Applied Cardiopulmonary Pathophysiology 15: 272-277, 2011

Extra-corporeal membrane oxygenation support in cardiac transplantation

Hartmuth B. Bittner

Division of Thoracic and Cardiovascular Surgery, Heart Center Leipzig of the University of Leipzig, Germany

Abstract

Objective: Extra-corporeal membrane oxygenation (ECMO) provides temporary cardiopulmonary-circulatory support with minimal surgical trauma in patients with therapy refractory cardiogenic shock and early graft failure following thoracic organ transplantation. The frequent use of echocardiography allows objectively the assessment of the biventricular myocardium and cardiac recovery potential, which may lead to ECMO weaning and discontinuation of circulatory support in the majority of patients with significantly improved myocardial function.
Methods and results: Between January 1997 and December 2009, 221 patients underwent orthotopic heart transplantation at our institution. Twenty-three patients (10 %) were treated for low cardiac output with ECMO support with a mean duration of 4 days (4 hours to 21 days). Peripheral access procedures for ECMO support were performed in all patients. Aorto-right atrial cannulation was always avoided, which would prevent sternal closure. Intra-aortic balloon counterpulsation was used in the majority of patients (18 of 23 patients). The early and one-year mortality rate of the ECMO supported patients were 61% and 74%, respectively. Primary graft failure (PGF) was a major indication for early ECMO support in 14 patients. Other indications were right heart failure and sepsis. Among the 14 patients supported with ECMO for PGF, 9 patients were weaned from the assisting device. The one-year survival rate for ECMO-supported PGF patients was 43%.
Conclusions: ECMO support is a reliable therapeutic option in severe PGF after cardiac transplantation. Although the 1-year survival is reduced, the use of ECMO is a valuable bridge to recovery strategy in heart transplant patients with graft failure related low cardiac output. Furthermore, our experience suggests that ECMO use is a feasible and cost-effective mechanical support technique to overcome severe cardiac allograft dysfunction.

Key words: ECMO, heart transplantation, thoracic transplantation, primary graft failure, cardiac surgery, weaning

Abbreviations

ECMO	Extra-corporeal membrane oxygenation
PGF	Primary graft failure
TEE	Transesophageal echocardiography

Introduction

The early post-operative care of the cardiac transplant recipient remains challenging, with approximately 12-15% of recipients not surviving the initial months following transplan-

tation according to the recent survival reports of the International Society for Heart and Lung Transplantation. The leading cause of early mortality after heart transplantation is primary graft failure (PGF). Since the pathophysiology of PGF is not always fully understood, its treatment and support remains still challenging today, despite the administration of the latest inotropic agents and phosphodiesterase inhibitors, liberal use of intra-aortic balloon pulsation and afterload lowering measurements, right ventricular support through NO and prostaglandine derivates lowering pulmonary resistance, and modified orthotopic transplantation techniques, such as bi-caval cardiac transplantation. Emergency re-transplantation in the setting of PGF carries a very limited role due to an unacceptable high operative mortality [1,2] and the unavailability of donor organs, and therefore has been abandoned.

Extracorporeal membrane oxygenation (ECMO) has been an established treatment option in adult patients with refractory cardiogenic shock, providing extended but temporary cardiopulmonary and circulatory support. Recent studies report improved in-hospital survival rates with the use of ECMO in the adult setting ranging from 20% to 50% and mortality rates of 50% to 70% [3,4].

Based on the experience of 517 consecutive adult patients treated with ECMO in our institution [4] tremendous experience was gained attenuating the well documented high incidence of bleeding complications and peripheral access related limb ischemia. Improvement of our ECMO strategy to reduce system-related complications allowed us to extend the duration and indication of ECMO therapy to heart transplant patients suffering from severe graft dysfunction as a bridge to recovery or more definitive support strategies.

