Artificial
Organs

Extracorporeal Membrane Oxygenation Support in Refractory Cardiogenic Shock: Treatment Strategies and Analysis of Risk Factors

*Antonio Loforte, *Giuseppe Marinelli, †Francesco Musumeci, *Gianluca Folesani, *Emanuele Pilato, *Sofia Martin Suarez, †Andrea Montalto, †Paola Lilla Della Monica, *Francesco Grigioni, *Guido Frascaroli, †Antonio Menichetti, *Roberto Di Bartolomeo, and *Giorgio Arpesella

*Department of Cardiovascular Surgery and Transplantation, S. Orsola-Malpighi Hospital, Bologna University, Bologna; and †Department of Cardiac Surgery and Transplantation, S. Camillo Hospital, Rome, Italy

Abstract: Two centrifugal pumps, the RotaFlow (Maquet, Jostra Medizintechnik AG, Hirrlingen, Germany) and Levitronix CentriMag (Levitronix LCC, Waltham, MA, USA), used in central or peripheral veno-arterial extracorporeal membrane oxygenation (ECMO) support systems have been investigated, in terms of double-center experience, as treatment for patients with refractory cardiogenic shock (CS). Between January 2006 and December 2012, 228 consecutive adult patients were supported on RotaFlow ($n = 213$) or CentriMag ($n = 15$) ECMO, at our institutions (155 men; age 58.3 ± 10.5 years, range: 19–84 years). Indications for support were: failure to wean from cardiopulmonary bypass in the setting of postcardiotomy ($n = 118$) and primary donor graft failure ($n = 37$); postacute myocardial infarction CS ($n = 27$); acute myocarditis ($n = 6$); and CS on chronic heart failure ($n = 40$). A peripheral ECMO setting was established in 126 (55.2%) patients while it was established centrally in 102 (44.7%). Overall mean support time was 10.9 ± 9.7 days (range: 1–43 days). Eighty-four (36.8%) patients died on ECMO. Overall success rate, in terms of survival on ECMO ($n = 144$), weaning from mechanical support ($n = 107$; 46.9%), bridge to mid-long-term ventricular assist device ($n = 6$; 2.6%), and bridge to heart transplantation ($n = 31$; 13.5%), was 63.1%. One hundred twenty-two (53.5%) patients were successfully discharged. Stepwise logistic regression identified blood lactate level and MB isoenzyme of creatine kinase (CK-MB) relative index at 72 h after ECMO initiation, and number of packed red blood cells (PRBCs) transfused on ECMO as significant predictors of mortality on ECMO ($P = 0.010$, odds ratio [OR] = 2.94; 95% confidence interval [CI] = 1.10–3.14; $P = 0.010$, OR = 2.82, 95% CI = 1.014–3.721; and $P = 0.011$, OR = 2.69; 95% CI = 1.06–4.16, respectively). Central ECMO population had significantly higher rate of continuous veno-venous hemofiltration need and bleeding requiring surgery events compared with the peripheral ECMO setting population. No significant differences were seen by comparing the RotaFlow and CentriMag populations in terms of device performance. At follow-up, persistent heart failure with left ventricle ejection fraction (LVEF) ≤40% was a risk factor after hospital discharge. Patients with a poor hemodynamic status may benefit from rapid central or peripheral insertion of ECMO. The blood lactate level, CK-MB relative index, and PRBCs transfused should be strictly monitored during ECMO support. In addition, early ventricular assist device placement or urgent listing for heart transplant should be considered in patients with persistent impaired LVEF after ECMO. **Key Words:** Heart failure—Mechanical circulatory assistance—Heart transplantation—Extracorporeal membrane oxygenation—Cardiogenic shock—Risks.

Since the early 1970s, extracorporeal membrane oxygenation (ECMO) support has been used in more than 200 centers worldwide in more than 40 000 severely ill patients with refractory cardiogenic shock (CS) or respiratory failure, as reported by the Extracorporeal Life Support Organization (ELSO) registry (1).

doi:10.1111/aor.12317

Received November 2013; revised February 2014.

Address correspondence and reprint requests to Dr. Antonio Loforte, Department of Cardiovascular Surgery and Transplantation, S. Orsola-Malpighi Hospital, Bologna University, Via Massarenti n.9, Bologna 40138, Italy. E-mail: antonioloforte@yahoo.it

ECMO offers several advantages: (i) it provides cardiac and pulmonary support; (ii) the eventual peripheral insertion of cannulas into vessels is simple and rapid, thus avoiding a sternotomy incision; (iii) it can be performed during cardiopulmonary resuscitation (CPR); (iv) it provides time to assess potential heart transplantation (Htx) or long-term ventricular assist device (VAD) candidates; and (v) it is less costly than other forms of mechanical circulatory support (MCS).

We report our double-center experience in using the RotaFlow (Maquet, Jostra Medizintechnik AG, Hirrlingen, Germany) and Levitronix CentriMag (Levitronix LCC, Waltham, MA, USA) centrifugal pumps in the setting of central or peripheral veno-arterial ECMO support systems as treatment for patients with primary or postcardiotomy refractory CS.

PATIENTS AND MATERIALS

ECMO System

In 2006, the ECMO circuit consisted of a polymethylpentene (PMP) oxygenator, Quadrox D (Maquet, Jostra Medizintechnik AG) and a centrifugal pump, RotaFlow (Maquet, Jostra Medizintechnik AG) ($n = 16$).

Since 2007, the more recent Permanent Life Support (PLS; Maquet, Jostra Medizintechnik AG) ECMO circuit was used and combined, traditionally, with the RotaFlow pump ($n = 197$) (2–4) or adapted for the Levitronix CentriMag ($n = 15$) (5–8). A heater-cooler (Stockert, Munchen, Germany) was added to the veno-arterial ECMO circuit.

Peripheral veno-arterial cannulation was performed in 126 (55.2%) patients using an arterial return cannula (DLP Biomedicus 15–19 Fr [mostly 17 Fr], Medtronic, Inc., Minneapolis, MN, USA), which was inserted into the femoral artery and a venous drainage cannula (DLP Biomedicus 17–23 Fr, Medtronic, Inc.), which was inserted into the femoral vein (4). Both insertions were performed using the Seldinger technique after anterior vessel wall exposure and secured with pledgeted, reinforced purse-string prolene sutures. In 14 patients belonging to the postcardiotomy cohort, a 19-Fr venous cannula into the right jugular vein (DLP Biomedicus, Medtronic, Inc.), was inserted primarily during the cardiopulmonary bypass (CPB) installation due to reoperation procedures.

The cannulation was performed centrally in 102 (44.7%) patients, using the right atrium through its lateral wall as access, and the left atrium between the right pulmonary veins as access for venous drainage. The employed cannulas were two 28-Fr wire-reinforced angled veno-atrial cannula (Jostra Venous Catheter OD, Maquet Cardiopulmonary AG, Hirrlingen, Germany) for both atria. The outflow cannula was always positioned into the ascending aorta (straight aortic perfusion cannula [22 or 24 Fr], Edwards Lifesciences LLC, Irvine, CA, USA). All cannulas were secured with pledgeted, reinforced purse-string prolene sutures, tunneled through subcostal incisions to allow chest closure, and then connected to the circuit, avoiding air in the system.

The Quadrox D oxygenator (2–4) has a PMP hydrophobic, hollow-fiber diffusion membrane with an effective surface area of 1.8 m^2, allowing long-term, high gas exchange performance; the oxygen transfer capacity and carbon dioxide transfer capacity are 288 and 230 mL/min, respectively; the pressure drop across the in and out lines of the device does not exceed 40 mm Hg at 4 L/min; and the priming volume is 250 mL. This oxygenator is compact with a decreased heat exchange surface area of the membrane (0.6 m^2), thus reducing the risk of clot formation.

