Extracorporeal Cardiopulmonary Resuscitation

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Abstract

Extracorporeal cardiopulmonary resuscitation (ECPR) is a method of resuscitation in which venoarterial (VA) extracorporeal membrane oxygenation(ECMO) is initiated during refractory cardiac arrest. ECPR promises to enhance outcomes after cardiac arrest by minimizing neurological deficits, stabilizing the patient for early reperfusion and hypothermia, and serving as a bridge to treatment or transplant. ECPR must be initiated according to structured guidelines and protocols, which are based on the patient's age, comorbidities, code status, neurological baseline, no flow time, and low flow time.

If a patient achieves return of spontaneous circulation on ECMO, the patient will receive post cardiac arrest care which includes but is not limited to therapeutic hypothermia, early reperfusion, intra-aortic balloon pump insertion, tight glycemic control, and low ventilation. While ECPR has been shown to improve outcomes, multiple complications including bleeding, infection, renal failure, limb ischemia, and stroke can result from the treatment. Nurses play a key role in monitoring these critical patients and achieving therapeutic outcomes.

As ECPR is expensive, carries high risk of complications, and can not always be performed under informed consent, thus there are ethical implications. A review of the literature indicates that low flow time, age, percutaneous intervention, and sustained ventricular fibrillation are independent factors that directly impact patient outcomes. With advances in ECPR and its use in the clinical setting, it is evident that randomized control trials and uniform ECPR protocols and guidelines are essential to improve evidence base practice and patient outcomes.

Extracorporeal cardiopulmonary resuscitation

Introduction

Cardiopulmonary resuscitation (CPR) has a unique if almost comical history. Stories of early resuscitation attempts began in the early ages and included everything from the Flagellation method, which consisted of whipping the victim with stinging nettles or wet cloths to stimulate a response, to the Heat method where warm ashes, hot water, and burning dried animal feces were applied to the individual with the intent of restoring heat and life to the dead body (American Heart Association, 2018). In the 1700's, a London Physician named William Hayes formed a British Royal Humane Society, which devoted itself to experimenting with various methods of bringing back the dead. Techniques performed and reported ranged from tickling the back of a victim's throat with a feather, rolling victims back and forth over a wine barrel, throwing the victim over the back of a galloping horse, and inserting ivory nostril pipes into the victim's nose (American Heart Association, 2018).

Among history's ineffective albeit creative methods of resuscitation, a few revolutionary ideas were formed. In the 1770's, electrical defibrillation was first described and mouth to mouth resuscitation was introduced in Paris (Butcher, 2017). In the 1800's, German scientists Moritz Schiff and Rudolph Boehm developed the foundations of chest compression (Butcher, 2017). In the 1960's, modern CPR was developed and popularized as a combination of chest compressions and mouth to mouth resuscitation with a sequence of interventions established under the acronym ABCD, which spells out Airway, Breathing, Chest compression and Defibrillation (Butcher, 2017).

Almost 60 years later, conventional CPR (CCPR) has fundamentally stayed the same and has been performed on millions around the world. While CCPR is cheap, easy to learn, life saving, requires little specialized equipment, and can be applied immediately, it is often performed incorrectly. CCPR can be traumatic and ineffective. In addition, it only achieves 25% of cardiac output (Butcher, 2017). Unlike illustrations on TV where 75% of patients survive cardiac arrest, only 2% of adults who collapse on the street will recover fully (Butcher, 2017). In addition, while 40% of patients will initially survive in-hospital cardiac arrest (IHCA), only 10-15% will survive to discharge. Out of these patients, only 50-80% will have favorable neurological outcomes (Butcher, 2017).

In general, survival of cardiac arrest patients is dependent on timely activation of the chain of survival which includes “quick recognition of cardiac arrest, activation of the emergency response system, good quality CPR, rapid defibrillation, advanced life support, and post cardiac arrest care” (Tan, 2017, p.446). However, some patients, such as those experiencing a massive pulmonary embolism, acute blockage of a coronary artery, severe metabolic acidosis, or poor coronary perfusion pressure may be refractory to these life saving measures (Stub et al., 2015). In refractory cardiac arrest patients, the use of extracorporeal cardiopulmonary resuscitation (ECPR) is being integrated into healthcare (Stub et al., 2015). ECPR is the insertion of venoarterial ECMO during refractory CPR. The goal of ECPR is to stabilize a patient long enough for recovery, transplant, or treatment. This innovative and potentially revolutionary practice will be explored from its mechanics, current protocols and guidelines, newfound research, and complications, to the nurse’s role, ethical concerns, and gaps in the literature.

Extracorporeal membrane oxygenation

Extracorporeal life support (ECLS) is a general term to describe “temporary support of cardiac or pulmonary function using mechanical devices when other measures are not able to support life” (Calhoun, 2018, p.394). Extracorporeal membrane oxygenation (ECMO) is a method of extracorporeal life support that assists in oxygenation, ventilation, and/ or cardiac output. These life saving functions are accomplished through a cannula inserted into the patient and connected to a circuit. This circuit pumps blood through an oxygenator and back to the patient (Mosier et al., 2015). ECMO was originally developed in the the 1950’s by John Gibson as a way of oxygenating an individual’s blood for prolonged cardiopulmonary bypass during operations (Calhoun, 2018).

Given the fact that ECMO did not require the open blood reservoir and intense anticoagulation necessary for a traditional cardiopulmonary bypass circuit, ECMO was seen as a less complex and more sustainable treatment choice for patients with refractory cardiovascular and respiratory failure outside of the operating room (Mosier et al., 2015). In the 1970’s, several reports were published regarding ECMO’s successful use in cases of shock-lung syndrome, adult capillary leaky syndrome, and cardiopulmonary failure (Calhoun, 2018). However, ECMO did not become popularized until the early 2000’s when the H1N1 pandemic hit. Since 2006, extracorporeal life support (ECLS) use in intensive care units throughout the United States has increased over 400% (Mosier et al., 2015). The two main types of ECMO are venovenous and venoarterial ECMO.

Venovenous Extracorporeal membrane oxygenation

Venovenous (VV) ECMO is used for patients with severe respiratory failure who are not being sufficiently supported by a ventilator. These include patients with acute respiratory distress syndrome, C02 retention (despite full ventilator support), influenza, pneumonia, acute pulmonary embolism, and patients on the lung transplant list (Calhoun, 2018). According to the Extracorporeal Life Support Organization (ELSO) guidelines, indications for VV ECMO would be a patient in hypoxic respiratory failure with a Pa02/FIO2 (P/F) ratio less than 100 and/ or a Murray score of 3-4. (Calhoun, 2018). VV ECMO functions by pulling blood from the inferior vena cava (IVC) through a circuit that removes carbon dioxide and oxygenates the blood. The blood is then returned into the venous system through the internal jugular vein. Most commonly, the femoral vein is used as the drainage cannula and the internal jugular functions as the return cannula. While VV ECMO provides mainly respiratory support to a patient, venoarterial (VA) ECMO supports both the respiratory and cardiac systems (Calhoun, 2018).

