Comparison of extracorporeal membrane oxygenation versus cardiopulmonary bypass for lung transplantation

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Objective: This study compared differences in patient outcomes and operative parameters for extracorporeal membrane oxygenation (ECMO) versus cardiopulmonary bypass (CPB) in patients undergoing lung transplants.

Methods: Between January 1, 2008, and July 13, 2013, 316 patients underwent lung transplants at our institution, 102 requiring intraoperative mechanical cardiopulmonary support (CPB, $n = 55$; ECMO, $n = 47$). We evaluated survival, blood product transfusions, bleeding complications, graft dysfunction, and rejection.

Results: Intraoperatively, the CPB group required more cell saver volume (1123 ± 701 vs 814 ± 826 mL; $P = .043$), fresh-frozen plasma (3.64 ± 5.0 vs 1.51 ± 3.2 units; $P = .014$), platelets (1.38 ± 1.6 vs 0.43 ± 1.25 units; $P = .001$), and cryoprecipitate (4.89 ± 6.3 vs 0.85 ± 2.8 units; $P < .001$) than the ECMO group. Postoperatively, the CPB group received more platelets (1.09 ± 2.6 vs 0.13 ± 0.39 units; $P = .013$) and was more likely to have bleeding (15 [27.3%] vs 3 [6.4%]; $P = .006$) and reoperation (21 [38.2%] vs 7 [14.9%]; $P = .009$). The CPB group had higher rates of primary graft dysfunction at 24 and 72 hours (41 [74.5%] vs 23 [48.9%]; $P = .008$; and 42 [76.4%] vs 26 [56.5%]; $P = .034$; respectively). There were no differences in 30-day and 1-year survivals.

Conclusions: Relative to CPB, the ECMO group required fewer transfusions and had less bleeding, fewer reoperations, and less primary graft dysfunction. There were no statistically significant survival differences at 30 days or 1 year. (J Thorac Cardiovasc Surg 2014;148:2410-6)

Since the advent of lung transplantation, the use of partial or full cardiopulmonary support has been a necessary component of the operation.¹ As the operative technique has become more streamlined, ventilation strategies have become more efficient, and hemodynamic support options have improved, the use of extracorporeal cardiopulmonary support is no longer ubiquitous in lung transplantation. Program-specific preferences, in addition to patient characteristics such as pulmonary hypertension, intolerance of single-lung ventilation, and right ventricular failure, however, still necessitate the use of cardiopulmonary support.

The use of cardiopulmonary bypass (CPB) has been shown to be a safe method of intraoperative management,^{2,3} but it remains controversial.⁴ CPB has been shown to be at least partly responsible for the development of lung injury and even acute respiratory distress syndrome in patients

undergoing operations other than transplants.⁵ The data on the causality of CPB in primary graft dysfunction (PGD) and recipient outcomes after lung transplants are varied and often confounded,^{6,7} but there is a theoretic risk of CPB inciting a biochemical cascade that could lead to a suboptimal early postoperative course.^{5,6} In addition to the risk of PGD, the use of CPB requires full systemic heparinization, which can lead to more substantial bleeding and use of blood products.⁸

The use of extracorporeal membrane oxygenation (ECMO) for intraoperative cardiopulmonary support has gained traction in recent years. There is growing experience with the preoperative use of ECMO as a bridge to a transplant in patients with refractory respiratory failure.⁹⁻¹² In addition, the use of ECMO in patients with severe PGD and acute rejection after a transplant has been documented with good results.^{13,14} Because of the potential pulmonary complications of CPB and the widespread use of ECMO, several lung transplant centers have begun to use intraoperative ECMO instead of CPB, with mixed results.¹⁵⁻¹⁷ ECMO has potential advantages in that there is no venous reservoir or cardiomyotomy suction, leading to lessened blood-air interface, and it also allows an easy transition to postoperative ECMO for cardiopulmonary support if necessary. Beginning in 2011, our transplant center began incorporating ECMO intraoperatively in lieu of CPB when feasible. In this study, we compare the outcomes of patients who underwent lung transplant requiring cardiopulmonary support between those with ECMO with those with CPB.

