Preoperative Venoarterial Extracorporeal Membrane Oxygenation Reduces Mortality in Advanced Structural Heart Disease

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Abstract

Introduction: Cardiac surgery for structural heart disease in the presence of cardiogenic shock or advanced heart failure has poor outcomes. We applied venoarterial extracorporeal membrane oxygenation (ECMO) to restore end-organ function and resuscitate patients prior to high-risk cardiac surgery. Methods: During a 2-year period (1/2018-12/2019) we reviewed all patients admitted to our Medical Centre with structural heart disease and cardiogenic shock, who had been resuscitated preoperatively by ECMO. Of these patients, 11 were included in the study. Patients were placed on ECMO preoperatively for 69 hours (range, 36-136 hours). Eight patients underwent valvular surgeries and 3 patients had ventricular septal defect repairs. Results: Mean age was 54± 15 years. Nine patients presented with cardiogenic shock, and two with advanced heart failure. Nine patients needed inotropes and four needed IABP support. Seven patients were admitted with acute kidney injury and five presented with metabolic acidosis. Average calculated EUROSCORE I was 56±23% and mean calculated APACHE II score was 17.18±6.26. The mean ECMO total time was 126±93 hours. Of the four postoperative deaths, three died within 10 days of surgery and one 2 months post-surgery. Conclusion: ECMO can be used as a bridge to heart valve or septal defect surgery in severely decompensated patients suffering from cardiogenic shock. Through recovery of end-organ function, ECMO may facilitate surgical correction of structural heart disease in patients in a very high risk for surgery.

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Keywords: ECMO; Cardiac surgery; Venoarterial extracorporeal membrane oxygenation; Cardiogenic shock; Structural heart disease; Mortality

Introduction

Cardiac surgery for acute structural heart disease in the setting of life-threatening advanced heart failure and cardiogenic shock has poor outcomes. Despite progress in invasive cardiology and surgical techniques, the mortality rate in these cases remains high (1). To counteract this problem, preoperative optimization of end-organ function is recommended to alleviate the operative risk (2). Venoarterial (VA) extracorporeal membrane oxygenation (ECMO) provides mechanical support in order to improve organ function and can be used as a bridge to definitive surgery.

Structural heart disease surgery is associated with high operational risk especially regarding reoperation valve surgery, ischemic ventricular septal defect (VSD) following acute myocardial infarction (MI) and ruptured papillary muscle repair. Critically ill patients with valve disease or VSD carry an operative mortality rate of >50% (3-5). Despite the advance in surgery and postoperative care, post-MI VSD carries the highest mortality rate of any procedure examined in The Society of Thoracic Surgeons risk score (3). These patients usually present with shock, decreased ejection fraction, end-organ dysfunction and often need postoperative mechanical support. However, these indicators have been shown to increase mortality in structural heart disease repair (3-5). Limited data exist regarding the efficacy and feasibility of using VA-ECMO preoperatively in the setting of advanced heart failure or cardiogenic shock in structural heart disease. Previous studies have reported that preoperative VA-ECMO support may reduce the risk score in patients with advanced structural heart disease (6, 7). We present the results of preoperative VA-ECMO, performed in our department, as a bridge to reparative surgery for patients who, despite optimal treatment due to acute structural heart disease, nevertheless suffer from cardiogenic shock with multi-organ failure.

Methods

Study design and population

The study was approved by the Institutional Ethics Committee (Protocol No 4257). Between 01.01.2018 and 31.12.2019, we performed a retrospective, observational study in a large teaching university hospital that included prospectively-collected data from consecutive patients diagnosed with structural heart disease. These patients presented with cardiogenic shock and advanced heart failure, and were resuscitated with VA-ECMO preoperatively as a bridge for reparative surgery.

Risk assessment included calculation of logistic EuroSCORE (8) and APACHE II score (9). Patient characteristics, clinical and laboratory information, surgical procedure, complications and outcome data were ascertained by reviewing hospital charts.

Surgical procedures and post-operative care

All patients were placed on VA-ECMO through open or percutaneous femoral access, and cannulation was done in the operating room or intensive care unit (ICU) either urgently or emergently. None of the patients was placed on VA-ECMO in the setting of cardiac arrest. Biomedicus cannulas (Medtronic, Minneapolis, MN, USA) were used in sizes from 23 French in diameter and 25 cm in length (23 F/25 cm) up to 29 F/50 cm for drainage and 19 F/18 cm up to 23 F/25 cm for return of the oxygenated blood. In these cases, the right femoral artery was cannulated, either percutaneously or with an open approach. When perfusion distal to the cannulation site was compromised, an 8 French catheter was inserted in the distal direction for retrograde perfusion. Biomedicus 550 consoles (Medtronic, USA) were used with a Maquet centrifugal pump (Maquet, Hirlingen, Germany) or Stöckert S3 or Stöckert CAPS roller pumps (Stöckert, Munich, Germany). The oxygenation of the blood and CO_2 removal were maintained by ECMO. The membranes were always ventilated with a FiO_2 of between 0.6 to 1.0 at a flow sufficient to maintain a $PvCO_2$ between 35-45 mm Hg. The blood temperature was regulated *via* heater. Heparin or bivalirudin was continuously infused to keep the activated clotting time (ACT) in a range between 180 and 220 seconds, which usually corresponded with an activated prothrombin time (APT) of 65-75 seconds. ECMO management included monitoring the brain and bilateral lower extremity saturations, as well as ambulation when feasible.

