Extracorporeal membrane oxygenation as perioperative right ventricular support in patients with biventricular failure undergoing left ventricular assist device implantation

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Abstract

Objective: Left-ventricular assist device (LVAD) implantation complicated by early right ventricle (RV) failure has a poor prognosis. This study details our center’s experience with veno-arterial extracorporeal membrane oxygenation (ECMO) as perioperative RV support in patients with preoperative biventricular failure undergoing LVAD implantation. Methods: Ten patients, who underwent LVAD implantation, were retrospectively analyzed. Six patients were already supported with ECMO before LVAD implantation. In four patients, the ECMO was implanted before weaning from cardiopulmonary bypass. Results: All patients showed reduced RV function with elevated right-ventricular end-diastolic diameter (RVEDD) (38 ± 4 mm) and RV systolic pressure (48 ± 14 mmHg). The mean pulmonary artery pressure (PAP) was 36 ± 9 mmHg. Nine patients showed dilatation of the tricuspid annulus (≥35 mm) with moderate tricuspid valve insufficiency and received tricuspid valve annuloplasty. After removal of the ECMO, none of the patients developed RV failure. ECMO was removed 4 ± 1 days after LVAD implantation. Four patients expired while on LVAD support due to not-device-related sepsis (two patients), mesenteric ischemia (one patient), and gastrointestinal bleeding (one patient), respectively. Overall survival was 60%. Conclusion: ECMO provided a satisfactory perioperative right-heart support in patients with preoperative biventricular failure undergoing LVAD implantations, who otherwise were better candidates for biventricular assist device. ECMO allowed time for the already compromised right ventricle to get attuned to the increasing preload, and avoids distension and RV failure.

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1. Introduction

Implantation of a left-ventricular assist device (LVAD) is an established treatment for end-stage heart failure. Right-ventricular dysfunction develops in 20–30% of LVAD recipients [1–6]. Depending on the pre-existing condition of the right ventricle (RV), an LVAD may have a beneficial effect by reducing afterload, or a detrimental effect by increasing preload to an already compromised RV, due to cardiomyopathy, ischemia, arrhythmias, or pulmonary hypertension. Although the incidence of post-LVAD right-ventricular failure has decreased with improved patient selection, it is still a major contributor of post-LVAD morbidity and prolonged length of hospital stay [7,8]. Even when right-ventricular support is not required, patients with severe RV failure may require prolonged inotropes, which interferes with their physical rehabilitation, and persistent elevation of the central venous pressure (CVP) may lead to liver dysfunction and poor resolution for impeding multiple organ failure. Therefore, prediction of potential RV failure after LVAD replacement is essential for optimal device selection and improved clinical outcome.

Clinically, it is well recognized that if pre-existing RV dysfunction is present at the time of LVAD implant, overt postoperative RV failure may occur [9,10]. Several studies have reported preoperative risk factors for the development of right-ventricular failure in patients with implantable LVADs [10–12]. Ochiai et al. concluded that preoperative circulatory support, female gender, and non-ischemic etiology of heart failure were significant predictors of RV failure [10]. Other series have demonstrated low pulmonary artery pressure (PAP) and low RV stroke work index to be significant risk factors [11]. Further, the grade of tricuspid incompetence (TI) and the geometry of the RV in relation to pulmonary vascular resistance (PVR) are most powerful predictors of RV failure after LVAD implantation [13].

RV failure compromises LVAD filling due to poor blood return from the pulmonary bed. Therefore, in addition to impaired
pulmonary perfusion from the failing RV, systemic perfusion is subsequently impaired. This cycle confers significant morbidity and mortality and reiterates the concept that the best treatment of RV failure is its avoidance [2].

This study details one center’s experience with venoarterial ECMO as perioperative RV support in patients with preoperative biventricular dysfunction undergoing LVAD implantation, who otherwise were better candidates for biventricular assist device.

2. Material and methods

2.1. Patients

All 10 patients, who underwent LVAD at our clinic from September 2006 to March 2009, were retrospectively reviewed and enrolled in this study.

Six patients with profound cardiogenic shock secondary to acute heart failure (myocarditis, one patient) and acute or chronic heart failure (known ischemic cardiomyopathy, one patient; known dilatative cardiomyopathy, four patients) were placed onto emergent ECMO for circulatory support before LVAD implantation. After LVAD implantation, ECMO was not removed, and was used as a perioperative right-heart support. The other four patients (known ischemic cardiomyopathy, one patient; known dilatative cardiomyopathy, three patients) were placed onto ECMO support perioperatively after LVAD implantation before weaning from cardiopulmonary bypass (Table 1). Reduced right-ventricular function in preoperative echocardiography was a visual diagnosis, in addition to the measurement of the right-ventricular end-diastolic diameter (RVEDD), systolic right-ventricular pressure (RVP), tricuspid valve insufficiency, and mean PAP. All patients in our study presented an elevated systolic RVP (48 ± 14 mmHg), mean PAP (36 ± 9 mmHg), and RVEDD (38 ± 4 mm), preoperatively. Further, 9 of 10 patients showed moderate-to-severe TI. We defined these findings as a moderate right-ventricular dysfunction (Table 1).

