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REVIEW ARTICLE

Use of Extracorporeal Membrane Oxygenation in Adult Patients During Cardiac Arrest

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Abstract

Background: Integrated extracorporeal membrane oxygenation (ECMO) in the treatment of cardiopulmonary resuscitation (CPR) is described as extracorporeal cardiopulmonary resuscitation (ECPR). It is used to ensure recovery of cardiac output when it is not possible to obtain sustained return of spontaneous circulation (ROSC) through conventional CPR methods. The comparison between ECPR and conventional CPR is a dilemma that has been frequently discussed.

Objective: To identify in the literature the use of ECMO in adult patients during cardiac arrest (CA) in and pre- and in-hospital settings.

Method: This is an integrative review using the following guiding question: What is the evidence in the literature on the use of ECMO in adult patients with cardiorespiratory arrest in the pre- and in-hospital setting? It consists of primary studies, published in full and available in Portuguese, English, and Spanish.

Results: The search identified 559 publications in the literature, of which 13 were articles read in full, after applying the inclusion criteria. Of these, 3 were disregarded due to unavailability in the complete format; 7 did not respond to the guiding question, and 3 studies were included. The studies were analyzed according to the 2020 version of the PRISMA Model.

Conclusion: ECPR is a practice adopted when CPR is refractory to conventional life support and concomitantly with this management. There are no significant differences in the rate of favorable neurological outcomes when comparing the pre- and in-hospital scenarios. In short, the development of institutional protocols with selection and exclusion criteria for ECPR is considered relevant.

Introduction

Extracorporeal circulation membrane oxygenation (ECMO) has been used in care situations for decades and was initially incorporated into cardiac surgery in 1954.[1] Subsequently, in certain contexts, such as during the outbreak of influenza A in 2009 and coronavirus disease in 2019, ECMO gained greater visibility due to its use in cases of more severe clinical conditions that were refractory to established conventional therapy.

ECMO is a mechanical circulatory device used for temporary support. Its installation is based on the joint decision of a trained medical team. This method has two basic modalities: venovenous, indicated in cases of pulmonary involvement, such as severe respiratory failure; and venoarterial for cardiac cases, such as cardiogenic shock, cardiac arrest (CA), among others. Both modalities can also be used concomitantly.[2] Therefore, the selection of one of the access routes for cannulation depends on the support provided: pulmonary and/or cardiac.

ECMO integrated into the treatment of CA is described as extracorporeal cardiopulmonary resuscitation (ECPR),

Keywords

Heart Arrest; Extracorporeal Membrane Oxygenation; Survival; Result of Treatment; Health Care Outcome Assessment.

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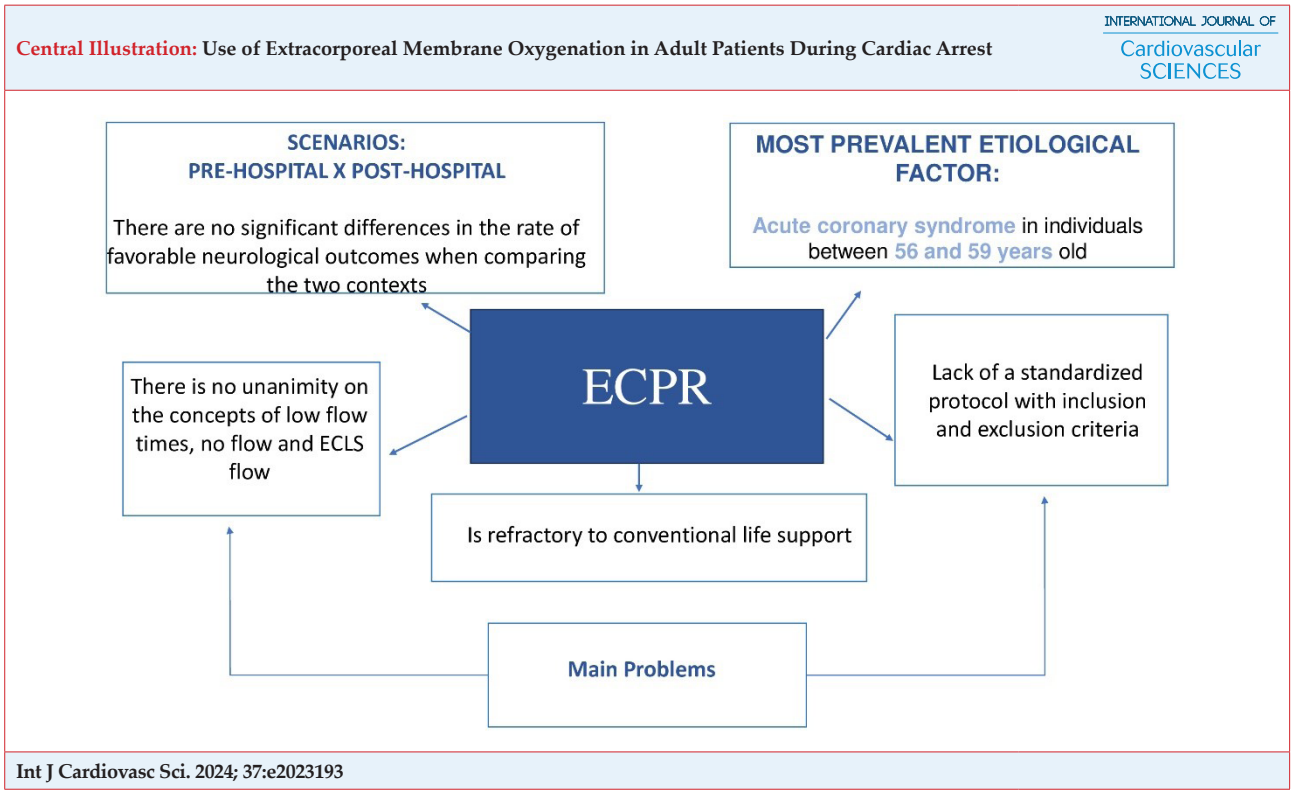