Venoarterial Extracorporeal cardiopulmonary resuscitation

VA ECMO is used for patients experiencing cardiogenic shock, decompensating heart failure, myocarditis, pulmonary embolism, myocardial infarction, and those in need of support before insertion of a more permanent device, such as an LVAD (Calhoun, 2018). VA ECMO drains deoxygenated blood from the right atrium via a venous cannula. This blood is drained by a centrifugal or roller, which actively draws venous blood and pumps it through the gas-exchange membrane (Calhoun, 2018). The carbon dioxide is eliminated in the oxygenator and fully oxygenated blood is returned to the patient through a large artery. The returned oxygenated blood supplies blood flow to all vital organs, including the brain. The most common form of cannulation is peripheral cannulation from the femoral vein-femoral artery (Swol et al., 2016). This type of cannulation produces a retrograde flow, which means that the blood from the ECMO is going against the body's normal circulation (Calhoun, 2018). Organ perfusion on VA ECMO is dependent on the patient's cardiac output as well as the ECMO's flow, which is typically anywhere from 3 to 5L/min (Calhoun, 2018).

ECPR eligibility guidelines

Recent research is starting to reveal the role VA ECMO can have in patients experiencing cardiac arrest. IHCA treated with conventional CPR (CCPR) typically has a survival rate of 15-17% and out of hospital cardiac arrest (OHCA) survival rate is lower at 8-10% (Michels et al., 2018). Research has shown coronary perfusion pressures to be a major factor in the low survival rate with conventional CCPR. The most important determinant of return of spontaneous circulation (ROSC) during CPR is myocardial blood flow, which is driven by coronary perfusion pressure. Coronary perfusion pressure is the "difference between the aortic and right atrial diastolic pressures" (Maryam et al., 2016, p.1111). ROSC is generally associated with a CPP of greater than 15. However, a study by Maryam et al. demonstrated that manual chest compression is unlikely to consistently exceed a CPP of 15 due to shallow compression, high ventilation rates, a high no flow fraction, and low mean compression rates (Maryam et al., 2016). Patients with the worst outcomes generally have a prolonged time to ROSC, which can lead to cerebral hypoperfusion. For patients with refractory CPR, early initiation of ECPR may reduce cerebral hypoperfusion and improve coronary perfusion pressures enough to achieve ROSC. As inserting VA ECMO during resuscitation requires specialized equipment and a highly skilled team of professionals, structured guidelines and protocols have come into place regarding who is eligible to receive ECPR.

Individuals being considered for ECPR must have no contraindications to ECMO, fit within the specific facility criteria, and be in refractory cardiac arrest. The American Heart Association stated in its latest guidelines the goal of ECPR was to “support patients in refractory cardiac arrest while reversible causes are identified and treated” (Tan, 2017, p. 446). ELSO’s 2013 recommendation agreed with these guidelines and concluded it may be medically futile to start ECPR if CPR has been unsuccessful for greater than thirty minutes (Tan, 2017). Currently there are no randomized, controlled studies on ECPR. As a result, standardized algorithms and selection criteria are lacking, but a general understanding of the guidelines can be formed through expert opinion and research.

In order to understand the guidelines for ECPR, refractory CPR must be defined. According to a large database of 64,339 patients with in hospital cardiac arrest (IHCA), half of patients achieve return of spontaneous circulation (ROSC) within 10 minutes of onset of arrest, one fourth in the subsequent ten minutes, and a few after more than thirty minutes of CPR. In OHCA, ROSC occurred within 16.1 minutes of CPR in 89.7% of patients with a good outcome. After 15 minutes, probability of good function to recover dropped to less than 2% (Fagnoul, Combes & De Backer, 2014). After evaluation of this data, cardiac arrest has been considered refractory to standard CPR after fifteen minutes. At the Erasme University Hospital, evaluation of a patient’s candidacy for ECPR begins at ten minutes of CPR (Fagnoul, Combes & De Backer, 2014).

While it is not fully understood why some patients are more resistant to CPR than others, refractory patients appear to have a greater amount of coronary artery disease as well as poor coronary perfusion pressure with CCPR, especially through the left anterior descending (LAD) coronary artery. Research has found refractory ventricular fibrillation represents the largest group of survivors with ECPR (Butcher, 2017). Nakashima studied subgroups of cardiac rhythm during OHCA. His study showed more favorable outcome in sustained ventricular fibrillation (VF) or ventricular tachycardia (VT) compared to rhythm change with the rate of favorable outcome increasing 5.5 fold for sustained VF/VT with ECPR (Nakashima, Tahara, Yasuda, 2015). While no standardized treatment pathway for ECPR patients has been formed as of yet, the University of Minnesota established an ECPR protocol defining eligibility for ECPR. The university found 45% of patients with out of hospital cardiac arrest who are placed on extracorporeal life support (ECLS) survive, compared to the 15% that survive with CCPR (Butcher, 2017).

Under the protocol, patients within the ages of 18-75 undergoing CPR for refractory ventricular fibrillation or tachycardia, who had conventional or mechanical CPR started less than ten minutes after cardiac arrest, are considered candidates and transported to the cardiac catheterization lab (Butcher, 2017). These candidates should have a suspected reversible cause of cardiac arrest such as hypoxia, hypovolemia, hypo- and hyperkalemia, hypothermia, pericardial tamponade, thromboembolism, pulmonary embolism, and tension pneumothorax (Michels et al., 2018).

In addition, these patients can have no absolute contraindications to ECMO implantation. These contraindications include individuals with end-stage cancer, immunosuppression, severe neurologic injuries, irreversible multi organ failure, intracranial hemorrhage, uncontrollable bleeding, severe trauma, severe aortic regurgitation, aortic dissection, “do not resuscitate” (DNR) orders, or chronic organ dysfunction such as renal failure, cirrhosis, and emphysema (Swol et al., 2016). Relative contraindications include elderly patients with multiple morbidities, individuals with dementia, patients with morbid obesity, and those with prolonged cardiac arrest time (Swol et al., 2016). If it is decided the patient can receive ECMO, the patient’s arterial and venous access will be evaluated under the ultrasound and the patients arterial blood gas and serum lactate are drawn (Butcher, 2017).

The blood gas and lactate are evaluated against some certain criteria. If the patient meets one or more criteria, the CPR is terminated and the patient is declared dead. The criteria are as follows: an end-tidal carbon dioxide less than 10%, a partial oxygen pressure of <50 mmHG, an oxygen saturation less than 85%, and a serum lactate greater than 18. These criteria serve as a measure of the effectiveness of CCPR. A high lactate indicates severe metabolic acidosis due to hypoperfusion. If none of the criteria are present, the patient is placed on AV ECMO (Butcher, 2017).

