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The Journal of Heart and Lung Transplantation

http://www.jhltonline.org

Impact of extracorporeal life support on outcome in patients with idiopathic pulmonary arterial hypertension awaiting lung transplantation

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KEY WORDS:
idiopathic pulmonary arterial hypertension;
extracorporeal life support;
bridge to transplant

BACKGROUND: Our management of patients with idiopathic pulmonary arterial hypertension (iPAH) awaiting lung transplantation changed in 2006 with the introduction of extracorporeal life support (ECLS) as an option to bridge these patients to transplantation (BTT).

METHODS: To study the effect of this change on waiting list mortality and post-transplant outcome, 21 consecutive iPAH patients listed for lung transplantation between January 2006 and September 2010 (second cohort) were compared with 23 consecutive iPAH patients listed between January 1997 and December 2005 (first cohort).

RESULTS: Between the first and second cohort, the number of patients admitted to the hospital as BTT increased from 4% (1 of 23) to 48% (10 of 21; $p = 0.0009$). Six patients were BTT with ECLS in the second cohort, including 4 with the Novalung device (Novalung GmbH, Hechingen, Germany) connected as a pumpless oxygenating right-to-left shunt between the pulmonary artery and left atrium. While on the waiting list, 5 patients (22%) died in the first cohort and none in the second cohort ($p = 0.03$). Time on the waiting list decreased from 118 ± 85 to 53 ± 40 days between the first and second cohort ($p = 0.004$). After lung transplantation, the 30-day mortality was 16.7% in the first cohort and 9.5% in the second cohort ($p = 0.5$). The postoperative intensive care unit stay increased from 17 ± 13 to 36 ± 30 days between the first and second cohort ($p = 0.02$). The long-term outcome after lung transplantation remained similar between both cohorts.

CONCLUSIONS: Aggressive management with ECLS of iPAH patients awaiting lung transplantation could have a major impact to reduce the waiting list mortality. This may, however, be associated with longer intensive care unit stay after transplant.

J Heart Lung Transplant 2011;30:997–1002

Idiopathic pulmonary arterial hypertension (iPAH) affects predominantly young women, with a mean age of 45 years at diagnosis.[1] Although the survival of patients with iPAH has improved during the past 15 years with the development of specific medical therapy, many patients continue to deteriorate despite maximal therapy, and lung transplantation remains the only therapeutic option for patients with advanced iPAH.[2] Unfortunately, the mortality rate on the waiting list for patients with iPAH is high, between 20% and 30%.[3,4]

The implementation of the lung allocation score (LAS) in the United States significantly reduced the waiting list mortality rate for patients with idiopathic pulmonary fibrosis and cystic fibrosis.[4] According to a recent analysis of the United Network for Organ Sharing (UNOS) data, however, the implementation of the LAS did not affect the waiting list mortality rate for iPAH patients.[4] Approximately 20% of the patients listed for lung transplantation in the United States still die on the waiting list within 1 year after being listed.[4] This is partially because iPAH patients die from

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1053-2498/$ -see front matter
doi:10.1016/j.healun.2011.03.002

right ventricular (RV) failure rather than lung failure, and parameters of RV failure are not currently taken into consideration for calculation of the LAS.[5]

During the past several years, a number of transplant programs have introduced extracorporeal life support (ECLS) devices as part of their armamentarium to bridge patients on the waiting list to lung transplantation (BTT).[6–9] The Novalung interventional lung assist device (Novalung GmbH, Hechingen, Germany) is a low-resistance oxygenator designed for pulsatile blood flow driven by the patient's cardiac output. It was originally designed as a pumpless device connected between the femoral artery and the femoral vein and was used in a variety of clinical situations, such as chest trauma, adult respiratory distress syndrome, pneumonia, and airway obstruction.[10,11]

Novalung was used for the first time as a BTT for patients with hypercapnic respiratory failure by the group in Hannover.[10] We and others have also demonstrated that this low-resistance membrane provides a unique option for patients with pulmonary hypertension by interposing the device between the pulmonary artery (PA) and the left atrium (LA), thereby resulting in an oxygenated right-to-left shunt and reducing RV afterload.[12,13]

In Toronto, our experience with Novalung as a BTT started in 2006. Novalung was used alternatively as a pumpless device between the femoral artery and femoral vein, or was connected with a pump for venovenous (VV) or veno-arterial (VA) extracorporeal membrane oxygenation (ECMO). In patients with PAH, the Novalung was used as a pumpless device connected between the PA and LA whenever it was feasible.[12] The goal of this study was to review the effect of this change in management on the waiting list mortality rate and post-transplant outcome specifically for patients with iPAH.