The RotaFlow is a centrifugal pump with a low prime volume (32 mL) that can provide high blood flow up to 10 L/min (2,4). This pump features a peg-top one-point sapphire bearing that lowers friction substantially without any metal shaft or seal. Its spiral housing ensures an optimized flow ratio with no stagnant zones. The pump rotor is magnetically suspended, and four flowing channels are generated inside the housing of the pump. These allow a continuous laminar flow with minimal turbulence and a reduced risk of hemolysis.

The Levitronix CentriMag blood pumping system was designed specifically for extracorporeal circulatory support applications as CPB or uni- or biventricular assistance (VAD) (5–8). The CentriMag motor is based on "bearingless" technology that combines the drive, magnetic bearing, and rotor into a single unit. The rotor is suspended and rotated by eight L-shaped iron cores (four pairs) with a drive and control wound together. The rotor position and rotation are continuously controlled by a feedback control system in radial directions. Another impeller motion is passively suspended with bias flux between the rotor and stator. The pump system consists of a single-use, disposable polycarbonate pump head (priming volume: 31 mL; connectors: 0.375-inch inlet/outlet ports), motor/bearing drive unit (diameter × height = 87 × 70 mm), cannulas, and a bedside controller. This system can generate flows up to 10 L/min with a priming volume of 31 mL; in Europe, the

system is licensed for use for 30 days, although longer periods of pump running and support have been reported. Recently, the CentriMag pump has also been adopted successfully for an ECMO support setting at several institutions (6–8).

In the circuit, the tubing and the oxygenator are coated with Bioline Coating (Maquet, Jostra Medizintechnik AG) (2–4). Recombinant human albumin is adsorbed on the extrinsic surface and acts as a heparin receptor. Covalent bonds and ionic interactions occur between the heparin molecules and albumin. Following this treatment, all the surfaces in contact with blood have highly stable covalent and ionic links with heparin. This coating provides high hemocompatibility, thus minimizing the activation of platelets, coagulation cascade, and complements.

The circuit was primed with saline. The priming procedure usually required 4–5 min, a process that proved to be useful in those patients who require immediate ECMO support in other hospital departments, such as intensive care units (ICUs), emergency departments, and hemodynamic laboratories.

In the novel adopted circuit, named PLS (Maquet, Jostra Medizintechnik AG) (2–4), the Quadrox D oxygenator has the housing reinforced with glass fibers to increase the mechanical resistance, and the polyvinyl chloride of the circuit is bis(2-ethylhexyl) phthalate-free. This circuit has been certified for a support period of 14 days (DEKRA Intertek Certification as a notified body of European Union, in accordance with the Directive 93/42/European Community).

Patients

Between January 2006 and December 2012, 12 242 adult patients underwent cardiac operations, mainly valvular procedures, at our institutions (S. Orsola-Malpighi Hospital, Bologna University, Bologna, Italy; S. Camillo Hospital, Rome, Italy). During the same period, 228 patients (1.86%) required veno-arterial peripheral or central ECMO support for primary or postcardiotomy CS (Tables 1 and 2). The contribution of the two institutions was comparable in terms of the number of cases referred (Bologna, $n = 119$ [52.1%] vs. Rome, $n = 109$ [47.8%]). This study was approved by the Institutional Review Boards of both centers.

The femoral route, involving 126 (55.2%) patients, was preferred initially to the open sternotomy route for ECMO support because the presence of an open sternotomy wound might have increased the risk of bleeding and infection and have made nursing care more difficult (4). Moreover, the femoral route was judged to be the easiest strategy to quickly restore the patient circulation in the case of CS. The central setting of ECMO support, involving 102 (44.7%) patients, was adopted over time after obtaining improvement in both physicians' and nurses' experience and skills concerning ECMO management.

Inclusion criteria for veno-arterial ECMO support to treat primary refractory heart failure (HF) and CS at our institution were the following: acute myocardial infarction (AMI); acute decompensation of end-stage dilated cardiomyopathy (DCMP); acute myocarditis; high-risk percutaneous transluminal coronary angioplasty (PTCA); and failure to wean from CPB after surgery.

Patients were excluded according to the following criteria: severe peripheral arteriopathy, severe and chronic renal failure, terminal malignancy, irreversible or severe degenerative brain diseases, and trauma.

ECMO support was installed most commonly in the operating room ($n = 202$) and, more rarely, in the ICU ($n = 26$; peripheral ECMO). Only 12 patients were transported while on peripheral ECMO support from other centers.

In the studied population, the vital status immediately before ECMO placement, as traditionally evaluated before any short-term mechanical support device placement at our institutions (4,5), was documented using the simplified acute physiology score (SAPS) II (Table 1). Briefly, the following data and score points were collected and calculated, respectively: age, heart rate, systolic blood pressure, body temperature (in °C), PaO_2/FiO_2, urine output, serum blood urea nitrogen, white blood cell count, serum potassium, sodium and bicarbonate level, plasma bilirubin level, Glasgow coma score, documented history of chronic disease (acquired immunodeficiency syndrome, hematologic malignancy, metastatic cancer), and type of admission.

The inotropic score, as calculated at our institutions (4,5), before ECMO placement was also evaluated (Table 1). Briefly, the doses of dopamine, dobutamine, and enoximone (in μg/kg body weight/min) were added, whereas the doses of epinephrine and norepinephrine were multiplied by 100 and then added.

ECMO Management

The ECMO blood flow was adequately adjusted during the first 24–48 h to maintain a cardiac index of 2.6 L/min/m^2, a mixed venous oxygen saturation (SvO_2) around 70%, and a mean arterial pressure of 60–65 mm Hg.

TABLE 1. *Demographic and preimplant clinical parameters of the different cohorts of patients supported by veno-arterial ECMO*

	Postcardiotomy ($n = 118$)	Donor graft failure ($n = 37$)	Post-AMI ($n = 27$)	Acute-on-chronic HF ($n = 40$)	Acute myocarditis ($n = 6$)
Mean age (years)	61.2 (40–84)	48.7 (23–64)	64.6 (40–71)	50.6 (19–55)	48.2 (44–56)
Male gender (n, %)	76 (64.4%)	26 (70.2%)	19 (70.3%)	29 (72.5%)	5 (83.3%)
BSA (m^2)	1.85 (1.74–1.88)	1.78 (1.68–1.88)	1.9 (1.85–1.95)	1.81 (1.78–1.86)	1.80 (1.67–1.86)
Etiology					
Coronary disease (n, %)	68 (57.6%)	—	27 (100%)	14 (35%)	—
Valvular disease (n, %)	50 (42.3%)	—	—	8 (20%)	—
DCMP (n, %)	—	—	—	18 (45%)	—
Preoperative LVEF (%)	48.2 (33–75)	—	—	—	—
Number of diseased coronaries	2.4 (2–3)	—	2.3 (2–3)	2.6 (2–3)	—
Previous cardiac operation	40 (33.8%)	16 (40%)	—	7 (17.5%)	—
Logistic EuroSCORE (%)	25.7 (10–46)	—	—	—	—
CPB time	204.5 (46–369)	246.4 (194–296)	—	—	—
Ischemic time	118.1 (64–198)	198.6 (157–215)	—	—	—
SAPS II score*	31 (28–45)	32 (26–45)	36 (28–50)	31 (15–41)	29 (15–45)
Inotropic score*	32 (20–45)	30 (20–38)	35 (20–50)	32 (15–38)	30 (20–40)
mSAP (mm Hg)	63 (50–65)	64.9 (50–68)	62.9 (48–65)	60.9 (50–70)	63.8 (50–68)
SvO_2 (%)	48 (40–55)	54 (48–58)	47 (40–55)	48 (45–55)	46 (40–56)
Lactate level (mg/dL)	13.6 (6.7–18.1)	12.5 (5.7–17.2)	14.8 (7.7–18.1)	12.9 (6.7–17.1)	11.9 (5.1–15.1)
CPR (n, %)	15 (12.7%)	—	11 (40.7%)	3 (7.5%)	—
CPR time (minutes)	28.1 (16–62)	—	31.5 (10–53)	25.5 (15–56)	—
IABP (n, %)	12 (10.1%)	—	27 (100%)	3 (7.5%)	—
Mechanical ventilation (n, %)	118 (100%)	37 (100%)	27 (100%)	3 (7.5%)	—

All values are presented as median and range or as percentage.