ECPR: extracorporeal cardiopulmonary resuscitation; ECLS: extracorporeal life support.

with the aim of ensuring cardiac output recovery when it is not possible to obtain sustained return of spontaneous circulation (ROSC) using conventional cardiopulmonary resuscitation (CCPR) methods.[3-6]

ECPR is currently a reality in the international context in both in- and out-of-hospital settings, while it is an incipient practice in Brazil. Thus, scientific evidence is needed regarding clarification of the appropriate timing for ECMO installation to obtain sustained ROSC, establishing well-defined inclusion and exclusion criteria, as well as discussing ethical aspects and dilemmas.

The comparison of ECPR and conventional CPR is a dilemma that has been frequently discussed, but no concrete support was identified in the literature regarding the use of ECMO being superior to conventional management or considered as an isolated practice. Some studies have shown the complementarity of these techniques, when the intervention with cardiopulmonary bypass does not interfere with the conduct recommended by advanced life support during CA.[3,7]

Although the Extracorporeal Life Support Organization (ELSO) has standardized information on handling ECMO, no standardized protocol was identified regarding the use of this extracorporeal therapy and, consequently, ECPR, making it difficult to control and monitor these practices.

The scarce evidence on the use of ECMO in CA justifies the relevance of the present study, whose objective is to identify aspects related to the use of ECPR, with the aim of bringing clear and concise recommendations.

Moreover, although some institutions follow established protocols with local applications, there are no standardized protocols, making it difficult to implement ECPR in all institutions and services accordingly.

Objectives

General objective

- Literature search on the use of ECMO in adult patients during CA in pre- and in-hospital contexts

Specific objectives

- Investigate the characterization and clinical profile of patients selected for ECMO during CA
- Gather evidence on the survival and clinical outcomes of patients undergoing ECMO during CA

• Correlate conventional management with the use of ECMO during CA

Methodology

This is an integrative review with the aim of obtaining a scientific basis, through a survey of studies in the literature, on the use of ECMO in patients during CA.

This review consists of the following aspects: a) definition of the guiding question and construction of the PICO strategy; b) choice of descriptors based on the Health Sciences Descriptors (Descritores em Ciências da Saúde [DeCS])/Medical Subject Headings (MeSH); c) selection of inclusion and exclusion criteria; d) search for studies in the main scientific databases: Cumulative Index to Nursing and Allied Health Literature (CINAHL), United States National Library of Medicine (MEDLINE/PubMed), and Scopus (Elsevier), accessed through the journal portal of the Coordination for the Improvement of Higher Education Personnel (Coordenação de Aperfeiçoamento de Pessoal de Nível Superior [CAPES]) and the Virtual Health Library (VHL); e) critical and concise analysis of the selected studies; f) data categorization; and g) information interpretation and presentation.