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Abbreviations and Acronyms

CPB	= cardiopulmonary bypass
ECMO	= extracorporeal membrane oxygenation
PGD	= primary graft dysfunction

MATERIALS AND METHODS

Patients

We retrospectively reviewed all lung transplants performed at our center between January 1, 2008, and July 13, 2013. During this time, we performed 316 lung transplants; of these, 102 (32.3%) required intraoperative cardiopulmonary support. Of these 102 patients, 47 (46%) received ECMO support (ECMO group) and 55 (54%) received CPB support (CPB group). All but 2 transplants in the ECMO group were performed after March 4, 2011, whereas there were only 10 performed in the CPB group after that date. Among the ECMO group, 22 patients (46.8%) had peripheral venoarterial support, 15 (31.9%) had central ECMO support, 6 (10.6%) had venovenous support, and 3 (4.3%) had a combination of central and peripheral cannulation. Among the CPB group, 52 patients (94.5%) had central CPB support, 2 (3.6%) had a combination of central and peripheral cannulation, and 1 (1.8%) had peripheral cannulation. The records of the 47 ECMO group patients and 55 CPB group patients were retrospectively reviewed. The preoperative, intraoperative, and postoperative data were compared between the 2 groups. Follow-up ended on September 20, 2013, and was 100% complete. This study was approved by the Columbia University institutional review board and performed in accordance with accepted ethical standards.

Operative Techniques

CPB was instituted through cannulation of the ascending aorta and right atrium in most cases. In 2 cases, we used an existing right internal jugular venous ECMO cannula for drainage with aortic cannulation, and in another case we used the common femoral vein and artery for peripheral cannulation. Before aortic cannulation, 300 IU/kg of intravenous heparin was administered to target an activated clotting time greater than 400 seconds. Protamine was given to antagonize heparin on weaning from CPB. The CPB circuit consisted of a Rotaflow pump (MAQUET Cardiovascular, LLC, Wayne, NJ), Sorin Synthesis oxygenator (Sorin Group, Milan, Italy), and Sorin tubing pack.

ECMO has been used routinely during lung transplants at our institution since 2011. The cannulation technique and types were variable. After a heparin bolus of between 3000 and 5000 units, patients were cannulated peripherally, centrally, or a combination.

When performing central or hybrid central and peripheral cannulation for ECMO ($n = 19$; 40.4%), we inserted a femoral venous drainage cannula and an aortic cannula for central support. We prefer this configuration if the patient has a relatively preserved intrinsic cardiac output but a lung function so poor that the carotid and coronary circulation is receiving inadequate oxygenated blood. In a femorofemoral venoarterial ECMO configuration, the retrograde arterial reinfusion does not provide adequate upper body oxygenation for these patients. We then make the decision to cannulate a peripheral artery or aorta according to the absence or presence of a persistently low Pao₂ from the right radial arterial line.

When performing peripheral cannulation, we use the femoral artery and vein except when the patient has an existing upper body ECMO configuration that uses the right internal jugular vein and subclavian artery. We do not routinely sew a beveled graft to the femoral artery except when we anticipate the need for postoperative ECMO or in cases of small vessels at risk for limb ischemia.

The ECMO system consisted of a Rotaflow (Maquet) centrifugal pump, Quadrox i or D (Maquet) membrane oxygenator, and Cobe Pack (Sorin) 3/8-inch tubing system. Intravenous heparin was given at the onset of

cannulation and maintained with a low-dose intravenous infusion during the case. No protamine was given on weaning. If ECMO was continued postoperatively, patients were maintained on a low-dose heparin infusion on arrival to the intensive care unit, with activated partial thromboplastin time maintained between 40 and 60 seconds.

Statistical Analysis

Data are expressed as mean $\pm$ SD or number with percentage. Survival was plotted with Kaplan-Meier curves and compared by the log-rank test. Means were compared with the 2-sample Student t test to determine statistical significance between groups. Categorical data were analyzed by χ^2 tests or, if expectations were too low, Fisher exact tests. Statistical analysis was performed with the SPSS software package (version 21.0; IBM, Armonk, NY).