* Definition is given by the same authors elsewhere (4,5).

AMI, acute myocardial infarction; BSA, body surface area; CBP, cardiopulmonary bypass; CPR, cardiopulmonary resuscitation; DCMP, dilated cardiomyopathy; HF, heart failure; IABP, intraortic balloon pump; LVEF, left ventricular ejection fraction; mSAP, mean systolic arterial pressure; SAPS, simplified acute physiology score; SvO_2, mixed venous oxygen saturation.

TABLE 2. *Outcome on veno-arterial ECMO support*

	Postcardiotomy (n = 118)	Donor graft failure (n = 37)	Post-AMI (n = 27)	Acute-on-chronic HF (n = 40)	Acute myocarditis (n = 6)
Peripheral ECMO setting	62 (52.5%)	17 (45.9%)	23 (85.1%)	18 (45%)	6 (100%)
Central ECMO setting	56 (47.4%)	20 (54.05%)	4 (14.8%)	22 (55%)	—
RotaFlow ECMO	110 (93.2%)	36 (97.2%)	25 (92.5%)	37 (92.5%)	5 (83.3%)
CentriMag ECMO	8 (6.7%)	1 (2.7%)	2 (7.4%)	3 (7.5%)	1 (16.6%)
ECMO time (days)	10.8 (2–43)	5.6 (3–10)	10.1 (1–24)	9.6 (8–21)	5.8 (3–12)
ECMO >6 days	88 (74.5%)	12 (32.4%)	19 (70.3%)	31 (77.5%)	1 (16.6%)
IABP on ECMO	118 (100%)	37 (100%)	27 (100%)	40 (100%)	6 (100%)
IABP time (days)	14.9 (2–42)	7.5 (3–13)	13.7 (6–30)	13.7 (8–18)	8.1 (3–15)
Intubation time (days)	20 (2–42)	10.1 (3–10)	19.2 (6–28)	19.3 (8–15)	10.2 (3–10)
Hospital stay (days)	41.2 (2–96)	21.6 (3–32)	38.5 (6–57)	38.4 (8–37)	20.5 (3–31)
Creatinine >3.5 (mg/100 mL)	19 (38%)	1 (12.5%)	5 (41.6%)	2 (66.6%)	1 (16.6%)
CVVH	65 (55.08%)	14 (37.8%)	15 (55.5%)	18 (45%)	1 (16.6%)
CVVH time (days)	8.3 (6–11)	3.1 (4–7)	8.1 (6–14)	7.6 (5–10)	3.2 (4–6)
Bleeding/tamponade	69 (58.4%)	19 (51.3%)	13 (48.1%)	21 (52.5%)	3 (50%)
Transfusion	118 (100%)	37 (100%)	27 (100%)	40 (100%)	6 (100%)
PRBCs	18 (3–52)	16.1 (3–48)	19.3 (3–51)	17.1 (3–55)	16.2 (3–46)
PLT units	16.5 (6–48)	15.8 (6–50)	15.9 (6–52)	16.1 (6–47)	15.7 (6–48)
FFP (1000 mL/unit)	5.6 (2–15)	5.2 (2–17)	6.1 (2–18)	5.1 (2–14)	5.2 (2–15)
Pulmonary complications	19 (16.1%)	4 (10.8%)	3 (11.1%)	3 (7.5%)	—
Liver failure	52 (44.06%)	10 (27.02%)	14 (51.8%)	7 (17.5%)	1 (16.6%)
Bilirubin >15 (mg/100 mL)	52 (44.06%)	10 (27.02%)	14 (51.8%)	7 (17.5%)	1 (16.6%)
PLT count	125.6 (40–198)	115.8 (95–188.1)	133.6 (88–177.5)	123.4 (105–166.1)	122.2 (105–169.2)
PFH (mg/dL)	46.5 (28–165)	43.5 (15–148)	48.9 (26–158)	44.3 (18–95)	43.4 (16–95)
CK-MB relative index (%)*	7.3 (5–28)	7.7 (4–20)	8.1 (5–25)	7.7 (5–19)	7.6 (4–18)
MOF	53 (44.9%)	10 (27.02%)	14 (51.8%)	7 (17.5%)	1 (16.6%)
Sepsis	26 (22.03%)	6 (16.2%)	6 (22.2%)	4 (10%)	1 (16.6%)
Brain death (cerebral hemorrhage)	20 (16.9%)	5 (13.5%)	8 (29.6%)	3 (7.5%)	—
Leg ischemia	7 (5.9%)	1 (2.7%)	—	5 (18.5%)	—
Survived on ECMO	66 (55.9%)	27 (72.9%)	13 (48.1%)	33 (82.5%)	5 (83.3%)
Central Setting (61.7%)	31	11	5	14	2
Peripheral Setting (64.2%)	35	16	8	19	3
Weaned from ECMO	65 (55.08%)	23 (62.1%)	12 (44.4%)	2 (5%)	5 (83.3%)
Central Setting (45.09%)	30	9	4	1	2
Peripheral Setting (48.4%)	35	14	8	1	3
Died on ECMO	52 (44.06%)	10 (27.02%)	14 (51.8%)	7 (17.5%)	1 (16.6%)
Central Setting (35.2%)	25	4	5	2	—
Peripheral Setting (38.09%)	27	6	9	5	1
VAD placement	1 (2%)	—	1 (8.3%)	4 (10%)	—
Htx	—	4 (10.8%)	—	27 (67.5%)	—
Discharged	55 (46.6%)	24 (64.8%)	10 (37.03%)	29 (72.5%)	4 (66.6%)
Central Setting (52.9%)	24	9	3	17	1
Peripheral Setting (53.9%)	31	15	7	12	3

All values are presented as mean and standard deviation or as percentage.

* Definition is given by Zhang et al. (9).

AMI, acute myocardial infarction; CVVH, continuous veno-venous hemofiltration; CK-MB, MB isoenzyme of creatine kinase; ECMO, extracorporeal membrane oxygenation; FFP, fresh frozen plasma; HF, heart failure; Htx, heart transplantation; IABP, intraortic balloon pump; MOF, multiple organ failure; PFH, plasma free hemoglobin; PLT, platelet; PRBCs, packed red blood cells; VAD, ventricular assist device.

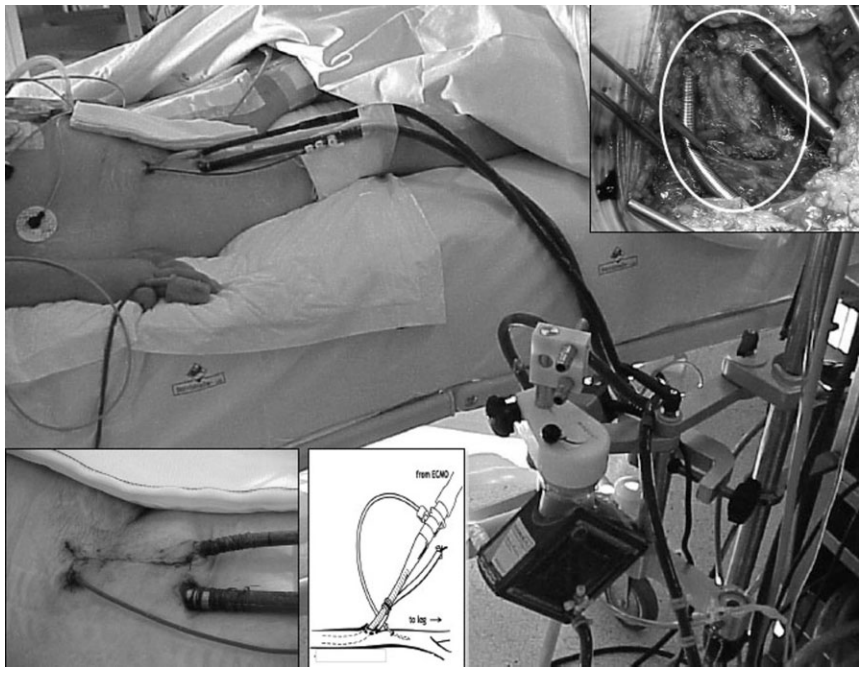

FIG. 1. Distal leg perfusion setting during peripheral veno-arterial ECMO support.

