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Central venoarterial extracorporeal membrane oxygenation as a bridge to recovery after pulmonary endarterectomy in patients with decompensated right heart failure

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INTRODUCTION: Patients with chronic thromboembolic pulmonary hypertension (CTEPH) and decompensated right heart failure (DRHF) have worse outcomes after pulmonary endarterectomy (PEA). We reviewed the role of central veno-arterial extracorporeal membrane oxygenation (VA-ECMO) as a bridge to recovery after PEA in these patients.

METHODS: Of 388 consecutive patients undergoing PEA, 40 (10.3%) were admitted with DRHF before PEA. This group was compared to the remaining 348 patients undergoing PEA (elective group). We also compared 2 periods: 2005-2013 (n = 120) and 2014-2019 (n = 268) after which early central VA-ECMO was introduced as a strategy to manage difficulty weaning from cardiopulmonary bypass (CPB).

RESULTS: The proportion of patients with DRHF remained similar between the first and second period (13% vs 9%, p = .2). The number of VA-ECMO bridge to recovery increased from 0.8% in 2005-2013 to 6.3% in 2014-2019 (p = .02). In the second period, 29% of DRHF patients were transitioned intraoperatively from CPB to central VA-ECMO for a median duration of 3 (2-7) days. After the introduction of central VA-ECMO as a bridge to recovery, the hospital mortality in patients with DRHF dropped from 31% in 2005-2013 to 4% in 2014-2019 (p = .03). In the long-term, the functional recovery and survival after discharged from hospital was similar between the DRHF group and the elective group. However, at 5 years, DRHF patients more frequently required PH targeted medical therapy (45% vs 20% in the elective group, p = .002).

CONCLUSIONS: Central VA-ECMO as a bridge to recovery is an important treatment strategy that can decrease hospital mortality in patients with DRHF and lead to excellent long-term outcome.

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Pulmonary endarterectomy (PEA) is an established procedure for patients with chronic thromboembolic pulmonary hypertension (CTEPH) with excellent early and long-term outcomes. Due to the success of PEA, experienced centers are increasingly comfortable treating patients with segmental and subsegmental disease .[1,2] However, CTEPH patients with distal disease and pulmonary vascular resistance (PVR) greater than 1200 Dynes.s.cm^{-5} in the context of decompensated right heart failure (DRHF) are at high risk of postoperative complications due to persistent hemodynamic compromise.[3] CTEPH programs have therefore started developing salvage strategies in order to maintain surgical options for these higher risk patients.

Extracorporeal membrane oxygenation (ECMO) is a well-accepted tool in cardiothoracic surgery to help in the management of lung transplantation, in advanced surgical resections or as a bridge to recovery for patients with acute cardiopulmonary failure.[4−9] Several studies have reported the use of ECMO as a bridge to recovery for complicated PEA patients by using veno-venous (VV) ECMO or veno-arterial (VA) ECMO either centrally or peripherally.[3,9,10,11] Most centers currently report the use of ECMO as a salvage procedure for critical situations in about 5% of all their patients undergoing PEA.[11-13] However, experience in lung transplantation for patients with pulmonary arterial hypertension and DRHF has shown that early VA-ECMO as a bridge to recovery in the immediate post-operative period was potentially beneficial.[14]

We performed our first case of central VA-ECMO bridge to recovery after PEA in 2014 for a CTEPH patient with DRHF. The right ventricle dysfunction improved within the first few days after PEA. This experience led us to consider early central VA-ECMO as a bridge to recovery in patients with hospital admission for DRHF combined with high PVR and segmental or subsegmental disease in the presence of difficulty weaning CPB due to hemodynamic instability or severe hypoxemia despite optimal medical management with nitric oxide (NO). Our objective is to review our experience to define the utility of central VA-ECMO as a bridge to recovery in patients with DRHF undergoing PEA. We therefore compared outcomes before and after introducing this concept in our program.

