneumothorax, subcutaneous emphysema, displacement of mediastinal structures to the left. Presence of a nasogastric tube. C. Mild pulmonary expansion with large subcutaneous emphysema. The chest tube is directed towards the pulmonary apex, a superior vena cava catheter is placed. D. Complete opacity of the left hemithorax with ipsilateral displacement of mediastinal structures, suggestive of atelectasis and presence of a hernia in the right lung. There is subcutaneous emphysema on both pulmonary fields. E. Severe right pneumothorax with complete collapse of the lung, right chest tube, mediastinal displacement to the left. F. Complete opacity of both pulmonary fields due to massive pleural effusion, right chest tubes and displacement of the trachea to the right. R: right side.

Table 2. ECMO indication, parameters and support

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Indication for ECMO	Hypercapnic respiratory failure Respiratory acidosis Right bronchopleural fistula 50% (Barotrauma) Cardiac arrest	Hypercapnic respiratory failure Respiratory acidosis VILI	Hypercapnic respiratory failure Respiratory acidosis	Hypercapnic respiratory failure Respiratory acidosis	Hypercapnic respiratory failure Respiratory acidosis	Hypercapnic respiratory failure Respiratory acidosis
Flow (L/min)	3,5	3,2	2	3	3,4	3
FiO_2 (%)	80	40	40	30	90	100
Gas flow (L/min)	2	3.5	3.5	2	3	4
ECMO time (h)	288	168	96	144	168	144
Blood transfusion						
RBC	16	3	2	4	2	0
FFP	20	0	0	0	0	0
Cryo	15	0	0	0	0	0
Vasoactive support (days)	12	6	N/A	4	N/A	4
Inotropic support (days)	2	6	N/A	N/A	N/A	N/A
Hemodialysis	Yes	No	No	No	No	No

VILI, ventilator induced lung injury; RBC, red concentrate blood; FFP, fresh frozen plasma; Cryo, cryoprecipitate.

Table 3. Patient complications during and posterior to ECMO and outcomes.

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Mechanical complications						
Circuit-related	No	No	No	No	No	No
Cannula-related	No	No	No	No	No	No
Medical complications						
Hemorrhage	No	No	No	No	No	No
Neurologic	No	No	No	TIA	No	No
Renal	AKI	No	No	No	No	No
Cardiovascular	Cardiac arrest, Ventricular fibrillation	Left ventricular dysfunction	No	Tamponade	No	No
Pulmonary	Left Pneumothorax, pulmonary hemorrhage	No	No	No	No	No
Metabolic	DIC	No	No	No	No	Hemolysis
Infectious	VAP	No	No	No	No	Pneumonia
Patient limb	No	No	No	No	No	No
VFD	0	23	26	9	26	26
ICU stay	13	9	8	18	8	11
Total Hospital Stay	13	11	9	19	0	0
Mortality	Yes	No	No	No	No	No

VAP, ventilator-associated pneumonia; DIC, disseminated intravascular coagulation; VFD, ventilator free-days.

condition worsened, and she became desaturated and fatigued, requiring intubation and the initiation of MV for hypercapnic respiratory failure.

Ventilating the patient proved challenging due to high airway resistance, leading to the administration of neuromuscular blockade with vecuronium and optimization of sedation with a ketamine infusion. A blood sample revealed an elevated white blood cell count, suggesting pneumonia, so antibiotics were initiated. The patient was then transferred to the ICU, where standard medical care continued, and nebulized adrenaline was added to the management. Nevertheless, her oxygen saturation continued to decline (SO_2 84%), and she became hypotensive (blood pressure 80/40 mmHg), with persistently high airway resistance. Vasoactive support and general anesthesia with sevoflurane were introduced. New ABG revealed mixed acidosis and severe hypercapnia, which proved refractory to management, with a MP of 7.2 J/min, prompting the initiation of ECMO (Figure 3). All microbiologic cultures and acute-phase reactants yielded negative results, and bronchoscopy revealed no remarkable findings, leading to the suspension of antibiotics. ABG values improved, as did ventilatory parameters, with a 53% decrease in MP (Table 1). Five days after ECMO initiation, the patient was successfully weaned from MV, achieving a VFD score of 23. She remained on ECMO for one more day, totaling 6 days (Table 2). A transthoracic echocardiogram reported moderate ventricular dysfunction with no other complications. She was discharged after a total of 11 days (Table 3) (Figure 4).