RESULTS

Preoperative Data

Between January 1, 2008, and July 13, 2013, a total of 316 patients underwent lung transplants. Among these, 102 patients (32.3%) required intraoperative cardiopulmonary support. Of these 102 patients, 47 (46%) received ECMO support and 55 (54%) received CPB support. Baseline patient characteristics were similar between the 2 groups (Table 1).

The underlying pathology leading to the lung transplant was not significantly different between the ECMO and CPB groups. In addition, the degree of patient illness, as measured by the 6-minute walk test, forced vital capacity and forced expiratory volume in 1 second, lung allocation score, and pretransplant pulmonary arterial systolic pressures, was not different between the groups. The ECMO group did have a higher percentage of pretransplant ECMO (10 [21.3%] vs 4 [7.3%]; $P = .04$; Table 1).

Operative Data

In the CPB group, 48 patients (87.3%) a sequential bilateral lung transplant and the remaining 7 (12.7%) received a single-lung transplant. In the ECMO group, 35 patients (72.9%) received a sequential bilateral lung transplant and the remaining 12 (27.1%) received a single-lung transplant. The mean ischemic times were similar between the 2 groups with the first, second, and single-lung ischemic times being 269 ± 81.1 , 351 ± 81.1 , and 335 ± 50.9 minutes, respectively, in the CPB group, and 281 ± 81.2 , 376 ± 81.2 , and 315 ± 68.9 minutes, respectively, in the ECMO group. Total cardiopulmonary support time was not significantly different between the CPB and ECMO groups (196 ± 80.2 vs 209 ± 73.6 minutes; $P = .387$). There was a statistically significant difference in cannulation location between groups, with 52 patients in the CPB group (94.5%) cannulated centrally and 29 patients in the ECMO group (61.7%) cannulated peripherally ($P < .001$; Table 2).

The intraoperative use of blood products was different between the 2 groups. The intraoperative transfusion of packed red blood cell units trended higher in the CPB group

TABLE 1. Baseline characteristics

Variable	CPB (n = 55)	ECMO (n = 47)	P value
Female	28 (50.9%)	22 (46.8%)	.68
Age (y)	46.9 ± 15.9	50.8 ± 14.9	.208
Body mass index (kg/m ²)	23.5 ± 5.5	24.0 ± 4.6	.65
Blood group			.431
A	19 (34.5%)	12 (25%)	
B	8 (14.5%)	12 (25%)	
AB	2 (3.6%)	3 (6.3%)	
O	26 (47.3%)	20 (41.7%)	
6-min walk test (m)	287 ± 156	260 ± 135	.364
Forced vital capacity (% predicted)	42.7 ± 15.3	42.6 ± 15.4	.97
FEV ₁ (% predicted)	36.6 ± 16.9	35.8 ± 18.6	.84
Cytomegalovirus risk			.742
Low	11 (20%)	11 (22.9%)	
Intermediate	24 (43.6%)	17 (35.4%)	
High	20 (36.4%)	19 (39.6%)	
Preoperative hospitalization	16 (29.1%)	16 (34.0%)	.591
Preoperative ICU	11 (20%)	14 (29.8%)	.252
Preoperative vasopressor or inotrope	1 (1.8%)	1 (2.1%)	>.999
Preoperative ECMO	4 (7.3%)	10 (21.3%)	.04
Preoperative mechanical ventilation	4 (7.3%)	6 (12.5%)	.507
Underlying pathology			.723
Cystic fibrosis	11 (20%)	12 (25.5%)	
COPD	7 (12.7%)	3 (6.3%)	
IPF or ILD	21 (38.2%)	19 (39.6%)	
Primary pulmonary hypertension	3 (5.5%)	1 (2.1%)	
Retransplant	4 (7.3%)	2 (4.3%)	
Other	9 (16.4%)	10 (21.3%)	
LAS	61.9 ± 20.0	62.0 ± 22.8	.989
Pretransplant systolic PAP (mm Hg)	54.8 ± 23.4	47.3 ± 22.1	.105

Data are represented as mean ± SD or number with percentage. CPB, Cardiopulmonary bypass; ECMO, extracorporeal membrane oxygenation; FEV₁, forced expiratory volume in 1 second; ICU, intensive care unit; COPD, chronic obstructive pulmonary disease; IPF, idiopathic pulmonary fibrosis; ILD, interstitial lung disease; LAS, lung allocation score; PAP, pulmonary arterial pressure.

