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The Effects of Prone Positioning with VV-ECMO Support in Adult Acute Respiratory Distress Syndrome Patients: A Scoping Review of the Evidence

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Abstract

Background

Cardiac surgery is a complex procedure that requires temporary circulatory support during the process. Cardiopulmonary bypass (CPB) is a technique used to provide this support. During CPB, blood is diverted from the heart and lungs to a machine that oxygenates it and pumps it back into the body. While this process occurs, the heart must be temporarily arrested to allow the surgeon to complete the surgery with a motionless field. Cardioplegia is a technique used to protect the heart during this period. It involves administering a solution that stops the heart's activity and protects it from injury.

Project Focus

There are different types of cardioplegia used during CPB, including microplegia, 4:1 cardioplegia, and Del Nido solution. Microplegia involves using a small amount of cardioplegia solution that is infused directly into the coronary arteries of the heart. 4:1 cardioplegia involves using a solution mixed with blood in a 4:1 ratio before being administered to the heart. Del Nido is a newer solution that has gained popularity due to its longer-lasting effects and potential benefits in complex cardiac procedures.

Method & Contribution to Cardiovascular Perfusion

This scoping review aims to identify and summarize the current literature on the different types of cardioplegia used on adults undergoing CPB. This review will provide an overview of the current state of knowledge in this area by examining the benefits and limitations of each type of cardioplegia. Additionally, this review will identify gaps in the current literature, which may guide future research in this field. Ultimately, the findings of this review may help cardiac surgeons and perfusionists select the most appropriate type of cardioplegia for their patients, which could lead to improved patient outcomes and reduced complications during cardiac surgery.

1. What is Cardioplegia?

In cardiac surgeries, cardiopulmonary bypass is required to provide physiological support through an extracorporeal circuit to allow a still, bloodless field (1). A critical component of cardiopulmonary bypass is the cardioplegia solution. Cardioplegia is delivered for every patient undergoing any sort of cardiac surgery in which CPB is required, ranging from valve cases, CABG cases to DHCA cases (2). The perfusionist is in charge of cardioplegia delivery and dosage during a bypass case.

The history of cardioplegia begins in the mid-1950s (3). In 1955, Dr. Melrose identified that high levels of potassium citrate could cause a reversible cardiac arrest which became the first solution to be used during cardiopulmonary bypass (3). Until the early 1990s, surgeons relied on hypothermia as the primary method for myocardial protection rather than a cardioplegic solution (3). In 1977, warm blood cardioplegia was introduced to prevent reperfusion injury after hypothermic cardioplegia (3). Its use resulted in accelerated recovery and reduced metabolic derangement (3). Continuous warm cardioplegia was believed to provide the heart with continuous oxygen delivery and metabolism, thus avoiding ischemia altogether (3). As the field advances, other methods have been developed to enhance cardioplegic delivery and optimize myocardial protection (3). Advances include different types of cardioplegia solutions, mechanical cardiac support, and pharmacological interventions (3). Despite the ongoing debate and research on the topic, the main goal remains to minimize myocardial damage during open heart surgery and improve patient outcomes (3).

Cardioplegia is a pharmacological agent administered during cardiac surgery to intentionally and temporarily arrest the heart (2). The main component of cardioplegia is the high levels of potassium; the potassium is used to induce temporary cardiac arrest (2). On a cellular level, cardioplegia acts by triggering a diastolic cardiac arrest. Normally, an influx of sodium ions will shift the membrane potential in myocytes from resting to depolarization; the membrane becomes more positively charged (2). When cardioplegia is delivered, the high levels of potassium in the solution can similarly depolarize the myocardial membrane and thus generate an action potential (2). As the surrounding concentration of potassium remains high, repolarization cannot occur, thus preventing further contractions; this mechanism is termed a diastolic arrest (2). Redosing of cardioplegia may be required throughout the surgery to prevent further electrical activity (2).

The primary goal of cardioplegia is to reduce myocardial oxygen demand and the ischemic effects of being on bypass to provide a relatively bloodless and motionless surgical field (2). Without cardioplegia, myocardial oxygen consumption will be uncontrolled and allow the myocardium to be prone to injury (4). Thus, by perfusing the heart with a cardioplegic solution to induce and maintain electromechanical arrest, myocardial oxygen consumption is reduced, and the heart can be protected.

