ECMO Management in Severely Hypothermic Cardiac Arrest Patients

Subjects: Cardiac & Cardiovascular Systems | Anesthesiology | Critical Care Medicine

Contributor: Hubert Hymczak , Aleksandra Gołąb , Sylweriusz Kosiński , Paweł Podsiadło , Dorota Sobczyk , Rafał Drwiła , Bogusław Kapelak , Tomasz Darocha , Dariusz Plicner

Accidental hypothermia, defined as an unintentional drop of the body core temperature below 35 °C, is one of the causes of cardiocirculatory instability and reversible cardiac arrest. Currently, extracorporeal life support (ECLS) rewarming is recommended as a first-line treatment for hypothermic cardiac arrest patients. The aim of the ECLS rewarming is not only rapid normalization of core temperature but also maintenance of adequate organ perfusion. Veno-arterial extracorporeal membrane oxygenation (ECMO) is a preferred technique due to its lower anticoagulation requirements and potential to prolong circulatory support. Although highly efficient, ECMO is acknowledged as an invasive treatment option, requiring experienced medical personnel and is associated with the risk of serious complications.

accidental hypothermia | cardiac arrest | extracorporeal membrane oxygenation | hypothermia

1. Introduction

Hypothermia is defined as a clinical condition in which the body core temperature falls below 35 °C. “Tc” will be used henceforth to denote “body core temperature”. According to etiology, hypothermia can be classified as unintentional (accidental), i.e., from exposure to cold, and intentional (therapeutic). The so-called therapeutic hypothermia, which means a targeted and controlled reduction in Tc, is used in cardiological, neurosurgical and cardiosurgical procedures or in intensive care units [1][2]. It has been established that this procedure improves survival and outcomes from some clinical conditions, including in out-of-hospital cardiac arrest survivors, mostly due to its neuroprotective effect and a decrease in the risk of encephalopathy [1]. However, the optimal target temperature management in this group of patients remains unknown. It has been established that lower temperature, i.e., below 34 °C, does not improve survival nor neurological outcome after normothermic cardiac arrest and increases the risk of arrythmias compared to mild hypothermia and normothermia [3][4][5][6]. It should be also emphasized that avoiding fever seems to be a more important issue [5][6]. In contrast, the survival after cardiac arrest, induced by hypothermia is higher compared to normothermic cases, which is related to a decrease in brain oxygen requirements. Nonetheless, in accidental, uncontrolled development of hypothermia, vital signs decrease and finally this condition may lead to death [2]. Some factors, including degree and cooling time, concomitant diseases and the availability of rewarming techniques influence the prognosis of accidental hypothermia [7].

2. In-Hospital Treatment of Accidental Hypothermia and the Role of Extracorporeal Membrane Oxygenation

2.1. Diagnosis of Accidental Hypothermia

Correct temperature measurement is a key element of proper diagnosis and implementation of optimal therapy in patients with accidental hypothermia. It has been previously thoroughly described how Tc measurement should be correctly performed [8]. A reference technique for Tc measurement is the pulmonary artery temperature reading [9]. However, in clinical settings, the temperature readings in the esophagus are considered to be a gold standard. Tympanic measurement using a thermistor technique is also a reliable option and is an alternative if invasive methods of Tc measurement are impossible to achieve, particularly in patients with preserved circulation. Furthermore, if the urine flow rate is within a normal range, the urinary bladder temperature would closely match the Tc. Temperature-sensing indwelling urinary catheters allow for the continuous drainage of urine and the constant measurement of body temperature. However, if Tc measurement is not available, the estimation of H-CA risk can be made by evaluating the vital signs according to the Swiss Staging System.

2.2. Initial Management and Qualification for Extracorporeal Membrane Oxygenation Support

Measures applied in the pre-hospital management of accidental hypothermia have been exhaustively described by Paal et al. [2]. According to the recent European Resuscitation Council (ERC) Guidelines all hypothermic patients with risk factors, i.e., Tc below 30 °C, ventricular arrythmias and systolic blood pressure below 90 mmHg and those with cardiac arrest, should be transported directly to the centers, where the extracorporeal membrane oxygenation (ECMO) rewarming methods are available [10]. However, there are still no clear criteria or algorithms for the qualification of hypothermic patients for ECMO therapy. Taking into account the fact that there are no absolute contraindications for ECMO support, the decision of its use should be balanced between possible complications and potential benefits [11][12].