Before cannulation, all patients received an intravenous heparin bolus (40–80 units/kg). During ECMO support, heparin was administered continuously to achieve an activated clotting time of 140–160 s and a prothrombin time value of 50–70. Infusion of antithrombin III (AT III) was required if the AT III serum level was below 80%. In patients with a motionless left ventricle, small doses of inotropes (dobutamine) were given to obtain minimal ventricular contraction, avoiding clot formation inside the left ventricle.

All ECMO support was conducted under normothermia. Patients who had cardiac arrest before starting ECMO were progressively cooled at 32–34°C for 24–36 h using a heater-cooler (Stockert).

Closed heart examinations by transesophageal echocardiography were performed to assess the left and right ventricle motion daily.

For peripheral cannulation, a continuous-wave Doppler image of the tibial artery flow and pulsatility was acquired every 2 days, in the presence of a consultant vascular surgeon, to evaluate and provide a correct distal leg perfusion. In 83 patients with absence of both anterior and posterior tibial artery flow and/or a mean pressure of the superficial femoral artery <50 mm Hg, distal perfusion was performed as soon as possible after mechanical support initiation to avoid the deleterious consequences of limb malperfusion (Fig. 1). Distal perfusion was performed through an 8-Fr catheter (flexible, soft balloon-tipped coronary catheter for selective anterograde cardioplegia infusion [Maquet, Jostra Medizintechnik AG]), via the T line coming off the main arterial femoral ECMO cannula, followed by vascular ultrasonography to assess the proximal and the distal flow separately. In the remaining 43 peripheral ECMO cases, the cannulas (most frequently 17 Fr) were found to not be fully occlusive for the femoral vessels, and distal perfusion catheter insertion was considered to be unnecessary.

All patients needed blood transfusions to achieve a hematocrit of 28–30%, and platelet infusions were given when the platelet count was <50 000–60 000.

Mechanical ventilation was continued throughout mechanical support using the same management for each patient in the studied population because of the accepted common policy of both institutions related to difficulties from the view of the ICU staff in managing awake patients while on ECMO as standard. The ventilator setting was commonly set at a tidal volume of 8 mL/kg, 8 breaths/min, positive end expiratory pressure <10 cm H_2O, and an FiO_2 of 0.40–0.60. An intra-aortic balloon pump (IABP) was employed in all patients to reduce the afterload and to improve coronary perfusion and maintain a pulsatile flow (10).

At our institutions, no attempts to wean off ECMO were usually considered during the first 72 h. Criteria for weaning include an SvO_2 ≥70%, a hematocrit of 28–30%, the absence of bleeding or tamponade, a left ventricular ejection fraction (EF) ≥35% with an aortic time–velocity integral >10 cm on echocardiography, the absence of left heart distension, good contraction of the right ventricle (EF >40%) with the

absence of moderate to severe tricuspid regurgitation, normal blood lactate levels (<1.5 mmol/L), and a normal urine output (>80 mL/h).

A gradual weaning by reducing the ECMO flow by 10% every ~12 h was our main strategy, together with close transesophageal echocardiography and Swan-Ganz catheter examinations. Once an ECMO flow of 1.5 L/min/m^2 was reached, in the presence of two or more consultant surgeons, the pump flow was radically reduced at 0.5 L/min/m^2 for ~40–60 min using an IABP set at 1:1. If the hemodynamics in terms of systemic arterial pressure (mean pressure >60 mm Hg), LV contractility (EF >35%), central venous pressure (10–15 mm Hg), wedge pressure (10–15 mm Hg), and SvO_2 (>70%) showed no significant changes without the addition of new inotropes, the heparin was stopped, and ECMO support was removed in the operating room within the next 1 h or, more rarely, at bedside ($n = 11$).

In both ECMO categories, all pledgeted purse-string sutures were successfully tied at the time of surgery for ECMO cannula removal. The entire peripheral ECMO population with a distal perfusion line (Fig. 1) required the removal of clot formation in the femoral artery at the site between the two perfusion cannulas (proximal and distal) due to blood stasis and a low anticoagulation regimen at the time of ECMO weaning. In these cases, a local vascular thromboembolectomy by deployment of a Fogarty arterial catheter (Edwards Lifesciences Corp.) ($n = 77$) or reconstruction of the femoral vessel with a pericardial patch ($n = 16$) was necessary.

Among the nonweanable patients, two were switched to prolong the support to the extracorporeal short- to mid-term Levitronix CentriMag LVAD configuration (5) by cannulating the left atrium and ascending aorta with further continuous intravenous heparin administration, to maintain a thromboplastin time of 50–60 s. Additionally, four patients were switched to an implantable long-term axial flow HeartMate II (Thoratec, Inc., Pleasanton, CA, USA) LVAD configuration (4) by cannulating the apex of the left ventricle and ascending aorta with postoperative anticoagulation management consisting of warfarin to maintain an international normalized ratio of 2.5–3.0, in association with a platelet aggregation inhibitor at low dosage (aspirin; 100 mg/day).

In all patients, the IABP support was maintained for at least 5 days after ECMO removal.

Statistical Analysis

Descriptive statistics are expressed as the means ± standard deviation or as the medians and range. A P value less than 0.05 was deemed to indicate statistical significance. Categorical variables are presented as percentages, and the χ^2-test was used to compare them. Analysis of variance for repeated-measures was employed for numerical variables. Continuous variables were evaluated using Student's t-test for independent variables. Univariate analysis was used as a screening process to identify predictor variables; those with $P < 0.05$ were selected. Stepwise logistic regression analysis was applied to determine the independent predictors of 30-day mortality.

A multivariate Cox proportional hazards regression analysis was performed to identify the independent predictors of survival after discharge of postcardiotomy and post-AMI cohorts. The Kaplan–Meier method was used to calculate the survival curves and determine survival outcomes for these cohorts.

All analyses were performed using SPSS for Windows, release 11.5 (SPSS, Inc., Chicago, IL, USA).

RESULTS

The mean age was 58.3 ± 10.5 years (range: 19–84 years), and 155 patients (67.9%) were males. The RotaFlow pump was used in 213 patients (93.4%), whereas the CentriMag was used in 15 patients (6.5%), and both groups were adapted for a central or peripheral veno-arterial ECMO support setting. The overall mechanical average support time was 10.9 ± 9.7 days (range: 1–43 days): 10.9 ± 9.8 days (range: 1–43 days) for peripheral ECMO and 10.6 ± 8.5 days (range: 3–32 days) for central ECMO. The overall survival on mechanical support was 63.1% ($n = 135$ [63.3%] for RotaFlow; $n = 9$ [60%] for CentriMag). One hundred seven patients (46.9%) were weaned off ECMO ($n = 99$ [46.4%] for RotaFlow; $n = 8$ [53.3%] for CentriMag), whereas 84 patients (36.8%) died during ECMO support ($n = 78$ [36.6%] for RotaFlow; $n = 6$ [40%] for CentriMag) due to multiple organ failure (MOF), which was mostly associated with sepsis and brain death (Tables 1 and 2). Among the patients who were weaned off ECMO, 122 (53.5%) were discharged ($n = 115$ [53.9%] for RotaFlow; $n = 7$ [46.6%] for CentriMag). Two patients (RotaFlow population) were switched to the Levitronix CentriMag using the short- to mid-term extracorporeal LVAD configuration. Death occurred in one case on support due to ischemic stroke. In another case, myocardial recovery occurred after 7 days of support, and the patient was discharged. In another four cases (RotaFlow population), the HeartMate II implantable long-term

LVAD was used, and four patients were discharged to their homes with no issues after more than 360 days of support.