Materials and methods

Extracorporeal circulatory support devices

The ECMO circuits consist of the Medtronic Carmeda heparin-bonded tubing (Medtronic Cardiopulmonary, Anaheim, CA) and a centrifugal blood pump (Biomedicus Biopump, Medtronic, Minneapolis, MN) or the Levitronix® (Centrimag®, Pharos LLC, Waltham, MA, USA) blood pumping system for prolonged support, which propells blood through a hollow-fiber membrane oxygenator (Affinity NT™, Medtronic, Anaheim, USA or Hilite 7000 LT™, or Medos Medizintechnik AG, Stolberg, Germany, and recently the Quadrox Bioline Jostra-Maquet Medizintechnik, Hirrlingen, Germany) with integrated heat-exchanger. An oxygen/air blender (Sechrist Industries, Anaheim, CA, USA) is used to ventilate the membrane oxygenator. Blood flows are monitored by a Doppler flow probe placed on the arterial side of the circuit. ECMO flows were 2.0 to 2.4 l/min/m^2. In order to prevent bleeding complications in heparinized patients following cardiopulmonary bypass for heart transplantation and ECMO support for the failing graft, heparin is completely antagonized through protamin. Aprotinine was routinely administered until the year 2006 using a modified Hammersmith protocol. More recently it was replaced by tranexam acid. Additional coagulation factors, platelets or coagulant agents were specifically substituted based on laboratory coagulation analysis or thrombelastography. Anticoagulation with heparin is initiated after chest drainage decreases to less than 50 mL/h. Heparin infusion is titrated to maintain an activated clotting time (ACT) between 160 to 180 seconds. The target partial thromboplastin time is between 50 and 60 seconds.

Cannulation techniques and surgical interventions

Peripheral access procedures for ECMO support are performed in all patients. Aorto-right atrial cannulation is always avoided, which would prevent sternal closure. The surgical access procedure consists of a cut down of the femoral artery and vein and of the right axillary artery. Monofilament 5-0 purse string sutures are applied to the anterior wall of the axillary or femoral artery and vein. The Seldinger cannulation technique is used to introduce the heparin-bonded venous (usually 22 Fr.) and arterial cannulas (18 Fr.). No left atrial or ventricular drainage is used. Transesophageal echocardiography (TEE) is applied to control the positioning of guide-wire and venous cannula within the right atrium, and in the event of intra-aortic balloon insertion, the tip of the balloon close to the origin of the left subclavian artery. Overall, the preferred access sites for ECMO circuit connection are the right axillary artery for arterial and the femoral vein for venous cannulation. This leads to optimal central and cerebral oxygenation and perfusion.

In order to avoid limb ischemia and access site complications with peripheral cannulation, we optimized the distal limb perfusion by using an 8-mm Dacron T-graft (end-to-side anastomosis to the femoral or subclavian artery), which is passed through a separate skin stab wound. The arterial cannula is passed through the Dacron graft until the tip of the cannula reaches the ananstomosis and points to the proximal site of the artery. This ascertains both central arterial blood flow and distal limb perfusion and lowers the risk of limb hyperperfusion. If hyperperfusion of the distal limb occurs a temporary snare applied distal to the anastomosis is usually flow reducing and protective. In the case of already existing femoral vessel cannulation from cardiopulmonary bypass support for heart transplantation surgery (our routine access site for redo-cardiac surgery) we connect these cannulas with the ECMO circuit. Controlled distal limb perfusion is reassured through a small 12 G -14 G angiocath or pediatric cardiac aortic cannula inserted distally through a separate purse string suture and connected to the side port of the proximal arterial cannula.

Right ventricular failure

Progressive right ventricular dysfunction or predominantly right ventricular failure is treated gradually by inotropic support, phosphodiesterase inhibitors, NO, prostaglandine E1, IABP, and continuous venous-venous hemofiltration. If these measurements fail to recover right ventricular function, the Levitronix® Centrimag® blood pumping system (Pharos LLC, Waltham, MA, USA) is used for prolonged but temporary right ventricular support. A Dacron prothesis is sutured end-to-side to the main pulmonary artery, then passed retrosternally through the anterior mediastinum, and brought out subxyphoidally next to a chest-tube drainage site. The cannula of the blood pump circuit is secured to the Dacron graft and venous drainage to the blood pump is performed through the already described femoral vein cannulation.