From a practical point of view, due to frequent Tc measurement unavailability in pre-hospital settings, interviews with eyewitnesses of the hypothermic event are crucial when making decisions. H-CA patients with a cold trunk, a history of cold exposure (indoor or outdoor) preceding asphyxia, with no serious injuries are those who should be rapidly transported to the ECMO centers to increase the likelihood of treatment success. Additionally, the most important principle of the patients' selection for ECMO therapy is in fact that it should not follow the guidelines for ECMO support for reasons other than accidental hypothermia. Hence, unwitnessed cardiac arrest and conditions such as asystole found at presentation, long or unknown no-flow time (the time from cardiac arrest to cardiopulmonary resuscitation), dilated and fixed pupils, advanced age and end-tidal carbon dioxide below 10 mmHg are not an absolute contraindication to ECMO [11][13].

The evidence supporting traditional triage with Tc and serum potassium level are weak (cut-off level at 30 °C and 7 mmol/L for avalanche victims with cardiac arrest or 12 mmol/L for other remaining cases of accidental hypothermia

with circulatory instability) [14]. Extreme hyperkalemia, reflected by an increased serum potassium concentration above the mentioned cut-off values, is regarded as an absolute contraindication to the ECMO, being a marker of cell death and indicating an unfavorable prognosis. In severe hypothermia, potassium concentrations vary, depending on the sampling site and the analytical method used [15]. The kidney and adrenal insufficiency, intoxication or rhabdomyolysis should be excluded in case of extreme hyperkalemia. Moreover, taking into account other factors that may affect survival, the decision-making should never rely on a single clinical marker [10][11]. Thus, the Hypothermia Outcome Prediction After extracorporeal life support (ECLS), which is known as the HOPE score has been proposed in order to establish the survival probabilities of H-CA patients [14]. A calculated probability of survival of ≥10% in adult H-CA patients provides an indication and justification for ECMO support [11][14]. An online calculator of the HOPE score is available at: www.hypothermiascore.org (accessed on 8 September 2023).

VA-ECMO circuit is indicated in H-CA patients with a potential for its reversibility. The beneficial effect of VA-ECMO is not only in rewarming but also in effective circulatory support as VA-ECMO provides extracorporeal gas exchange and adequate organ perfusion [16].

In summary, the following measures should be taken to make the final decision about VA-ECMO support use in H-CA patients:

- Interview regarding the circumstances of cooling and appropriate Tc measuring.
- Blood samples from ultrasound-guided puncture of the femoral venous (mainly to assess the serum potassium concentration) [15].
- Estimation of the survival rate according to the HOPE score [14].
- Consideration of all possible complications and potential benefits of ECMO therapy.
- Cardiopulmonary resuscitation should be continued during ECMO cannulation.
- Further therapy is dependent on the patient's condition and is the same as for normothermic cardiac arrest patients [11].

2.3. Extracorporeal Membrane Oxygenation Cannulation Techniques and Complications

Cannulation in severely H-CA patients has different specificity compared to normothermic subjects. Depending on the patient's characteristics and the skills of the medical staff, the cannulation of the peripheral vein and artery is performed by the following methods [11][16]:

- Percutaneous modified Seldinger technique, which is associated with a lower risk of bleeding and infection. Rapid implementation is a benefit of this method, but it can be difficult to perform in hypothermic patients with prolonged cardiopulmonary resuscitation. This technique should be performed using ultrasound guidance.
- By using the surgical open cutdown technique, when percutaneously cannulation is not possible. This method is preferred in many centers.
- Combination of the surgical open cutdown and Seldinger techniques.
- During cannulation chest compressions should be continued with the best achievable quality until sufficient ECMO flow is achieved. Chest compressions can then be terminated [11].

Similarly, to the occurrence of problems and pitfalls in the qualification procedure for the ECMO, difficulties are also observed in cannulation. One of the most serious complications is associated with inadequate distal leg perfusion, which is related to the femoral artery cannulation and results in lower extremity ischemia (about 20% of ECMO patients) [16][17]. Hence, a separate perfusion line is usually placed in the distal superficial femoral artery by direct cutdown for retrograde perfusion. This catheter is connected to the side port of the arterial cannula using a 6–8 French extension tubing with an intervening three-way stopcock [16]. Notably, Takayama et al. showed that insertion of the smaller arterial cannulas is associated with lower arterial complication rates compared to the larger ones, while clinical support was comparable [18]. Despite this, limb ischemia is a common cause of premature ECMO system removal [19].