Case 3

A 53-year-old woman sought care at an external institution due to 3 days of worsening dyspnea and a dry cough. She presented with tachypnea, use of accessory muscles, and generalized wheezing in both lung fields. Inhalation therapy with a beta-2 agonist and an IV steroid regimen was initiated, but the patient had a poor response, leading to intubation and the initiation of MV. Subsequently, she was transferred to our institution. Upon admission, her vital signs were as follows: blood pressure 135/75 mmHg, heart rate 120 beats per minute, respiratory rate 35 breaths per minute, SO_2 at 98%, and a temperature of 36 degrees Celsius. Physical examination revealed decreased breath sounds and wheezing. Standard care for SA was initiated and MV was continued. A chest X-ray showed no remarkable

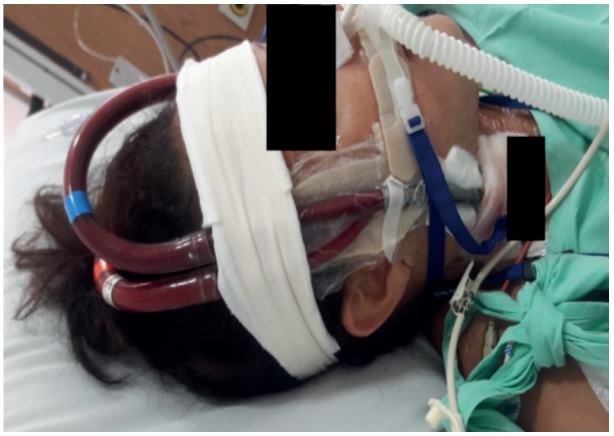

Figure 3. Appearance of the 27 Fr Avalon cannula located in the right internal jugular vein in the veno-venous system, under ultrasound guidance.

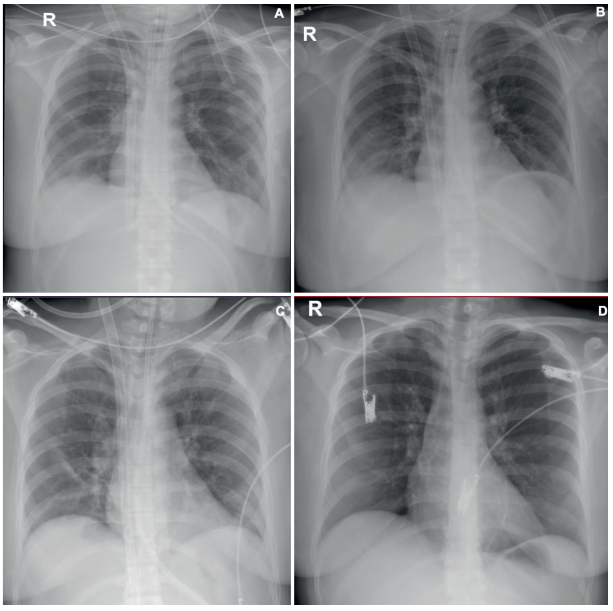

Figure 4. Sequential chest X-ray of case 2. A. thickening of the peribronchial weave, nasogastric tube, ECMO cannula in place and right subclavian catheter with its distal end in the right atrium. There are no areas of consolidation or pleural effusion. B. Veiling of the right costophrenic angle due to a small pleural effusion, with no areas of consolidation. C. Small band of right flat atelectasis, patent airway, presence of ECMO cannula and right subclavian catheter. D. Recovery chest X-ray showing a normal cardiac silhouette, normal pulmonary fields and a normal mediastinum.

findings besides air trapping7, and the initial ABG analysis indicated respiratory acidosis.