Material and methods

All iPAH patients listed for lung or heart-lung transplantation in our program between January 1997 and September 2010 were retrospectively reviewed after the University Health Network Research Ethics Board approved the study and waived the need for informed consent. Patients with familial or anorexigen PAH were included in the study. However, the study excluded patients with PAH associated with connective tissue disorders or congenital heart disease because they often present with systemic manifestations of their disease or complex congenital anomalies that preclude the use of ECLS.

In our program, we recommend that iPAH patients be assessed for transplant when intravenous epoprostenol is being considered, with a plan to list them when they deteriorate clinically to New York Heart Association function class III or IV despite optimal medical therapy, including intravenous epoprostenol. In general, we believe that early assessment is crucial for these patients, even if the time of listing is delayed by several years through the use of medical treatment, to ensure that patients understand the implication of the transplant option and to be able to provide rapid listing in the event their clinical course is more precarious than expected. The use of intravenous epoprostenol started in 1997 in our institution.

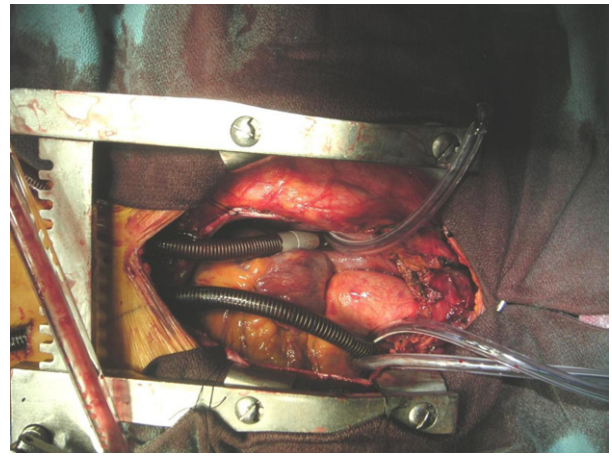

Figure 1 Sternotomy to insert the pumpless pulmonary artery to left atrium Novalung. One cannula is placed in the main pulmonary artery and the second is placed in the left atrium through the right superior pulmonary vein.

The management of our patients on the waiting list changed in 2006 with the introduction of ECLS as a potential BTT option. To analyze the effect of this change on outcome in iPAH patients, we divided the cohort of patients into 2 eras according to the time of listing, from January 1997 to December 2005 and from January 2006 to September 2010. Before 2006, atrial septostomy was the predominant therapeutic option considered for decompensating iPAH patients as a BTT, whereas since 2006, patients have been admitted to the intensive care unit (ICU) for inotropic support and/or intubation and placed on the Novalung in the event these options were not sufficient to stabilize them.

Technique of insertion of PA-LA Novalung

The PA-LA Novalung was always inserted in the operating room (Figure 1). The femoral vein and artery were first dissected and exposed under local anesthesia because of the high risk of hemodynamic collapse with induction of general anesthesia. Patients were then placed on VA-ECMO through the femoral vessels, anesthetized, and intubated. Once stable on VA-ECMO, a sternotomy was performed, a right-angled cannula was placed into the LA through the right superior pulmonary vein, and a straight cannula was placed into the main PA. The pumpless Novalung was connected and VA-ECMO weaned. The sternotomy was closed in a standard fashion, the femoral cannulas were removed, the femoral vessels repaired, and the groin was closed.

Patients were transferred back to the ICU with the pumpless PA-LA Novalung. Heparin was started in the operating room and continued to maintain an activated clotting time of 160 to 200 seconds and/or an unfractionated heparin level of 0.4 to 0.6 U/ml until the transplant. Inotropic drugs were weaned and attempts were made to extubate the patients. The Novalung device was changed when oxygenation and/or blood flow across the membrane decreased due to fibrin deposition. The exchanged was performed at the bedside by briefly clamping the inflow and outflow cannulas.