Materials and methods

All patients undergoing PEA at the Toronto General Hospital between January 2005 and December 2019 were reviewed after approval by our institutional research ethics board (REB 19-5181). Informed written consent was waived. A total of 388 consecutive patients with a CTEPH diagnosis undergoing PEA were identified in the database and divided into two groups: those who presented with a diagnosis of DRHF before PEA (n = 40) and those who did not (n = 348). The DRHF group was defined as patients who required hospital admission for the management of severe fluid overload with signs of low cardiac output such as low blood pressure and tachycardia due to severe right heart failure occasionally associated with secondary dysfunction of other organs such as kidneys and liver. Treatment included intravenous diuretics and oxygen delivered via high flow nasal cannula or face mask as well as inotropic and vasoconstrictor support in the presence of persistent low blood pressure, and circulatory support with femoral VA-ECMO inserted under local anesthesia if necessary. We also defined two periods, 2005-2013 and 2014-2019, corresponding to the implementation of central VA-ECMO as a bridge to recovery after PEA.

All patients referred to the CTEPH program were discussed at our multidisciplinary CTEPH board meeting involving chest radiologists, thoracic surgeons, dedicated pulmonary hypertension physicians and anesthesiologists. All potential PEA candidates underwent a complete work-up with history and physical examination, ventilation-perfusion (VQ) scan, computed tomography pulmonary angiogram (CTPA), echocardiogram, right heart catheterization, 6-minute walk test (6MWT), pulmonary function tests and blood work that included brain natriuretic peptide (BNP). Patients with an established diagnosis of CTEPH were selected for PEA regardless of the severity of the PVR. In particular, out-of-proportion PVR was not considered an exclusion criterion even in the presence of segmental and subsegmental disease as long as the diagnosis was established and the disease accessible for PEA.

PEA was performed through a sternotomy using a standardized technique with deep hypothermic circulatory arrest (DHCA) at 20°C.[1] The type of endarterectomy material was classified according to the Jamieson classification.[1] Since 2014, the possible need for VA-ECMO as a bridge to recovery was systemically discussed prior to surgery in high-risk patients. The decision to start central VA-ECMO as a bridge to recovery was made intra-operatively based on the ability to wean CPB, the hemodynamic parameters and the gas exchange. Central VA-ECMO was instituted in the presence of: (1) Persistent hemodynamic compromise despite high doses of noradrenaline and vasopressin infusion, (2) Worsening hemodynamic parameters in the presence of residual isosystemic pulmonary artery pressures (PAP), (3) Severe hypoxemia despite optimization of mechanical ventilation and use of nitric oxide, or (4) Severe hemoptysis.

Central VA-ECMO was initiated using the same technique for all patients. Briefly, an EOPA (Medtronic) arterial cannula (22 Fr) was used for the aortic cannulation and a straight single stage venous cannula (28 Fr) was used for the venous drainage from the right atrium. Cannulas were secured with 2 purse strings, snugged and tied to the cannulas. We then proceeded to close the skin, keeping the sternum open with both cannulas exiting through the sternotomy. The patients remained fully sedated until decannulation. Postoperatively, invasive arterial lines and Swan-Ganz catheter were monitored to ensure that pulsatile flow was preserved through the lungs with a cardiac index of at least 1-1.5 L/min/m^2. The VA-ECMO flow was typically running at 2.5-3 L/min to maintain pulsatile flow through the lungs with a mean pulmonary artery pressure ranging between 20-25 mmHg. Lactate values were continuously monitored to ensure normalization. Anticoagulation was started 6 to 12 hours after surgery with intravenous unfractionated heparin. ECMO weaning was evaluated after 36-48 hours once lactate normalized, inotropic requirement was reduced and heparin reached therapeutic range using anti-Xa levels of 0.3-0.5. The weaning strategy involved decreasing the ECMO flow to 1-1.5 L/min/m^2 in the intensive care unit with transesophageal echocardiographic monitoring. If the patient remained hemodynamically stable, decannulation was then performed in the operating room and the chest was closed. In case of hypoxemia or hypercapnia, the central VA-ECMO was switched to peripheral VV-ECMO after chest closure to minimize the ventilator pressure requirements and achieve adequate gas exchange to prevent pulmonary reactive vasoconstriction.

Demographics, hemodynamic measurements and long-term outcomes were analyzed and compared between the 2 groups (DRHF vs elective) and for both periods (2005-2013 vs 2014-2019). Data were reported as mean ± standard deviation or as median and range. Categorical variables were compared by χ^2 analysis and continuous variables by Student's *t*-test. Survival was calculated using the Kaplan-Meier method and survival comparison was performed by using the log-rank test. The initiation of PH targeted medical therapy was subject to censoring and calculated accounting for death without PH targeted medical therapy as a competing risk.[15] Hospital mortality was not subject to censoring and comparison was performed as binary variables using χ^2 analysis. Statview (Abacus Concept, Berkeley, CA) was used as the software tool. p-value < .05 was considered significant.

