

Extracorporeal membrane oxygenation in adults: experience from the Middle East

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Abstract

Background: The literature reports conflicting results for survival after extracorporeal membrane oxygenator support, and survival differs in pediatric and adult patients. We present our institutional experience of adult extracorporeal membrane oxygenator support.

Methods: From January 2007 to December 2009, 19 adult patients required extracorporeal membrane oxygenator support after cardiac surgery or catheter interventions. It was provided on an emergency basis to 11 patients, urgently to 5, and electively to 3. Indications included post-cardiotomy cardiogenic shock, post-cardiotomy acute respiratory failure, emergency cardiac resuscitation, and post-percutaneous coronary intervention cardiogenic shock. The mean duration of support was 4 days (range, 1–11 days).

Results: Seven (36.84%) patients could be weaned off extracorporeal membrane oxygenator support; one (14.28%) of them survived to hospital discharge and the other 6 (85.71%) died in hospital. Twelve (63.15%) patients could not be weaned off and died while still on extracorporeal membrane oxygenator support. Overall 30-day hospital mortality was 94.73%, and survival to discharge was 5.26%.

Conclusion: Our institutional experience of extracorporeal membrane oxygenator support for cardiac indications in adult patients indicates poor survival. It significantly increased costs by delaying imminent death and prolonging stay in the intensive care unit.

Keywords

Cardiopulmonary resuscitation, extracorporeal membrane oxygenation, life support care, respiratory distress syndrome, adult, shock, cardiogenic

Introduction

The literature reports mixed survival outcomes after extracorporeal membrane oxygenator (ECMO) support, and survival differs in pediatric and adult populations.^{1,2} Thiagarajan and colleagues³ studied outcomes and predictors of hospital mortality after ECMO use for cardiopulmonary resuscitation; they found 38% survival to hospital discharge. In a review and quantitative analysis, Chalwin and colleagues⁴ stated that the role of ECMO has not been formally validated for patients with adult respiratory distress syndrome. Our institution, being a tertiary care center, deals with a large cohort of adult and pediatric patients with complex cardiorespiratory problems. ECMO support is readily available at our institute, being more extensively utilized in pediatric patients than the adult group. Results in the pediatric group

are comparable with those in the literature, but the data of adult patients has not been previously subjected to formal analysis. After a retrospective review of patient records from January 2007 to December 2009, we present our institutional results of ECMO use in adult patients.

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Patients and methods

The study was conducted in accordance with the ethical principles contained in the Declaration of Helsinki (2000), the ICH Harmonized Tripartite Good Clinical Practice Guidelines, the policies and guidelines of the Research Advisory Council of the institution, and the laws of the country. A waiver of written informed consent was obtained from the Research Advisory Council of the hospital.

Between January 2007 and December 2009, 19 adults aged 18 years and older, who required ECMO support after open heart surgery or catheter interventions were included in the study. There were 9 (47.4%) men and 10 (52.6%) women. The mean age was 55.6 ± 16.2 years (range, 21–79 years). Body surface area ranged between 1.3 and 2 m^2 (mean, 1.7 m^2). Mean EuroSCORE was calculated as 11.3 (range, 4–26), and mean left ventricular ejection fraction was 40% (range, 15%–55%). Four patients underwent redo sternotomies. The patient data were identified and obtained through the institutional computerized database. Collected data were entered into a statistical analysis database designed for this particular retrospective study. Demographic and clinical data of the patients are presented in Table 1. The patients were divided in 4 groups based on the primary indication for ECMO support: group 1 comprised 8 patients who had post-cardiotomy cardiogenic shock, group 2 was 8 patients who had ECMO during emergency cardiac resuscitation, group 3 was 2 patients who had post-cardiotomy acute respiratory failure, and group 4 was one patient who suffered cardiogenic shock after a percutaneous coronary intervention (Table 2). Eleven patients had ECMO support in emergency situations (cardiac or respiratory arrest in 8, failed weaning from cardiopulmonary bypass in 2, impending cardiac arrest in 1), 5 required urgent support (poor hemodynamics in 2,

Table 1. Demographics and clinical data of 19 patients who had extracorporeal membrane oxygenator support.