The present review is guided by the following question: What evidence exists in the literature regarding the use of ECMO in adult patients during CA in pre- and in-hospital contexts? To this end, we adopted the PICO strategy, an acronym for "P" (patient/population), referring to adult patients in CA; "I" (intervention), for the use of ECMO; "C" (comparison), which does not apply; and "O" (outcome), survival as treatment outcome and evaluation of health care outcomes.

This study was conducted using DeCS/MeSH. The selected descriptors correlating to the PICO strategy were combined with Boolean operators as follows: "(heart arrest) OR (CPR) AND (extracorporeal membrane oxygenation — ECMO) OR (extracorporeal circulation) AND (treatment outcome) AND (outcome assessment, health care) AND (survival)."

The defined inclusion criteria consisted of primary studies, published in full and available in Portuguese, English, and Spanish, comprising adult patients and considering CA in both in- and out-of-hospital settings. The period covered by the studies was 2017 to 2022, with the beginning year established due to the need to survey updated research and reformulate the theme based on updated evidence.

The exclusion criteria were duplicate studies; those with an approach divergent to the subject of the present research; and secondary studies such as theses, thesis chapters, books, book chapters, congress or conference proceedings, technical and scientific reports, and ministry documents, among others.

The search for studies in the literature databases was conducted between April and July 2022, and the survey and analysis were performed in pairs. The studies found were included in the Rayyan platform, an automation tool for the refinement of studies, avoiding the analysis of duplicate studies and those with a non-corresponding study design. It automatically detects terms corresponding to the established exclusion criteria.

The subsequent stage consisted of building the PRISMA model with all the studies found in the literature.

Results

In the initial search for the integrative review, we identified 559 scientific productions. After applying the inclusion and exclusion criteria, we excluded 546 articles corresponding to 8 duplicate publications; 36 records marked as ineligible by automation tools; and 502 articles in the selection of pertinence by title, theme, and abstract for not belonging to the theme or not answering the guiding question, for being secondary studies, or for having a population other than the one considered.

Once this stage was completed, 13 studies were analyzed, with 3 articles excluded for not presenting the articles in full and 7 for not answering the research question as per the reviewers' evaluation. Finally, 3 scientific studies were included according to the selection flowchart of primary studies presented below.

Figure 1 displays the PRISMA 2020 Flow Diagram, referring to the PRISMA 2020 model for new systematic reviews that included searches in databases and registries only.[8]

Subsequently, the main results of the included studies were extracted and outlined in two tables.

In Table 1, the results are grouped according to the characterization and clinical profile of the patients selected for ECMO during CA.

Table 2 displays the analysis of survival and clinical outcomes of patients undergoing ECMO during CA (ECPR).