Lung and heart lung transplantation

Donor retrieval, transplant procedure, and postoperative management have been reviewed in details elsewhere.[14,15] Bilateral lung

Table 1 Patient Characteristics at the Time of Listing

Variable[a]	1998–2005 (n = 23)	2006–2010 (n = 21)	p-value
Age, years	35 ± 15	37 ± 18	0.7
Female sex	18 (78)	14 (67)	0.7
NYHA class	3.1 ± 0.3	3.4 ± 0.6	0.04
6-MWT distance, meters	343 ± 92	293 ± 127	0.1
Right atrial pressure, mm Hg	14 ± 8	11 ± 6	0.2
Cardiac output, liters/min	3.3 ± 0.7	3.7 ± 0.9	0.1
PVR, dynes · sec · cm^{-5}	1173 ± 314	1145 ± 537	0.8
Patients on IV epoprostenol	18 (78)	13 (62)	0.2
Duration of IV epoprostenol, mon	16 ± 17	21 ± 27	0.5
Patients on oral therapy	8 (35)	14 (67)	0.002

IV, intravenous; NYHA, New York Heart Association; PVR, pulmonary vascular resistance.
[a]Data are presented as number (%) or mean ± standard deviation.

transplant was chosen as the preferred option for all iPAH patients, unless there was evidence of severe left ventricular (LV) dysfunction on echocardiogram and/or the presence of technical limitations to conduct a bilateral lung transplant. Bilateral lung transplants were performed through a clamshell incision and heart-lung transplant through a clamshell incision or a sternotomy. Cardiopulmonary bypass (CPB) was used for all transplants. The Novalung cannulas were removed from the PA and LA at the time of transplant. Severe primary graft dysfunction (PGD) was defined according to the International Society for Heart and Lung Transplantation (ISHLT) definition as grade III PGD during the initial 72 hours after transplant.

Statistical analysis

Data are expressed as mean ± standard deviation. The Student's t-test was used to test differences between continuous variables, and the chi-square test was used for categoric variables. Waiting list mortality included all patients who died on the waiting list or were removed from the waiting list due to clinical deterioration. Follow-up was complete for all patients until death or October 2010. Survival was calculated with the Kaplan-Meier method and survival curves were compared using the log-rank test. StatView V software (SAS, Cary, NC) was used for all analyses. Values of $p < 0.05$ were considered significant.

Results

Of 123 iPAH patients referred for lung transplantation since 1997, 44 were listed. The 23 patients who were listed between January 1997 and December 2005 were the first cohort, and the 21 patients listed between January 2006 and September 2010 were the second cohort. The number of patients referred and listed were similar between the first and the second cohort: 23 listed of 69 referrals (33%) vs 21 listed of 54 referrals (39%), respectively; ($p = 0.5$). Almost all patients were treated with intravenous epoprostenol. However, the number of patients treated with oral vasodilative agents significantly increased in the second cohort due to increasing availability of these drugs during the past decade (Table 1).

At the time of transplant, 13 patients (5 in the first cohort and 8 in the second cohort) were not treated with intravenous epoprostenol because of symptoms suggestive of veno-occlusive disease in 8, mild emphysematous changes associated with iPAH in 2, and significant hemoptysis before starting intravenous epoprostenol in 1. An additional 2 patients received transplants because of a large aneurysm of the pulmonary artery of 9.5 cm and 8.3 cm, respectively, and they were not treated with intravenous epoprostenol before their transplant. The first patient was listed for heart-lung transplantation because of progressive enlargement of the aneurysm and the second patient was urgently assessed and listed for heart-lung transplantation because of unrecognized iPAH and the requirement of ECMO to come off CPB after elective repair of the aneurysm.

The number of patients admitted to hospital for BTT increased from 4% in the first cohort to 48% in the second cohort ($p = 0.0009$). In the first cohort, 2 patients were BTT with an atrial septostomy, whereas in the second cohort, 10 patients were in the hospital at the time of transplant to be started on high-flow oxygen, inotropic support, ECLS, or a combination of these options (Table 2).