Variable	No. of patients
Male	9 (47.4%)
Female	10 (52.6%)
Mean age (years) [range]	55.6 [21–79]
Weight (kg) [range]	67.7 [42–94]
Height (cm) [range]	157.7 [138–180]
BSA (m^2) [range]	1.7 [1.3–2.0]
EuroSCORE [range]	11.3 [4–26]
LVEF [range]	40.0% [15%–55%]
ACT (s) [range]	165.8 [120–200]

ACT: activated clotting time; BSA: body surface area; LVEF: left ventricular ejection fraction.

poor hemodynamics and acute lung injury in 1, acute lung injury in 1, cardiogenic shock in 1), and 3 were supported electively (poor hemodynamics in 2, acute lung injury in 1).

Our hospital is a regional tertiary care center with an annual workload of approximately 1500 cases comprising the whole range of adult (40%) and congenital (60%) cardiac surgical procedures. ECMO support is utilized much more extensively in the pediatric group than in adults. We used a Medtronic Bio-Medicus console incorporating a Bio-Medicus BPX-80 centrifugal pump, a Medos 7000 LT heparin-coated oxygenator, and Medos heparin-coated circuit tubing. Standard arterial and venous wire-reinforced cannulae were used for peripheral or central cannulation. The circuit was primed with an isotonic saline solution resembling normal extracellular fluid, including $4\text{--}5 \text{ mEq}\cdot\text{L}^{-1}$ of potassium. Access was decided according to the individual patient's situation. In this study population, 11 patients were supported with central venoarterial access, whereas 8 had peripheral venoarterial ECMO support. Target blood flow ($3\text{--}5 \text{ L}\cdot\text{min}^{-1}$) was gradually achieved and maintained according to the body weight and body surface area. To avoid limb ischemia, distal femoral artery perfusion was achieved with a shunt created from the side-arm of the femoral arterial cannula.

Anticoagulation was maintained with heparin infusion to keep activated clotting time at 180–210 s.

Table 2. Indications for ECMO support and surgical procedures in 19 patients.

Variable	No. of patients	Outcome
Indication		
Post-cardiotomy cardiogenic shock	8 (42.1%)	Died
Post-cardiotomy respiratory failure	2 (10.5%)	1 survived
Emergency cardiac resuscitation	8 (42.1%)	Died
Post PCI cardiogenic shock	1 (5.3%)	Died
Status		
Emergency	11 (57.9%)	Died
Urgent	5 (26.3%)	Died
Elective	3 (15.8%)	1 survived
Procedure		
Valve	8 (42.1%)	Died
Valve + CABG	3 (15.8%)	Died
CABG	3 (15.8%)	Died
Post PCI	2 (10.5%)	Died
Heart transplant	1 (15.3%)	Died
Adult congenital	1 (15.3%)	Died
Pulmonary thromboendarterectomy	1 (15.3%)	Survived

CABG: coronary artery bypass grafting; PCI: percutaneous coronary intervention; EMCO: extracorporeal membrane oxygenator.

One patient with heparin-induced thrombocytopenia received lepirudin, and adequate anticoagulation was maintained by keeping activated partial thromboplastin time at 1.5- to 2-times the normal range. The platelet count was maintained above 100, hemoglobin above 80 mg·dL⁻¹, and oxygen saturation >95%. Medical bleeding was treated with tranexamic acid infusion after target activated clotting time, activated partial thromboplastin time, and platelet counts were achieved and surgical bleeding was ruled out. Vasopressors were titrated according to the lowest possible doses allowing adequate perfusion pressure. Urine output and mixed venous saturation were used to monitor perfusion pressure. Mechanical ventilation was maintained with a low rate, low fraction of inspired O₂, and a long inspiratory time. Positive end-expiratory pressure was carefully manipulated between 5 and 15 cm H₂O so that it did not compromise diastolic filling of the heart. Fluids were carefully administered to keep central venous pressure between 5 and 10 cm H₂O. Diuretics and hemofiltration were used to manage fluid status. Full caloric and protein requirements were provided via the enteral route if possible, and total parenteral nutrition was used when indicated. Antibiotic therapy was initiated if there was a break in sterility during the procedure, or for documented infection or unexplained persistent fever.

Data were analyzed using SAS software package version 9.2 (SAS, Inc., Cary, NC, USA). Descriptive statistics (mean, standard deviation, and percentage) are reported for all variables. All continuous variables were compared by using Student's *t* test, and categorical variables were compared by the chi-squared test. The level of significance was set at $p < 0.05$; however, due to small numbers, all p values need to be interpreted with caution.