Apart from potassium, there are various other components found in a cardioplegic solution, such as calcium, sodium, and magnesium, which all play a beneficial role in reducing oxygen consumption and protecting the myocardium (2). Additionally, components such as lidocaine, bicarbonate, and glucose have been added to various solutions to add further protection for the patient (2). Since its initial discovery, cardioplegia solution composition has been subjected to various changes, and a variety of techniques have been used for delivery (3). Crystalloid cardioplegia and blood cardioplegia of varying ratios, such as Del Nido solution and microplegia, are all commonly used and, therefore, are the subject of this research. Thus, it is critical that the different types of cardioplegia used on adults undergoing cardiopulmonary bypass are understood to help make evidence-based decisions in the patient's best interest.

2. Challenges of Cardioplegia

Although cardioplegic solutions are indicated to protect cardiac cells from ischemia, a detrimental injury may occur during delivery due to inadequate delivery of a cardioplegic solution, toxicity, or the maldistribution of a solution distal to total coronary occlusions (5). In addition, there is the potential for a reperfusion injury during each infusion and after the aortic cross-clamp removal (5). Each of the various types of solutions may have its own unique complications. For example, when del Nido cardioplegia is delivered for adult aortic root surgeries, the ischemic time of the patient is increased (5). However, it is also critical to understand how an adult myocardium is subjected to ischemia in order to understand cardioplegia dosing. The relative sensitivity of the adult myocardium to ischemia could be explained by its reduced capability for anaerobic metabolism in the setting of ischemia, as the adult myocardium uses fatty acids to derive its energy (6). Also, the adult myocardium is found to be less capable of utilizing glucose after an ischemic insult (6). This difference in myocardial physiology might explain the need for a more aggressive cardioplegia strategy for adult cardiac surgery (6). Other important factors that may influence cardioplegia include pre-existing pathophysiology and renal function (6). The suboptimal renal function of patients may impair the clearance of the potassium load, and thus a cardioplegia solution with a lower concentration of potassium may be considered (6). Other factors such as diabetes, could play a role in the outcomes of patients. Many cardioplegic solutions contain dextrose in the solution and may worsen patient glucose levels (5). Thus, diseased states must be considered when determining optimal cardioplegia solutions for patients.

3. What is Known About Cardioplegia

Due to advancements in technologies and further research in cardioplegia, the components of cardioplegic solutions are constantly changing. Other factors, such as temperature and route of delivery, are also subject to change (7). Cardioplegia compositions are separated into two different categories: blood-based and crystalloid cardioplegia (7). Blood cardioplegia provides an advantage in its ability to act as a buffer, act as a free radical scavenger, and improved oxygen delivery while maintaining normal oncotic pressure (7). On the contrary, the benefits of crystalloid cardioplegia lie in its ability to reduce oxygen consumption and thus protect the myocardium from ischemic damage (7). Commonly used blood cardioplegia include St Thomas' (4:1), Microplegia, Del Nido's cardioplegia (1:4), while the most common crystalloid cardioplegia solution is the Custodiol solution (7). A general description of each solution has been provided below.

St. Thomas (4:1 cardioplegia)

St Thomas' Cardioplegia solution is commonly used as a blood cardioplegia diluted 4:1 (blood: crystalloid), but can also be used in crystalloid solutions (8). The solution contains a high potassium concentration, which depolarizes the cell membrane and sodium channel blockers to aid in depolarization (7). The method involves repetitive dosing every 20-30 minutes, which may result in inadequate myocardial protection if not timed appropriately (9). Repetitive dosing may interrupt the operation and may result in inadequate myocardial protection if the timing of cardioplegia is not appropriately followed (8). Additives are commonly included to make the solution as physiological as possible and to avoid acidity that can damage the heart (7). St Thomas' solution has been made with different configurations, with St Thomas' 2 being developed in 1981 (7). The post-operative outcomes of using St. Thomas' solution have not been well examined in the literature, and thus, is an area of interest.