2.4. Extracorporeal Membrane Oxygenation Circuit and Patient-Related Management

The success of the ECMO therapy depends also on proper surveillance during extracorporeal gas exchange and perfusion. The most important principles of circuit and patient-related management in H-CA patients are listed below.

2.4.1. Blood Flow, Oxygenation and Hemodynamics Support

According to the 2017 Extracorporeal Life Support Organization (ELSO) guidelines, to assure optimal systematic perfusion, the blood flow should be between 3 and 4 L/min in adult patients [20]. Blood flow along with vascular resistance have an impact on hemodynamics during ECMO treatment. The mean arterial pressure goal ranges between 50 and 70 mmHg. Hypovolemia is frequently observed in hypothermic patients as a result of endothelium damage and fluid shifts. The most reliable indicator of adequate flow seems to be venous oxygen saturation over 70% [20]. Of note, decreased oxygen demand observed in hypothermia might be a cause of venous oxygen saturation elevation [11].

Refractory ventricular fibrillation may occur during rewarming, which is resistant to the standard therapy until Tc > 30 °C is reached. In case of bradycardia and hemodynamic instability after achieving normothermia, when

pharmacological treatment is ineffective, internal cardiac pacing should be considered [11].

The ECMO support should be completed when normothermia with sufficient hemodynamic stability is achieved or persistent asystole/irreversible ventricular fibrillation occurs, despite normothermia [21]. Complications, such as severe respiratory failure, septic shock with high vasopressors demand and post-resuscitation chest trauma, may delay weaning. With echocardiographic evidence of cardiac recovery, ECMO blood flow should be reduced gradually to a minimum rate of 1.2 to 1.5 L/min. The criteria of the weaning from ECMO are same for hypothermic as well as normothermic patients, i.e., left ventricle ejection fraction ≥ 25%, aortic velocity-time interval ≥ 12 cm on minimal ECMO support settings (1.5 L/min), mitral annulus peak systolic velocity ≥ 6 cm/s, no major valvular pathologies, mean blood pressure > 60 mmHg and central venous pressure < 18 mmHg [22].

2.4.2. Temperature Management

Continuous Tc measurement should be held in two sites simultaneously [23]. Several sites are possible, such as the esophagus, urinary bladder, rectum, tympanic membrane, pulmonary artery or venous inflow [8]. However, ERC strongly recommend esophageal measurement [10]. The target position of the tip of the probe is located in the lower third of the esophagus. However, the esophageal temperature may not correspond to the Tc, which might be caused by warm blood outflow in the vicinity of the tip of the esophageal probe. According to the ERC guidelines, the target Tc during ECMO support is ≥32 °C.

The rewarming rate is calculated as a change of Tc per unit of time during ECMO therapy (°C/h). The optimal rewarming rate is still unknown for hypothermic patients but is usually targeted to ≤5 °C/h [24]. Faster rewarming rates until the return of spontaneous circulation may be recommended, but 10 °C/h should not be exceeded, followed by slower rewarming of about 1–2 °C/h. The heat exchanger should not be set above 37 °C to prevent brain tissue overheating [20]. Normothermia should be achieved within 24 h after the return of spontaneous circulation. When continuous renal replacement therapy is carried out simultaneously, the temperature should be set to 37–38 °C.

2.4.3. Anticoagulation and Hemostasis Disturbances

ECMO protocols routinely include the use of heparin in order to counteract the development of the prothrombotic state and decrease the risk of pump malfunction, oxygenator failure and thromboembolic events, including stroke or pulmonary embolism [24][25][26][27]. Bolus of unfractionated heparin should be administered (50–100 units per kg) at the time of cannulation and then by continuous infusion [20][25]. An activated clotting time (ACT) targeted at 160–220 s is recommended [25]. The benefit of the ACT is rapid assessment of the haemostasis at the patients' bedside. However, several factors can affect ACT, including hypothermia itself [27][28]. Recent reports have analyzed the alternative anticoagulation strategies, which include bivalirudin or nafamostat mesilate use instead of heparin [29][30]. This issue requires further studies.