Cannulation Procedure

The goal for patients eligible to receive ECPR is for full ECLS to begin within sixty minutes of cardiac arrest. In order to connect the VA ECMO to the patient, arterial and venous vascular access is required. The inguinal vessels are primarily used during the procedure and an ultrasound is utilized to visualize the vessel diameter in order to increase safety (Swol et al., 2016). The size of the cannula depends on the individual’s body size and the flow requirements. Typically, a 17 French cannula is inserted into the femoral artery after percutaneous puncture and dilation using the Seldinger technique. A 23 French venous cannula is then inserted into the femoral vein on the same or opposite side. The tip of the venous cannula should be positioned in the right atrium (Swol et al., 2016). A guide wire the length of 100-150cm is recommended for venous access (Swol et al., 2016). Stiff catheterization guide-wires may provide more support than cannulation guide-wires but fluoroscopic imaging should be used with stiff guide-wires (Swol et al., 2016).

Overall, performing cannulation under resuscitation can prove to be a major challenge. It is difficult to find appropriate blood vessels with such poor circulatory conditions (Swol et al., 2016). A mobile, miniaturized ultrasound could prove beneficial for this procedure. In addition, fast surgical cut-down is an option if vessels can not be visualized. In fast surgical cut-down, the femoral vein is exposed surgically and a cannula is inserted into the vein under direct vision (Swol et al., 2016). If fluoroscopy is available, this technology can be used to ensure the guide wires are in a good position prior to their insertion. In addition, regional brain tissue oxygen saturation measurement may be helpful during the process to assess the patient's circulation (Swol et al., 2016).

After the cannulation, a chest x ray should be completed to verify placement of the venous access cannula and endotracheal tube (Stub et al., 2014). Then the dry and primed ECLS system is connected with polyvinyl cellulose (PVC) tubing to the cannula. Heparin is usually administered at 100 IU/kg, or an estimated dose of 5,000 IU of heparin (Calhoun, 2018). The ECLS function is initiated by a roller or centrifugal pump at a blood flow rate of 3-4L/min to achieve a cardiac index of 2.2-2.5L/min/m2 and an oxygen fraction of 50%. This oxygen fraction should be gradually brought up from 50%

to 100% due to the risk of hyperoxygenation during reperfusion. Blended oxygen may be considered to reduce this complication (Swol et al., 2016).

Once the ECLS is functioning, a transesophageal ultrasound is used to confirm correct cannula positioning, appropriate left and right ventricular unloading, and best flow conditions in relation to cannula position. Best flow conditions are defined as “the highest flow with lowest ECMO revolutions per minute” (Swol et al., 2016, p.182). If venous drainage is found to be low after cannulation, the venous cannula should be checked to make sure it is not being inhibited by the intra-atrial septum (Swol et al., 2016). In addition, the patient’s fluid volume can be checked by placing the patient in Trendelenburg, which is when the body is laid supine with the feet elevated 15-30 degrees above the head, and by administering fluid. If the venous flow improves after administration of fluid, the patient was most likely hypovolemic. However, if the maneuver is ineffective, an additional venous cannula may be placed in the iliac or inferior vena cava through the contra-lateral femoral vein to improve venous drainage (Swol et al., 2016). The ECLS is usually continued for up to ninety minutes. If return of spontaneous cardiac function is achieved, the patient is admitted to the intensive care unit. If the patient has not achieved return of spontaneous circulation, the patient is pronounced dead (Butcher, 2017).

After defining ECPR eligibility and the cannulation procedure, Butcher provides an example of the process through which potentially eligible ECPR patients are siphoned. Butcher describes published data detailing outcomes for seventy-two patients with OHCA. The patients presented with ventricular fibrillation and were transported by EMS after three unsuccessful shocks and Amiodarone. After these interventions, ten did not meet transport criteria. Three patients had manual CPR only, one patient had Pectus Excavatum, two had morbid obesity, three had a time from 911 to the cardiac catheterization lab that was greater than ninety minutes, one was greater than eighty years, one had stage IV renal cancer, and two were declared DNR on arrival (Butcher, 2017). Of the sixty-two patients that met early transport criteria, seven were declared dead due to failure to meet ECLS bloodwork initiation criteria. Five patients had ROSC before arrival, and fifty were placed on ECLS. Eight were declared dead after ECLS was unable to re-establish rhythm after ninety minutes. Forty-seven were admitted to the CICU. Twenty-eight of the forty-seven survived to discharge, twenty-six with a cerebral performance category of 1-2 (Butcher, 2017). The cerebral performance category (CPC) score is the most commonly used tool to assess long term neurological and functional outcomes from a resuscitation attempt. A CPC of 1 indicates good cerebral performance and a CPC of 2 indicates moderate cerebral disability. A CPC of 3 indicates severe cerebral disability, a CPC of 4 indicates coma or vegetative state, and a CPC of 5 indicates brain death (Reynolds & Soar, 2014). According to Butcher's published data, twenty- six patients survived three months after discharge with a CPC of 1. In total, 55% of the admitted patients survived to three months after discharge with none to minimal neurological deficits (Butcher, 2017).

Using VA ECMO for refractory cardiac arrest promises to enhance outcomes. By supporting systemic circulation, ECPR can provide time for recovery from underlying insults causing arrest such as electrolyte abnormalities, hypothermia, cardiac tamponade, and pneumothorax. ECPR also serves sustained perfusion to the brain and rapidly restores oxygen metabolism. These factors may contribute to the efficacy of ECPR in terms of cerebral resuscitation (Sakamoto et al., 2014). Another reason for better neurological outcomes in ECPR patients may be related to the fact that early supply of oxygenated blood to failing myocardium during ROSC prevents irreversible ischemia and acts as a bridge to percutaneous coronary intervention by maintaining circulation (Sakamoto et al., 2014). When there is particularly gross damage to the heart, ECPR can also be a bridge to treatment with cardiac transplantation or a left ventricular assist device (Riggs, Becker & Sugarman, 2015).

Post Cardiac Arrest Care

It is important to understand that ECPR makes up only one aspect of post-cardiac arrest care, which also includes "therapeutic hypothermia, early perfusion for best patient outcome, tight glycemic control, low tidal volume ventilation, and treatment of the root cause" (Tan, 2017, p. 447). The purpose of these interventions are to address the potential cause of injury, reduce effects of metabolic acidosis and ischemia, and to reduce reperfusion injury or post resuscitation syndrome. Reperfusion injury is the tissue damage caused when blood supply returns to tissue. After a refractory CPR event there is damage to tissue, acidosis, and accumulation of metabolic intermediates. During reperfusion, there is a sudden increase in oxygen radicals and dead and dying tissue are washed into the systemic circulation (Napp, Kuhn, & Bauersachs, 2017). The introduction of these oxygen radicals and dead tissue particles into the circulation produces intravascular coagulation, diffuse inflammatory response, and systemic vascular permeability. Respiratory distress syndrome can develop if the ischemic injury is severe. In addition, renal failure or multi organ failure can also occur (Napp, Kuhn, & Bauersachs, 2017).