Microplegia

Standard formulation of blood cardioplegia is delivered in a four-part blood to one-part crystalloid ratio. However, an alternative to 4:1 blood cardioplegia involves delivering pure blood cardioplegia where the cardioplegia solution is a reduced volume that is delivered intermittently (10).

The main advantage of microplegia is that it helps to reduce hemodilution and, as a result, reduces myocardial edema (10). In addition, microplegia has been shown to be effective in managing harmful inflammatory responses and reducing inflammatory mediators that arise due to ischemia and reperfusion (10). Microplegia is able to offer additional benefits while retaining all the advantages of blood cardioplegia, such as superior oxygen-carrying capacity, better osmotic properties and antioxidant capability (11). Its main reason for use is to reduce hemodilution, such as in patients with CHF or pediatric patients (10). Moreover, the reduction of hemodilution is especially important for populations such as Jehovah Witnesses, as blood conservation is a critical consideration for optimizing these patients during cardiac surgery (10). However, the clinical advantage of microplegia continues to be debated, and is an area for further research.

Del Nido

Del Nido cardioplegia is a longer-lasting arrest solution administered as a single dose at the induction of arrest (6). Using high potassium and a high sodium concentration, DNP is delivered in a 1:4 ratio of one part blood and four parts crystalloid (6). It was initially developed for intended use in pediatric cardiac surgery and is now used in adult populations (6).

Del Nido cardioplegia is composed of lidocaine, magnesium, and adenosine (6). The lidocaine in the cardioplegic solution helps to reduce incidences of ventricular fibrillation and intraoperative arrhythmia (6). Unexpected arrhythmias are large sources of oxygen consumption and damage; thus del Nido helps to protect the myocardium (6). However, it is important to take into account the possibility of lidocaine toxicity when using Del Nido solution as a cardioplegic agent. Although the solution has been shown to be effective and safe in clinical practice, it is recommended to conduct thorough calculations to determine the appropriate dosage to prevent lidocaine toxicity. Del Nido also includes magnesium sulfate in the solution. Magnesium is known to stabilize cell membranes and prevent calcium overload, especially during the removal of cross-clamp (6). The crystalloid solution of

Del Nido cardioplegia is plasmalyte A, which has a physiologically similar electrolyte composition to plasma (6). Thus, the physiologic nature of the solution makes it suitable to be delivered at a 1:4 ratio (blood: CP) without changing hemostasis, even in combination with other additives (6).

There are also some concerns related to the Del Nido cardioplegia. One of the major problems is that the Del-Nido solution is not standardized across the globe, resulting in multiple variations of the formula with the same name but with different chemical combinations (12). Thus, various modifications can result in changed outcomes, making it impossible to correlate the measured outcomes to del-nido or the modifications. Furthermore, patients on del-nido cardioplegia are at risk of being hyperkalemic due to the high potassium content of del Nido solution (12). Hyperkalemia results in coronary vasoconstriction and consequently complicates myocardial ischemia (12). Despite the variability in composition, Del Nido remains one of the most understood cardioplegic solutions due to it's popularity across the globe.

Custodiol Cardioplegia

Custodiol cardioplegia, also known as histidine tryptophan ketoglutarate, is a crystalloid cardioplegic solution that induces diastolic cardiac arrest by hyperpolarizing the myocyte (13). Each component of the solution aids in myocardial protection, with histidine buffering acidosis accumulated by anaerobic metabolism, tryptophan stabilizing the cell membrane, ketoglutarate improving adenosine triphosphate (ATP) production during reperfusion, and mannitol decreasing cellular edema (14). Overall, Custodiol improves ATP production, stabilizes cell membranes, and maintains osmotic regulation of the cell membrane (15). Overall, Custodiol improves ATP production, stabilizes cell membranes, and maintains osmotic regulation of the cell membrane. It can provide myocardial protection for up to 3 hours when administered as a single dose, allowing complex procedures to be performed without interruption (9).