relative to the ECMO group (5.24 ± 5.7 vs 3.6 ± 3.2 units; $P = .081$). Intraoperative cell saver use was also higher in the CPB group (1123 ± 701 vs 814 ± 826 mL; $P = .043$). More units of fresh-frozen plasma were transfused in the CPB group during the operation as well (3.64 ± 5.0 vs 1.51 ± 3.2 ; $P = .014$). Platelet transfusion was significantly higher in the CPB group relative to the ECMO group (1.38 ± 1.6 vs 0.43 ± 1.25 6-packs; $P = .001$). In addition, cryoprecipitate was used more frequently in the CPB group than in the ECMO group (4.89 ± 6.3 vs 0.85 ± 2.8 units; $P < .001$). Although the CPB group did require more intraoperative blood products, the estimated blood loss was not significantly different between the CPB and ECMO groups (604 ± 723 vs 634 ± 1004 mL; $P = .862$; Table 2).

TABLE 2. Intraoperative data

Variable	CPB (n = 55)	ECMO (n = 47)	P value
Double lung transplant	48 (87.3%)	35 (72.9%)	.098
Associated cardiac procedure	5 (9.1%)	0 (0%)	.06
First lung ischemic time (min)	269 ± 81.1	281 ± 81.2	.477
Second lung ischemic time (min)	351 ± 81.1	376 ± 81.2	.158
Single lung ischemic time (min)	335 ± 50.9	315 ± 68.9	.521
Bypass time (min)	196 ± 80.2	209 ± 73.6	.387
Cannulation location			<.001
Central	52 (94.5%)	16 (34%)	
Peripheral	1 (1.8%)	29 (61.7%)	
Combined	2 (3.6%)	3 (6.4%)	
Cannulation configuration			<.001
Venovenous	0 (0%)	6 (12.8%)	
Venoarterial	1 (1.8%)	22 (46.8%)	
Venovenousarterial	0 (0%)	1 (2.1%)	
Vena cava/RA-aorta	52 (94.5%)	15 (31.9%)	
Other	2 (3.6%)	3 (6.4%)	
Intraoperative blood products			
PRBCs (units)	5.24 ± 5.7	3.6 ± 3.2	.081
Cell saver (mL)	1123 ± 701	814 ± 826	.043
FFP (units)	3.64 ± 5.0	1.51 ± 3.2	.014
Platelets (6-packs)	1.38 ± 1.6	.43 ± 1.25	.001
Cryoprecipitate (units)	4.89 ± 6.3	.85 ± 2.8	<.001
Estimated blood loss (mL)	604 ± 723	634 ± 1004	.862

Data are represented as mean ± SD or number with percentage. CPB, Cardiopulmonary bypass; ECMO, extracorporeal membrane oxygenation; RA, right atrium; PRBCs, packed red blood cells; FFP, fresh-frozen plasma.

Postoperative Data

Postoperatively, 3 patients in the CPB group (5.5%) and 5 in the ECMO group (10.6%) required continued support ECMO ($P = .465$), and 4 patients in the CPB group (7.3%) and 4 in the ECMO group (8.5%) required reinstitution of ECMO during the intensive care unit stay ($P > .999$). The difference in the use of blood products in the postoperative period was not as statistically significant as during the intraoperative period, although the CPB group still tended to require more transfusions. Packed red blood cell unit transfusion trended higher in the CPB group (4.75 ± 11.9 vs 1.57 ± 2.6 units; $P = .077$). The difference in fresh-frozen plasma unit transfusion nearly reached statistical significance, with the CPB group requiring 3.67 ± 10.1 units versus 0.68 ± 2.4 units in the ECMO group ($P = .051$). Postoperative platelet transfusion, in fact, did reach statistical significance, with the CPB group requiring 1.09 ± 2.6 units versus $0.13 \pm .39$ 6-packs in the ECMO group ($P = .013$).