Use of targeted temperature management (TTM) after cardiac arrest for a minimum of 12 hours followed by gradual rewarming is considered standard procedure. Early introduction of therapeutic hypothermia (TH) may reduce the severity of ischemic reperfusion injury or post resuscitation syndrome. Cerebrally, during reperfusion there is a major increase in ipsilateral cerebral blood flow that is above the metabolic demands of the brain tissue. This rapid oxidant burst that occurs in response to reperfusion after systemic ischemia, is suspected to be reduced with hypothermia (Tan, 2017). TTM has also been found to prevent lactate production, acidosis, and reduce the oxygen demand of the heart. Hypothermia also preserves brain metabolism and the auto regulation of the body. Therapeutic hypothermia decreases cerebral metabolic rate by 6-7% for any 1 degree drop in temperature. In addition, TTM helps preserve the blood brain barrier, decrease intracranial pressure, and reduces swelling in the brain (Tan, 2017). A retrospective review conducted by Pang et al. evaluated therapeutic hypothermia and its impact on neurological outcome in ECPR patients. The study was conducted for 225 consecutive adult patients treated with ECLS between July 2003 and January 2016. The study found that therapeutic hypothermia at 34 degrees Celsius maintained for 24 hours improved neurologically favorable survival rates. Patients with TH had a favorable neurological survival at 42.9% in comparison with those with normothermia who had a favorable survival rate of 15.4% (Pang et al., 2017).

Care is also devoted to avoid hyperoxia and hypocapnia in reperfusion in order to reduce brain damage or loss of cerebral perfusion autoregulation. High oxygen partial pressures during ECPR may result in production of superoxide, as a result, careful control of oxygen partial pressure is necessary during ECPR and may be managed with low oxygen fraction in ECMO gas. (Swol et al., 2016). In addition, early reperfusion through percutaneous coronary intervention (PCI) for patients with acute coronary syndrome and arrest of cardiac origin has proven to increase survival rates and reduce mortality (Swol et al., 2016).

Intra-aortic balloon pump insertion can also be considered to improve coronary and peripheral perfusion via diastolic balloon inflation. The balloon pump can improve ventricular function by reducing afterload and increasing perfusion to the coronary arteries during diastole. The literature regarding IABP insertion in post ECPR patients is not robust but may be a valuable future assessment (Swol et al., 2016).

After stabilization, it is important to collect a detailed case history and perform diagnostic procedures to determine potential causes of cardiac arrest. Some reversible causes of cardiac arrest include hypoxia, acidosis, hypokalemia, hypoglycemia, tension pneumothorax, thrombosis, toxins, cardiac tamponade, hypovolemia, and hypoxia (Calhoun, 2018). Patients should be weaned off ECMO as soon as underlying illness is addressed and the patient is hemodynamically stabilized. Most literature states that up to a week is usually enough time to regain organ function (Calhoun, 2018).

At this time, turndown echocardiograms are performed to see if the patient can tolerate coming off of ECMO. During a turndown echocardiogram, a transthoracic echocardiogram is brought to the bedside and a physician looks at the patient’s heart function as they turn down the flow of the ECMO machine. For patients with a pulsatile flow, where native cardiac output is present, the extracorporeal blood flow can be decreased and a trial of clamping the extracorporeal circuit can be performed (Swol et al., 2016). If the patient’s vital signs remain stable and heart function appears to have returned, decannulation is the next step. However, if the patient doesn't seem to tolerate being weaned off the ECMO machine, a more permanent device such as an LVAD may be advised (Calhoun, 2018).

Post Cardiac Protocols

In order to have a full picture of post cardiac treatment for patients undergoing ECPR, the specific treatment protocols for one study will be discussed. This study by Sakamoto et al. compared the difference in neurological outcomes between ECPR and conventional CPR in OHCA patients with VF or VT on the initial ECG at one month and six months after cardiac arrest. Forty-six facilities participated in the study with the approval of the ethical committee of each hospital. Twenty-six hospitals were enrolled in the ECPR group and 20 hospitals in the non-ECPR group. Between October 2008 and March 31, 2012, a total of 454 patients were registered. The ECPR group consisted of 260 patients and the non ECPR group had 194 patients (Sakamoto et al., 2014).

Patients included in criteria for the study were those who were in ventricular fibrillation or ventricular tachycardia on the initial electrocardiogram(ECG), who arrived at the hospital within forty-five minutes from reception of the emergency call or the onset of cardiac arrest to hospital arrival. Exclusion criteria included those under the age of twenty and older than 75 years, a non-cardiac origin, a core body temperature less than thirty degrees, and no informed consent from individuals representing patients (Sakamoto et al., 2014). Every patient in the trial had a post cardiac arrest treatment bundle including therapeutic hypothermia, IABP, and early reperfusion, as tolerated. For patients undergoing ECPR, respiratory protocols involved maintaining PaC02 between 36-44, avoiding hypoxemia, and preventing hyperventilation. When acute coronary syndrome was suspected, emergency coronary angiography was to be performed to improve patient circulation. In addition, orders were set in place to avoid hypotension by maintaining a MAP of 65 or above, targeting timed urine volume to 0.5 mL/h or more, maintaining a lactate less than 4, keeping mixed venous oxygen saturation at 65% or above, maintaining a superior vena cava oxygen saturation at 70% or above, and achieving a central venous pressure (CVP) between 12-15. Patients were also to be kept on a 12 lead ECG and an x ray was to be utilized to verify placement of the venous and arterial cannula (Sakamoto et al., 2014).

Regarding therapeutic hypothermia, temperatures were monitored with a temperature sensing foley, rectal temperature probe, or VA ECMO machine in order to achieve a core body temp of 32-34 degrees with a cooling rate of at least one degree Celsius an hour. Target body temperature was to be achieved in four hours and a state of hypothermia was to be maintained for twenty-four hours or more. Rewarming after the allotted twenty-four time was to be gradual to at least 36 degrees and less than 37 degrees. Anticonvulsants and sedative were utilized when shivering occurred. If shivering could not be controlled, muscle relaxants and deeper sedation was to be administered to reduce metabolic demand. Glucose levels were also to be controlled in order to avoid hyperglycemia (Sakamoto et al., 2014).

For patients receiving percutaneous cardiopulmonary support (PCPS) also known as ECPR, onset from arrest was ideally no more than sixty minutes and as long as ninety minutes. The PCPS flow rate was to be set at a maximal flow rate of 4L/min at the start and adjusted as appropriate. In addition, anticoagulants were to be administered per agency and the frequency of oxygenator exchange was also to be changed per protocol.

According to the study, patients were to be assessed for lower extremity ischemia related to ECMO through skin color, joint stiffness, progression of acidosis and increase in lactate, decrease in Doppler blood flow, palpability of the dorsalis pedis artery, and difference in the right and left sole temperature. Criteria for weaning was based on blood pressure, heart rate, left ventricular wall motion, left ventricular ejection time, cardiac index, end-tidal carbon dioxide concentration, and urine volume (Sakamoto et al., 2014). Meanwhile, criteria for discontinuation, according to the study, were severe circulatory failure where PCPS flow rate could not be maintained, cerebral nervous system disorder, and uncontrollable bleeding (Sakamoto et al., 2014).