Signs of right-heart failure were defined by the occurrence of two of the following criteria in the first 48 h after ECMO explantation, in the absence of signs of cardiac tamponade, based on a definition prepared by an international working group: mean arterial pressure < 55 mmHg, CVP ≥ 16 mmHg, mixed venous saturation ≤ 55%, and inotropic support.

Table 1. Patient characteristics.

| Age (years) | 53 ± 10 |
| Gender |
| Female |
| Male |
| Etiology |
| Ischemic |
| Nonischemic |
| Myocarditis |
| Cardiac index (l min⁻¹ m⁻²) | 1.9 ± 0.3 |
| Ejection fraction (%) | 20 ± 7 |
| RVEDD (mm) | 38 ± 4 |
| Right ventricular pressure (mmHg) | 48 ± 14 |
| Mean PAP (mmHg) | 36 ± 9 |

2.2. ECMO

The ECMO circuit consisted of a closed, heparin surface-coated circuit of polymethylpenten tubing (Maquet) and either a Biomedicus Biopump (Medtronic) or a Josta-Maquet Rotaflow RF 32 (Josta Medizintechnik, Hirrlingen, Germany), a centrifugal pump that propels blood through a hollow-fiber membrane oxygenator (Quadrox PLS, Maquet). Blood flow was monitored by using a Doppler flow probe placed on the arterial side of the circuit. Veno-arterial ECMO was instituted through peripheral cannulation (common femoral artery and vein) in eight patients and subclavian artery and femoral vein cannulation in two patients. To avoid limb ischemia observed in some early cases 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 was tied on a 20F arterial cannula (Medtronic) to ascertain both central arterial blood flow and distal limb perfusion. Patients were heparinized as early as possible to achieve a partial thromboplastin time (PTT) between 50 and 60 s.

Maintenance of adequate systemic blood flow was monitored by mean arterial pressure, blood lactate concentrations, central or mixed venous oxygen saturation, and urine output. Mean arterial pressure was maintained between 50 and 80 mmHg with vasopressor or vasodilator administration. Maintaining residual left-ventricular ejection was also expected to reduce the risk of intracardiac clot formation. Whenever pulsations disappeared, volume expansion or inotropic support was immediately started until pulsatile systemic blood flow reappeared.

2.3. The device

In all patients, an intracorporeal LVAD was implanted (Heart Mate II, Thoratec Corp., Pleasanton, CA, USA). Left-heart support was achieved by cannulating the apex of the left ventricle and the ascending aorta. In the first 6 h after LVAD implantation, the patients did not receive any anticoagulation. After 6 h without bleeding, we started anticoagulation with heparin (PTT 50–55 s), and we maintained this anticoagulation protocol till ECMO explantation. Long-term anticoagulation consisted of coumarins, together with a platelet aggregation inhibitor at low dosage.

We left the operating room with an LVAD flow between 4 and 5 l min⁻¹ and an ECMO flow between 2.5 and 4 l min⁻¹. The ECMO flow was adjusted to CVP (below 15 mmHg), LVAD flow (higher than 3.5 l min⁻¹), and echocardiography controls. After 24 h, we started weaning from ECMO under echocardiographic controls and careful observation of CVP, LVAD flow, PAP, and liver and renal function, as described previously by Scherer et al. [14]. It is challenging to assess the right-ventricular function under ECMO support; hence, we developed our own weaning protocol. As a second step to prevent RV failure after LVAD implantation, nine patients with tricuspid valve insufficiency and ring dilatation before ECMO implantation received reconstruction of the tricuspid valve by annuloplasty with a flexible band (Cosgrove).

To sort out problems of neurologic damage before LVAD implantation, we reduced the sedative medication. If the
patient showed signs of neurological disorders, we performed a computed tomography.

2.4. Hemodynamic measurements

A preoperative right-heart catheter was used to measure PAP, right atrial pressure (RAP), and cardiac index (CI). A preoperative transthoracic echocardiography was performed to evaluate the degree of TI, RVEDD, and left-ventricular ejection fraction (EF).