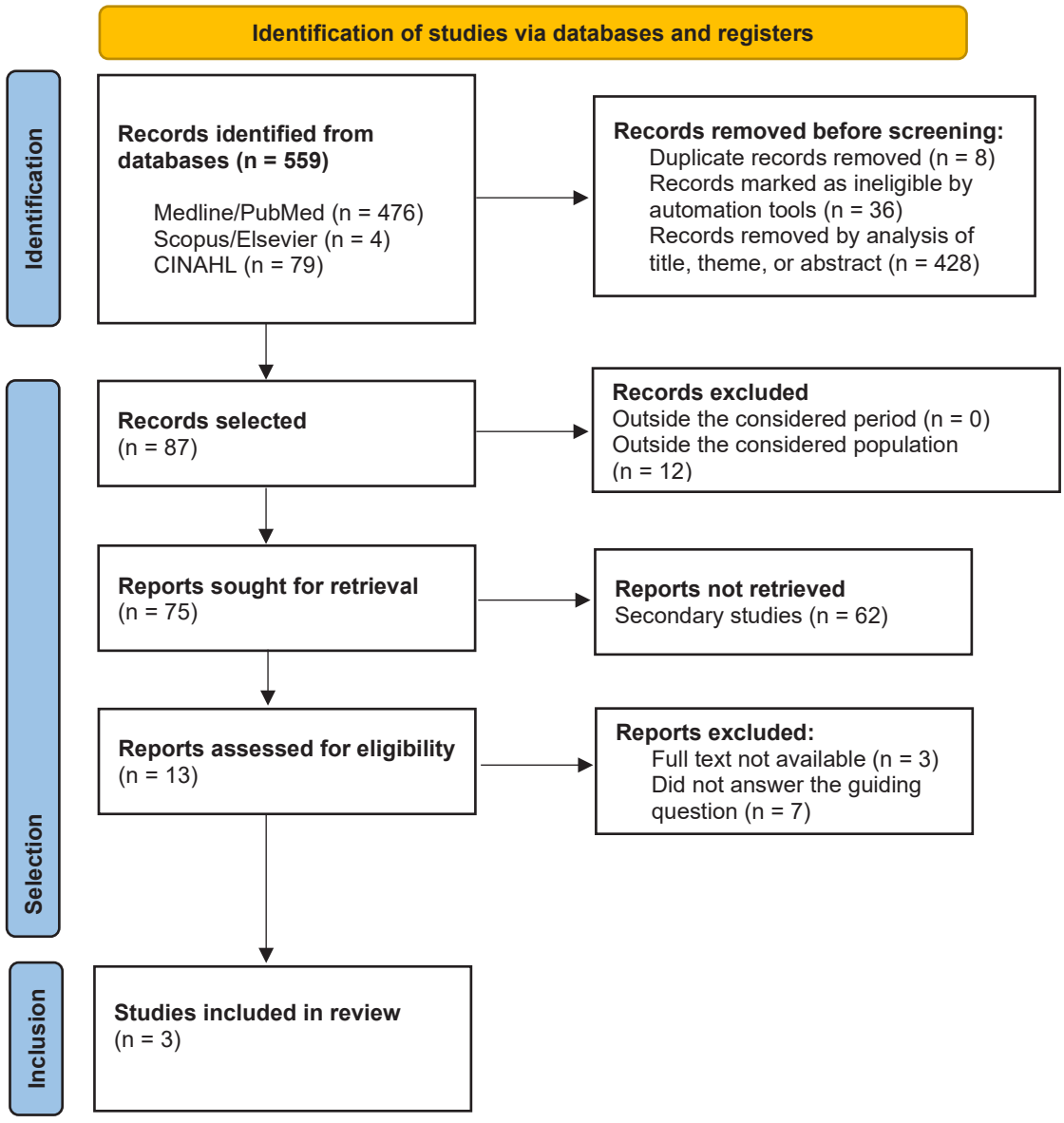

Figure 1 – PRISMA 2020 flow diagram for new systematic reviews which included searches of databases and registers only. Source: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71. Available at: https://www.prisma-statement.org/. Accessed 23 Sept 2022. (Adapted by the author).[8] CINAHL: Cumulative Index to Nursing and Allied Health Literature

Discussion

The patients' ages in this review ranged from 56 to 59 years.[9,10] However, a study by Yu et al. (2018) considered patients of all ages, categorizing them into the following groups: 18 to 65 years, 65 to 75 years, and > 75 years; the first group was the most prevalent. The studies included in this review confirmed the absence of a consistent standardization in the literature, due to which age range was considered for excluding patients from ECPR.[11]

Such age diversification makes it difficult to analyze variables, such as the clinical profile, clinical outcome, and patient survival, as, when older individuals are considered, there is a greater likelihood of unfavorable clinical results. This finding was corroborated by one of the studies in this review, which reported that, in the 1-year period, the survival

Table 1 – Characterization and clinical profile of patients chosen for ECMO in cardiorespiratory arrest (ECPR)

Main author, journal	Title	Country of publication, database, year	Design, sample	Objective	Results
Cesana et al.,[9] *European Heart Journal: Acute Cardiovascular Care*	Effects of ECPR on neurological and cardiac outcome after refractory ischemic CA.	Italy, PubMed, 2018	Cohort, 459 patients	To compare clinical evolution in patients with CA of ischemic origin and ROSC during CCPR versus patients with refractory CA who require ECPR.	63 patients underwent ECPR (mean age: 59 ± standard deviation: 10). There was a lower prevalence of major cardiovascular risk factors: diabetes, hypertension, obesity, dyslipidemia, and smoking when compared to patients who underwent CCPR.
Djordjevic et al.,[10] *Journal of Artificial Organs*	Risk factors associated with 30-day mortality for out-of-center ECMO support: experience from the newly launched ECMO retrieval service	Germany, PubMed, 2019	Retrospective, observational; 28 patients	Present risk factors that predict 30-day mortality for patients receiving ECMO support in a newly launched ECMO recovery facility.	28 patients underwent ECMO (mean age 56 ± 15 years) with heart, lung, or heart and lung failure. Of this total, 15 patients (54%) were cannulated under CPR conditions.
Yu et al.,[11] *Intensive Care Medicine*	Effect of interplay between age and low-flow duration on neurological outcomes of ECPR	Taiwan, Scopus, 2018	Prospective, observational; 482 patients	Evaluate the effects of the interaction between age and prolonged low-flow duration on hospital survival rates in elderly patients to identify subgroups that may benefit from ECPR.	The 18 to 65 age group was the most prevalent with 340 patients. In this group, when considering the underlying causes of CPR, there was a higher percentage of patients with ACS 118 (34.7%).