Despite continuous salbutamol nebulization and ketamine infusion, the patient continued to have a poor response, experiencing high airway pressures that hindered adequate ventilation. Respiratory acidosis worsened, and MP reached 9.5 J/min (Table 1). Consequently, she was transferred to the ICU, where the medical team determined that she would benefit from VV ECMO. After 12 hours of ECMO, the patient achieved normocapnia, had adequate oxygenation, and experienced a 79% decrease in MP. A sputum chain polymerase reaction was positive for rhinovirus/enterovirus, while her white blood cell count was normal, and acute phase reactants were negative. She was weaned from MV two days later with a VFD score of 26. Her ECMO support lasted for a total of 4 days (Table 2), and she did not encounter any complications. The patient was discharged after a total of 9 days (Table 3).

Case 4

A 55-year-old female patient consulted an external institution due to progressive dyspnea. She was tachypneic, requiring the use of accessory muscles, and her SO_2 dropped below 80% despite management with NIMV, terbutaline and dexamethasone nebulizations, and IV steroid. The patient was subsequently transferred to our institution with the following vital signs: blood pressure 153/93 mmHg, heart rate 126 beats per minute, respiratory rate 27 breaths per minute, SO_2 at 93%, and a temperature of 35.7 degrees Celsius. She displayed no neurological response. Intubation was performed and MV was initiated along with standard care. A chest X-ray revealed air trapping, and the initial ABG analysis indicated respiratory acidosis. She was then transferred to the ICU, where management continued, adding neuromuscular blockade, ketamine, and prophylactic antibiotics due to the possibility of bronchoaspiration. Vasoactive support was also initiated.

Despite these interventions, the patient continued to experience severe bronchospasm, respiratory acidosis, and high ventilatory parameters, with a MP of 11 J/min (Table 2). ECMO was considered, but during the procedure, the patient suffered cardiac tamponade, requiring drainage through a pericardial window. Following the procedure, anisocoria was documented but resolved within 24 hours, suggesting a transient ischemic attack. A cerebral computerized tomography (CT) scan yielded unremarkable results (Table 3). Gas exchange began to improve, as did ventilatory parameters, with a decrease in MP of 82.8% (Table 1). An attempt to extubate was made 3 days after ECMO initiation, but the patient exhibited agitation, dyspnea, and severe bronchospasm, requiring reintubation, despite normal ABG. Two days later, a tracheostomy was performed due to persistent bronchospasm. ECMO support continued for a total of 6 days (Table 2). After 18 days in the ICU, when there was no evidence of bronchospasm and her oxygenation was adequate, she was transferred to the intermediate care unit to continue the weaning process from MV and undergo pulmonary rehabilitation. The patient experienced no other complications and was discharged after a total of 19 days with a VFD score of 9 (Table 3) (Figure 5).

Case 5

A 17-year-old female patient arrived at an external primary care center with a two-hour history of worsening dyspnea and a dry cough. Initial treatment included nebulizations with a short-acting beta-2 agonist, IV steroid, and magnesium sulfate. Despite these interventions, the patient did not respond well and her respiratory condition continued to deteriorate, necessitating an urgent transfer to our institution. Upon admission, she was in respiratory failure with altered sensorium, requiring immediate intubation and MV. Her vital signs were as follows: blood pressure 137/84 mmHg, heart rate 101 beats per minute, respiratory rate 40 breaths per minute, SO_2 98%, and temperature 36.7 degrees Celsius. During the physical examination, she exhibited the use of accessory muscles, basal bilateral hypoventilation, and universal inspiratory and expiratory wheezing. Standard management was initiated. Chest X-ray revealed air trapping, and the first ABG showed severe respiratory acidosis. Furthermore, high airway pressures and a MP of 20.2 J/min were documented, leading to the initiation of ECMO. The patient exhibited rapid