Thirty-one patients (13.5%) ($n = 30$ [14.08%] for RotaFlow; $n = 1$ [6.6%] for CentriMag) were successfully bridged to Htx after an average ECMO support time of 9.8 ± 8.6 days (range: 3–18 days). Among these transplanted patients, eight (RotaFlow population; acute-on-chronic HF cohort) required veno-arterial ECMO support a second time (RotaFlow system) for graft failure after Htx at the time of weaning from CBP and further successful ECMO weaning and removal. Overall, 27 patients were successfully discharged home from the transplant units of both institutions.

Seventy-three patients (32.01%) required ECMO ($n = 67$ [31.4%] for RotaFlow; $n = 6$ [40%] for CentriMag) to treat a primary CS. Twenty-seven of them, referred mostly from other institutions, had a large myocardial infarction (left main, $n = 15$) and had undergone treatment by primary PTCA ($n = 25$ [11.7%] for RotaFlow; $n = 2$ [13.3%] for CentriMag). Six patients had acute myocarditis as evaluated by the pathologist after biopsy ($n = 5$ [2.3%] for RotaFlow; $n = 1$ [6.6%] for CentriMag); additionally, 40 patients, who were on the waiting list for Htx, showed acute decompensation on chronic HF due to end-stage DCMP ($n = 37$ [17.3% for RotaFlow; $n = 3$ [20%] CentriMag).

One hundred eighteen patients (51.7%) received ECMO support ($n = 110$ [51.6%] for RotaFlow; $n = 8$ [53.3%] CentriMag) after cardiac surgery procedures due to failure to wean from CPB. Postcardiotomy procedures included the following: coronary artery bypass grafting (CABG) in 28 patients; combined mitral valve replacement and tricuspid valve repair in 27 patients; combined CABG and ascending aorta replacement in 22 patients; Bentall procedure in 15 patients; aortic valve replacement in 10 patients; combined CABG and aortic valve replacement in 10 patients; and mitral valve replacement in six patients.

Additionally, 37 patients (16.2%) required ECMO support ($n = 36$ for RotaFlow; $n = 1$ for CentriMag) to treat an early primary graft failure (PGF) after Htx.

In the overall described population, 29 patients (12.7%) received ECMO ($n = 26$ [16.9%] for RotaFlow; $n = 3$ [20%] for CentriMag) during CPR with a mean CPR time of 30.3 ± 13.1 min (range: 10–62 min).

The preoperative risk profile and postoperative parameters are listed in Tables 1 and 2. An IABP was inserted into all of the patients before ECMO support according to the Hausmann et al. (10) IABP score for mechanical support initiation.

In all of the patients, blood lactate, MB isoenzyme of creatine kinase (CK-MB), and the CK-MB relative index (the ratio of CK-MB to total CK) were measured during overall ECMO support. All of the evaluated parameters showed a significant reduction during the first 72 h of support (Tables 1–3).

Table 3 shows the first statistical screening process (univariate analysis) used to identify all possible predictors defining all of the risk variables in the

TABLE 3. *Comparison of the survivors and nonsurvivors variables*

	Survivors ($n = 144$)	Nonsurvivors ($n = 84$)	P value
Age (years)	48.1 ± 9.1	66.7 ± 11.3	0.03
Female gender	21 (14.5%)	52 (61.9%)	<0.01
Lactate level (mg/dL) before ECMO	10.7 ± 3.8	30.1 ± 24.2	<0.01
CPB time (min) in postcardiotomy cohort	174.5 ± 87.5	244 ± 112.5	0.03
Aortic cross-clamping time (min) in postcardiotomy cohort	89.6 ± 56.3	144.4 ± 72.3	<0.01
CPR before ECMO	8 (5.5%)	21 (25%)	<0.01
Inotropic score before ECMO*	11.1 ± 4.2	33.4 ± 6.3	0.02
Intubation time (days) on ECMO	9.7 ± 7.2	18.9 ± 5.1	0.02
MOF on ECMO	1 (0.6%)	84 (100%)	<0.01
PRBCs on ECMO	8.5 ± 4.6	23.1 ± 12.7	<0.001
PLT units on ECMO	13.8 ± 6.9	26.7 ± 15.4	0.03
FFP (1000 mL/unit) on ECMO	3.6 ± 3.2	9.9 ± 8.6	0.02
Blood lactate level (mmol/L) 72 h after ECMO initiation	2.1 ± 1.23	7.9 ± 5.61	<0.01
Blood level of CK-MB (U/L) 72 h after ECMO initiation	145.2 ± 133.4	356.3 ± 234.4	0.01
CK-MB relative index (%) 72 h after ECMO initiation**	7.5 ± 3.42	21.2 ± 12.3	<0.001
PFH (mg/dL) 72 h after ECMO initiation	33.6 ± 10.3	93.7 ± 14.7	<0.01

All values are presented as mean and standard deviation or as percentage.
Only significant results ($P < 0.05$) of the analysis are shown in this table.
* Definition is given by the same authors elsewhere (4,5).
** Definition is given by Zhang et al. (9).
CBP, cardiopulmonary bypass; CK-MB, MB isoenzyme of creatine kinase; CPR, cardiopulmonary resuscitation; ECMO, extracorporeal membrane oxygenation; FFP, fresh frozen plasma; IABP, intraortic balloon pump; MOF, multiple organ failure; PFH, plasma free hemoglobin; PLT, platelet; PRBCs, packed red blood cells.

nonsurvivor population on ECMO. Next, stepwise logistic regression analysis was applied to determine definitively the independent predictors of 30-day mortality.

The blood lactate level 72 h after ECMO initiation ($P = 0.01$), the CK-MB 72 h after ECMO initiation ($P = 0.01$), and the CK-MB relative index 72 h after ECMO initiation ($P < 0.001$) demonstrated statistically significant differences between survivors and nonsurvivors on ECMO (Table 3).

Logistic regression analysis revealed blood lactate levels (3 mmol/L) at 72 h after initiation of ECMO and the CK-MB relative index 72 h after ECMO initiation to be significant predictors of mortality on ECMO support ($P = 0.010$, odds ratio [OR] = 2.94; 95% confidence interval [CI] = 1.10–3.14; $P = 0.010$, OR = 2.82, 95% CI = 1.014–3.721).

Thus, when the level of lactate in blood has a value of 3 mmol/L after 72 h of ECMO support initiation, the predicted probability of mortality would be 50%. Moreover, the predicted probability of mortality on ECMO therapy would be 50% if the relative CK-MB index 72 h after ECMO initiation had a value of 10%.

All of the patients were transfused (Table 2). Furthermore, hemoglobin levels >10 mg/dL would not be expected in critically ill patients and is higher than is necessary for appropriate perfusion. The patients who died had a higher number of red blood cell transfusions ($P < 0.01$), a higher number of platelets ($P = 0.03$), and a higher number of units of fresh frozen plasma (FFP) transfusions ($P = 0.02$; Table 3).

The stepwise logistic regression analysis revealed that the number of packed red blood cells transfused is an independent predictor of mortality during ECMO support ($P = 0.011$, OR = 2.69; 95% CI = 1.06–4.16).