Potentially life-threating bleeding is recognised as a complication during VA-ECMO, but data on the optimal strategy for anticoagulant therapy are limited and largely based on experts' opinion [17]. However, to avoid systemic

anticoagulation and to reduce the risk of bleeding, heparin-coated ECMO systems and high-flow techniques are used [12][31]. All lesions found in computed tomography, like intracranial bleeding, brain masses or skull fractures, should be consulted with neurosurgeons to establish the risk-benefit ratio of ECMO support. On the other hand, low and nonpulsatile blood flow is associated with the prothrombotic clot phenotype and, thus, predisposes to thrombosis [32][33][34], which could be another complication of the ECMO support. The observed hypercoagulability is also a result of ECMO biomaterial-mediated activation of the coagulation and inflammation pathways and increased platelet activation [33][34]. Of note, echocardiography examination may mistakenly indicate intracardiac coagulation, but in fact, this phenomenon is associated with increased blood echogenicity and slow flow induced by hypothermia [11]. Systemic anticoagulation may be waived within the first 24 h in case of coagulopathy induced by the ECMO system, bleeding or high risk of its occurrence [35].

2.4.4. Ventilation

The lung protective ventilation strategy, based on the smallest possible volume and driving pressure, includes a tidal volume of 6 to 8 mL/kg ideal body weight with a maximum positive end-expiratory pressure of 10 cmH_2O or a plateau pressure of 20–25 cmH_2O [20][36]. The latter setting should be adjusted according to cardiorespiratory function. An initial ventilator setting of FiO_2 is 1.0 [11]. To avoid the risk of alveolar damage and hyperoxia, FiO_2 should be reduced to the lowest possible value. Moreover, management should focus on pulmonary edema prevention [20].

References

1. Tveita, T.; Sieck, G.C. Physiological Impact of Hypothermia: The Good, the Bad, and the Ugly. Physiology 2022, 37, 69–87.
2. Paal, P.; Pasquier, M.; Darocha, T.; Lechner, R.; Kosinski, S.; Wallner, B.; Zafren, K.; Brugger, H. Accidental Hypothermia: 2021 Update. Int. J. Environ. Res. Public Health 2022, 19, 501.
3. Sanfilippo, F.; La Via, L.; Lanzafame, B.; Dezio, V.; Busalacchi, D.; Messina, A.; Ristagno, G.; Pelosi, P.; Astuto, M. Targeted Temperature Management after Cardiac Arrest: A Systematic Review and Meta-Analysis with Trial Sequential Analysis. J. Clin. Med. 2021, 10, 3943.
4. Fernando, S.M.; Di Santo, P.; Sadeghirad, B.; Lascarrou, J.B.; Rochwerg, B.; Mathew, R.; Sekhon, M.S.; Munshi, L.; Fan, E.; Brodie, D.; et al. Targeted temperature management following out-of-hospital cardiac arrest: A systematic review and network meta-analysis of temperature targets. Intensive Care Med. 2021, 47, 1078–1088.
5. Nielsen, N.; Wetterslev, J.; Cronberg, T.; Erlinge, D.; Gasche, Y.; Hassager, C.; Horn, J.; Hovdenes, J.; Kjaergaard, J.; Kuiper, M.; et al. TTM Trial Investigators. Targeted temperature management at 33 °C versus 36 °C after cardiac arrest. N. Engl. J. Med. 2013, 369, 2197–2206.