Of note, in all the described cannulation procedures, central access is avoided allowing chest closure in an immunosuppressed patient in all situations. This cannulation technique allows decannulation at the bedside in the intensive care unit.

Management strategy

Pump flows are chosen to supply adequate systemic circulatory support (2.0 to 2.5 L · min^{-1} m^{-2}). Pulsatile pulmonary artery flow is maintained by means of right ventricular filling with intravenous fluid and blood products. A continuous cardiac output pulmonary artery catheter is used to assess pulmonary blood flow. Inotropic support is reduced or withdrawn to decrease myocardial oxygen demand and facilitate myocardial recovery. Norepinephrine is infused to maintain a

mean systemic arterial pressure of more than 70 to 75 mm Hg. To oxygenate any blood delivered to the lungs by the patient's heart and to minimize atelectasis and lung injury, low tidal volume (5 to 6 mL/kg tidal breaths) mechanical ventilation with positive end-expiratory pressure at 8 to 10 cm H_2O is applied.

Weaning protocol

Cardiopulmonary recovery was assessed daily by hemodynamic, clinical and echocardiographic measurements to define the time of weaning. Routinely, full ECMO flow was instituted for 48-72 hours before weaning process was started. If a pulsatile arterial waveform is maintained for at least 24 h and the echocardiographic evaluation demonstrated systolic heart function recovery and pulmonary blood oxygenation is not compromised, a rigid ECMO-weaning protocol is applied. Weaning was cautiously begun only under stable hemodynamic and metabolic conditions starting from full flow to approximately 1 l/min during a 36-48 hour process observing intrinsic cardiac output, metabolic status, venous saturation and end organ perfusion allowing medical adjustment when necessary. When signs of malperfusion occurred during ECMO weaning the flow was increased again to full flow allowing prolonged ECMO support. During the weaning all patients received at least one daily TEE control. This includes to progressively reducing the pump flow to <1 l min^{-1} (respecting the minimum rotational speed of 1500 rpm to prevent retrograde flow) by gradually decreasing the flow every 12 hours by 0.5 l min^{-1}. Inotropic support is routinely used during the weaning procedure. The ECMO is usually removed on the ICU since the sternum is always closed.

Results

Between January 1997 and December 2009, 223 patients underwent orthotopic heart transplantation at our institution. Twenty-three patients (10%) were treated with ECMO support for therapy-resistant low cardiac output and primary graft failure. Peripheral access procedures for ECMO support were performed in all patients (right axillary artery cannulation: 13 patients; femoral artery cannulation: 10 patients). Aorto-right atrial cannulation was always avoided. Primary graft failure (PGF) was the major indication for ECMO support: 14 patients. Other indications of ECMO support were right heart failure (4 patients) and sepsis (5 patients, heart transplantation for infected assist devices). Initiation of ECMO support ranged from intra-operatively (2 patients) to 11 days post-operatively (mean 2.2 days). The mean duration of ECMO support was 4 days (12 hours to 21 days). Intra-aortic balloon counterpulsation was used in the majority of patients (18 of 23). Continuous venovenous hemofiltration was initiated early to regulate intravascular volume and overall fluid balance and to enable the rapid administration of blood and blood products without the induction of volume overload. To decrease right ventricular afterload, inhaled nitric oxide was used in 6 patients with predominantly right ventricular dysfunction. One patient was bridged to a chronic pulsatile right ventricular assist system.

The in-hospital and one year-mortality rates of the ECMO supported patients were 61% and 74%, respectively. Right heart failure associated with low cardiac output and sepsis were major risk factors for death: all 9 patients. Use of ECMO support for PGF in 14 patients showed improved outcome: 9 of 14 patients were weaned successfully. The one-year survival rate for ECMO-supported PGF patients was 43%. Implementation of ECMO support in PGF patients occurred early (< 12 hours post-operatively).