A moderate reduction in platelet count was observed (overall, 236.4 ± 81.7 K/μL before ECMO vs. 133.4 ± 91.7 K/μL at 72 h of ECMO support [$P = 0.01$], with no significant further reduction at the overall average time of ECMO support and no significant difference between survivors and nonsurvivors). Ten patients (4.3%) (RotaFlow population) showed a reduction in the platelet count <50 K/μL with a diagnosis of heparin-induced thrombocytopenia type II, and fondaparinux (2.5 mg per day) was used as an alternative to intravenous heparin administration (11). Of these patients, only one died due to MOF and brain death (cerebral hemorrhage); all others were successfully weaned from ECMO support (postcardiotomy cohort).

Peripheral complications of femoral access included leg ischemia (5.7%), which required immediate distal perfusion catheter insertion, and femoral site infection (3.9%); no inferior vena cava or femoral vein thrombosis was noted. No isolated mediastinitis occurred in the central ECMO population. As shown in Table 4, the central ECMO population had more bleeders (62.7 vs. 48.4%) and a higher rate of a requirement for continuous veno-venous hemofiltration (CVVH) (56.8 vs. 43.6%) compared with the peripheral ECMO population.

The mean follow-up time was 20.1 ± 20.7 months (range: 1–68 months). The overall survival rates for patients belonging to the postcardiotomy ($n = 55$) and post-AMI ($n = 10$) cohorts who survived until hospital discharge were 60% (39/65) in the first year and 18.4% (12/65) in the third year. The late deaths (death after hospital discharge) were considered to be cardiac related. A postoperative left ventricle ejection fraction (LVEF) ≤40% before hospital discharge was the only independent risk factor for late death (hazard ratio: 12.3; 95% CI: 4.1–34.8; $P < 0.0001$). The 1-year survival rates for survivors of postcardiotomy and post-AMI cohorts with a postoperative LVEF >40 and ≤40% were 69.7% (30/43) and 40.2% (9/22), respectively, whereas the 2-year survival rates were 27.9% (14/43) and 9.09% (2/22), respectively. Figure 2 shows the Kaplan–Meier survival curves of this population. The mean survival time of patients with a postoperative LVEF ≤40% was 15.4 months (range: 1–31 months).

The overall 5-year conditioned survival of PGF patients was similar to that of recipients ($n = 498$) not

TABLE 4. *Comparison of the peripheral and central ECMO populations variables (significant results only)*

	Peripheral ECMO ($n = 126$)	Central ECMO ($n = 102$)	P value
CVVH	55 (43.6%)	58 (56.8%)	0.01
Bleeding/tamponade	61 (48.4%)	64 (62.7%)	0.01
PRBCs on ECMO	9.6 ± 4.5	14.8 ± 12.4	0.02
PLT units on ECMO	15.5 ± 6.4	20.1 ± 14.6	0.03
FFP (1000 mL/unit) on ECMO	4.6 ± 3.9	8.2 ± 7.2	0.03

All values are presented as mean and standard deviation or as percentage.
Only significant results ($P < 0.05$) of the analysis are showed in this table.
CVVH, continuous, veno-venous hemofiltration; ECMO, extracorporeal membrane oxygenation; FFP, fresh frozen plasma; PFH, plasma free hemoglobin; PLT, platelet; PRBCs, packed red blood cells.

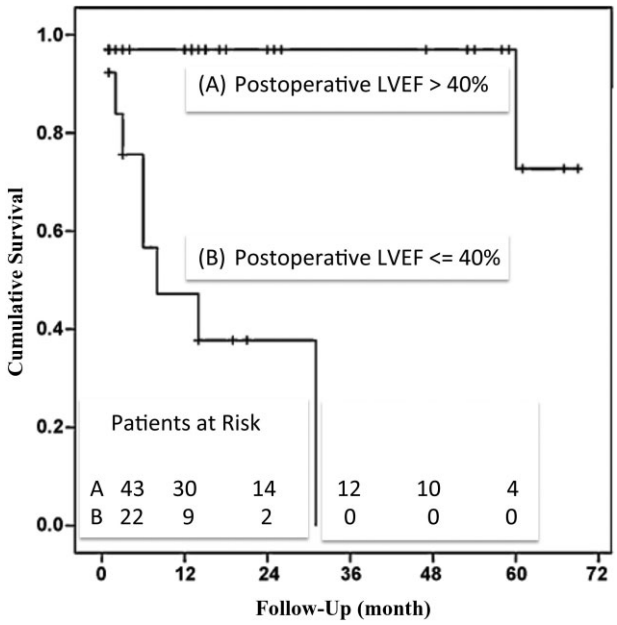

FIG. 2. Kaplan–Meier survival curves of survivors with a stable postoperative (just before hospital discharge) left ventricular ejection fraction (LVEF) >40% and ≤40% (log-rank test, $P < 0.0001$).

requiring ECMO support after Htx in both institutions ($70.3 \pm 15.1\%$ vs. $72.1 \pm 9.5\%$, respectively; $P = 0.8$) during the same period, as described elsewhere (12,13).

DISCUSSION

ECMO support is a well-established technology that provides full circulatory support with the possibility of recovery from organ injury in patients who present with cardiac arrest or severe hemodynamic instability associated with MOF (1–4,6–9,12–25).

The novel material PMP, which we adopted, is likely the key to the success of the latest generation of oxygenators and ECMO systems in terms of high gas exchange efficiency in a small surface, low prime volume, low pressure gradient, and no plasma leakage for periods of more than 7 days compared with the hollow-fiber polypropylene membrane oxygenators that were introduced in the early 1990s. Above all, no randomized study has compared several oxygenators for ECMO support.

The PMP Quadrox D oxygenator and the entire ECMO circuit had to be changed in 34 (14.9%) patients ($n = 31$ for RotaFlow; $n = 3$ for CentriMag) who had an aggressive sepsis (postcardiotomy and post-AMI cohorts) with consequent difficult anticoagulation management by our teams, leading to clinical hemolysis (defined as an increase of more than twofold in lactate dehydrogenase and plasma free hemoglobin in compared with the values on the third day after surgery, together with hyperbilirubinemia, severe anemia with hemoglobin <8 g/dL, and the need for red blood cell transfusion in the absence of bleeding) and evident clots or deposit formation in both the oxygenator and tubing of the ECMO circuit. Additionally, the ECMO circuit was changed at the beginning of our experience in 17 other patients ($n = 14$ for RotaFlow; $n = 3$ for CentriMag) because prolonged support was needed (>15 days), as advised by the manufacturers of both pump systems, even in the absence of clinical adverse event issues or severe ECMO circuit failure (at the oxygenator, the pressure drop was >130 mm Hg, and the PaO_2 was <70 at a FiO_2 of 100% in only five patients; $n = 4$ for RotaFlow and $n = 1$ for CentriMag). Moreover, in these cases, all components of the ECMO systems were macroscopically evaluated to detect clots or fibrin deposits; no circuit had macroscopic alterations.

Several studies reported the mean ECMO duration to be 1.7–7.1 days (1–4,6–9,12–25). In our experience, the mean ECMO duration was 10.2 ± 7.3 days (range: 2–43 days), which is higher than reported in the literature. The cause may be that there was no concern about the optimal performance of the Quadrox D oxygenator assembled with the RotaFlow or CentriMag pumps; thus, most of our patients were supported for more than 7 days (Table 2).

Bleeding remains a serious problem in patients supported by ECMO. Several studies have reported high frequencies of transfusions with red blood cell units, platelets, and FFP (1–4,6–9,12–25).