2.5. Laboratory data

Serum glutamic–oxaloacetic transaminase (GOT), serum glutamic–pyruvic transaminase (GPT), and creatinine were evaluated before LVAD implantation and after ECMO explantation.

3. Statistical methods

Data are presented as mean ± standard deviation.

4. Results

Patient characteristics, preoperative right-heart catheter data (PAP, RAP, and CI), and preoperative transthoracic echocardiography data (EF and RVEDD) are presented in Table 1.

4.1. Pre-ECMO status — patients with preoperative cardiogenic shock (six patients)

Two patients required ventilator support before ECMO implantation, and four patients were intubated for ECMO implantation. One patient needed dialysis, and one patient was on intra-aortic balloon support. Liver enzymes were elevated in all patients with an average of GOT 206 ± 107 U l⁻¹ and GPT 334 ± 207 U l⁻¹. All patients had elevated creatinine with a mean of 2.1 ± 1 mg dl⁻¹ (Table 2).

4.2. Time of LVAD implantation — patients with preoperative cardiogenic shock on ECMO support (six patients)

During ECMO support, liver function improved. GOT decreased from 206 ± 107 U l⁻¹ at the time of ECMO implantation to 71 ± 33 U l⁻¹ at the time of LVAD implantation. Further, GPT decreased from 334 ± 207 U l⁻¹ to 78 ± 40 U l⁻¹. The creatinine level decreased from 2.1 ± 1 mg dl⁻¹ to 1.2 ± 0.2 mg dl⁻¹ (Table 2). The patient with dialysis showed improvement of the renal function and started to have urine output 1 day after ECMO implantation.

4.3. Time of LVAD implantation — other patients (four patients)

In these patients, the levels of GOT and GPT were 114 ± 103 U l⁻¹ and 133 ± 159 U l⁻¹, respectively. The creatinine level was 1.2 ± 0.2 mg dl⁻¹ (Table 2).

4.4. One day after ECMO explantation (all patients)

One day after ECMO explantation, the liver enzymes and creatinine levels were slightly elevated (Table 2).

4.5. Neurological complications

The patient with myocarditis showed left hemiparesis due to middle cerebral artery infarction confirmed by computed tomography after reduction of sedative medication. The patient had arrived intubated at our institution, and it was not possible to determine whether stroke occurred during hemodynamic crash or was induced by ECMO. Because of the good prognosis in this young patient, we decided to implant the LVAD system. The other patients had no neurological complications.

4.6. Hemostatic complications

Two patients required re-exploration for bleeding after cannulation of the subclavian artery for ECMO implantation, and six patients needed re-exploration for extensive bleeding after LVAD implantation. Three patients, who needed re-exploration for bleeding after LVAD implantation, were previously not on ECMO support. One patient with ECMO, preoperatively, due to cardiogenic shock developed bleeding 4 days after ECMO explantation (arrosion bleeding on diaphragma) and needed re-exploration. Anticoagulation with heparin (PTT 50—55 s) on ECMO does not seem to be the reason for excessive bleeding postoperatively. In the first 6 h after LVAD implantation, the patients did not receive any anticoagulation. After 6 h without bleeding, we started anticoagulation with heparin (PTT 50—55 s). This anticoagulation protocol was maintained till ECMO explantation.

4.7. Infections

One patient developed a Staphylococcus infection on the right shoulder after removal of the subclavian cannula. Despite wound revision and antibiotic therapy, she expired.

| Table 2. Laboratory data. |
|---------------------------|----------------|----------------|----------------|----------------|
|                            | Pre-ECMO       | LVAD-implantation patients with preoperative cardiogenic shock | LVAD-implantation other patients | ECMO-implantation all patients | 1 day after ECMO-implantation all patients |
| Creatinine (mg dl⁻¹)       | 2.2 ± 0.9      | 1.1 ± 0.2      | 1.2 ± 0.3      | 1.8 ± 0.6      | 2 ± 1          |
| GOT (U l⁻¹)                | 206 ± 107      | 102 ± 83       | 114 ± 103      | 69 ± 24        | 70 ± 28        |
| GPT (U l⁻¹)                | 334 ± 207      | 125 ± 120      | 133 ± 159      | 83 ± 62        | 95 ± 94        |
while on LVAD support due to Staphylococcus sepsis. Another patient developed empyema of the right pleural cavity. Despite surgical revision and antibiotic therapy, he expired while on LVAD support due to Staphylococcus sepsis.

4.8. Other complications

Two patients expired while on LVAD support due to mesenteric ischemia and gastrointestinal bleeding, respectively.