Results

Among a total of 388 consecutive patients undergoing PEA for CTEPH between January 2005 and December 2019, 40 (10.3%) had a recorded admission for DRHF that occurred 30 ± 36 days prior to PEA (DRHF group). The proportion of patients with DRHF remained similar between the first and the second periods (13% in 2005-2013 vs 9% in 2014-2019, p = .2). General demographics such as age, sex, history of deep venous thrombosis (DVT), antiphospholipid syndrome and anticoagulation strategies were not different between patients with or without DRHF (Table 1). Preoperatively, 50% of the patients in the DRHF group were on PH targeted medical therapy in contrast to only 21% in the elective group (p < .0001). The functional status, 6MWT, BNP, and total pulmonary resistance (TPR) were significantly worse in the DRHF group with a majority of patients (72.5%) presenting with TPR>1200 dynes.s.cm^{-5} (Table 1).

No difference was observed in the characteristics of patients with DRHF between the first and the second periods (Supplemental Table 1). The preoperative use of PH targeted medical therapy remained stable over time (55% in 2005-2013 vs 45% in 2014-2019, p = .41). Preoperative PH targeted medical therapy included predominantly phosphodiesterase type 5 inhibitor (PD5-I, n = 44) or soluble guanylate cyclase simulator (SCG, n = 33). Endothelin receptor antagonists (ERA, n = 18) and epoprostenol (n = 7) were used less frequently, and often in combination with PD5-I or SGC (n = 9). PD5-I was most frequently used in patients with DRHF (Table 1).

The duration of DHCA and aortic cross clamp time, the proportion of Jamieson type 3 disease and the proportion of combined cardiac procedures such as coronary aortic bypass graft (CABG) was similar between patients with or without DRHF (Table 2). The duration of CPB was significantly longer in the DRHF group, reflecting the difficulty in weaning CPB in this group of patients. Postoperatively, the duration of intubation, length of ICU stay and hospital stay were significantly longer in the DRHF group compared to the elective group (Table 2).

The hospital mortality for the whole cohort was 3.1% and remained stable between the first and the second period (4.2% in 2005-2013 vs 2.6% in 2014-2019, p = .41). The hospital mortality was significantly higher in the DRHF

Table 1 Demographics and Preoperative Data for all Patients Undergoing PEA 2005-2019.

	Elective PEA (n = 348)	DRHF PEA (n = 40)	p-value
Age (years)	57±14.6	58±15.5	0.6
Sex (female)	173 (49.7%)	24 (60%)	0.21
History of DVT	129 (37.1%)	16 (40%)	0.7
Antiphospholipid syndrome	7 (2%)	1 (2.5%)	0.8
DOAC anticoagulation	122 (35.1%)	12 (30%)	0.8
Preoperative PH targeted medical therapy	73 (20.9%)	20 (50%)	<0.0001
- Soluble guanylate cyclase stimulator (SCG)	34 (9.8%)	3 (7.5%)	0.64
- Phosphodiesterase type 5 inhibitor (PD5-I)	31 (8.9%)	15 (37.5%)	<0.0001
- Endothelin receptor antagonist (ERA)	13 (3.7%)	5 (12.5%)	0.01
- Epoprostenol	2 (0.6%)	5 (12.5%)	<0.0001
- Combination therapy	7 (2%)	3 (7.5%)	0.04
Preoperative balloon pulmonary angioplasty	1 (0.3%)	0	0.7
Functional class NYHA IV	22 (6.3%)	34 (85%)	<0.0001
6MWD (m)	391 ± 129	157 ± 138	<0.0001
BNP (pg/ml)	227 ± 332	834 ± 691	<0.0001
Right heart catheterization (RHC)			
- RAP (mmHg)	9.7±5.4	14.7±6.3	<0.0001
- Mean PAP (mmHg)	42.5 ± 12.8	51.1 ± 10.8	<0.0001
- Cardiac Index: (L/min/m^2)	2.24 ± 0.63	1.53 ± 0.36	<0.0001
- TPR (dynes/sec/cm^{-5})	878 ± 433	1493 ± 612	<0.0001
- TPR >1,200 dynes.s.cm^{-5}	69 (19.8%)	29 (72.5%)	<0.0001
Time RHC-surgery (months)	3±1	1±0.5	<0.0001
Preoperative inotropic/vasopressor support	0	8 (20%)	<0.0001
Preoperative VA-ECMO	0	1 (2.5%)	0.1

Table 2 Surgical Characteristics and Postoperative Outcomes 2005-2019.