Of 8 patients admitted to the ICU since 2006, 4 were BTT with PA-LA Novalung, 2 with VA-ECMO, and 2 with inotropic support only (Table 3). Of 4 patients bridged to bilateral lung transplantation using the pumpless Novalung in a PA to LA mode, 3 were weaned from all inotropic support and extubated while waiting for their transplant. PAH therapies were stopped, including intravenous epoprostenol, in all 3 patients. A pericardial hematoma developed in the fourth patient on PA-LA Novalung along the right atrium and the patient remained intubated, on inotrope support, and intravenous epoprostenol until the transplant. PA-LA Novalung was maintained for 9, 21, 30, and 69 days until the transplant (median, 26 days). No complications occurred related to infection, embolic events, stroke, or device dislodgement or malfunction during that period.

Two patients were bridged to heart-lung transplant on VA-ECMO. The first patient had experienced a cardiorespi-

Table 2 Pre-transplant Management

Variable	1998–2005 (n = 23) No. (%)	2006–2010 (n = 21) No. (%)	p-value
In-hospital pre-transplant	1 (4)	10 (48)	0.0009
Atrial septostomy	2 (9)	0	0.2
Extracorporeal life support	0	6 (29)	0.006
PA-LA Novalung	0	4	
VA ECMO	0	2	
Inotropic support	0	5 (25)	0.01
Intubated	0	4 (20)	0.02
Waiting list mortality	5 (22)	0	0.03
Type of transplant			0.05
Bilateral lung	18	17	
Heart-lung	0	4	

ECMO, extracorporal membrane oxygenation; LA, left atrium; PA, pulmonary artery; VA, venoarterial.

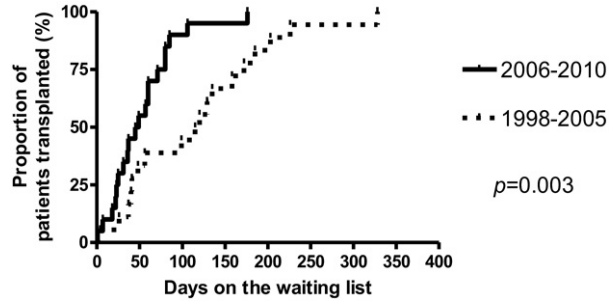

Figure 2 Life-table analysis shows the time between listing and transplant in both eras. The waiting time decreased significantly in the second era.

ratory arrest on arrival in the operating room for insertion of the PA-LA Novalung and was therefore maintained on VA-ECMO. The second had unrecognized iPAH and required VA-ECMO to come off CPB after elective repair of a PA aneurysm. Both of these patients underwent heart-lung transplantation after 1 and 3 days on VA-ECMO, respectively.

After implementation of this aggressive management in 2006, the waiting list mortality rate decreased from 22% in the first cohort to 0% during the second cohort (p = 0.03). Five patients died on the waiting list in the first cohort from consequences of RV failure after 104 ± 164 days on the waiting list. The time between listing and transplant decreased significantly between the 2 cohorts, from 118 ± 83 days in the first cohort to 53 ± 40 days in the second (Figure 2).

Despite aggressive management and the use of ECLS before transplant, the rate of severe PGD and the 30-day mortality rate remained similar between the 2 cohorts (Table 4). However, the post-transplant ICU and hospital lengths of stay increased for the second cohort (Table 4). Severe PGD developed in 9 patients, and 5 of them died within 30 days after transplant: 3 in the first cohort and 2 in the second cohort. The long-term outcome remained similar between the 2 cohorts (Figure 3). Of the 4 patients bridged to bilateral lung transplantation with PA-LA Novalung, 3 are alive and well after 5, 26 and 28 months since the transplant. One patient died postoperatively of severe PGD.

Discussion

This study suggests that an aggressive management strategy for patients with iPAH on the waiting list can decrease the waiting list mortality rate without increasing the postoperative risk for severe PGD or the 30-day mortality rate. We believe that the use of the Novalung between the PA and LA is an excellent option to bridge iPAH patients to lung transplantation because it provides an oxygenated, low-resistance right-to-left shunt and effectively unloads the RV. Patients can be weaned from their inotropic drugs and PAH therapy, extubated, and rehabilitated in the ICU with the Novalung until their transplant.