Postoperative complications, including cerebrovascular accident, initiation of renal replacement therapy, tracheostomy, vascular complications, and cardiopulmonary

TABLE 3. Postoperative outcomes

Variable	CPB (n = 55)	ECMO (n = 47)	P value
Postoperative ECMO	3 (5.5%)	5 (10.6%)	.465
Secondary ECMO	4 (7.3%)	4 (8.5%)	>.999
Postoperative blood products			
PRBCs (units)	4.75 ± 11.9	1.57 ± 2.6	.077
FFP (units)	3.67 ± 10.1	0.68 ± 2.4	.051
Platelets (6-packs)	1.09 ± 2.6	0.13 ± 0.39	.013
Cryoprecipitate (units)	0.82 ± 2.6	0.43 ± 2.9	.478
Complications			
CVA	2 (3.6%)	3 (6.4%)	.66
Hemodialysis	8 (14.5%)	4 (8.5%)	.346
Tracheostomy	18 (32.7%)	10 (21.3%)	.196
Reoperation	21 (38.2%)	7 (14.9%)	.009
Vascular complications	2 (3.6%)	3 (6.4%)	.66
Bleeding	15 (27.3%)	3 (6.4%)	.006
CPR or cardiac arrest	7 (12.7%)	3 (6.4%)	.335
ICU stay (d)	13.0 ± 13.1	10.4 ± 8.4	.25
30-d survival	53 (96.4%)	44 (93.6%)	.66
Rejection	15 (27.3%)	10 (21.3%)	.483
Any PGD at 24 h	41 (74.5%)	23 (48.9%)	.008
PGD grade at 24 h			.067
Grade 0	14 (25.5%)	24 (51.1%)	
Grade 1	16 (29.1%)	9 (19.1%)	
Grade 2	8 (14.5%)	5 (10.6%)	
Grade 3	17 (30.9%)	9 (19.1%)	
Any PGD at 72 h	42 (76.4%)	26 (56.5%)	.034
PGD grade at 72 h			.188
Grade 0	13 (23.6%)	20 (43.5%)	
Grade 1	21 (38.2%)	14 (30.4%)	
Grade 2	7 (12.7%)	5 (10.9%)	
Grade 3	14 (25.5%)	7 (15.2%)	
FEV ₁ (% predicted)	57.0 ± 19.3	52.5 ± 15.2	.22

Data are represented as mean ± SD or number with percentage. CPB, Cardiopulmonary bypass; ECMO, extracorporeal membrane oxygenation; PRBCs, packed red blood cells; FFP, fresh-frozen plasma; CVA, cerebrovascular accident; CPR, cardiopulmonary resuscitation; ICU, intensive care unit; PGD, primary graft dysfunction; FEV₁, forced expiratory volume in 1 second.

resuscitation or cardiac arrest, were similar between the 2 groups. More patients in the CPB group than in the ECMO group had significant postoperative bleeding, defined as reoperation for bleeding or transfusion of more than 6 units of packed red blood cells (15 [27.3%] vs 3 [6.4%]; *P* = .006). In addition, there were more reoperations in the postoperative period in the CPB group than in the ECMO group (21 [38.2%] vs 7 [14.9%]; *P* = .009). According to the International Society for Heart and Lung Transplantation lung transplant injury grades for PGD, the CPB group was more likely to have any PGD at both 24 and 72 hours than was the ECMO group (41 [74.5%] vs 23 [48.9%]; *P* = .008; and 42 [76.4%] vs 26 [56.5%]; *P* = .034; respectively; Table 3). There were no statistically significant differences in 30-day and 1-year survivals between the CPB group and the ECMO group (Figure 1).

FIGURE 1. Kaplan-Meier survival curve out to 1 year. CPB, Cardiopulmonary bypass; ECMO, extracorporeal membrane oxygenation.