ECPR survival rates

Now that ECPR eligibility, cannulation protocol, and the guidelines for post cardiac arrest care have been described, the research supporting current practice for ECPR will be explored. The databases that were utilized for this research included Medline, CINAHL, Pubmed, Google Scholar, Cochrane library, Embase and Proquest. Over fifty articles were initially reviewed and these articles were narrowed down to twenty-four articles. The twenty-four articles incorporated in the paper were published within the last five years. These articles were then evaluated based on the Melnyk Framework for levels of evidence (Melnyk & Fineot-Overhold, 2015). Of the twenty-four articles, twelve articles had a level five evidence. Nine of these articles were expert opinion and clinical expertise and three articles were case reports. Seven articles had a level four evidence. Of these articles, three articles were a retrospective review and four articles were prospective observational studies. Of the prospective observational studies, one study was multi center and two studies were single center. The last five articles had a level one evidence and all five articles were a meta-analysis and systematic review. Out of the literature review, no randomized control trials were found. A randomized control trial would be considered a level two evidence according to the framework utilized for this paper (Melnyk & Fineot-Overhold, 2015).

The study that has spearheaded interest in ECPR is the CHEER trial. The CHEER trial was a single center, prospective, observational study conducted at the Alfred Hospital in Australia. The trial had twenty-six patients with a mean age of fifty-two years. Patients selected for the trial were in refractory OHCA and IHCA of greater than thirty minutes, an age between 18-65, had a no flow time of less than ten minutes, had a mechanical CPR machine available, and were in ventricular fibrillation with a suspected cardiac etiology (Stub et al., 2014). Patients with severe chronic airway disease, cirrhosis, renal failure, and terminal illness were excluded from the trial. Patients chosen for the trial were treated with a treatment bundle that consisted of mechanical CPR, hypothermia, ECMO, and early reperfusion. Mechanical CPR was accomplished with an autopulse machine and hypothermia was initiated through the administration of 30 mL/kg of ice-cold saline rapid administration. This hypothermia was then maintained for twenty-four hours in the intensive care unit at thirty-three degrees celsius (Stub et al., 2015). The study found a survival of 45% for patients with OHCA, and 60% survival of patients with IHCA with a CPC of 1-2. Together, 54% of patients survived to discharge with a CPC of one (Stub et al., 2015).

The remarkable finding in the CHEER trial was not just the survival rate of ECPR patients but the high neurological outcomes. A retrospective propensity matched study by Patricio et al. found improved long-term neurological outcomes with ECPR as compared to CCPR. The retrospective analysis was of a prospective database of cardiac arrest patients, which included all consecutive adult patients admitted to the intensive care department after cardiac arrest between January 2012 and December 2017. The decision to initiate ECPR was made by the attending physician and ECPR was performed by an ECPR team with ICU physicians. The primary outcomes of the study were survival to ICU discharge and favorable 3-month neurologic outcome, assessed by a CPC score of 1-2. From 635 patients with CA during the study period, 80 ECPR patients were matched to 80 CCPR patients. ROSC rates were 77/80 for ECPR and 30/80 for CCPR. Survival to ICU discharge was 18/80 for ECPR versus 14/80 for CCPR. At 3 months, 17/80 ECPR patients and 9/80 CCPR patients had a favorable outcome (Patricio et al., 2019).

A meta-analysis by Wang et al. also demonstrated favorable neurological outcomes with ECPR versus CCPR. The systematic review examined six studies with 2,260 patients. The purpose of the review was to study the survival rate to discharge and long-term neurological outcomes of ECPR versus CCPR. The study found survival with a favorable CPC score in 19.4% of those with ECPR versus 7.4% with CCPR (Wang et al., 2017).

A meta-analysis of thirteen cohort studies by Ouweneel et al. supports the findings of Wang and Patricio. The meta-analysis compared the mortality rates of patients in refractory cardiac arrest and cardiogenic shock treated with and without ECLS support. The study found that the use of ECLS was associated with an absolute increase of 30-day survival of 13% compared with conventional CPR (Ouweneel et al., 2016).

January 1st, 2015, the Extracorporeal Life Support Organization (ELSO) released the international ECLS registry report, which was based on its experience with 1,657

ECPR patients. A total of 639 or 39% of patients survived initial ECPR; of these, 471 or 74% of patients survived till discharge. Other observation studies have found improvements in mortality with the use of ECPR. Cardarelli performed a meta-analysis of observation studies on ECPR involving 135 adults (Tan, 2017). The study showed overall survival to hospital discharge was 40%, and the most common cause of cardiac arrest was acute myocardial infarction. He also found those in the age group of 17-41 years had a higher survival rate compared to those in the 41-56 years' age group. The meta-analysis also revealed patients who had CPR performed for more than thirty minutes were more likely to die than those who received less than thirty minutes of ECPR. This data suggests that ECPR may have better outcomes in younger patients who receive a shorter duration of CPR with early implantation of ECMO (Tan, 2017).

Survival and Neurological Predictors of ECPR

A meta-analysis of clinical trials by Wang et al., identified key survival and neurological predictors of ECPR (2018). The study reviewed a total of 16 studies, in which 1,162 patients were enrolled. The study concluded the following:

> IHCA, witnessed cardiac arrest (CA), bystander CPR, initial shockable rhythm, shorter CPR duration and arrest-to-ECMO duration, higher baseline PH, lower baseline lactate and PCI were favorable survival predictors of adult ECPR, and shockable rhythm and shorter CPR duration were good neurological outcome predictors of adult ECPR. (Wang, Qingbian, Zhang, Liu & Zheng, 2018, p.13257)

Another study by Schmidt et al. evaluated pre-ECMO predictors of in-hospital survival. The study acknowledged the large financial and human resources that ECPR can have and the importance of allocating this technology to patients with high survivability. The study evaluated patients with refractory cardiogenic shock treated with VA ECMO between January 2003 and December 2013 by examining records from the International Extracorporeal Life Support Organization Registry. Of 3,846 patients with cardiogenic shock treated with ECMO, 1,601 (42%) were alive at hospital discharge. The study found “Chronic renal failure, longer duration of ventilation prior to ECMO initiation, pre-ECMO organ failure, pre-ECMO cardiac arrest, congenital heart disease, lower pulse pressure, and lower serum bicarbonate” were risk factors associated with mortality (Schmidt et al., 2015, p. 2246). Whereas “younger age, lower weight, acute myocarditis, heart transplant, refractory ventricular tachycardia or fibrillation, higher diastolic blood pressure, and lower peak inspiratory pressure” were factors associated with reduced mortality (Schmidt et al., 2015, p. 2246).

From these risk factors and protective factors discovered in the study, a survival after venoarterial-ECMO (SAVE) score was developed. The SAVE score looks at 12 items to predict survival. A save score of zero is equivalent to 50% survival and positive scores represent a higher chance of survival. It is hoped that the SAVE score can help guide clinician decision regarding patient survivability and increase the efficiency and success of ECPR (Schmidt et al., 2015).