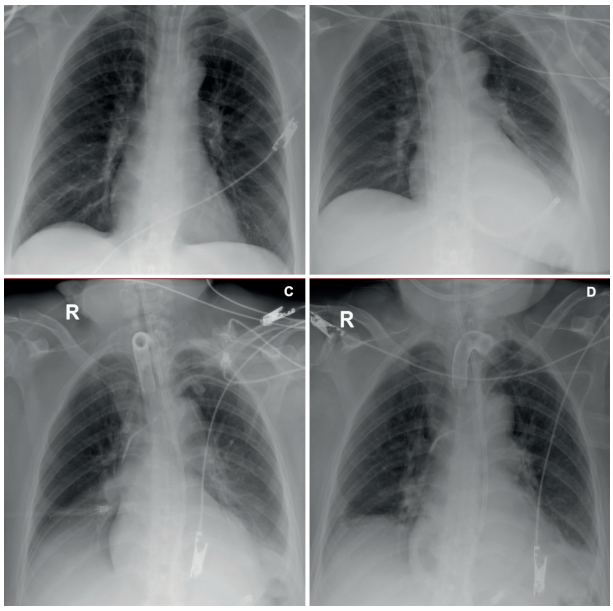

Figure 5. Sequential chest X-ray of case 4. A. Chest X-ray with adequate pulmonary expansion, orotracheal tube correctly positioned. B. A left basal opacity is identified, secondary to pleural effusion with increased retrocardiac density due to atelectasis/consolidation, presence of ECMO cannula in right jugular vein. C. Tracheostomy cannula, pulmonary congestion and bilateral pleural effusion. D. Tracheostomy cannula, unremarkable pulmonary hila, subsegmentary bilateral basal atelectasis with small pleural effusion, enteral feeding tube and left subclavian catheter.

improvement in ABG (Table 1), with a subsequent decrease in MP by 89.2%. After two days, she was successfully extubated, achieving a VFD score of 26. ECMO support continued for a total of 8 days (Table 2). The patient experienced no complications and was discharged after 8 days (Table 3).

Case 6

A 49-year-old male patient sought medical attention at a peripheral primary healthcare facility due to a gradual onset of dyspnea, bronchospasm, and cyanosis. Initial treatment consisted of inhalation therapy with beta-2 agonist and anticholinergic inhalers but yielded a limited response, prompting the need for intubation and the subsequent transfer to our institution. Upon admission, the patient exhibited the following vital signs: blood pressure 196/91 mmHg, heart rate 125 beats per minute, respiratory rate 22 breaths per minute, SO_2 73%, and a temperature of 36 degrees Celsius. During the physical examination, diffuse wheezing was observed. The orotracheal tube was changed from 7.0 to 8.0, and MV was initiated in conjunction with standard therapy. A chest X-ray showed hyperinflation, with no other apparent findings. The patient showed no response to initial management, presenting severe respiratory acidosis, high airway resistance, and a MP of 15.6 J/min. Consequently, he was promptly transferred to the operating room, where ECMO was initiated, and vasoactive support was added. After 12 hours, the patient exhibited mild improvement but remained hypoxemic. MP had decreased by 74.4% (Table 1). After 2 days, he was extubated but experienced desaturation without hemodynamic instability or an increase in respiratory effort. Therefore, NIMV was continued, resulting in a VFD score of 26. The patient also exhibited symptoms of fever and hemoptysis, which prompted the collection of cultures and the initiation of antibiotic treatment. Given the suspicion of pneumonia, a chest X-ray was requested, which revealed a right basal consolidation. Additionally, a bronchoscopy was performed, revealing the presence of a foreign object in the right mainstem bronchus, which was subsequently extracted. It was a 12 cm long, hollow plastic fragment, that resembled an aspiration probe. While the object's exact origin could not be definitively determined, there was suspicion that it may have been introduced at the primary care health center during respiratory therapy or intubation, as this type of probe is not used in our institution. Following this procedure, ABG values returned to normal, and the airway obstruction resolved. However, the patient developed moderate thrombocytopenia and hemolysis. Considering the risk-benefit relationship, ECMO was removed after 5 days (Table 2). The patient experienced no further complications and was discharged after a total of 11 days (Table 3) (Figure 6).

Discussion

Over the past decade, ECMO has emerged as a last-resort treatment for patients with SA and NFA who do not respond to standard medical therapy. While the available evidence primarily derives from case reports and retrospective cohort studies, ECMO

appears to be an effective rescue therapy, contributing to a reduction in asthma-related mortality rates [10]. In the context of acute respiratory distress syndrome (ARDS), survival rates are estimated to be approximately 67% for patients who are successfully weaned off ECMO, with a 52% survival rate upon hospital discharge. In contrast, when ECMO is utilized in other medical scenarios, such as cardiac arrest, cardiogenic shock, or following cardiac surgery with cardiopulmonary bypass, reported survival rates typically fall within the range of 20% to 30% [11].