Results

The mean duration of ECMO support was 4 days (range, 1–11 days). Seven patients (36.8%) were

weaned off ECMO support; one (14.3%) of them survived, and 6 (85.7%) died later due to multisystem organ failure. There was a significant association between weaning and outcome (Fisher's exact test, $p = 0.00001$). Twelve (63.2%) patients could not be weaned off and died while on ECMO support. Mortality was 100% in the emergency and the urgent groups and 33.33% in the elective group (Figure 1). Overall 30-day hospital mortality was 94.73%, and survival to discharge was 5.26%. Using Student's *t* test, there was no significant difference between the EuroSCORE ($p = 0.5164$) and left ventricular ejection fraction ($p = 0.5520$) of the patients weaned off ECMO and those who could not be weaned off. Similarly, the difference in age ($p = 0.1467$) and EuroSCORE ($p = 0.5164$) between those who survived and those who died did not reach statistical significance. Figures 1, 2, and 3 depict outcome according to urgency status, groups, and individual indications, respectively.

All 8 patients who were supported with ECMO for post-cardiotomy cardiogenic shock died; 5 had valve surgery (1 mitral valve replacement, 1 tricuspid valve replacement, 2 aortic root replacements, 1 redo aortic valve replacement), 2 had mitral valve replacement and coronary artery bypass grafting, and one underwent heart transplantation. Three of these patients were supported with ECMO on an urgent basis, 2 had elective support, and 3 were emergency cases. Mean predicted mortality by logistic EuroSCORE was 13.5% (range, 7%–26%) on admission, and mean duration of ECMO support was 4.37 days (range, 1–7 days). Six patients died on ECMO, 5 due to multisystem organ failure and 1 due to severe heart failure. Two patients were weaned off but died later, one due to multisystem organ failure and sepsis and the other due to severe heart failure.

Eight patients were supported with ECMO for emergency resuscitation after cardiac arrest or impending arrest. Mean duration of ECMO support was 3.87 days and mean logistic EuroSCORE was 10.37%.

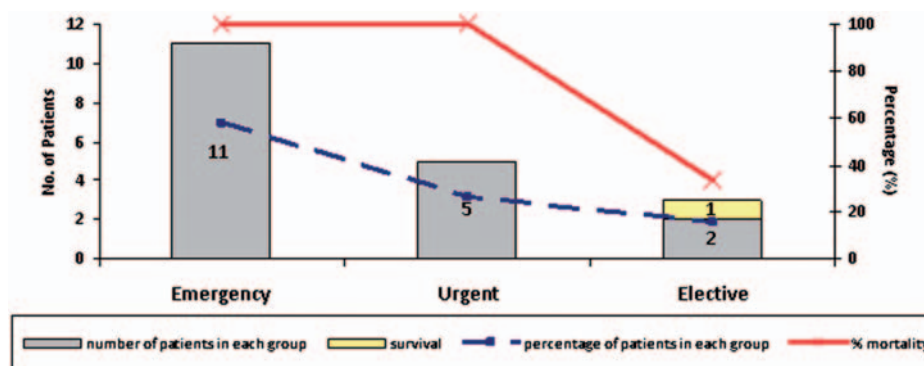


Figure 1. Survival outcome according to urgency status.

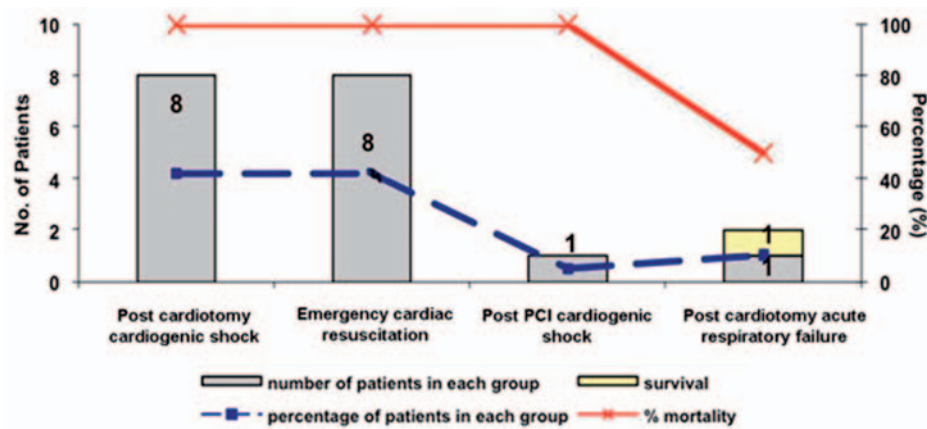


Figure 2. Survival outcome according to groups.