4.8.1. ECMO support

The ECMO—LVAD time interval was 8 ± 4 days (range 4–13 days). There were three patients with a duration of 11, 13 and 18 days, respectively. Two patients had an infection (pneumonia), and we implanted the LVAD after reduction of the signs of infection (C-reactive protein (CRP) and leucocytes). The other patient was the one with left hemiparesis. In this case, we needed more time to discuss the case with our neurologist and to take the decision for LVAD implantation. In these three patients, recovery of the liver and kidney function could be seen after 4 days of ECMO support. In the other three patients, the ECMO—LVAD duration was 4, 5, and 6 days. In eight patients, we removed the ECMO 3 days after LVAD implantation. The other two patients underwent ECMO explantation 4 days after LVAD implantation. After removal of the ECMO, there was no right-heart failure. None of the patients needed inotropic support after ECMO explantation.

4.9. Survival rate

All patients could be successfully transferred from ECMO to LVAD and were weaned from the ECMO after LVAD implantation. Four patients expired while on LVAD support due to non-device-related sepsis (two patients), mesenteric ischemia (one patient), and gastrointestinal bleeding (one patient), respectively. Overall survival was 60%.

4.10. Long-term follow-up

Four patients have undergone transplantation of which two patients are alive. One patient died 1 day postoperatively, and the other 5 days postoperatively due to hemorrhagic complications and heart failure. One patient developed cancer, and had to be removed from the waiting list. He is still on LVAD support. The heart function of the patient with stroke recovered during LVAD support, and the system could be successfully removed. Further, the neurological status improved and the patient shows now only a minimal motoric weakness of the left arm and left leg.

5. Discussion

Right-ventricular dysfunction after LVAD implantation is a well-recognized complication but remains ill defined and difficult to predict [6, 15]. Right-ventricular assist device (RVAD) use has declined with the use of pulmonary vasodilators and improved patient selection [16]. However, varying degrees of right-ventricular dysfunction requiring prolonged inotropic support are underestimated in a vast majority, resulting in multiple organ failure and decreased survival [11].

The ability of the RV to supply the left heart and, thus, the LVAD with adequate volume is critically related to intrinsic RV contractility and PVR. Factors that influence right-ventricular dysfunction that worsens after LVAD implantation are unclear but include myocardial stunning, ischemia, arrhythmias, and PVR [15]. PVR is usually elevated in patients with congestive heart failure, and is further increased in the early postoperative period by the effects of cardiopulmonary bypass and blood product administration [17].

Clinically, it is well recognized that if pre-existing right-ventricular dysfunction is present at the time of LVAD implantation, overt postoperative RV failure may occur [9, 10]. Despite the frequency and significance of RV failure in LVAD recipients, few studies have identified predictors of post-LVAD RV failure. More concerning is the lack of consensus among these [10, 11, 18–20]. Dang et al. reported that elevated CVP predicts post-LVAD right-ventricular failure, but no study has corroborated these findings [18]. Similarly, Kormos et al. identified pulmonary edema, fever without infection, and preoperative mental impairment as predictors of RVAD use, but no subsequent study has provided confirmation [20].

The prediction of right-ventricular failure after LVAD implantation remains difficult. Sophisticated echocardiographic indices of right-ventricular dysfunction now exist, but are not yet universally applied to this patient population [21]. Potapov et al. defined the following echocardiographic parameters as predictors for post LVAD right-ventricular dysfunction: TI, RVEDD (cut-off > 35 mm), RV EF (cut-off < 30%), and right atrial dimension (cut-off > 50 mm) [13]. In addition, there are multiple scores for monitoring RV function, but more concerning is the lack of consensus among these [13, 22, 23]. These studies are published in 2008, but we implanted most of our patients (seven patients) in 2006 and 2007. At this time, an internationally agreed-upon definition of right-ventricular dysfunction and failure was not common; hence, we applied our own definition of right-ventricle dysfunction because we had earlier lost some patients after LVAD implantation due to right-ventricular failure.

The ability to predict right-ventricular dysfunction before LVAD implantation based on available laboratory and hemodynamic indicators would be an invaluable aid with which the development or progression of right-ventricular dysfunction with subsequent multiorgan failure could be aborted early. The findings in the study from Kavarana et al. emphasize that no single laboratory or hemodynamic data on its own can reliably predict right-ventricular dysfunction. They found no association of elevated RAP and right-ventricular dysfunction [19].