As our experience and confidence with the PA-LA Novalung increased, our indication for using it as a BTT has evolved. Initially in our experience, we tended to use this option as a very last resort, and consequently, cardiorespiratory arrest occurred in 1 patient on the way to the operating room, and a brief cardiorespiratory arrest occurred in 1 patient while the femoral cannulas were being inserted for VA-ECMO. More recently, considering the favorable expe-

Table 3 Patients Bridged to Lung Transplant With Extracorporeal Life Support

Patient	ECLS mode	ECLS duration (days)	Extubation & rehab	Inotropic support	Type of transplant	Outcome	Follow-up (mon)
1	VA-ECMO	1	No	Yes	Heart-lung	Died, BO	18
2	PA-LA Novalung	21	No	Yes	Bilateral lung	Alive & well	28
3	PA-LA Novalung	30	Yes	No	Bilateral lung	Alive & well	26
4	VA-ECMO	3	No	Yes	Heart-lung	Died, PRES	2
5	PA-LA Novalung	9	Yes	No	Bilateral lung	Alive & well	5
6	PA-LA Novalung	69	Yes	No	Bilateral lobar lung	Died, PGD	0.2

BO, bronchiolitis obliterans; ECLS, extracorporeal life support; ECMO, extracorporeal membrane oxygenation; LA, left atrium; PA, pulmonary artery; PRES, posterior reversible encephalopathy syndrome, PGD, primary graft dysfunction; VA, venoarterial.

Table 4 Early Post-transplant Outcome

Variable	1998–2005 (n = 18)	2006–2010 (n = 21)	p-value
30-day mortality, No.	3	2	0.5
Severe PGD[a], No.	4	5	0.9
LOS (mean ± SD)			
Intensive care unit	17 ± 13	36 ± 30	0.02
Hospital	35 ± 27	66 ± 68	0.08

LOS, length of stay; PGD, primary graft dysfunction; SD, standard deviation.

[a]Defined by PGD III persistent during the initial 72 hours after transplant.

rience that we have had with the PA-LA Novalung, we resort to using this option earlier on in the management of PAH patients if they do not rapidly stabilize on inotropic support after being admitted to the ICU.

The optimal time for iPAH patients to receive a transplant is when the RV starts failing despite optimal medical treatment, but before severe RV failure occurs, therefore leaving a very narrow window of opportunity between the time of listing and the transplant.[16,17] Unfortunately, this narrow window of opportunity results in a high risk of death on the waiting list, with most patients dying from RV failure. The right-to-left shunt provided by the PA-LA Novalung results in oxygenation and unloading of the RV and therefore appears to be an ideal strategy for a safe BTT for these patients once the RV starts failing. The unloaded RV promptly recovers in function, and similarly, the improved hemodynamics results in improved end-organ (eg, renal, hepatic) decompression and perfusion, with preservation of function.

Since 2006, we have used the PA-LA Novalung in 6 patients, 4 patients with iPAH reported in this series and in 2 patients with pulmonary hypertension related to connective tissue disease and sarcoidosis, respectively. This mode of ECLS provides both unloading of the RV and oxygenation of the blood, and resulted in immediate hemodynamic stabilization in all 6 patients. Unloading the RV was associated with major reduction in the RV filling pressure, potentially allowing these patients to be in better condition at the time of their transplant. In theory, diverting pulmonary blood flow could result in some remodeling of the pulmonary vasculature and potentially be associated with reduction of the flow through the Novalung over time. However, considering that the pressure gradient across the Novalung membrane is only 6 mm Hg, a pressure head of only 25 to 30 mm Hg appears sufficient to generate adequate flow through the device.[12] As a consequence, it is not surprising that we did not observe a reduction in flow through the device that could be ascribed to an improvement in pulmonary blood flow with time.