Discussion

Temporary ECMO circulatory support is required in patients following cardiac transplan-

tation for primary graft failure with severe hemodynamic instability. PGF is the leading cause of early mortality after heart transplantation. Pre-transplant recipient and donor organ characteristics are associated with the onset of PGF: increased pulmonary vascular resistances, preservation and reperfusion injury or even intrinsic organ donor dysfunction. The following risk factors have been identified: ischemic time donor age and pretransplant VAD therapy [5-8].

In these patients the implantation of an extracorporeal membrane oxygenation device is an easily applicable and widely accepted option of temporary mechanical circulatory support allowing cardiac and pulmonary recovery or bridging until further therapeutic alternatives are carefully considered [3-5]. In heart transplant patients suffering of PGF, the successful ECMO weaning rate ranges from 68% to 82% and corresponds to a hospital mortality rate of 50%. [9,10]. In our transplant center the one-year survival rate for ECMO-supported PGF patients was 43% when the decision was made early to use ECMO support as a bridge to recovery. Delayed consideration for ECMO support in heart transplant patients (> 24 hours) or other than PGF indications led to near 100% unfavorable outcome. The perioperative decision for ECMO support in PGF remains challenging and is poorly based on scientific data but also on individual considerations, because ECMO support is associated with a high morbidity that includes bleeding and ischemic or thromboembolic events and end organ failures. Transplant surgeons have to carefully balance the high perioperative morbidity, man power and resource utilization in ECMO treatment against the probability of survival.

ECMO is one reasonable treatment option for temporary mechanical circulatory support in PCS patients and was preferred in our institution over other assist devices because of its versatility. ECMO allows rapid restoration of circulation during primary cardiac surgery or active resuscitation, fits to almost all patients and clinical scenarios, is cost-saving, offers varying cannulation options and covers biventricular and lung function. In these patients ECMO allows to bridge patients for further evaluation and decision making and to judge neurological status. Despite the administration of antifibrinolytic agents, selective coagulation factors and blood product transfusions postoperative bleeding was one of the major problems in postoperative ECMO care. Reasons for excessive bleeding in these patients included the preceding surgical trauma, thrombocytopenia, activation of leucocytes as well as the anticoagulation treatment and led to rethoracotomy in one-third of the patients. Other major complications as limb ischemia or mediastinitis, and sternotomy wound healing problems were rarely observed since peripheral access procedures with reassurance of distal limb perfusion and sternotomy closures were performed in all ECMO cases. In particular, the peripheral access preference for ECMO cannulation and connection allowed to close the chest and attenuated the care of the patient with subsequent weaning, discontinuation, and ECMO de-cannulation in the intensive care unit. Complications are reduced by minimizing the duration of mechanical support, meticulously maintaining anti-coagulation parameters and blood cell counts, and closely surveying the cannula, oxygenator and circuit to prevent thrombus formation and bleeding. The frequent use of echocardiography allows objectively the assessment of the biventricular myocardium and its recovery potential, which may lead to ECMO weaning and discontinuation of circulatory support in patients with significantly improved cardiac function.

Conclusions

Based on our results implementation of ECMO should be considered early in the face of cardiac allograft pump failure. If decision for ECMO is made it is reasonable not to wait until secondary organ damage, resuscitation or profound metabolic acidosis occurs. EC-

MO support is a reliable therapeutic option in severe PGF after cardiac transplantation. Although the 1-year survival is reduced, the use of ECMO is a valuable bridge to recovery strategy in heart transplant patients with graft failure related low cardiac output. Long-term outcome of hospital survivors is comparably good. ECMO use is a feasible and cost-effective mechanical support technique to overcome severe cardiac allograft dysfunction. However, because of the high morbidity ECMO indication has to be considered on an individual risk profile and the underlying cause of graft dysfunction. Because of the high device related morbidity further efforts have to be made to develop less traumatic devices allowing fast and easy applicable devices for temporary circulatory support.

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Correspondence address
Hartmuth B. Bittner, MD, PhD
Division of Thoracic and Cardiovascular Surgery
Heart Center Leipzig
University of Leipzig
Struempell Str. 39
04289 Leipzig
hartmuth.bittner@medizin.uni-leipzig.de