As mentioned earlier, while the correction of respiratory acidosis remains a crucial goal in ECMO therapy, preventing VILI is one of the critical factors influencing the mortality of these patients. In fact, the sole mortality in this case series was observed in a patient who had already developed VILI and extensive barotrauma before ECMO initiation. Ventilator-related causes of VILI include large tidal volumes, high pressures, elevated respiratory rates, and large inspiratory flow rates, all of which contribute to the MP equation, as well as pneumothorax [12]. Despite emerging evidence regarding MP, there are no established goals or "normal" limits [7]. However, it is expected that as pulmonary compromise worsens, the threshold for VILI becomes lower. The thresholds for stress, strain, power, and energy may vary, but they depend on the degree of underlying tissue integrity and the extent of the injury [13].

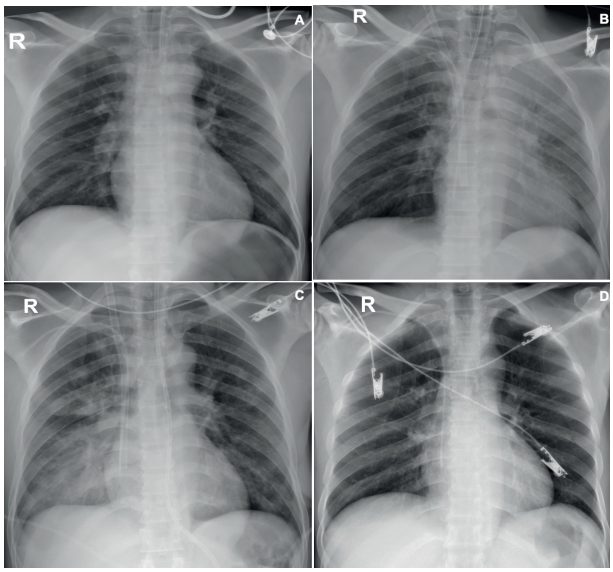

Figure 6. Sequential chest x-ray of case 6. A. Normal cardio aortic silhouette, central trachea, normal mediastinum, orotracheal tube in proper position. There are no consolidations, adequate pulmonary expansion. An image is observed that may correspond to a probe projected to the right intermediate bronchus. B. central trachea, orotracheal tube correctly positioned, right jugular cannula ending in the right atrium. Appearance of consolidation with air bronchogram in the left upper lobe. C. Opacity in the right lower lobe, ECMO cannula in position, enteral feeding tube. There is no evidence of pleural effusion. This image is posterior to the extraction of the foreign body located in the right intermediate bronchus. D. Image prior to discharge showing a normal trachea, normal cardiac silhouette, mediastinum and lung fields. There is no evidence of pneumothorax or pleural effusion.

Nevertheless, a reduction in MP as an indicator of the risk of developing VILI should be considered a safety measure in therapy. Therefore, when evaluating the efficacy of ECMO, one should not only focus on ABG values but also on the decrease in ventilatory parameters, especially those variables contributing to MP. Calculating MP can be complex, involving mathematical processes and the manipulation of the ventilator to measure certain variables. Some simpler formulas have been proposed, such as the one described by Giosa *et al.* (Figure 1), which we used in this case series [14]. This formula is intended for use in volume-controlled ventilation and includes variables like minute ventilation, peak pressure, positive end-expiratory pressure (PEEP), and inspiratory flow.

It should be noted that the formula proposed by Giosa *et al.* made a significant assumption that could introduce bias in calculations. This assumption involved a fixed value for respiratory system resistance at 10 cm H_2O/L/sec, which is an average value commonly found in the literature for mechanically ventilated patients [14]. However, certain conditions, such as COPD and asthma, primarily impact airway resistance, potentially leading to higher respiratory system resistance values and consequently an increase in mechanical power [14,15]. Nevertheless, during the development of this simplified formula, a secondary analysis was conducted on patients with respiratory system resistances greater than 15 cm H_2O/L/sec, with a median value of 18.9 cm H_2O/L/sec. This analysis revealed a minor underestimation bias, which still ensures the accuracy of the formula when applied to patients with elevated resistances [14].