6. Dankiewicz, J.; Cronberg, T.; Lilja, G.; Jakobsen, J.C.; Levin, H.; Ullén, S.; Rylander, C.; Wise, M.P.; Oddo, M.; Cariou, A.; et al. Hypothermia versus Normothermia after Out-of-Hospital Cardiac Arrest. N. Engl. J. Med. 2021, 384, 2283–2294.
7. Takauji, S.; Hayakawa, M. Intensive care with extracorporeal membrane oxygenation rewarming in accident severe hypothermia (ICE-CRASH) study: A protocol for a multicentre prospective, observational study in Japan. BMJ Open 2021, 11, e052200.
8. Hymczak, H.; Gołąb, A.; Mendrala, K.; Plicner, D.; Darocha, T.; Podsiadło, P.; Hudziak, D.; Gocoł, R.; Kosiński, S. Core Temperature Measurement-Principles of Correct Measurement, Problems, and Complications. Int. J. Environ. Res. Public Health 2021, 18, 10606.
9. Shin, J.; Kim, J.; Song, K.; Kwak, Y. Core temperature measurement in therapeutic hypothermia according to different phases: Comparison of bladder, rectal, and tympanic versus pulmonary artery methods. Resuscitation 2013, 84, 810–817.
10. Lott, C.; Truhlář, A.; Alfonzo, A.; Barelli, A.; González-Salvado, V.; Hinkelbein, J.; Nolan, J.P.; Paal, P.; Perkins, G.D.; Thies, K.C.; et al. European Resuscitation Council Guidelines 2021: Cardiac arrest in special circumstances. Resuscitation 2021, 161, 152–219.
11. Swol, J.; Darocha, T.; Paal, P.; Brugger, H.; Podsiadło, P.; Kosiński, S.; Puślecki, M.; Ligowski, M.; Pasquier, M. Extracorporeal Life Support in Accidental Hypothermia with Cardiac Arrest-A Narrative Review. ASAIO J. 2022, 68, 153–162.
12. Jarosz, A.; Kosiński, S.; Darocha, T.; Paal, P.; Gałązkowski, R.; Hymczak, H.; Drwiła, R. Problems and Pitfalls of Qualification for Extracorporeal Rewarming in Severe Accidental Hypothermia. J. Cardiothorac. Vasc. Anesth. 2016, 30, 1693–1697.
13. Darocha, T.; Debaty, G.; Ageron, F.X.; Podsiadło, P.; Hutin, A.; Hymczak, H.; Blancher, M.; Kosiński, S.; Mendrala, K.; Carron, P.N.; et al. Hypothermia is associated with a low ETCO2 and low pH-stat PaCO2 in refractory cardiac arrest. Resuscitation 2022, 174, 83–90.
14. Pasquier, M.; Hugli, O.; Paal, P.; Darocha, T.; Blancher, M.; Husby, P.; Silfvast, T.; Carron, P.N.; Rousson, V. Hypothermia outcome prediction after extracorporeal life support for hypothermic cardiac arrest patients: The HOPE score. Resuscitation 2018, 126, 58–64.
15. Pasquier, M.; Blancher, M.; Buse, S.; Boussat, B.; Debaty, G.; Kirsch, M.; de Riedmatten, M.; Schoettker, P.; Annecke, T.; Bouzat, P. Intra-patient potassium variability after hypothermic cardiac arrest: A multicentre, prospective study. Scand. J. Trauma Resusc. Emerg. Med. 2019, 27, 113.
16. Rao, P.; Khalpey, Z.; Smith, R.; Burkhoff, D.; Kociol, R.D. Venoarterial Extracorporeal Membrane Oxygenation for Cardiogenic Shock and Cardiac Arrest. Circ. Heart Fail. 2018, 11, e004905.
17. Cheng, R.; Hachamovitch, R.; Kittleson, M.; Patel, J.; Arabia, F.; Moriguchi, J.; Esmailian, F.; Azarbal, B. Complications of extracorporeal membrane oxygenation for treatment of cardiogenic

shock and cardiac arrest: A meta-analysis of 1866 adult patients. Ann. Thorac. Surg. 2014, 97, 610–616.