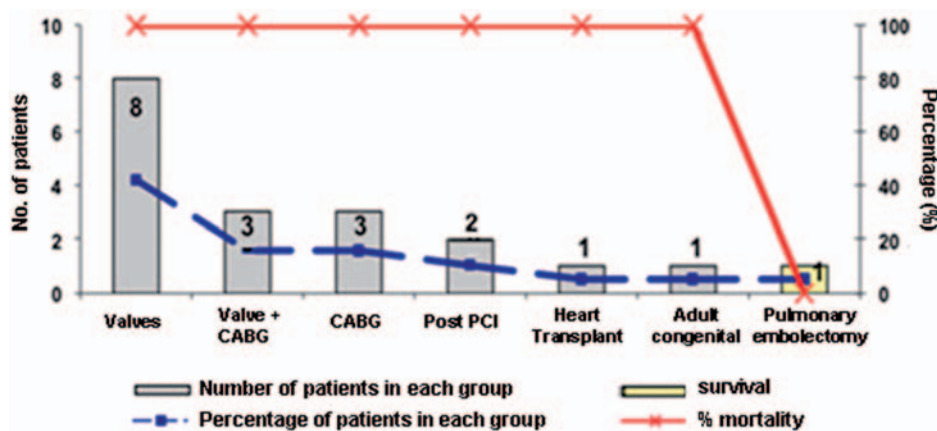


Figure 3. Survival outcome according to individual indications.

Three had undergone valve surgery (1 aortic root replacement, 1 mitral and tricuspid valve replacement, 1 redo triple-valve replacement), 2 had coronary artery bypass grafting for acute coronary syndrome, 1 had aortic root replacement and coronary artery bypass grafting, 1 had a redo Fontan procedure for adult congenital heart disease, and 1 developed severe refractory cardiogenic shock during a percutaneous coronary intervention and was supported for emergency cardiac resuscitation. All patients died in this group, due to multisystem organ failure in 2, sepsis and multisystem organ failure in 3, and brain death in 3. Four of these patients died while still on ECMO.

Two patients were supported with ECMO for post-cardiotomy acute respiratory failure. The first was admitted with acute coronary syndrome and chronic obstructive pulmonary disease and underwent coronary artery bypass grafting. The second patient underwent pulmonary thromboendarterectomy for chronic pulmonary embolism. Both developed acute lung injury postoperatively. The first patient was supported on an urgent basis and the other was supported electively for progressive deterioration in arterial blood gases and

right ventricular impairment. Mean duration of ECMO support was 7 days (range, 3–11 days) and mean preoperative logistic EuroSCORE was 6.5% (range, 4%–9%). The first patient died on ECMO due to multisystem organ failure. The second patient could be weaned off ECMO, survived until discharge, and is still alive.

One patient developed cardiogenic shock after a percutaneous coronary intervention for acute coronary syndrome. He developed stent thrombosis, underwent multiple angioplasties, and drifted into cardiogenic shock with multisystem dysfunction despite intraaortic balloon pump and inotropic support. He was supported urgently with ECMO for 3 days. His predicted mortality by logistic EuroSCORE was 10%. He died on ECMO due to multisystem organ failure.

Discussion

Post-cardiotomy severe myocardial dysfunction requiring mechanical support beyond intraaortic balloon pumping constitutes an indication for ECMO for obvious reasons. It provides combined cardiopulmonary

support which is vital for a failing heart after cardiomy. Circulation can be urgently restored during resuscitation with ECMO, and it is relatively cheaper and more readily available than other devices.⁵ Reported outcomes of ECMO support are variable. Extracorporeal Life Support Organization data yielded a 37% survival rate in patients receiving ECMO for postcardiotomy shock.⁶ Fiser and colleagues⁷ reported 16% survival, whereas Kawahito and colleagues,⁸ Smith and colleagues,⁹ and Wang and colleagues¹ reported 39%, 41%, and 52% long-term survival rates, respectively. Recently, Hsu and colleagues¹¹ reported 67% hospital mortality and 29% survival at 1-year.