DISCUSSION

In current practice, most lung transplants are not performed with intraoperative cardiopulmonary support. At our institution, we have performed 316 transplants in the last 5 years, and only 102 (32.3%) required intraoperative extracorporeal mechanical support. There are many situations in which the use of either CPB or ECMO is unavoidable, however, and these include inability to tolerate single-lung ventilation, right ventricular failure, and pulmonary hypertension. Historically, CPB was the mechanical support system of choice because it had proved successful in cardiac surgery for decades and more recently in lung transplantation as well.^{2,3} The use of an extracorporeal mechanical support system, however, is not without risk. There is concern that the CPB system can incite an inflammatory response that damages end organs and should be avoided in lung transplantation.⁴ There is additional data that CPB can lead to acute lung injury and acute respiratory distress syndrome in patients undergoing operations other than transplants, which would make its utility for lung transplants even more questionable.⁵ Further data, including those from the International Society for Heart and Lung Transplantation working group on lung PGD, have suggested that CPB can be directly linked to worse postoperative outcomes and higher rates of PGD.⁶⁻⁸ To avoid the potential complications of CPB, many groups have begun replacing CPB with intraoperative ECMO when mechanical circulatory support is required. Preliminary data regarding the utility of ECMO relative to CPB is varied. A study by Bittner and colleagues¹⁶ in 2006 suggested that ECMO use led to higher rates of blood product transfusions, as well as worse 1-year survivals.¹⁶ A more recent report from Ius and coworkers¹⁵ in 2012 demonstrated lower blood product transfusion rates and improved survivals at 3, 9, and 12 months in the ECMO group relative to the CPB group.¹⁵

With a recent paradigm shift at our institution from intraoperative CPB to ECMO, we sought to compare intraoperative and postoperative outcomes between the 2 groups. Although we did not demonstrate a statistically significant 1-year survival difference between the 2 groups, there were several clinically meaningful outcomes in favor of the ECMO group. Patients who received intraoperative ECMO required fewer intraoperative and postoperative blood product transfusions. In addition, the ECMO group had fewer instances of postoperative bleeding and required fewer posttransplant reoperations. Patients who received intraoperative CPB were also more likely to have any PGD at both 24 and 72 hours than were those in the ECMO group. We believe that the lower PGD rates in the ECMO group can be explained both by the fewer blood product transfusions and by the relative blood biocompatibility advantage of the ECMO circuit. The ECMO circuit is simpler than the CPB circuit, has less blood-tubing interface surface area, has less blood-air interface, and lacks a cardiomy reservoir, all of which lead to a theoretic decrease in activation of a systemic inflammatory response.

Study Limitations

This study was a single-center, retrospective review. The results also may be confounded by the fact that the transplants performed with CPB were performed mostly in the first 3 years of the study, whereas the transplants performed with ECMO were performed in the final 2.5 years of the study. This should not have significantly affected outcomes, however, because the same 3 surgeons performed all 102 transplants with the same operative techniques during the short 5-year course of the study. The follow-up for the ECMO group, although complete, did not extend to 1 year for 15 patients (31.9%), potentially influencing 1-year survival results. When reviewing all patients at our center, however, there was no statistically significant difference between observed and expected 1-year survivals between the first half of the study and the second half of the study. From January 1, 2008, through June 30, 2010, the 1-year survival was 89.4% (based on 118 transplants), with an observed to expected *P* value of .624. From July 1, 2010 through December 31, 2012, the 1-year survival was 91.4% (based on 144 transplants), with an observed to expected *P* value of .240.^{18,19} Because this comparison was made among all transplant patients, whether they required cardiopulmonary support or not, it suggests that any difference in improved outcome was not related to an improvement in overall survival between the 2 periods.

CONCLUSIONS

Intraoperative use of ECMO for lung transplants was associated with lower transfusion requirements and use of cell saver relative to CPB. Postoperatively, the ECMO group had less bleeding, underwent fewer reoperations,

received less fresh-frozen plasma, and had less PGD. In addition, ECMO confers the benefit of easy conversion to posttransplant extracorporeal cardiopulmonary support if required. There were, however, no statistically significant survival differences between the 2 groups at 30 days and 1 year. ECMO has become our institution's preferred method for intraoperative cardiopulmonary support when required during lung transplantation.

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Discussion

Dr Michael J. Weyant (*Aurora, Colo*). Dr Biscotti, I enjoyed reading the article that you sent me well in advance. You and your coauthors are to be congratulated for exploring these novel ways of supporting our patients through lung transplants, because we all know the incidence of needing to support these patients will probably go up as we continue to do lung transplants.