4. Knowledge Gaps

It is evident that there is abundant literature on many different types of cardioplegia, but the conclusive evidence surrounding each type of cardioplegia solution varies greatly. Many papers are unable to present clear advantages and disadvantages for one solution over another. This may be due to the lack of comparative effectiveness studies, leading to a lack of standardization that should be a cause for concern in this era of evidence-based medicine (4). Furthermore, the studies that do exist lack similar measurements of post-operative outcomes, which prevents comparison between treatment groups. Without effective comparisons, evidence-based decisions can not be made, thus limiting the ability of clinicians to target solutions directly to pathology. Another limitation is that current literature has shown extreme variability in terms of cardioplegia delivery protocol and solution makeup. Although the paper may cite a specific solution type, modifications may have been made to the solution which may alter the outcomes reported by the paper. Ideally, a general understanding of the true solution composition and outcomes is required.

An assessment of all literature surrounding various cardioplegia solutions and their outcomes allows for standard protocols to be developed for cardioplegia delivery based on evidence-based research. This scoping review is intended to compile all evidence surrounding different cardioplegia methodologies used in the field of cardiac surgery. The overall goal of this capstone paper is to review the current literature with the goal of presenting a clearer understanding of clinical outcomes related to the various types of cardioplegia. Thus, the capstone project aims to investigate the various types of cardioplegia used on adults undergoing cardiopulmonary bypass and their postoperative outcomes.

5. Methods

Research Design and Approach

For this paper, we will conduct a comprehensive scoping review. This scoping review aims to identify and map the available evidence on cardioplegia. This review will be a valuable method for synthesizing a large body of literature and identifying gaps in knowledge. The first step we will take in writing this scoping review is to define the research question. In this case, the research question is: What are the different types of cardioplegia used in cardiac surgery? This question is broad enough to capture all relevant literature but specific enough to guide the search process. The next step is to conduct a systematic search of the literature. This involves searching multiple databases, such as PubMed, Embase, and Cochrane Library, for relevant studies. The search will include all types of peer-reviewed literature and use keywords and subject headings to capture all relevant literature. The search strategy will be documented in detail to ensure transparency and reproducibility. Once the search is complete, the next step is to screen the literature. This involves reviewing the titles and abstracts of all identified studies to determine their relevance to our research question. Studies that are clearly irrelevant will be excluded, while those that are potentially relevant will be retained for full-text review. The final step is to analyze and synthesize the results. This involves identifying patterns and trends in the data and mapping the available evidence on the different types of cardioplegia used in cardiac surgery. The results will be presented clearly and concisely, using tables and figures to aid in visualization. To conclude, writing a scoping review about the different types of cardioplegia used in cardiac surgery involves defining the research question, conducting a systematic search, screening the literature, extracting data, and analyzing and synthesizing the results. By following these steps, we can produce a comprehensive overview of the available evidence on this topic and identify gaps in knowledge that can guide future research.

Quantitative and Qualitative Data

In order to achieve a comprehensive scoping review on cardioplegia, it is essential to analyze the available literature using both quantitative and qualitative procedures. Quantitative procedures involve the use of statistical methods to analyze numerical data. In our case, quantitative procedures involve analyzing the frequency of use of different types of cardioplegia or the outcomes associated with different types of cardioplegia. Quantitative procedures can provide us with a broad overview of the available evidence, allowing us to identify patterns and trends in the data. This type of analysis is useful in determining the prevalence of different types of cardioplegia used in cardiac surgery and the outcomes associated with them.

On the other hand, qualitative procedures involve the analysis of non-numerical data, such as text or images. In our case, qualitative procedures involve analyzing the descriptions of different types of cardioplegia or the experiences of patients and healthcare providers with different types of cardioplegia. Qualitative procedures can provide a more in-depth understanding of the experiences and perspectives of patients and healthcare providers, allowing us to identify areas for further research and improvement. This type of analysis is useful in understanding the patient experience with different types of cardioplegia and the perspectives of healthcare providers on the use of different types of cardioplegia.

In the scoping review process, both quantitative and qualitative procedures are essential. By using both types of procedures, we can gain a comprehensive understanding of the current state of knowledge on this topic. This comprehensive understanding will enable us to identify gaps in knowledge and areas for further research and improvement.