	Elective PEA (n = 348)	DRHF PEA (n = 40)	p-value
Cardiopulmonary bypass time (min)	245 ± 36	266 ± 40	0.0006
Aortic cross-clamp time (min)	132 ± 29	136 ± 30	0.4
Total circulatory arrest time (min)	41 ± 14	42 ± 13	0.6
Jamieson type 3	36%	35%	0.9
Combined cardiac procedure	4.9%	2.5%	0.5
Duration of intubation (days)	3.5±4.5	10.6±14.0	<0.0001
ICU LOS (days)	5.8±5.8	13.8±15.0	<0.0001
Hospital LOS (days)	16.6±14.1	35.8±37.5	<0.0001
Hospital mortality	2%	15%	<0.0001

group compared to the elective group (15% vs 2%, respectively; $p < .0001$). The utilization of central VA-ECMO was associated with significant reduction in hospital mortality for patients with DRHF from 31% in 2005-2013 to 4% in 2014-2019 (Figure 1). The benefit of VA-ECMO in DRHF also translated into a reduction in the hospital mortality for patients with TPR >1,200 dynes.s.cm^{-5}, which decreased from 13.2% in 2005-2013 to 1.7% in 2014-2019 ($p = .02$). Among patients with TPR >1,200 dynes.s.cm^{-5} in the second cohort (2014-2019), the use of central VA-ECMO was more frequent in patients with Jamieson type 3 disease compared to type 1 and 2 disease (26.9% vs 5.9%, respectively; $p = .02$).

The overall ECMO utilization rate was 5.2% ($n = 20$) for the whole cohort with 13 central VA-ECMO, 5 peripheral VA-ECMO and 2 VV-ECMO. The rate of VA-ECMO utilization increased from 0.8% ($n = 2$) in 2005-2013 to 6.3% ($n = 18$) in 2014-2019 ($p = .02$).

In the second period (2014-2019), 9 out of 24 DRHF patients (38%) required VA-ECMO. The majority ($n = 7$, 78%) were transitioned intra-operatively to central VA-ECMO for persistent iso-systemic pulmonary artery pressures and worsening hemodynamic parameters after weaning CPB ($n = 3$), residual pulmonary hypertension combined with hemodynamic instability and inability to wean CPB ($n = 2$) and hemodynamic instability associated with severe hypoxemia despite nitric oxide and optimization of ventilatory settings ($n = 2$).

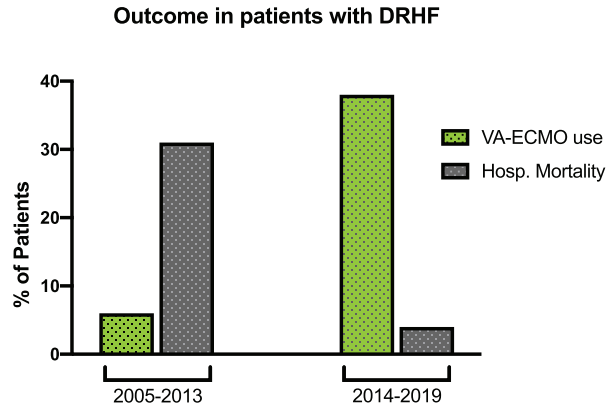

Figure 1 Outcomes in patients with decompensated right heart failure (DRHF) before and after 2014 when central VA-ECMO as a bridge to recovery was implemented.