All patients in our study presented an elevated RVP (48 ± 14 mmHg), mean PAP (36 ± 9 mmHg), and REDD (38 ± 4 mm), preoperatively. Further, 9 of 10 patients showed moderate TI, and received tricuspid valve reconstruction by annuloplasty. We defined these findings as a moderate right-ventricular dysfunction and a risk factor for post-LVAD implantation right-heart failure. Hence, we decided to support the right heart perioperatively with the ECMO system.
Right atrium to pulmonary artery bypass using ECMO circuit or paracorporeal devices is a widely accepted modality. The disadvantage of this technique is the necessary re-operation to remove the right atrial and pulmonary artery cannula with additional risk for wound but also device infections. ECMO offers several advantages: (1) it provides both cardiac and pulmonary support for hypoxic patients, (2) through extrathoracic insertion of the cannulas, it avoids a resternotomy for removal of the cannulas, and (3) it is less costly than other forms of mechanical circulatory support. Despite these advantages, ECMO support has several disadvantages that limit its applicability as long-term support: hemolysis, bleeding, stroke, and limited ability to adequately decompress the left ventricle in poorly functioning hearts [24–26].

Right-heart support after LVAD implant was maintained for 4 days. Weaning from ECMO was done as previously described by our group under echocardiography controls and controls of the CVP and LVAD flow. After removal of the ECMO system, none of the patients showed signs of right-heart failure defined by the occurrence of two of the following criteria in the first 48 h after surgery, in the absence of signs of cardiac tamponade, based on a definition prepared by an international working group: mean arterial pressure ≤ 55 mmHg, CVP ≥ 16 mmHg, mixed venous saturation ≤ 55%, and inotropic support.

6. Limitation

Data collection was not complete in every field, and therefore was not as accurate as in a prospective trial.

7. Conclusion

ECMO provided a satisfactory perioperative right-heart support in patients with preoperative biventricular dysfunction undergoing LVAD implantation, who otherwise were better candidates for biventricular assist device. ECMO allowed time for the already compromised right ventricle to get attuned to the increasing preload, and avoids distension and RV failure leading to poor filling of the LVAD. An internationally agreed-upon definition of right-ventricular dysfunction and failure is necessary. Further, additional studies are needed to establish universal selection criteria for the institution of univentricular and biventricular support.

References

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Appendix A. Conference discussion

Dr T. Mihaljevic (Cleveland, OH, USA): I just have a few questions for you. I think this is a very challenging group of patients, but there are several things that I do not necessarily understand. The majority of your patients were on ECMO before you put an LVAD in — is that right?

Dr Scherer: Yes.

Dr Mihaljevic: And then the preoperative right ventricular pressures, how were they determined if patients were already on ECMO? Was that determination done before the ECMO?

Dr Scherer: It was before ECMO implantation, upon arrival in our clinic.

Dr Mihaljevic: Some patients received an elective LVAD implant, but you decided to insert an ECMO because their right ventricle didn’t look good, although they were never weaned off bypass. My understanding was that the ECMO is inserted even before they were weaned off bypass. Is that correct or am I misunderstanding?

Dr Scherer: We had the signs of right ventricular dysfunction preoperatively, so it was our opinion that these patients were at risk for developing right ventricular problems after LVAD implantation, and we decided to put the patients on ECMO support for right heart support perioperatively.

Dr Mihaljevic: Most of us would try to come off, because in some patients the right heart behaves better after the left heart is unloaded. Do you think that you could have avoided putting an ECMO in these patients had you just given them a chance to come off with the left ventricular assist device working?

Dr Scherer: We tried this for one time in the first patient that we had implanted at our clinic. The patient developed right ventricular failure 3 hours later in the ICU, so we had to put this patient on ECMO support. But it was too late for the patient, he died on ECMO support, and he died because of right heart failure. So we decided to support these patients with preoperative right ventricular dysfunction to avoid right ventricular failure after LVAD implantation.

Dr Mihaljevic: And the last question is: do you use right ventricular stroke index to determine the risk of right ventricular failure after LVAD?

Dr Scherer: Actually no. Because it was a retrospective study, I don’t have all the data so I could not present this data. For this study I only used the right ventricular end-diastolic diameter and echo controls preoperatively on arrival in our clinic.

Dr K. Toda (Osaka, Japan): I understand that some of your patients had an LVAD on the left side and also had peripheral VA-ECMO to prevent right ventricular failure. But I am afraid that if you use peripheral VA-MO with LVAD, LVAD flow will decrease. That may cause thromboembolic events from the LVAD. So how do manage that.

Dr Scherer: We left the operating room at the end of the operation with an LVAD flow between 3 and 4 liters and an ECMO flow between 3 and 4 liters. So 24 hours after operation we started weaning from the ECMO support. We reduced the ECMO flow and we saw that the LVAD flow increased. We didn’t have any thromboembolic complications.