IHCA survival rates with ECPR versus CCPR

In a retrospective single center, propensity matched analysis, Shin studied IHCA patients in a single center who received CPR for more than ten minutes. The study showed significantly improved survival rates in the ECPR group as compared to the CCPR group in terms of survival to discharge and six-month survival (Tan, 2017). In a two-year follow-up study in 2013, Shin showed a four-fold increase in survival with minimal neurological deficit in the ECPR group. Similar to Cardarelli's meta-analysis, Shin found that an age less than sixty-five years and CPR duration less than thirty-five minutes were independent predictors of survival with minimal neurologic injury (Tan, 2017). Chen also performed a propensity analysis comparing ECPR to CCPR in IHCA patients. The study favored ECPR in terms of survival to discharge, 30-day survival rate and one-year survival rate. Chen reported a cumulative 30-day survival rate of 34% for ECLS. The probability of survival to discharge was 50% when ECMO flow was initiated within thirty minutes of IHCA, 30% between thirty and sixty minutes, and 18% after sixty minutes (Tan, 2017).

OHCA survival rates with ECPR versus CCPR

A retrospective study of 21 patients with OHCA by Fjolner found seven patients survived at a 33% survival rate. Survivors had a cerebral performance category of 1 and 2 at hospital discharge (Fjolner et al., 2017). Sakamato et al. studied the difference in neurological outcomes between ECPR and conventional CPR in OHCA patients with ventricular fibrillation or pulseless ventricular tachycardia on the initial ECG at one month and six months after cardiac arrest (Sakamato et al., 2014). Neurological outcomes were defined by the cerebral performance category. At one month, 13.7% of the ECPR group were CPC 1-2 compared to 1.9% of the CCPR group. At six months, 12.4% if the ECPR group were CPC 1-2 compared to 3.1% of the CCPR group (Tan, 2017). ECPR combined with therapeutic hypothermia and intra-aortic balloon pump placement was recently shown to improve neurologic outcomes for OHCA patients with ventricular fibrillation or pulseless ventricular tachycardia. The study discussed in an article from

Critical Care: The Official Journal of the Critical Care Forum demonstrated survival with a favorable CPC at six months for 11.2% of ECPR patients versus 2.6% of conventional CPR (Mosier et al., 2015).

Improving ECPR Outcomes

After reviewing the literature, time to ECMO flow from cardiac arrest has been found to be a critical determinant of outcome with survival rates of 50% when initiated with thirty minutes of IHCA, 30% between thirty and sixty minutes, and 18% after sixty minutes (Fagnoul, Combes & De Backer, 2014). Reduction of low flow time appears to be one of the primary goals for ECPR. A no flow period less than five minutes, bystander CPR, and rapid transport mechanical CPR are all factors that may maintain quality of CPR before ECMO flow is initiated (Fangoul, Combes & De Backer, 2014). Another study by Kane and colleagues reflects these findings. The study found that those with severe metabolic acidosis at the time of ECPR initiation had higher mortality. Thus, one of the primary goals of ECPR is minimizing cardiac arrest time and the suboptimal cardiac output and oxygen delivery from CCPR through rapid initiation of ECPR. In order for these goals to be met, a rapid decision to pursue ECPR and activation of an advanced ECPR program with institutional protocols for notification and deployment of a team is necessary (Min-Sing, 2016).

Another important factor which has shown to directly influence ECPR outcome is sustained ventricular fibrillation. A multicenter prospective observational study was conducted in 46 hospitals by Nakashima. A total of 457 patients with OHCA aged 20-47 years were registered in the study. These patients had an initial rhythm of VF and a duration from collapse to hospital arrival time of 45 minutes. After CPR for more than 15 minutes, these patients received ECPR and therapeutic hypothermia. Of the patients who underwent ECPR, 2 groups were identified. Group A consisted of patients who had sustained VF during CPR and Group B consisted of patients who changed from VF to a non-shockable rhythm ((Nakashima, Tahara & Yasuda, 2015). The outcome of the groups was defined as a CPC of 1-2, 6 months after collapse. Group A had a favorable outcome rate of 19.7% as compared to Group B, whose favorable outcome rate was 3.3%. The results of this study indicated the importance of rhythm change in determining ECPR outcomes and the need to factor in rhythm change when considering a patient's eligibility and survivability from ECPR (Nakashima, Tahara & Yasuda, 2015).

Another factor that could improve outcomes in ECPR patients is intra-arrest PCI versus delayed reperfusion. Kagawa noted the high incidence of acute coronary syndrome in cardiac arrest patients and improvement of outcome with postresuscitation PCI and investigated the effectiveness of intra-arrest PCI associated with ECPR. Kagawa reported higher survival rates in intra-arrest PCI groups compared with delayed PCI. Patients with intra-arrest PCI were found to have a thirty-day survival of 36% versus those with delayed PCI who had a thirty-day survival of 12% (Fagnoul, Combes & De Backer, 2014).

In order to promote best practice during the cannulation process, the literature has found randomized controlled or prospective studies comparing fluoroscopically guided with ultrasonically guided ECLS placement may be beneficial. In addition, "miniature circuits with smaller prime volumes and improved biocompatibility of the ECLS circuit components could decrease the inflammatory response and the need for blood component transfusions for patients receiving ECPR" (Ming-Sing, 2016, p.1140). Additionally, implementation of a left ventricular microaxial pump or impella could be considered to improve outcomes for patients with no pulsatility or only minimal left ventricular contractility. (Michels et al., 2018).

Putting a Team Together

A successful ECLS program requires a multidisciplinary team that is committed to having the necessary resources and personnel (Mosier et al., 2015). Facilities must have access to blood products, laboratory services, elecrocardiography, angiography, transesophageal echocardiography, duplex ultrasounds, cannulation equipment, and an uninterrupted power system that supports all devices for at least one hour. The ECLS team can be structured in addition to or separate from other ECMO programs with an institution (Mosier et al., 2015). ECLS teams should be trained in general CPR with physicians, specialized nurses, and perfusionists. Personnel trained in VA cannulation, circuit management, and post-resuscitation should be available 24/7 and a physician trained in ECLS should provide 24-hour on call coverage for these patients (Swol et al., 2016).

The team should also comprise of selected physicians trained in insertion, maintenance, and surveillance of VA ECMO. The nurse patient ratio during post cardiac arrest care should be at least 1:1 (Swol et al., 2016). Predetermined inclusion and exclusion criteria, as well as guidelines on when to remove a patient from ECMO, should be clearly outlined. Hospitals with a higher volume of ECLS cases (>30 cases/ year) have been shown to have a lower mortality rate than facilities with low volume of ECLS cases (<6 cases/year) (Tan, 2017). According to Michels et al., a caseload of at least 30

ECLS/ECMO placements per year and per hospital with an ECMO/ECLS program is important to achieve high quality care (Michels et al., 2018).