ACS: acute coronary syndrome; CCPR: conventional cardiopulmonary resuscitation; CPR: cardiopulmonary resuscitation; ECMO: extracorporeal membrane oxygenation; ECPR: extracorporeal cardiopulmonary resuscitation; CA: cardiac arrest; ROSC: return of spontaneous circulation. Source: the authors.

after undergoing ECPR was higher in younger than in older patients.[11] However, the same study also showed that age was not a significant factor for neurological outcome.[11]

Regarding the clinical profile, the patients had cardiovascular and non-cardiovascular risk factors. A study by Cesana et al. (2018) showed a lower prevalence of cardiovascular risk factors compared to the group undergoing conventional management. However, another study identified acute coronary syndrome (ACS), in 118 of the patients (34.7%), as the main cause of CA in those undergoing ECPR.[9,10]

A systematic review suggested that the etiology of the CA may be an important factor for survival. It stated that only non-cardiac etiologies had a notably higher survival rate compared to cases that included cardiac etiologies.[12]

Regarding the neurological outcome, according to the ELSO guidelines for ECPR (2021), to date, there is no scientific basis for the relationship between the increase in the number of patients with neurological injury and the increasing use of ECPR. Although some studies indicate favorable results and others show

Table 2 – Analysis of survival and clinical outcomes of patients undergoing ECMO during CA (ECPR).

Main author journal	Title	Country of publication, database year	Design/ sample	Objective	Results
Cesana et al.,[9] *European Heart Journal: Acute Cardiovascular Care*	Effects of resuscitation cardiopulmonary bypass on neurological and cardiac outcome after refractory ischemic CA	Italy, PubMed, 2018	Cohort, 459 patients	To compare the clinical evolution in patients with CA of ischemic origin and ROSC during CCPR versus patients with refractory CA who require ECPR.	In the 1-year period, 98% of discharged patients who underwent CCPR and 92% of those who underwent ECPR were alive. Good neurological outcome (CPC 1-2) was achieved in more than 90% of discharged patients, with no significant difference between ECPR and CCPR patients (92% versus 94%), despite longer duration of cerebral hypoxia in the former group.
Djordjevic et al.,[10] *Journal of Artificial Organs*	Risk factors associated with 30-day mortality for out-of-center ECMO support: experience from the newly launched ECMO retrieval service	Germany, PubMed, 2019	Retrospective, observational; 28 patients	Present risk factors that predict 30-day mortality for patients receiving ECMO support in a newly launched ECMO recovery facility.	15 of the patients (54%) were cannulated under CPR conditions; 40% survived at 1 week, and 33.3% at 1 month, 6 months, and 1 year.
Yu et al.,[11] *Intensive Care Medicine*	Effect of interplay between age and low-flow duration on neurological outcomes of ECPR	Taiwan, Scopus, 2018	Prospective, observational; 482 patients	Evaluate the effects of the interaction between age and prolonged low-flow duration on hospital survival rates in elderly patients to identify subgroups that may benefit from ECPR.	Hospital survival rates were higher in younger patients compared to those aged > 75 years. Age was not a significant factor for neurological outcome.