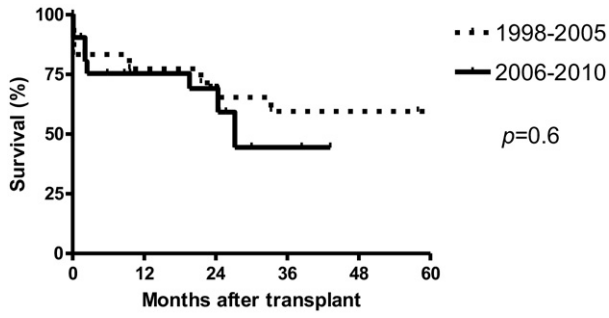

Figure 3 Long-term outcome after lung transplantation is shown for 1998–2005 (dotted line) and 2006–2001 (solid line). The outcome remained similar between both eras.

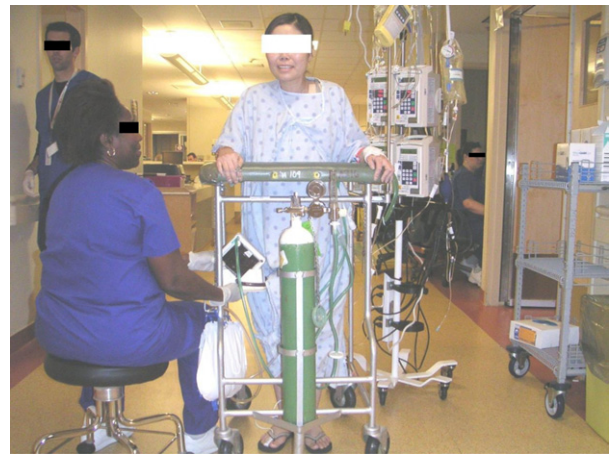

Figure 4 Photograph shows a patient ambulating while being supported in the intensive care unit with the pulmonary artery-to-left atrium Novalung. Permission was granted from the team members to appear in Figure 4.

The PA-LA Novalung and VA-ECMO have been used to bridge iPAH patients to transplant.[12,18] The main disadvantage of the PA-LA Novalung is that a sternotomy is required. The central cannulation, however, offers the advantage of allowing patients to start ambulating once they are extubated while waiting for their transplant (Figure 4). This is a major advantage compared with femoral cannulation and VA-ECMO, which confines patients in bed until the transplant even though they can be awake and spontaneously breathing.[18]

The PA-LA Novalung is also pumpless and can be maintained for several weeks with minimal blood damage and remarkably low morbidity. The Novalung membrane was changed every 2 to 3 weeks and was required on 6 occasions in our experience. These switches were always done at the bedside in the ICU, except for the first case that was performed at the bedside in the operating room. The membrane exchange is performed by briefly clamping and quickly disconnecting and reconnecting the inflow and outflow cannula to change the Novalung device. We did not experience any problem with the switch in any patients (3 patients were and remained extubated at the time of exchange).

Bilateral lung transplantation has been our preferred option for all patients supported by the PA-LA Novalung. The PA and LA cannulas were removed at the time of transplant once CPB had been initiated. The insertion sites were repaired, and the double-lung transplant was completed using our standard technique. Removal of the cannulas added minimal time to the transplant procedure. We always used a

transesophageal echocardiogram to ensure that there was no clot in the LA related to the cannula. Although no clot was seen in the atrium in any patient, we frequently observed a small amount of organized thrombi at the insertion site of the LA cannula in the superior pulmonary vein that was removed at the time of the atrial anastomosis. These fibrin deposits have not been of any clinical significance and have not been associated with any complication.

This study has limitations due to its retrospective nature, the small number of patients, and the potential change in medical management during the course of the study period. However, despite the potential effect of a shorter waiting time, a reduction in the number of patients treated with intravenous epoprostenol, and better general care of PAH patients may have had on the waiting list mortality rate in the recent cohort of patients, we do believe that all patients started on the PA-LA Novalung or VA-ECMO would have died before their transplant if they could not have been stabilized by ECLS. Future studies will be required to confirm if this mode of support, along with changes in the LAS, can help reduce the overall waiting list mortality for iPAH patients.

Disclosure statement

Novalung supported a clinical trial for lung transplant candidates at the Toronto General Hospital.

Dr de Perrot received speaking fees from Actelion. None of the other 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.

Presented as an oral presentation at the Thirtieth Meeting of the International Society for Heart and Lung Transplantation, Chicago, Illinois, April 21–24, 2010.