The remaining 2 patients had salvage peripheral VA-ECMO initiated pre-operatively as a bridge to surgery ($n = 1$) or after PEA on postoperative day 7 ($n = 1$) for hemodynamic instability. Compared to the elective group, patients with DRHF requiring VA-ECMO were more frequently women (100% vs 53%, $p = .01$), had higher preoperative TPR (1870 ± 763 dynes.s.cm^{-5} vs 1282 ± 534 dynes.s.cm^{-5}, respectively; $p = .04$), higher preoperative BNP levels (1100±814 pg/ml vs 542 ± 322 pg/ml, $p = .03$) and a greater proportion of Jamieson type 3 disease (66% vs 36%, $p = .05$).

The duration of central VA-ECMO ranged from 2 to 7 days (median 3 days). Two patients required VV-ECMO after central VA-ECMO decannulation. All patients were decannulated and discharged from hospital (Table 3).

Another 8 patients required VA-ECMO in the absence of preoperative DRHF during the period 2014-2019, using either central VA-ECMO for hemoptysis ($n = 3$), residual pulmonary hypertension with hemodynamic instability ($n = 2$), and left ventricular dysfunction ($n = 1$), or peripheral VA-ECMO for hemodynamic instability on postoperative day 7 and 13 after PEA ($n = 2$) (Table 4). Overall, out of the 13 patients requiring central VA-ECMO, 12 patients were decannulated and discharged from hospital (92%).

At 1 year follow-up, patients in the DRHF group had major improvements in functional class and 6MWD, reaching similar levels as the elective group in functional class (NYHA 1.7 ± 0.8 in the DRHF group vs 1.5 ± 0.7 in the elective group, $p = .2$) and in 6MWD (449 ± 152m in the DRHF group vs 468 ± 129 m in the elective group, $p = .4$). After a median follow-up of 29 months (range, 2-160 months), the proportion of patients requiring PH targeted medical therapy was higher in the DRHF group than the elective group (45% at 5-year vs 20% at 5-year, respectively; $p = .002$), but the long-term survival of patients who survived to hospital discharge was similar between both groups, reaching 84% and 90% at 5-year, respectively (Figure 2). There were no long-term complications related to the use of ECMO.

Discussion

CTEPH patients presenting with DRHF are the most difficult group of patients to manage. However, PEA generally

Table 3 ECMO Support After PEA in Patients With Preoperative DRHF (2014-2019).

ECMO type	Indic.	Sex	Age	Preop TPR (Dyn.s.cm^{-5})	Jamieson type	ECMO Initiation	ECMO (days)	Successful weaning	Discharge (days)
CVA-VV	RVF	F	57	1508	Type 3	Post-CPB	4 + 11	Yes	Yes (105)
CVA	RVF	F	45	2667	Type 3	Post-CPB	3	Yes	Yes (232)
CVA	RVF	F	56	2442	Type 3	Post-CPB	2	Yes	Yes (40)
CVA	RVF	F	71	1309	Type 3	Post-CPB	2	Yes	Yes (179)
CVA-VV	RVF	F	48	1111	Type 1	Post-CPB	4 + 5	Yes	Yes (49)
CVA	RVF	F	60	2982	Type 1	Post-CPB	2	Yes	Yes (36)
PVA	RVF	F	72	1415	Type 1	Pre-PEA	7	Yes	Yes (43)
CVA	RVF	F	79	2462	Type 3	Post-CPB	3	Yes	Yes (39)
PVA	RVF	F	61	933	Type 3	POD 7	7	Yes	Yes (96)

Abbreviations: CVA, central VA-ECMO; PVA, peripheral VA-ECMO; CVA-VV, central VA-ECMO followed by peripheral VV-ECMO; POD, postoperative day; RVF, right ventricle failure; CPB, cardiopulmonary bypass; F, female.

Table 4 ECMO Support After PEA in Patients Without Preoperative DRHF (2014-2019).

ECMO type	Indic.	Sex	Age	Preop TPR (Dyn.s.cm^{-5})	Jamieson type	ECMO Initiation	ECMO (days)	Successful weaning	Discharge (days)
CVA	Hemoptysis	53	F	1675	Type 3	Post-CPB	3	Yes	Yes (33)
CVA	LVF	54	M	696	Type 1	Post-CPB	3	Yes	Yes (30)
CVA	RVF	68	F	1520	Type 3	Post-CPB	2	Yes	Yes (39)
PVA	RVF	57	M	834	Type 3	POD13	7	No	No
CVA	RVF	66	M	1412	Type 1	Post-CPB	2	Yes	Yes (24)
VV-PVA	RVF	48	F	1380	Type 3	POD 6	1+8	Yes	No
CVA	Hemoptysis	33	M	494	Type 2	Post-CPB	1	Yes	Yes (23)
CVA-VV	Hemoptysis	68	F	426	Type 2	Post-CPB	2+11	Yes	No