You suggest from your study that ECMO may be a more beneficial method of supporting these patients through lung transplant, and you suggest the reasons for that are your decreased blood transfusions, the circuit being simpler, and the mechanical injury of the blood cells being less.

I have a few questions, but I thought this study overall was quite novel, and I plan to adopt some of these practices in my own work with lung transplants. The first is that in looking at the patients who had ECMO support in the operating room, were there any conversions from ECMO to standard CPB? If there were, what were the reasons for that?

Dr Biscotti. There were several instances in which we had to convert to CPB, and these were mostly because of difficulty in controlling bleeding where we needed cardiotomy suction. We didn't want to use several rounds of the cell saver, which tends to deplete factors and can create its own set of problems. We generally convert to CPB from ECMO when we encounter extensive bleeding.

Dr Weyant. It's not "several," it's a small number, which I actually don't think you emphasized enough, because the vast majority of patients who went to the operating room didn't have their strategy changed. And so to a critic of the use of ECMO, for example, for this purpose, that would be your defense. And I think when you submit the final article, maybe emphasizing that will be more important.

And the other thing is that about a third of the patients in the ECMO group you are talking about have what you describe as central ECMO cannulation. Now, we all know what central cannulation might be, but can you elaborate more on the actual cannulation strategy for central ECMO versus peripheral ECMO? I'm assuming the difference is most likely the placement of the arterial cannula, but how do you decide where to put it?

Dr Biscotti. We don't typically do it in the same way as the CPB. We often use a femoral venous drainage cannula and then insert an aortic cannula for central support, which can be done through either a clamshell or thoracotomy, which are our preferred surgical approaches to the chest. This is because if the patient has a good intrinsic cardiac output but poor lung function, the carotid and coronary circulation will have inadequate oxygenated blood because retrograde venoarterial ECMO does not provide good upper body perfusion. In those cases that where we have to convert from our typical groin arterial cannulation to our central aortic cannulation, we can maintain the same peripheral drainage. If we have any doubts or notice a severe and persistent drop in PaO₂ from the right radial artery, we will use or convert to a central ECMO cannulation strategy.

Dr Weyant. For my final question, you mentioned your anticoagulation strategy for both your standard CPB and ECMO. For those who are going to institute ECMO more as a way of supporting their patients, you seem to run it a little looser, without monitoring of activated clotting time and so on. What would you suggest for programs that would initiate more ECMO support versus CPB support and the use of activated clotting times and more firm monitoring of the anticoagulation process?

I thought your talk was great and really enjoyed reading your article.

Dr Biscotti. Thank you; I appreciate that. Our intraoperative anticoagulation approach was greatly influenced by our experience with our intensive care unit-managed ECMO patients. We did manage them with activated clotting time during the infancy of the ECMO program; however, after demonstrating that there really was no difference in system failure or cannula issues such as clotting, whether the activated clotting time was measured or we just followed partial thromboplastin times every 6, 12, or 24 hours, we then transitioned to not using activated clotting times, and that is our current intraoperative protocol. Our perfusionists will check an activated clotting time after the initial heparin bolus to confirm that it has increased from baseline, but that is the last clinical use of activated clotting time during the operation. Also, because the ECMO technology, specifically biocompatibility, has improved so much in the last 5 to 10 years, I think that low anticoagulation levels are probably reasonable for a 3- to 6-hour ECMO run.

Dr Daniel L. Miller (*Marietta, Ga*). I had done lung transplants for 20 years and stopped December 31st when I went to my new position, and I can't believe I am asking a lung transplant question. But my question is, I saw about a third of your circulatory support was for an indication of interstitial lung disease and a very small percentage was for primary pulmonary hypertension. Do you have any insight into the patients who had interstitial lung disease? What was the degree of pulmonary artery hypertension, and did that correlate with your outcomes or need for CPB versus ECMO?

Dr Biscotti. Thank you for the question. I know between the 2 groups, at the very least, there was no difference in pulmonary arterial pressures; however, I think that this is something that could be looked at as far as the comparison of our pulmonary artery pressures in these patients versus the ones who don't require mechanical circulatory support. I think generally one of the reasons we make the decision preoperatively that we are going to use bypass or ECMO is because, as you know, the pulmonary arterial pressures are very high, but I don't have a subgroup analysis of just the patients with interstitial lung disease per se.