References

1. Frost AE, Badesch DB, Barst RJ, et al. The changing picture of pulmonary arterial hypertension (PAH) Patients in the United States: how the REVEAL Registry differs from historic and non-US contemporary registries. Chest 2011;139:128-37.
2. Benza RL, Miller DP, Gomberg-Maitland M, et al. Predicting survival in pulmonary arterial hypertension: insights from the Registry to Evaluate Early and Long-Term Pulmonary Arterial Hypertension Disease Management (REVEAL). Circulation 2010;122:164-72.
3. Dandel M, Lehmkuhl HB, Mulahasanovic S, et al. Survival of patients with idiopathic pulmonary arterial hypertension after listing for transplantation: impact of iloprost and bosentan treatment. J Heart Lung Transplant 2007;26:898-906.
4. Chen H, Shiboski SC, Golden JA, et al. Impact of the lung allocation score on lung transplantation for pulmonary arterial hypertension. Am J Respir Crit Care Med 2009;180:468-74.
5. Benza RL, Miller DP, Frost A, Barst RJ, Krichman AM, McGoon MD. Analysis of the lung allocation score estimation of risk of death in patients with pulmonary arterial hypertension using data from the REVEAL Registry. Transplantation 2010;90:298-305.
6. Mangi AA, Mason DP, Yun JJ, Murthy SC, Pettersson GB. Bridge to lung transplantation using short-term ambulatory extracorporeal membrane oxygenation. J Thorac Cardiovasc Surg 2010;140:713-5.
7. Garcia JP, Iacono A, Kon ZN, Griffith BP. Ambulatory extracorporeal membrane oxygenation: a new approach for bridge-to-lung transplantation. J Thorac Cardiovasc Surg 2010;139:e137-9.
8. Fadel E, Mercier O, Mussot S, et al. Long-term outcome of double-lung and heart-lung transplantation for pulmonary hypertension: a comparative retrospective study of 219 patients. Eur J Cardiothorac Surg 2010;38:277-84.
9. Fischer S, Hoeper MM, Tomaszek S, et al. Bridge to lung transplantation with the extracorporeal membrane ventilator Novalung in the veno-venous mode: the initial Hannover experience. ASAIO J 2007; 53:168-70.
10. Hoeper MM, Welte T. Extracorporeal lung assist: more than kicking a dead horse? Eur Respir J 2008;32:1431-2.
11. Fischer S, Simon AR, Welte T, et al. Bridge to lung transplantation with the novel pumpless interventional lung assist device NovaLung. J Thorac Cardiovasc Surg 2006;131:719-23.
12. Strueber M, Hoeper MM, Fischer S, et al. Bridge to thoracic organ transplantation in patients with pulmonary arterial hypertension using a pumpless lung assist device. Am J Transplant 2009;9:853-7.
13. Schmid C, Philipp A, Hilker M, et al. Bridge to lung transplantation through a pulmonary artery to left atrial oxygenator circuit. Ann Thorac Surg 2008;85:1202-5.
14. de Perrot M, Waddell TK, Shargall Y, et al. Impact of donors aged 60 years or more on outcome after lung transplantation: results of an 11-year single-center experience. J Thorac Cardiovasc Surg 2007;133: 525-31.
15. de Perrot M, Chaparro C, McRae K, et al. Twenty-year experience of lung transplantation at a single center: Influence of recipient diagnosis on long-term survival. J Thorac Cardiovasc Surg 2004;127:1493-501.
16. Glanville AR, Estenne M. Indications, patient selection and timing of referral for lung transplantation. Eur Respir J 2003;22:845-52.
17. Orens JB, Estenne M, Arcasoy S, et al; Pulmonary Scientific Council of the International Society for Heart and Lung Transplantation. International guidelines for the selection of lung transplant candidates: 2006 update—a consensus report from the Pulmonary Scientific Council of the International Society for Heart and Lung Transplantation. J Heart Lung Transplant 2006;25:745-55.
18. Olsson KM, Simon A, Strueber M, et al. Extracorporeal membrane oxygenation in nonintubated patients as bridge to lung transplantation. Am J Transplant 2010;10:2173-8.