Complications of Venoarterial ECMO

VA ECMO carries a high risk of hemorrhage, vessel rupture, hyperfibrinolysis, stroke, air embolism, limb ischemia, kidney failure, and infection (White & Fan, 2016). A meta-analysis of twenty studies and 1,866 patients by Cheng et al. explored the most common complications of ECPR. The meta-analysis found the pooled estimate rates of complications with 95% confidence interval to be as follows:

> lower extremity ischemia, 16.9%; fasciotomy or compartment syndrome, 10.3%; lower extremity amputation, 4.7%, stroke, 5.9%; neurologic complications, 13.3%; acute kidney injury, 55.6%; renal replacement therapy, 46.0%; major or significant bleeding, 40.8%; rethoracotomy for bleeding or tamponade in postcardiotomy patients, 41.9%; and significant infection, 30.4%. (Cheng et al., 2014, p. 610)

Data shows at least one large complication occurs with over half of patients on ECMO. Nurses play a key role in helping prevent complications, keeping patients safe and observing changes in a patient’s status.

Bleeding

Bleeding occurs in 30-40% of patients on ECMO and it most commonly occurs at the cannulation or surgical sites. Bleeding is directly related to continuous heparin infusion and platelet dysfunction. Bleeding can occur in the brain and cause neurological damage. In order to reduce the risk of bleeding, platelet counts should be maintained at >1 lakh/mm3 (Calhoun, 2018). If bleeding occurs, heparin infusions should be decreased per protocol and activated clotting time (ACT) should be maintained at 160 seconds (Calhoun, 2018). If the patient is suspected of having heparin induced thrombocytopenia, heparin infusions should be replaced with non-heparin anticoagulants. Surgical exploration may be used if major bleeding occurs and plasminogen inhibitors can be given. However, these inhibitors may increase the risk of circuit thrombosis. A circuit thrombosis can turn into an emboli and potentially obstruct blood flow to the heart and the lungs. Sudden changes in pressure gradient on the ECMO machine could be indicative of thrombus formation. As the nurse, it is important to evaluate patients for pressure gradient changes. In addition, nurses should also be aware of bleeding indicators which include decreased cardiac output, blood in the urine, petechiae, retroperitoneal bruising, and tachycardia (Calhoun, 2018).

Vessel Perforation

With cannulation, vessel perforation, arterial dissection, and bleeding can occur. VA cannulation carries a high risk of arterial injury. Around 18% of patients requiring VA ECMO experience this complication and most patients require surgical repair (Mosier et al., 2015). In order to reduce these risks, image-guided cannulation is strictly recommended and manipulation or dilation of the vessel should not be performed against resistance. In addition, in order to avoid accidental deccanulation, patients with any type of femoral cannulation must be kept well sedated (Calhoun, 2018). Nurses must perform daily wakeups to check for neurological status and practice excellent care to prevent skin breakdown in these immobile patients (Calhoun, 2018).

Ischemia

Another issue seen with femoral artery cannulation and retrograde flow is ischemia in the lower limbs. Ischemia can occur when a cannula partially occludes the artery and as a complication of the retrograde flow of venoarterial ECMO (White & Fan, 2016). It is important for nurses to monitor for ischemia by observing for coolness, mottling, and pallor in the feet. There is minimal pulsatility in VA ECMO, so it is challenging to feel for the pulses on a patient's limb. A Doppler ultrasound can be used to find the dorsalis pedis and posterior tibial arteries. Pulses should be checked at least every four hours. If ischemia occurs, the physician should be notified immediately and a small reperfusion catheter can be inserted (White & Fan, 2017). The catheter is inserted into the femoral artery distal to the main arterial cannula and it diverts blood from the ECMO circuit and down through the femoral artery, returning blood flow to the limb. In some facilities, it is standard to insert a reperfusion catheter while inserting the VA ECMO catheter. This practice has been shown to greatly decrease leg ischemia in these patients (Calhoun, 2018).

Considerations

For patients with poor heart function, caution must be practiced regarding the ECMO flow rate. A flow rate that is too high for the patient could cause excessive afterload and make it more challenging for the left ventricle to fully contract and eject blood. This resistance could lead to left ventricular distention, increased left ventricular filling pressures, pulmonary edema or thrombosis. In order for the nurse to evaluate the left ventricular output, the nurse can observe for pulsatility on the arterial waveform. If contractions are absent, ECMO flow may need to be adjusted or the patient may have severe left ventricular dysfunction requiring left ventricular venting (Swol et al., 2016).

ECMO is preload dependent as well as afterload sensitive. As a result, nurses should recognize a reduction in flow may be seen because of decreased inflow due to hypovolemia, thrombosis, and a tension pneumothorax, or due to increased afterload because of mechanical obstruction of the cannula, increased systemic vascular resistance or increased atrial pressure (Calhoun, 2018). With VA ECMO, the body's intrinsic blood flow can compete with ECMO's retrograde flow. The retrograde ECMO output meets the antegrade left ventricular output at a zone called the "watershed" (Napp, Kuhn & Bauersachs, 2017). The watershed is found between the aortic root and the diaphragm, depending on the native hearts cardiac output. The higher the left ventricular output, the more distal the watershed. Pulse pressure measured at the right radial artery serves as an estimate of left ventricular output. According to Napp et al. A blood pressure of "80/70 mm HG at an ECMO flow of 4.5 1/min indicates a watershed in the aortic root, whereas a blood pressure of 140/70 mm HG at the same flow would suggest a watershed in the descending thoracic aorta" (Napp, Kuhn & Bauersachs, 2017, p. 34). The competition between intrinsic blood flow and retrograde blood flow becomes problematic when respiratory lung function is poor due to the fact that oxygenation of blood from the left ventricle depends on lung function.

When the lungs are severely compromised, deoxygenated blood goes through the left ventricle. This deoxygenated blood can result in hypoxemia of the upper parts of the body and hyperoxia of the lower body. This complication is known as north-south syndrome and may lead to coronary and/ or cerebral hypoxia (White & Fan, 2016).

Nurses should be aware of this phenomenon and observe patients for cyanosis. In order to receive the most accurate reading of blood oxygenation to the heart and brain, blood gas should be drawn from the right radial artery. In order to prevent north-south syndrome, a patient's lung function should be optimized with a high ventilator setting or high frequency oscillatory ventilation. Diuretics may also be administered to promote fluid removal. In addition, the use of venoarteriovenous ECMO could be incorporated in which oxygenated blood is returned to both arterial and venous systems. Another potential option could be increasing the patient's ECMO flow as tolerated (Calhoun, 2018).

It is vital for the bedside nurse to care for this patient population with excellence. Patients should be assessed for pupil changes, changes in skin color, changes in skin temperature, drops in oxygen saturation, and increasing or decreasing blood pressure. These small changes could be a significant indicator for a development in the patient's status and it is crucial for the nurse to recognize these changes and take the proper course of action (Calhoun, 2018).