Reparative structural heart surgery was performed via a median sternotomy approach in all patients. Cardiopulmonary bypass was established by connecting to the ECMO cannulas. Myocardial protection was achieved by using antegrade and/or retrograde cold blood cardioplegia.

After surgery all patients were admitted to the ICU directly from the operating room. Following discharge from the ICU, patients were transferred either to a step-down unit or directly to the floor, from where they were discharged either to their home or to a rehabilitation facility. Throughout the study no major changes in hospital policy, surgical or anesthesiological techniques were introduced. All patients received standard anesthesia.

Data are presented as mean ± standard deviation. Categorical variables are given as frequencies and percentages. Statistical significance was assumed when the null hypothesis could be rejected at $p< 0.05$. All p -values are the results of two-sided tests.

Results

Patient characteristics at admission

Eleven patients presented with cardiogenic shock were included in this study, with a mean age of 54 years (29-69 years). Diagnoses included severe acute mitral regurgitation, post-infarction VSD, severe aortic stenosis after transcatheter aortic valve implantation (TAVI), acute prosthetic aortic valve thrombosis and severe tricuspid regurgitation. Five patients had severe metabolic acidosis (pH <7.3), and nine patients (80%) were supported also by inotropes. In their decompensated state, the mean ejection fraction was 24%, and an intra-aortic balloon pump was inserted together with the VA-ECMO support in four cases. Other comorbidities included hypertension (n=4), diabetes (n=1), ischemic heart disease and past interventional coronary catheterization (n=2), atrial fibrillation (n=2), prior cerebrovascular accident (n=1), chronic kidney disease (n=1), chronic infections of hepatitis C virus and tuberculosis (n=1), prior cardiac surgery (n=1), previous TAVI (n=1), and previous thoracic endovascular aortic repair (n=1). The mean logistic EuroSCORE I was 56.15±23% and the mean preECMO APACHE II score was 17.18±6.26 (Table 1).

Extracorporeal membrane oxygenation data

Patients were on VA-ECMO support for an average of 69 hours prior to surgery (range, 36-136 hours). Nine patients were ventilated while being supported by ECMO and the average ECMO flow was 75-85% from the calculated cardiac output. Preoperative VA-ECMO support improved the hemodynamic, organ function and metabolic parameters. Lactate, pH and creatinine levels normalized according to lab tests taken 1-2 days after ECMO initiation. Moreover, immediate preoperative APACHE score was significantly declined after ECMO support, from 17.2±6.3 to 7.36±1.8 (See Fig 1). Seven patients were weaned from ECMO at the time of surgery, while 4 patients could not be weaned from cardio-pulmonary bypass and left the operating room on VA-ECMO, with a mean duration of 179±93.6 hours (64-262 hours) postoperatively. ECMO-related complications included lower limb ischemia, which led to above the knee amputation (n=1), revisions related to bleeding due to heparin administration during ECMO support (n=4), and intracardial thrombus formation after the heparin dose was decreased (n=1).

Structural heart repair surgery and outcomes

The performed surgical procedures included: 5 isolated mitral valve replacements, 1 aortic valve replacements, 2 isolated VSD repairs, and 3 patent combined procedures (See Table 2). Mean postoperative ventilation time was 8.18±4 days, mean ICU stay was 14.5± 6.1 days, and mean hospital stay was 19.3 ± 7.5 days. Postoperative complications included re-exploration due to bleeding or tamponade in 4 patients, tracheostomy due to prolonged ventilation time, with the need for respiratory rehabilitation in 2 patients, sepsis in 3 patients and acute kidney injury that required renal replacement therapy in 3 patients (Table 2).

There were 3 cases of 30-day mortality. Two patients died with sepsis and multi-organ failure after 7 and 9 days post-surgery (a case of aortic valve replacement after TAVI and a case of mitral valve replacement and VSD closure). The third patient underwent mitral valve replacement surgery that was complicated with an emergency reopening due to tamponade, followed by a re-reopening due to a large intracardial thrombus. The patient died on the fourth postoperative day while on ECMO support. Furthermore, one patient died 2 months post tricuspid valve replacement and closure of patent foramen ovale (after emergent TEVAR) due to sepsis and multi-organ failure. Four patients were discharged home and three patients were transferred to a rehabilitation facility.