18. Takayama, H.; Landes, E.; Truby, L.; Fujita, K.; Kirtane, A.J.; Mongero, L.; Yuzefpolskaya, M.; Colombo, P.C.; Jorde, U.P.; Kurlansky, P.A.; et al. Feasibility of smaller arterial cannulas in venoarterial extracorporeal membrane oxygenation. J. Thorac. Cardiovasc. Surg. 2015, 149, 1428–1433.
19. Mohite, P.N.; Fatullayev, J.; Maunz, O.; Kaul, S.; Sabashnikov, A.; Weymann, A.; Saez, D.G.; Patil, N.P.; Zych, B.; Popov, A.F.; et al. Distal limb perfusion: Achilles' heel in peripheral venoarterial extracorporeal membrane oxygenation. Artif. Organs 2014, 38, 940–944.
20. Extracorporeal Life Support Organization: General Guidelines for All ECLS Cases. Available online: https://www.elso.org/portals/0/elso%20guidelines%20general%20all%20ecls%20version%201_4.pdf (accessed on 8 September 2023).
21. Foggle, J.L. Accidental Hypothermia: 'You're Not Dead Until You're Warm and Dead'. Rhode Isl. Med. J. 2019, 102, 28–32.
22. Ortuno, S.; Delmas, C.; Diehl, J.L.; Bailleul, C.; Lancelot, A.; Naili, M.; Cholley, B.; Pirracchio, R.; Aissaoui, N. Weaning from veno-arterial extra-corporeal membrane oxygenation: Which strategy to use? Ann. Cardiothorac. Surg. 2019, 8, E1–E8.
23. Swol, J.; Brodie, D.; Napolitano, L.; Park, P.K.; Thiagarajan, R.; Barbaro, R.P.; Lorusso, R.; McMullan, D.; Cavarocchi, N.; Hssain, A.A.; et al. Indications and outcomes of extracorporeal life support in trauma patients. J. Trauma. Acute Care Surg. 2018, 84, 831–837.
24. Saczkowski, R.; Kuzak, N.; Grunau, B.; Schulze, C. Extracorporeal life support rewarming rate is associated with survival with good neurological outcome in accidental hypothermia. Eur. J. Cardiothorac. Surg. 2021, 59, 593–600.
25. McMichael, A.B.V.; Ryerson, L.M.; Ratano, D.; Fan, E.; Faraoni, D.; Annich, G.M. 2021 ELSO Adult and Pediatric Anticoagulation Guidelines. ASAIO J. 2022, 68, 303–310.
26. Lorusso, R.; Whitman, G.; Milojevic, M.; Raffa, G.; McMullan, D.M.; Boeken, U.; Haft, J.; Bermudez, C.A.; Shah, A.S.; D'Alessandro, D.A. 2020 EACTS/ELSO/STS/AATS expert consensus on post-cardiotomy extracorporeal life support in adult patients. Eur. J. Cardiothorac. Surg. 2021, 59, 12–53.
27. Extracorporeal Life Support Organization: Anticoagulation Guideline. Available online: https://www.elso.org/portals/0/files/elsoanticoagulationguideline8-2014-table-contents.pdf (accessed on 8 September 2023).
28. Kander, T.; Brokopp, J.; Friberg, H.; Schött, U. Wide temperature range testing with ROTEM coagulation analyses. Ther. Hypothermia Temp. Manag. 2014, 4, 125–130.

29. Seelhammer, T.G.; Bohman, J.K.; Schulte, P.J.; Hanson, A.C.; Aganga, D.O. Comparison of Bivalirudin Versus Heparin for Maintenance Systemic Anticoagulation During Adult and Pediatric Extracorporeal Membrane Oxygenation. Crit. Care Med. 2021, 49, 1481–1492.
30. Sanfilippo, F.; Currò, J.M.; La Via, L.; Dezio, V.; Martucci, G.; Brancati, S.; Murabito, P.; Pappalardo, F.; Astuto, M. Use of nafamostat mesilate for anticoagulation during extracorporeal membrane oxygenation: A systematic review. Artif. Organs 2022, 46, 2371–2381.
31. Biderman, P.; Einav, S.; Fainblut, M.; Stein, M.; Singer, P.; Medalion, B. Extracorporeal life support in patients with multiple injuries and severe respiratory failure: A single-center experience? J. Trauma. Acute Care Surg. 2013, 75, 907–912.
32. Undas, A.; Ariëns, R.A. Fibrin clot structure and function: A role in the pathophysiology of arterial and venous thromboembolic diseases. Arterioscler. Thromb. Vasc. Biol. 2011, 31, e88–e99.
33. Olson, S.R.; Murphree, C.R.; Zonies, D.; Meyer, A.D.; Mccarty, O.J.T.; Deloughery, T.G.; Shatzel, J.J. Thrombosis and Bleeding in Extracorporeal Membrane Oxygenation (ECMO) Without Anticoagulation: A Systematic Review. ASAIO J. 2021, 67, 290–296.
34. Meyer, A.D.; Rishmawi, A.R.; Kamucheka, R.; Lafleur, C.; Batchinsky, A.I.; Mackman, N.; Cap, A.P. Effect of blood flow on platelets, leukocytes, and extracellular vesicles in thrombosis of simulated neonatal extracorporeal circulation. J. Thromb. Haemost. 2020, 18, 399–410.
35. Hoyler, M.M.; Flynn, B.; Iannacone, E.M.; Jones, M.M.; Ivascu, N.S. Clinical Management of Venoarterial Extracorporeal Membrane Oxygenation. J. Cardiothorac. Vasc. Anesth. 2020, 34, 2776–2792.
36. Schmidt, M.; Pellegrino, V.; Combes, A.; Scheinkestel, C.; Cooper, D.J.; Hodgson, C. Mechanical ventilation during extracorporeal membrane oxygenation. Crit. Care 2014, 18, 203.