Not much is known about the long-term complications and quality of life for patients that have undergone ECMO. ECMO survivors may experience a poor quality of life, anxiety, depression, and post-traumatic stress disorder. In addition, with the complications, cost, and resources required to successfully perform ECPR, it is important to consider risk and benefits carefully before considering ECPR (Mosier et al., 2015)

Ethical Concerns

ECPR has ethical challenges that should be addressed as the technology slowly integrates into healthcare practice. Some of these challenges include "ECPR's uncertain risk-benefit profile, the difficulty in obtaining express informed consent in most cases, the high costs of ECPR, and the challenge in ensuring fair access to ECPR" (Riggs, Becker & Sugarman, 2015, p. 73). Regarding ECPR's uncertain-risk benefit profile, ECPR has been associated with potential harms and complications. While one study showed ECPR improved survival rates and neurological outcomes for those who experienced cardiac arrest, the same study also revealed higher rates of coma and vegetative state with ECPR. It is possible ECPR may increase the chances for patients to experience outcomes that could be considered worse than death. ECPR can also lead to something called the bridge to nowhere. This bridge to nowhere is a situation where the patient is awake on ECMO but he/she is not a candidate for a transplant or life saving procedure (Riggs, Becker & Sugarman, 2015). As a result, these patients are dependent on the life support they receive from the ECMO machine and have little hope of recovering to the point where they can be successfully weaned off the equipment. Another downside to ECPR is the potential trauma, anxiety, and stress families undergo if their loved one is removed from ECMO support (Riggs, Becker & Sugarman, 2015).

Informed consent

While consent for conventional CPR is generally assumed, it is not evident whether consent to ECPR should be presumed. Potential patients who may be eligible for ECPR may not find the risks of ECPR worth the treatment and could hypothetically refuse the intervention if medically able. As a result, ethic guidelines recommend resuscitation preferences be discussed with in hospital patients who are at a high risk of cardiac or respiratory failure. The discussion could also be a part of a routine code discussion after hospital admission. This practice could significantly reduce the ethical concern regarding informed consent and ECPR (Riggs, Becker & Sugarman, 2015).

Fair Criteria

Another ethical challenge of ECPR is the difficulty in creating a fair criterion for ECPR. Studies use inclusion criteria aimed at targeting patients that are most likely to benefit from ECPR and to prevent the initiation of futile and aggressive care. As discussed, some studies do not offer ECPR after an individual arrives at the hospital greater than forty-five minutes after their cardiac arrest. While it is true the time from cardiac arrest to full flow time directly correlates with the patient's recovery, survival has been reported in patients where ECPR was started after more than 150 minutes of conventional CPR. As a result, strict futility can not be an argument for time limitation criterion. Another criterion that may be seen as controversial is age cutoffs for ECPR. Most protocols do not include patients greater than seventy-five years old. However, in the United States, "age is not generally used as a basis for access to therapy that could be potentially beneficial" (Riggs, Becker & Sugarman, 2015, 73).

Expenses

The substantial costs associated with making ECPR available may also be considered an ethical issue. The equipment and training necessary to successfully carry out ECPR is very expensive. In addition, large costs may be incurred in caring for survivors of cardiac arrest. Costs may even reach hundreds of thousands of dollars per patient, especially when survivors are neurologically compromised (Riggs, Becker & Sugarman, 2015).

Organ Donation

Another potential ethical complication with ECPR has to do with organ donation. One third of non survivors after ECPR die from postanoxic brain damage, but only a minority will present with brain death. Patients with absence of recovery of cardiac activity and poor neurologic state may be candidates for non heart beating organ donation. While organ donation has the potential to save many lives, it can be a challenging process, especially when family members are opposed or feel as if the healthcare team does not have the patient's best interest in mind (Fagnoul, Combes & De Backer, 2014).

Recommendations

In order to reduce some of the ethical considerations associated with ECPR, it is important for stakeholders to be committed to developing more evidence base for ECPR. Most studies are focused on short-term mortality after ECPR but more evidence is required regarding long-term survival, patient and family experiences, as well as short- and long-term disability. This information could be gathered through registries. The Extracorporeal Life Support Organization (ELSO) currently has more than 170 participating institutions that keep records of extracorporeal life support and ECPR cases. The ELSO registry is currently focused on short-term survival and complications, but it should expand to researching other outcomes. Other ways to improve understanding of ECPR outcomes include efforts to study ECPR through randomized trials and a commitment of institutions that provide ECPR to send data to the ELSO registry (Fagnoul, Combes & De Backer, 2014). A meta-analysis by Holmberg et al. expressed the need for randomized control trials to improve the quality of research in support of ECPR for adults and children. The systematic review found observational studies to be one of the highest levels of evidence among the research and overall could not conclusively support the use of ECPR for OHCA and IHCA in adults and children (Holmberg et al., 2018).

Regarding informed consent, institutions that provide ECPR should update their code status policies. They should inform patients of their options regarding ECPR so that their preferences about ECPR are directly received from patients. (Riggs, Becker, & Sugarman, 2015). In addition, data should be collected through representative surveys from stakeholders on whether ECPR should be provided without informed consent. Cost-effective analyses can be used to inform ECPR policy. It is important to compare the costs of ECPR per quality adjusted life year with conventional CPR. It is essential to assess the economic impact that ECPR can have and to propose further research regarding this issue (Swol et al., 2016).

Conclusion

While convenient, CCPR has been found to be minimally effective in the face of refractory cardiac arrest and poor coronary perfusion pressure. According to research, ECPR has improved neurological outcomes and survival rates for patients in refractory OHCA and IHCA as compared to CCPR. ECPR is a temporary intervention that can stabilize patients to allow for early reperfusion and therapeutic hypothermia, and serve as a bridge to transplant. Although ECPR has a great potential for transforming lives, significant ethical and logistical hurdles still exist. Some of these hurdles include lack of definitive data on complication rates, functional outcomes, and survival as well as economic costs and resource utilization (Mosier, 2015). In addition, there is currently a lack of uniform guidelines for ECPR eligibility. Greater integration of tools such as the

SAVE score should also be utilized to assist in predicting survival of patient's undergoing ECPR.

After a review of the literature, it is clear that a patient's age and the time to ECMO flow from cardiac arrest are both critical determinants in the survival outcomes of ECPR patients. The sensitivity of low flow time to patient survival explains the poorer OHCA outcomes in relation to IHCA outcomes. In order to reduce low flow time, rapid communication between EMS and a highly trained ECPR team is essential. Research regarding improving outcomes of ECPR patients with OHCA should be conducted. The literature also reveals several gaps in ECPR research regarding best practice. In order to potentially improve outcomes, studies comparing fluoroscopically guided and ultrasonically guided ECLS placement can be evaluated. In addition, a uniform protocol for the routine insertion of an anterograde arterial cannula to reduce limb ischemia should be discussed. In order to promote the strength of ECPR research, large, prospective, randomized control trials should be developed. Research examining the use of an intra aortic balloon pump and Impella device to improve post cardiac function in ECPR patients should also be conducted. In addition, collaborative efforts from biochemical engineers and pharmacy to improve the biocompatibility of ECLS circuits may help reduce inflammatory response to the ECMO device.

One important consideration for the future development of ECPR and an ECPR team, is the production of more literature defining the nurse's role in caring for ECPR patients during the cannulation procedure and post cardiac arrest recovery. Critical care and emergency nurses are on the front lines of caring for these patients and should be properly equipped, educated, and trained in order to promote quality care and produce good critical thinking that could potentially avert complication.

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