Discussion

We report here the results of emergent VA-ECMO treatment prior to structural valve repair surgery in a single tertiary medical center. Currently, most data in the literature regarding ECMO support concentrate on cardiogenic shock due to heart failure and describe its use as a bridge to transplantation, recovery, or decision. Limited data exist regarding the role of preoperative VA-ECMO in critically ill patients in order to stabilize them in preparation for major cardiac surgery. In 2018, Gammie *et al.* (6) reported on the efficacy of preoperative VA-ECMO in optimizing moribund patients with structural heart disease presenting with cardiogenic shock or end-organ dysfunction, and its ability to reduce surgical risk. Another study by Gregoric *et al* (10) compared 8 patients who received a percutaneous assist device (TandemHeart, LivaNova, Houston, TX, USA) for 7 ± 3 days prior to repair of ischemic VSD with 3 patients who required the device postoperatively. They demonstrated markedly improved hemodynamics with preoperative mechanical circulatory support as well as improved survival.

In this study we report on our experience using VA-ECMO as a support to optimize critically ill patients before they undergo surgical repair of structural heart disease associated with cardiogenic shock or advanced heart failure. While we expect this report to complement the current literature, we realise that further studies are needed in order to establish guideline recommendations for the use of preoperative VA-ECMO in patients in the acute setting arising from structural heart disease.

Advanced structural heart disease leading to cardiogenic shock or end-organ dysfunction carries significant operative risk. Several reports have been published regarding the operative mortality of VSD ranging from 19-60% depending on several aspects such as: patient's hemodynamic status, anatomical location of the rupture and surgical technique (4, 11, 12). Moreover, urgent VSD repair surgery and heart failure have been shown to be independent risk factors for mortality (13). In the patients with acute severe mitral regurgitation due to papillary muscle rupture, the operative mortality remains at a substantial 40%. Moreover, when these patients develop low cardiac output or renal failure, the chances of survival are extremely poor (5). In addition, hospital mortality for prosthetic valve thrombosis ranges from 13-40%, with heart failure as the strongest predictor for mortality (14,15).

In this group of patients, mechanical support of VA-ECMO has led to preoperative improvement in organ function and metabolism followed by physiologic parameters, including pH, creatinine, lactate, bilirubin and liver enzymes. This improvement resulted in decreased surgical mortality risk.

We believe that the role of preoperative VA-ECMO is to delay surgical intervention until after the patient is stabilized, and to perform the curative operation when the surgical risk is lower. Furthermore, an additional advantage of delaying surgery in particular cases of acute VSD, is that the time on ECMO may enable organization of the surrounding infarcted septum.

Cardiogenic shock following cardiac surgery carries a mortality rate of 50-80% (16-18). Many of our study patients share the risk factor of post-cardiotomy cardiogenic shock, such as renal failure, lactic acidosis, cardiogenic shock and heart failure. The operative and first-year survival rates for preoperative ECMO are better than those of post-cardiotomy shock patients who require salvage ECMO. This series suggests that preoperative ECMO may offer a higher survival rate in those at risk for post-cardiotomy shock.

Some may focus on endovascular treatments for these patients. However, outcomes of endovascular procedures for structural heart disease are poor (1, 19-22). Transcatheter aortic valve replacement in the setting of cardiogenic shock has high procedural (20- 30%), and 1-year (64-83%) mortality (1, 22). Transcatheter therapy for ischemic VSD has demonstrated significant procedural complications, with 1-month adverse event-free survival at 56%, and only 30% among those in cardiogenic shock (23).

There are case reports of successful aortic (24) and mitral (25) interventions following stabilization with VA-ECMO. Preoperative, short-duration VA-ECMO to physiologically optimize patients may hold promise for patients undergoing transcatheter interventions as well as conventional surgery.

This research has some limitations. There were only 11 patients which is a small sample from which to deduce strong conclusions. Moreover, this was a retrospective study without a comparative control group of patients who were not supported with ECMO preoperatively. Despite these limitations, we have shown that ECMO can be used as a bridge to heart valve or septal defect surgery in severely decompensated patients suffering from cardiogenic shock or advanced heart failure. Furthermore, by restoring end-organ function and resuscitating patients prior to high-risk cardiac surgery, ECMO could offer successful surgical correction of structural heart disease in patients considered inoperable or in a very high risk, as well as transform a salvage situation to a kind of elective one. Additional research with a larger patient cohort is needed in order to further substantiate the advantages of this preoperative procedure.

Author contributions statement

This study was supervised by L.S and A.K . who also took part of conceptualization review and editing. T.J has been part of conceptualization, data curation, investigation , writing the original draft , reviewing and editing . E.R was part of editing and reviewing . Y.K , D.V and Y.G were part of date curation**.** All authors are accountable for all aspects of the work (if applied, including full data access, integrity of the data and the accuracy of the data analysis) in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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