In our case series experience, we observed that after 12 hours of ECMO support, not only did we achieve correction of respiratory acidosis, but we also noted a significant reduction in all ventilatory parameters and a decrease in MP ranging from 52.8% to 89% (Tables 1 and 3). Furthermore, among the 5 surviving patients, all but one, who required a tracheostomy, had a high VFD score, with a mode 26 days (Table 3). This highlights a substantial reduction in ventilation time.

On the other hand, ECMO is a complex process that demands specific resources and multidisciplinary management and may result in serious, and even fatal, complications [16]. These complications can be categorized as mechanical or medical, with the former being associated with the circuit and cannulation process, device-related issues, insertion complications, anticoagulation, or the therapy's effects on distal organs [17]. Common complications reported include cardiovascular issues (particularly the need for inotropes during therapy), renal problems, culture-proven infections, the presence of clots in the oxygenator, and hemorrhagic complications (mainly related to cannula and surgical site bleeding) [11,17]. Survival rates for these complications range from 47% to 58%, decreasing to 28% to 30% for rarer but more severe complications like central nervous system infarction and hemorrhage, as well as disseminated intravascular coagulation, respectively [18].

A retrospective cohort study, based on the ELSO registry, analyzed survival and complication rates in 1257 cases. Out of these, 24 patients received ECMO for SA, while the remaining cases were non-asthmatic. Asthmatic patients were younger, received less MV before ECMO initiation, had shorter ECMO durations, exhibited greater acidosis, and less hypoxia. The survival rate among asthmatics was 83.3% compared to 50% in the non-asthmatic group. The complication rate was 79.2%, with mechanical and bleeding complications being the most prevalent [5]. Similarly, in our experience, the survival rate is high (83%), as evident in this case series where only one out of six patients died. We encountered a total of 9 complications, with cardiovascular issues being the most common. Apart from a cardiac tamponade during cannulation, no patient experienced significant hemorrhage.

Conclusions

ECMO finds utility in a diverse range of medical scenarios, including the management of SA/NFA when conventional treatments prove ineffective. Our experience indicates that ECMO is an effective therapy capable of addressing acidosis and mitigating VILI, resulting in a notably high survival rate, despite the relatively elevated complication rate (40.2%) [19]. It is crucial to recognize that ECMO serves as a life-saving intervention for critical situations. Additionally, the growing use of MP as a tool to enhance safe ventilation is promising, even though more extensive data is required for a comprehensive evaluation of its role in assessing the risk of VILI development and the overall success of ECMO therapy.

Abbreviations

SA: Status asthmaticus
NFA: Near fatal asthma
ICU: Intensive Care Unit
MV: Mechanical ventilation
ECMO Extracorporeal membrane oxygenation
ELSO: Extracorporeal life support organization
CO_2: Carbon dioxide
VILI: Ventilator induced lung injury
MP: Mechanical power
IV: Intravenous
P_{plat}: Plateau pressure
cm H_2O: Centimeter of water
PaO_2/FiO: Oxygen arterial pressure/inspired fraction of oxygen
CNS: Central nervous system
ABG: Arterial blood gasses
VFD: Ventilator-free days
SO_2: Oxygen saturation
BE: Base excess
VV: Venovenous
BVM: Bag-Valve-Mask
$PaCO_2$: Arterial carbon dioxide tension
PO_2: Partial pressure of oxygen
HCO_3: Bicarbonate
NIMV: Non-invasive mechanical ventilation
CT: Computerized tomography
PEEP: Positive end-expiratory pressure
ARDS: Acute respiratory distress syndrome