In our experience, we have observed a slight reduction in blood component transfusions and lower plasma-free hemoglobin (PFH) levels, in terms of the hemolysis rate, in patients who survived on ECMO compared with those who died on ECMO (Table 3). No significant differences were noted between the RotaFlow and CentriMag systems (Table 5) in terms of the pump failure event rate, blood component transfusions needed, or PFH levels at both 3 days after ECMO initiation and at the average support time of each ECMO system population (RotaFlow: 10.9 ± 9.9 days, range: 1–43 days; CentriMag: 10.2 ± 7.6 days, range: 3–32 days).

We reported an overall mortality of 36.8% and an overall survival rate on ECMO of 63.1% (Table 2); these rates are similar to those reported previously (1–4,6–9,12–25) but with a longer ECMO duration. Several interpretations are possible. On the one hand, if the patient could not be weaned off ECMO within 7 days, then Htx or a VAD implantation is required. On the other hand, the possibility of

TABLE 5. *Comparison of the RotaFlow and CentriMag ECMO systems variables*

	RotaFlow ECMO ($n = 213$)	CentriMag ECMO ($n = 15$)	P value
Pump failure	—	—	—
PFH (mg/dL) 72 h after ECMO initiation	43.5 ± 12.3	43.7 ± 10.5	0.88
PFH (mg/dL) at the average time of ECMO support	48.9 ± 12.6	48.1 ± 11.7	0.91
Bleeding/tamponade	117 (51.3%)	8 (53.3%)	0.77
PRBCs on ECMO	9.1 ± 3.6	9.0 ± 4.1	0.62
PLT units on ECMO	15.7 ± 4.4	14.7 ± 5.4	0.75
FFP (1000 mL/unit) on ECMO	4.1 ± 2.8	4.4 ± 3.1	0.81

All values are presented as mean and standard deviation or as percentage.

ECMO, extracorporeal membrane oxygenation; FFP, fresh frozen plasma; PFH, plasma free hemoglobin; PLT, platelet; PRBCs, packed red blood cells.

leaving the patient on ECMO for more than 7 days, before attempting weaning off of support, has to be considered seriously, particularly by adoption of PMP oxygenators and latest-generation centrifugal pumps.

Additionally, the routine use of IABP support in each patient (10) might have contributed to the encouraging outcome of our ECMO population with, fortunately, no negative side effects, for example, renal malperfusion or vascular complications.

The decision regarding the optimal timing of device insertion and duration of support to either bridge or recovery is difficult to provide in a precise fashion but remains a key confounder when comparing transplant unit experiences. Moreover, the question of whether to bridge to transplant or use a long-term device remains controversial. Our goal was to adopt an ECMO support as a bridge to Htx if there was no evidence of recovery after weaning attempt(s) following neurological recovery and multiple organ improvement because the average waiting time to Htx in Italy is historically shorter than that in the USA (40 vs. 250 days). We noticed no significant difference between the patients who survived and those who died on ECMO in terms of the mean ECMO duration (9.3 ± 3.6 vs. 10.3 ± 5.2 days, respectively; $P = 0.71$).

Regarding the ECMO outcome, the ELSO reported the data from the international summary of the Extracorporeal Life Support (ECLS) registry, in which the proportions of survival to ECLS and survival to discharge for cardiac patients are 48 and 34%, respectively, and the survival to ECLS and survival to discharge for patients suffering from cardiac arrest are 36 and 27%, respectively (1). Some authors (1–4,6–9,12–25) reported a survival to discharge of 24–45% and rates of weaning off of ECMO of 46–64%.

By considering all of the data mentioned before, we believe that the peripheral/central RotaFlow and CentriMag ECMO systems with Quadrox D PMP oxygenator are an optimal strategy and have to be seriously considered even when a perfusion longer than 7 days is forecasted.

Presently, no specific guidelines exist for the management of ECMO, and the decision to discontinue support remains a challenge and is entrusted to the experience of each center.

Hyperlactatemia (blood lactate >3 mmol/L) during CPB is associated with increased mortality and appears to be related to a state of inadequate perfusion (1–4,6–9,12–25). In our study, we observed that patients who survived to 30 days showed a significantly lower level of blood lactate at 72 h than nonsurvivors (Table 3). Similar to other reports (4,22), we confirmed that a blood lactate level (>3 mmol/L) after 72 h is predictive of the probability (50%) of 30-day mortality.

Consequently, an eventual decision concerning the discontinuation of ECMO treatment may be supported by the above-evaluated predictor at 72 h after initiation of mechanical support. Alternatively, it might be eventually discussed as an earlier intervention by considering a switch to a mid-term BVAD (CentriMag) to provide better output and systemic perfusion with a lactate level >3 mmol/L, a clear sign of severe acidosis and tissue hypoxia.

Moreover, similar to the study of Zhang et al. (9), we observed that patients who presented with an index of CK-MB at 72 h of 10% had a predicted probability of mortality of 50%, and patients not weaned off of ECMO (mostly nonsurvivors) had a CK-MB relative index significantly higher than those who were weaned off (Table 3), as reported previously in a smaller ECMO population (4).

The plasma CK-MB is a feasible molecular marker for the evaluation of myocardial injury. In skeletal muscle, CK-MB can comprise up to 2% of total CK; however, in cardiac muscle, CK-MB makes up 20–46% of total CK (9,24). The relative CK-MB index results appear to have a high specificity and much better utility for the detection of myocardial injury (4,9,24).

Consequently, for a CK-MB index at 72 h of 10%, which suggests no possibility of myocardial recovery, earlier intervention involving a switch to long-term VAD or Htx would be prudent to improve the outcome.

In addition, the rate of bleeding and need for blood transfusions during ECMO remain high and are associated with an increase in mortality (21,22) (Table 3), suggesting the need for optimization of the anticoagulation strategy and surgical techniques in such a delicate patient population. The latter findings should be emphasized more in a central ECMO setting, despite our data suggesting more bleeders and a higher rate of requirement for CVVH than in the peripheral ECMO population, likely due to the high rate of acute volume-depletion events that led to acute renal injury.

During the study period, both the postcardiotomy and post-AMI cohorts demonstrated higher bilirubin levels, and developed MOF and sepsis more frequently compared with the remainder of the population, which comprised a preoperative severely ill cohort of patients who belonged to clinically more delicate categories (1–4,6–9,12–25). Moreover, these patients also had preoperative higher SAPS II and inotropic scores before ECMO installation and late referral by other peripheral institutions, as did the post-AMI population.

Veno-arterial PLS ECMO support was successful if delivered early in the post-Htx graft failure population (Tables 1–3), with a resulting shorter average period of support than that of other patient cohorts, as advocated elsewhere (4,12,13,25). Thus, veno-arterial PLS ECMO support remains our first choice if an MCS is necessary.

Few recent studies available in the literature (6–8) have reported successful adoption of the novel, magnetically levitated CentriMag blood pumping system, even in the ECMO configuration, in terms of patient outcome and device performance. This study included only 15 patients supported by the CentriMag ECMO system, and the results were encouraging ($n = 9$ patients [60%] survived on ECMO; $n = 1$ patient [6.6%] transplanted; $n = 8$ patients [53.3%] successfully discharged); however, further investigation is necessary.

Despite the high cost, the PLS set was combined with the CentriMag pumphead, thus requiring excision of the RotaFlow pumphead, which is usually implemented in every PLS set itself to have, at least at the beginning of our experience, the same materials and blood-contact surfaces on ECMO support and provide a better evaluation of our ECMO population to be studied over time.

In the present study, 22 patients in the survivors of postcardiotomy and post-AMI cohorts (22/65) experienced severe HF with a reduced LVEF (mean decrease, 8.5% ± 6.2%) after surgery. The postoperative (but not the preoperative) LVEF was the only independent risk factor for mortality after hospital discharge. Cardiac surgery may improve the LVEF by recruiting the hibernating myocardium, or may worsen the LVEF due to inadequate intraoperative myocardial protection. Regardless, impaired LVEF after surgery is an ominous sign. Close follow-up and earlier intervention, using either a VAD or urgent listing for Htx, will improve the survival of these patients.