Dr Miller. From your experience, if you have elevated pulmonary arterial pressures, which would you prefer?

Dr Biscotti. It seems that ECMO does a pretty good job in our hands.

Dr Si Mai Pham (*Baltimore, Md*). I have 2 questions. First, in which patients would you recommend using ECMO versus CPB if you need to use cardiopulmonary support during a lung transplant operation? Second, there was a study from Germany several years ago from Friedrich Mohr's group in which they compared ECMO versus CPB in lung transplant operation, and they abandoned the use of ECMO because the ECMO group had more bleeding and more complications. So I wonder whether you are familiar with that work, and what are differences between your work and theirs?

Dr Biscotti. Thank you for your questions. To answer your second question first, I am not sure whether it's the same as that 2007 study that you were talking about, but I think it could be that they ran their anticoagulation higher; additionally some of the circuitry is different from what we use now. Perhaps the technology wasn't quite there in 2007, or maybe they were using a more complex circuit than ours, which is relatively simple and less thrombogenic. Also, they studied their lung transplant program in its infancy; from what I understand, they had just started their program. So it is not necessarily comparable.

And I think for your first question, why we use ECMO versus CPB or CPB versus ECMO, I know that if we anticipate a lot of bleeding or if we will have to do some intracardiac procedure, such as closing an atrial septal defect, then we would definitely use CPB. But at this point in our institution, we use ECMO unless one of those situations arises.

Dr Michael S. Mulligan (*Seattle, Wash*). What was your incidence of limb complications in your groin access group?

Dr Biscotti. I don't remember the exact number. I know that there was no difference between the groups. We generally don't use distal perfusion cannulas if we don't have to, only if we anticipate that we will have to continue support postoperatively.

Dr Mulligan. What was your incidence of insufficient drainage with groin cannulation? This is a common problem that surgeons will talk about, and in fact it came up in the transplant symposium yesterday that people were concerned about this. Are you seeing this as a problem?

Dr Biscotti. I can't answer that. I don't know the answer to that, but I think it is a reasonable question.

Dr Matthew Bacchetta (*New York, NY*). We actually have not had to insert extra drainage cannulas. We choose cannulas based on the expected need of the patient, which is a function of their remaining native lung function and calculated cardiac output. If we are doing a double-lung transplant, we approach them sequentially and transplant the worst lung first (based on

ventilation/perfusion scan data). This approach generally allows us to flow at partial support levels even for patients with severe pulmonary hypertension. We have found that 60% to 75% of their calculated flow is more than adequate to support them physiologically.

Regarding limb ischemia, we have not had a problem with compromised limbs because we carefully size the femoral vessels preoperatively with an ultrasound. If the required arterial cannula looks close to causing limb ischemia, we cut down onto the artery and sew a graft on it. Then, we cannulate the tunneled graft. This approach eliminates the risk for limb ischemia.

Dr Mulligan. I may have misheard, but it sounds like you had situations where you may have had groin venous cannulation and central aortic cannulation, and if you are already in the chest and you are going to centrally cannulate for a return, paint me a scenario in which you wound up having sort of one purpose for each access.

Dr Bacchetta. If the patient's native lung function is extremely poor and she might not tolerate partial flow with sequential transplant, or if she develops severe hemodynamic instability while I have the chest open, I can cannulate the aorta while my resident cannulates the femoral vein. It saves a small amount of time, but mostly it keeps the venous cannula out of the right atrium, which can be mildly nettlesome when clamping the pulmonary veins/left atrium.

Dr Mulligan. So this is not a planned strategy in which you have something in the groin and something in the chest?

Dr Bacchetta. Sometimes it is part of the plan since I prefer to keep venous cannulas out of the right atrium. I don't like having a dual-stage venous cannula in the atrium because, as I mentioned earlier, it can make clamping the pulmonary veins/left atrium more cumbersome. I usually insert the femoral venous cannula up to the atrial-inferior vena cava junction, which allows for good drainage while keeping it out of the right atrium.