ACS: acute coronary syndrome; CCPR: conventional cardiopulmonary resuscitation; CPC: cerebral performance category; CPR: cardiopulmonary resuscitation; ECMO: extracorporeal membrane oxygenation; ECPR: extracorporeal cardiopulmonary resuscitation; CA: cardiac arrest; ROSC: return of spontaneous circulation. Source: the authors.

unfavorable neurological results, several limiting aspects have been observed, thereby compromising the findings.[6]

When comparing the survival of patients undergoing CCPR and extracorporeal management (ECPR), Cesana et al. (2018) showed that, in patients who received ECMO during CA, there was lower 1-year survival and good neurological result obtained in more than 90% of the patients who were discharged; moreover, despite longer duration of cerebral hypoxia in the first group, no significant difference was noted between patients with ECPR and CCPR (92% versus 94%).[9]

In the comparison between CCPR and ECPR, we noted that, in the literature, especially with regard to evidence, large organizations and bodies, such as the American Heart Association (AHA), Advanced

Cardiovascular Life Support (ACLS), and ELSO, emphasize the need to maintain CCPR in CA as the first choice, adopting ECPR once the patient's risk-benefit has been carefully discussed and considered and in situations of refractoriness to CCPR.

The 2021 ELSO guidelines for ECPR reinforce the need to adopt measures, such as assigning the role of supervising CCPR in the treatment of CA to the team leader, in parallel to the cannulation process and ECMO functionality.[6] In addition, care must be taken not to defibrillate the patient after starting the insertion of the guidewire to avoid any risk to cannulators.[6,13,14]

Although the use of ECPR in pre-hospital settings is not currently a reality in Brazil, this practice has been adopted in many countries in similar situations, to the detriment of the in-hospital setting. The studies included in this review considered both contexts, but, when they were correlated, a rate of favorable neurological outcomes was identified that was almost equal between the two. They showed no significant differences for the distance and time of arrival at the peripheral hospital, as well as the in- or out-of-hospital ECMO implantation time.[9-11]

As the first choice in cases of refractory CA in patients eligible for ECPR, in the pre-hospital setting, the literature recommends quickly taking the patients to the nearest hospital that provides support in order not to compromise their survival.[6]

According to the 2021 ELSO guidelines for ECPR, the inclusion criteria for patients undergoing ECPR are the following: age < 70 years; arrest to first CPR ("no-flow interval") < 5 min (that is, bystander CPR); initial cardiac rhythm of ventricular fibrillation/pulseless ventricular tachycardia/pulseless electrical activity; arrest to ECMO flow < 60 min ("low-flow interval"); end-tidal CO_2 > 10 mmHg (1.3 kPa) during CCPR before cannulation for ECMO; and intermittent ROSC or recurrent ventricular fibrillation. The guidelines also suggest excluding patients with previously known life-limiting conditions, such as end-stage heart failure, chronic obstructive pulmonary disease, kidney failure, and aortic valve incompetence.[6]

Aiming at more homogeneity among the studies, greater significance of the results, and less limiting aspects, we need to consider studies in which the inclusion and exclusion criteria of patients for ECPR are applied according to the ELSO guidelines.

Conclusion

ECPR is a procedure that is adopted when CA is refractory to conventional life support. Concomitantly with this management, it is used in and pre- and in-hospital contexts in several countries worldwide, with greater predominance in pre-hospital care, which differs from the Brazilian reality.

There are no significant differences in the rate of favorable neurological outcomes when comparing the two contexts. However, some recommendations prefer ECMO cannulation in the in-hospital setting as the first choice, thus emphasizing the need for concise and comparative studies on the positive and negative aspects of both care contexts.

According to the eligible studies, we observed that patients selected for ECMO during CA aged between 56 and 59 years with risk factors of cardiovascular and non-cardiovascular origin, presenting a predominance of ACS as an etiologic factor of CA in one of the studies.

Nevertheless, the inclusion and exclusion criteria for patients selected for ECPR are defined by organizations such as ELSO, but there is no standardized protocol, which makes it difficult to analyze studies on this subject. In addition, as there is no unanimity in the concepts of times of low flow, no flow, and ECLS flow, the interpretation of the variables and results found may be compromised.

The development of institutional protocols with well-defined and standardized selection and exclusion criteria for ECPR is extremely important, in addition to the encouragement of scientific research to minimize gaps on a given topic and guarantee improvements in the provision of extracorporeal life support.

Author Contributions

Conception and design of the research, analysis and interpretation of the data and critical revision of the manuscript for intellectual content: Alves C, Pimentel SQ, Lopes FJ; acquisition of data: Alves C; writing of the manuscript: Alves C, Lopes FJ.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

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Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee on Animal Experiments of the Diretoria de Ensino e Pesquisa da Sociedade Beneficente de Senhoras do Hospital Sírio-LibanÊs under the protocol number 2658.

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