The pediatric group in our institution has 38% survival to discharge after ECMO use;¹² unfortunately, this could not be achieved in the adult population. Our weaning rate was 36.84%, and only one (14.28%) patient was weaned off EMCO support and survived. Other studies have reported weaning rates of 40%–100% and survival rates of 25%–80%.^{13–15} We observed 100% mortality in the emergency and urgent groups. Elective support had 33.33% mortality. We presume, from our clinical experience, that prolonged and persistent suboptimal hemodynamic status during the course of events leading to heart failure before ECMO is initiated, triggers end-organ damage. It is believed that in post-cardiotomy patients, ECMO support is initiated after severe injury has already occurred, which may contribute to the poor survival outcome in this group.¹⁶ Chung and colleagues¹⁷ recently reported better survival with pre-intervention initiation of ECMO support.

The dominant cause of mortality in our series was multisystem organ failure, as reported by other studies.^{18,19,20} Massive transfusion of blood and blood products for excessive bleeding, particularly after central ECMO support for post-cardiotomy patients with an open chest, is associated with transfusion complications. Ischemia-reperfusion injury and an exaggerated inflammatory response due to neutrophil, platelet, and cytokine activation is common during extracorporeal circulation.^{16,21} Sepsis, although a late complication and not always a limiting factor for weaning, is still a strong predictor of mortality in patients on ECMO.²¹ Neurologic complications, whether hemorrhagic or embolic, are not infrequent during ECMO.¹³ Compounding effects of all these complications may result in the development of multisystem organ failure and contribute to the final outcome of ECMO support. We had 50% mortality due to multisystem organ failure and 22.22% due to sepsis with multisystem organ failure. Brain death occurred in 16.66% patients and persistent severe heart failure was the cause of mortality in 11.11%. All these observations, including ours, suggest that an aggressive approach towards early initiation of ECMO for persistent heart failure may

prevent multisystem organ failure and thus improve survival results of ECMO support. However, the cause and consequence relationship between multisystem organ failure, cardiac collapse, and ECMO is still debated.¹³ Several studies reported the use of intraaortic balloon pumping as a predictor of better survival, and proposed that a balloon pump should be routinely used in patients supported by ECMO.^{14,16,22} However, 2 recently published studies did not find a significant difference in survival in patients with or without a balloon pump during ECMO support.^{17,23}

Unfortunately, our clinical experience with adult ECMO for cardiac indications is not consistent with the higher success rates published in the literature. Despite much scrutiny, we are unable to explain this. Possible explanations include inappropriate case selection, lack of experience of adult ECMO support, and a learning curve. We believe that short-term ECMO is the “bailout” alternative when mechanical support beyond balloon pumping is required for post-cardiotomy patients. In general, for reasons not clearly known, the theoretical benefits of cardiopulmonary support provided by ECMO are not translated into actual clinical practice, and the variable reported outcomes of adult ECMO support this argument.^{6–11} However, patients do not die as a direct consequence of ECMO support, rather complications such as renal failure, hemorrhage, infections, adult respiratory distress syndrome, ischemia, pancreatitis, and cerebral complications constitute grounds for high mortality. Initiation of ECMO support before end-organ damage ensues, and prevention of complications, are crucial for better survival. Unfortunately, not much progress has been made in the past several decades to overcome these issues. From our own experience, we presume that for better survival and cost-effectiveness of ECMO support, particularly in post-cardiotomy adult patients, a radical change in clinical practice requires a more selective attitude for initiation of ECMO support, preemptive identification and management of complications, and timely initiation of support.

On the other hand, in the current era, much user friendly implantable ventricular assist devices should be considered as an alternative option if only cardiac support is required. These devices are implanted centrally and chest can be closed readily. This minimizes the threat of surgical bleeding and infection as compared to open chest for central ECMO. Further more the groin vessels are spared that eliminates the danger of limb ischemia which, otherwise, is a constant threat in peripheral ECMO support. If respiratory failure develops at any stage in the post operative period in these patients while on ventricular assist device, it can be addressed by concomitant use of interventional lung assist such as Nova Lung²⁴ which can be implanted percutaneously at the femoral vessels.

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Conflict of interest statement

None declared.

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