Data Bases and Collection

Data sources and collection procedures are crucial components in conducting a scoping review. The first step we will take in our scoping review is to identify the data sources that will be used to gather relevant literature. Regarding our topic on cardioplegia, potential sources include electronic databases such as PubMed, Embase, and Cochrane. These databases provide access to a vast array of scholarly articles, peer-reviewed journals, and other resources related to cardioplegia. Electronic databases have become increasingly important as they allow us to access a wider range of scholarly articles and relevant resources. PubMed, Embase, and Cochrane are just some of the commonly used databases that we will use to gather literature on cardioplegia. Another useful resource in this regard is Google Scholar, which can help us to identify relevant literature that may not be included in traditional databases. In addition to electronic databases, other potential data sources we will include is grey literature, such as reports and unpublished studies, as well as relevant websites and professional organizations. It is essential that we include a diverse range of data sources to ensure that the scoping review is comprehensive and representative of the current state of knowledge in the field.

Once the data sources have been identified, developing a data collection plan will be next. This plan will describe the data collection instruments used to gather information from each source. In the case of electronic databases, these instruments include search terms, inclusion and exclusion criteria, and screening tools to identify relevant articles. For instance, cardioplegia is also known as a "heart arresting agent". Thus we will conduct searches using both "cardioplegia" and "heart arresting agent" as search terms to ensure we capture all relevant articles. Additionally, on PubMed, we will utilize mesh terms for various types of cardioplegia. For instance, "microplegia" will be the mesh term for "mini-cardioplegia." Regarding inclusion criteria, we will only consider recent papers published from the year 2000 onwards. This will ensure we have access to the most recent and updated information available. Furthermore, our sample population will only include adults to maintain a specific focus. We have opted to exclude pediatrics from our analysis to ensure that our research remains narrowly targeted to the adult population.

In addition to these instruments, we will develop data extraction forms to record information from the relevant literature. These forms will include fields for the author, title, publication date, study design, and key findings, among other variables. It is also crucial that we establish a clear process for managing and organizing the collected data. This might include creating a spreadsheet to record and track the information. Developing a coding system to categorize the data and identify key themes and trends in the literature will also be necessary.

By identifying a diverse range of data sources and developing clear and comprehensive data collection instruments, we can ensure that our scoping review is comprehensive, representative, and informative of the current state of knowledge in the field of cardioplegia.

6. Limitations

One of the main limitations of scoping reviews is setting appropriate inclusion and exclusion criteria. In this case, cardioplegia is a specific topic, but there may be a vast literature on the subject. Therefore, it is important to ensure that the inclusion and exclusion criteria are clear and concise. This can help to ensure that relevant studies are included and irrelevant studies are excluded. To mitigate the impact of this limitation, we will carefully define our inclusion and exclusion criteria. When selecting inclusion and exclusion criteria for our research, we need to ensure that we are targeting the specific area of interest, while also excluding any extraneous data that may skew our results. In order to do this, we have decided to focus on the use of three main cardioplegia solutions in adult cardiac surgery: Del Nido, 4:1, and microplegia. These three solutions are of particular interest to us because they represent some of the most commonly used and well-studied options in the field of cardiac surgery. By focusing on these solutions, we hope to gain a deeper understanding of their respective benefits, drawbacks, and potential applications, and to identify any areas where further research may be needed.

At the same time, we recognize that the term "cardioplegia" is a broad and varied one, with many different formulations and applications in the context of cardiac surgery. To ensure that our research is as targeted and specific as possible, we have also established a set of exclusion criteria that will help us to filter out any data that is not directly relevant to our area of interest. These exclusion criteria include a publication date of greater than 2000, as well as any studies involving pediatric populations or uncommon variations of the cardioplegia solutions we are focused on. By excluding these data points, we can ensure that our research is focused on the most current and relevant information available, and that we are able to draw meaningful conclusions that can help to drive progress in the field of cardiac surgery.

Overall, our approach to selecting inclusion and exclusion criteria is designed to ensure that our research is as targeted and specific as possible, while also remaining open to new ideas and perspectives that may emerge as we delve deeper into the topic at hand. By taking this approach, we hope to make a meaningful contribution to the field of cardiac surgery, and to help improve patient outcomes for years to come. We will also conduct a pilot study to ensure that our criteria are effective in identifying relevant studies. This step is crucial in ensuring that the scoping review is comprehensive and relevant to the current literature on cardioplegia.