References

1. Louie S, Morrissey BM, Kenyon NJ, Albertson TE, Avdalovic M. The Critically Ill Asthmatic—from ICU to Discharge. Clin Rev Allergy Immunol. 2012 Aug 1;43(1):30–44.
2. Leatherman J. Mechanical Ventilation for Severe Asthma. Chest 2015;147(6):1671–80.
3. Holley AD, Boots RJ. Review article: Management of acute severe and near-fatal asthma. Emerg Med Australas 2009;21(4):259–68.
4. Kaur BP, Lahewala S, Arora S, Agnihotri K, Panaich SS, Secord E, et al. Asthma: Hospitalization Trends and Predictors of In-Hospital Mortality and Hospitalization Costs in the USA (2001-2010). Int Arch Allergy Immunol 2016;168(2):71–8.
5. Mikkelsen ME, Woo YJ, Sager JS, Fuchs BD, Christie JD. Outcomes using extracorporeal life support for adult respiratory failure due to status asthmaticus. ASAIO J 2009;55(1):47-52.
6. Tonna JE, Abrams D, Brodie D, Greenwood JC, Mateo-Sidron JAR, Usman A, et al. Management of Adult Patients Supported with Venovenous Extracorporeal Membrane Oxygenation (VV ECMO): Guideline from the Extracorporeal Life Support Organization (ELSO). ASAIO J 2021;67(6):601–10.
7. Marini JJ. How I optimize power to avoid VILI. Crit Care 2019;23(1):326.
8. Chiu LC, Lin SW, Chuang LP, Li HH, Liu PH, Tsai FC, et al. Mechanical power during extracorporeal membrane oxygenation and hospital mortality in patients with acute respiratory distress syndrome. Crit Care 2021;25:13.
9. ECLS Registry Forms | ELSO | ECMO | Extracorporeal Life Support (Internet). (cited 2023 Oct 3). Available from: https://www.elso.org/registry/datadefinitions,forms, instructions.aspx
10. Yeo HJ, Kim D, Jeon D, Kim YS, Rycus P, Cho WH. Extracorporeal membrane oxygenation for life-threatening asthma refractory to mechanical ventilation: analysis of the Extracorporeal Life Support Organization registry. Crit Care 2017;21(1):297.
11. Vyas A, Bishop MA. Extracorporeal Membrane Oxygenation in Adults. In: StatPearls (Internet). Treasure Island (FL): StatPearls Publishing; 2023 (cited 2023 Oct 3). Available from: http://www.ncbi.nlm.nih.gov/books/NBK576426/
12. Gattinoni L, Marini JJ, Collino F, Maiolo G, Rapetti F, Tonetti T, et al. The future of mechanical ventilation: lessons from the present and the past. Crit Care 2017;21(1):183.
13. Marini JJ, Rocco PRM. Which component of mechanical power is most important in causing VILI? Crit Care 2020;24(1):39.
14. Giosa L, Busana M, Pasticci I, Bonifazi M, Macrì MM, Romitti F, et al. Mechanical power at a glance: a simple surrogate for volume-controlled ventilation. Intensive Care Med Exp 2019;7:61.
15. Hurley JJ, Hensley JL. Physiology, Airway Resistance. In: StatPearls (Internet). Treasure Island (FL): StatPearls Publishing; 2023 (cited 2023 Oct 31). Available from: http://www.ncbi.nlm.nih.gov/books/NBK542183/
16. Na SJ, Chung CR, Choi HJ, Cho YH, Sung K, Yang JH, et al. The effect of multidisciplinary extracorporeal membrane oxygenation team on clinical outcomes in patients with severe acute respiratory failure. Ann Intensive Care 2018;8(1):31.
17. Brodie D, Slutsky AS, Combes A. Extracorporeal Life Support for Adults With Respiratory Failure and Related Indications: A Review. JAMA 2019;322(6):557–68.
18. Extracorporeal Life Support Organization. ECLS Registry Report, International Summary (Internet). 2019 (cited 2023 Oct 4). Available from: https://www.elso.org/registry/internationalsummaryandreports.aspx
19. Vaquer S, de Haro C, Peruga P, Oliva JC, Artigas A. Systematic review and meta-analysis of complications and mortality of veno-venous extracorporeal membrane oxygenation for refractory acute respiratory distress syndrome. Ann Intensive Care 2017;7:51.

Received for publication: 7 February 2021 Accepted for publication: 9 November 2023

Licensee Mattioli 1885, Italy
Multidisciplinary Respiratory Medicine 2024; 19: 943
doi: 10.5826/mrm.2024.943