Limitations

The present study was retrospective and based on a double-center experience. Two different pumpheads for ECMO treatment were compared, despite the possible biases.

A higher frequency of a peripheral ECMO setting (55.2%) versus a central ECMO setting (44.7%) resulted in the retrospective nature of this report and is related to the learning curve of both institutions in terms of the surgical treatment of CS management. Prospectively, our common policy consists of offering a peripheral ECMO to primary CS patients (postmyocarditis, post-AMI, acute decompensation on chronic HF related to an end-stage DCMP) as the first salvage treatment. This guarantees full cardiocirculatory support. A central ECMO is offered for postcardiotomy syndrome and no weaning from CPB with the chest already open and heart or great vessels exposed for cannulation, thus improving cardiac unloading and full biventricular support. The switch from peripheral to central ECMO should be considered early in cases with inadequate cardiac output, unsatisfactory cardiac unloading, or vascular complications related to the cannulation site.

Despite the advent of newer VADs that are more suitable for temporary and mid-term support, the above-mentioned ECMO therapy has been preferred by our institutions as being simple to establish and cost-effective to operate.

CONCLUSION

In summary, our study outcomes correspond to those published elsewhere, and the statistical analysis revealed significant results. Further studies are necessary to identify a valid score that can be used for prediction of mortality in all adult cardiac patients supported by extracorporeal membrane oxygenation.

Acknowledgment: The authors would like to thank the entire "MCS" team of the Deutsches Herzzentrum Berlin, Berlin, Germany, for continuous support. The study was carried out within Dr. Loforte's PhD Program in "Transplantation" awarded by Rome Tor Vergata University, Italy, in cooperation with the Deutsches Herzzentrum Berlin, Germany.

Conflict of Interest: There was no source of funding for this study. None of the authors has a financial relationship with a commercial entity that has an interest in the subject of the presented manuscript or other conflicts of interest to disclose.

REFERENCES

1. Extracorporeal Life Support Organization. ELSO Registry. Available at: http://www.elso.med.umich.edu/registry.htm. Accessed September 15, 2013.
2. Horton S, Thuys C, Bennet M, Augustin S, Rosenberg M, Brizard C. Experience with the Jostra Rotaflow and Quadrox D oxygenator for ECMO. *Perfusion* 2004;19:17–23.
3. Toomasian JM, Schreiner RJ, Meyer DE, et al. A polymethylpentene fiber gas exchange for long-term extracorporeal life support. *ASAIO J* 2005;51:390–7.
4. Loforte A, Montalto A, Ranocchi F, et al. Peripheral extracorporeal membrane oxygenation system as salvage treatment of patients with refractory cardiogenic shock: preliminary outcome evaluation. *Artif Organs* 2012;36:53–61.
5. Loforte A, Montalto A, Ranocchi F, et al. Levitronix CentriMag third-generation magnetically levitated continuous flow pump as bridge to solution. *ASAIO J* 2011;57:247–53.
6. Aziz TA, Singh G, Popjes E, et al. Initial experience with CentriMag extracorporeal membrane oxygenation for support of critically ill patients with refractory cardiogenic shock. *J Heart Lung Transplant* 2010;29:66–71.
7. Russo CF, Cannata A, Lanfranconi M, et al. Veno-arterial extracorporeal membrane oxygenation using Levitronix centrifugal pump as bridge to decision for refractory cardiogenic shock. *J Thorac Cardiovasc Surg* 2010;140:1416–21.
8. Mikus E, Tripodi A, Calvi S, Del Giglio M, Cavallucci A, Lamarra M. CentriMag venoarterial extracorporeal membrane oxygenation support as treatment for patients with refractory postcardiotomy cardiogenic shock. *ASAIO J* 2013;59:18–23.
9. Zhang R, Kofidis T, Hiroyouki K, et al. Creatine kinase isoenzyme MB relative index as predictor of mortality on extracorporeal membrane oxygenator support for postcardiotomy cardiogenic shock in adult patients. *Eur J Cardiothorac Surg* 2006;30:617–20.
10. Hausmann H, Potapov EV, Koster A, et al. Prognosis after the implantation of an intra-aortic balloon pump in cardiac surgery calculated with a new score. *Circulation* 2002;106(12 Suppl. 1):I203–1206.
11. Pappalardo F, Scandroglio A, Maj G, Zangrillo A, D'Angelo A. Preliminary experience with fondaparinux. Treatment of heparin-induced thrombocytopenia after cardiac surgery. *J Thorac Cardiovasc Surg* 2010;139:790–2.
12. Arpesella G, Loforte A, Mikus E, Mikus PM. Extracorporeal membrane oxygenation for primary graft failure. *Transplant Proc* 2008;40:3596–7.
13. Lonetti C, Manfredini V, Potena L, et al. Role of donor recipient match in determining the risk for primary graft failure after heart transplantation. *J Heart Lung Transplant* 2013; 32(4S):S255. [Abstract].
14. Chen JS, Ko WJ, Yu H, et al. Analysis of the outcome for patients experiencing myocardial infarction and cardiopulmonary resuscitation refractory to conventional therapies necessitating extracorporeal life support rescue. *Crit Care Med* 2006;34:950–7.
15. Doll N, Kiaii B, Borger M, et al. Five-year results of 219 consecutive patients treated with extracorporeal membrane oxygenation for refractory postoperative cardiogenic shock. *Ann Thorac Surg* 2004;77:151–7.
16. Hoefer D, Ruttmann E, Poelzl G, et al. Outcome evaluation of the bridge to bridge concept in patients with cardiogenic shock. *Ann Thorac Surg* 2006;82:28–34.
17. Saito S, Nakatani T, Kobayashi J, et al. Is extracorporeal life support contraindicated in elderly patients? *Ann Thorac Surg* 2007;83:140–5.
18. Smedira N, Moazami N, Golding CM, et al. Clinical experience with 202 adults receiving extracorporeal membrane oxygenation for cardiac failure: survival at five years. *J Thorac Cardiovasc Surg* 2001;122:92–102.
19. Ko W, Lin C, Chen RJ, Wang SS, Lin FY, Chen YS. Extracorporeal membrane oxygenation for adult postcardiotomy cardiogenic shock. *Ann Thorac Surg* 2002;73:538–45.
20. Liden H, Wilklund L, Haraldsson A, Berglin E, Hultman J, Dellgren J. Temporary circulatory support with extracorporeal membrane oxygenation in adult with refractory cardiogenic shock. *Scand Cardiovasc J* 2008;16:1–7.
21. Ang AL, Teo D, Lim CH, Leou KK, Tien SL, Koh MB. Blood transfusion requirements and independent predictors of increased transfusion requirements among adult patients on extracorporeal membrane oxygenation—a single centre experience. *Vox Sang* 2009;96:34–43.
22. Formica F, Leonello A, Colagrande L, et al. Extracorporeal membrane oxygenation to support adult patients with cardiac failure: predictive factors of 30-day mortality. *Interact Cardiovasc Thorac Surg* 2010;10:721–6.
23. Luo XJ, Wang W, Hu SS, et al. Extracorporeal membrane oxygenation for treatment of cardiac failure in adult patients. *Interact Cardiovasc Thorac Surg* 2009;57:612–4.
24. Capellan O, Hollander JE, Pollack D Jr, et al. Prospective evaluation of emergency department patients with potential coronary syndromes using initial absolute CK-MB versus CK-MB relative index. *J Emerg Med* 2003;24:361–7.
25. D'Alessandro C, Aubert S, Golmard JL, et al. Extra-corporeal membrane oxygenation temporary support for early graft failure after cardiac transplantation. *Eur J Cardiothorac Surg* 2010;37:343–9.