Moreover, a main challenge we encounter when exploring our topic is the widespread and varied use of the term "cardioplegia" in the context of cardiac surgery. There are many different types of Del Nido solution, each with unique characteristics and applications, and this is just one example of the many ways cardioplegia can be used. To ensure that we focus on the specific area of interest, it's crucial to establish a clear and specific definition of cardioplegia that we will use throughout our research. By taking the time to define the term "cardioplegia" in the context of our research, we can properly explore the topic and build on existing work. This involves reviewing relevant literature and consulting with experts to gain a deeper understanding of the various ways the term is used. We must then develop a concise definition that will guide our work moving forward. Ultimately, this will be a key component of our research and will help us make meaningful contributions to the field of cardiac surgery and improve patient outcomes.

Another limitation of our scoping review is the lack of quality assessment of the included studies. This means that studies of poor quality may be included in the review, which can affect the overall conclusions. To mitigate this limitation, we will assess the quality of the included studies by ensuring the credibility of the journal. This will help to ensure that only studies of high quality are included in the review, which will increase the reliability and validity of the results. This step is essential in ensuring that the review is trustworthy and credible.

Lastly, scoping reviews is that it can be time-consuming, especially if there is a vast literature on the topic. This can limit the number of studies that can be included in the review, which can affect the overall conclusions. To mitigate this limitation, we will allocate sufficient time for the review to ensure that we can include as many relevant studies as possible. We will also use appropriate search strategies and tools to ensure that we can efficiently identify relevant studies. This includes assigning time to search multiple databases that are available. By doing so, we can ensure that we have a comprehensive review of the literature on cardioplegia.

7. Contributions

Contributions to clinical practice

When making evidence-based decisions, it is important to understand and analyze the existing literature on hand to ensure that current practices are well understood and supported. A summarization of cardioplegic solutions allows surgeons and perfusionists to make educated decisions backed by research supporting the type of cardioplegic solution chosen. Currently, each cardiac center has adopted its specific cardioplegia practice resulting in wide variations of cardioplegic solutions and delivery methods. However, clinical decisions need to be based on evidence-based medicine in order to determine best practices and to reduce bias in the decision-making process. Before making clinical decisions, the literature surrounding cardioplegia needs to be thoroughly understood, and the outcomes associated with each cardioplegic solution need to be factored in when determining a medical plan for a patient. Each individual has unique pre-existing conditions and may require different types of cardiac operations that utilize different cardioplegic solutions. An overall understanding of cardioplegia allows standard protocols to be developed for cardioplegia delivery based off evidence-based research.

Contributions to Knowledge

One of the critical impacts of this scoping review is the identification of gaps in the literature on cardioplegia. By comprehensively examining the literature on the various types of cardioplegia used in cardiac surgery, we can identify areas where further research is needed. For instance, we may come across a lack of studies that compare the effectiveness of Del Nido and Microplegia in adult populations. This gap in knowledge could be addressed through further research studies, which could be conducted to identify the most effective type of cardioplegia for specific patient populations.

In addition to the benefits mentioned above, this review could also be instrumental in identifying any safety concerns associated with different types of cardioplegia. Through a thorough analysis of the existing literature on the use of cardioplegia in cardiac surgery, we can gain valuable insights into any potential risks that may exist and contribute to the development of safer surgical practices. Furthermore, this scoping review will serve as a comprehensive guide to the current state of research on the different types of cardioplegia used in cardiac surgery. Through this review, we can identify gaps in the existing research and areas where further studies are needed to enhance our understanding of this vital aspect of cardiac surgery. Another key impact of our scoping review is the synthesis of existing knowledge. With this review, we can identify key concepts, theories, and findings that have emerged from previous research. This helps identify areas where there is consensus in the literature, as well as areas where there are conflicting findings. Our scoping review can also help to identify areas where more research is needed. This can help to inform future research directions and priorities in the field of cardiac surgery.

In conclusion, this scoping review will significantly impact our understanding of the different types of cardioplegia used in cardiac surgery. By identifying knowledge gaps, synthesizing existing knowledge, identifying research priorities, and identifying clinical implications, this scoping review can help inform future research and clinical practice in cardiac surgery. This can ultimately lead to improved patient outcomes and a better understanding of the optimal use of cardioplegia in cardiac surgery.

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