Abbreviations: CVA, central VA-ECMO; PVA, peripheral VA-ECMO; CVA-VV, central VA-ECMO followed by peripheral VV-ECMO; POD, postoperative day; RVF, right ventricle failure; LVF, left ventricle failure; CPB, cardiopulmonary bypass; F, female.

remains the best treatment option for these patients despite greater risk of complications and higher operative mortality. Options to reduce the surgical risk in these patients have included the use of PH targeted medical therapy before PEA. More recently, considerations was also given for BPA either concomitantly with an hybrid intraoperative approach or postoperatively as a rescue strategy.[16,17] Preoperative BPA may also be a possibility for patients with subsegmental disease in the left lower lobe that may be more difficult to access surgically.

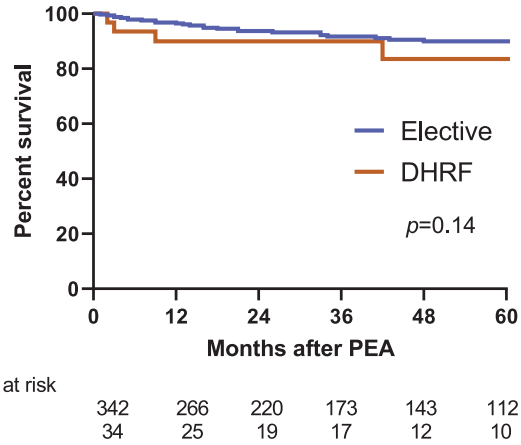

Figure 2 Survival after hospital discharged in patients with decompensated right heart failure (DRHF) and the remaining patients undergoing elective PEA. The survival reached 90% at 1-year and 84% at 5-year in DRHF compared to 96% at 1-year and 89% at 5-year in elective PEA.

In our experience, we observed that the use of central VA-ECMO in patients with hemodynamic instability when coming off CPB may provide important advantages by allowing the right ventricle and the pulmonary vasculature to recover from the prolonged CPB, thus preventing the development of pulmonary edema and worsening of right heart failure. The concept of slow weaning from VA-ECMO has been shown to be beneficial in patients with end-stage pulmonary arterial hypertension undergoing lung transplantation.[14] Currently, there are limited data on the use of central VA-ECMO after PEA and most studies describe small numbers of patients using ECMO as a salvage strategy. Typically, cannulation sites are peripheral, allowing for chest closure and bedside postoperative care. The successful weaning rates range between 50% and 65% and long-term follow-up is rarely reported.[18,19]

The majority of CTEPH patients do not need ECMO bridging to achieve full recovery. However, our experience shows that central VA-ECMO can benefit patients presenting with DRHF and hemodynamic instability with right

ventricular failure coming off CPB. VA-ECMO support was needed in 29% of the patients presenting with DRHF between 2014 and 2019. The need for VA-ECMO was particularly high in the context of DRHF with segmental disease and TPR greater than 1,200 Dynes.s.cm^{-5}. These patients may have some residual pulmonary hypertension immediately postoperatively despite improvement in PVR that may lead to difficulty weaning CPB. We observed that the pulmonary artery pressures continue to improve within the first 12 to 24 hours after PEA if the pulmonary vascular bed and the right ventricle are adequately unloaded. Therefore, post-operative central VA-ECMO with gentle weaning strategies over 48 to 72 hours provided important benefit by allowing the right ventricle to recover from prolonged CPB and allowed time for the pulmonary arterial bed to recover from the PEA.

Central VA-ECMO was preferred over peripheral VA-ECMO for several reasons. First and foremost, the cannulation sites are already established for CPB and thus easy to switch to central VA-ECMO. Second, avoiding peripheral VA-ECMO limits the risk of other potential complications that are typically related to peripheral cannulation such as limb ischemia or Harlequin syndrome. Third, a central approach may provide better control of the pulsatile flow through the lungs. Central VA-ECMO may, in counterpart, be associated with an increased risk of bleeding, but the use of low unfractionated heparin level targets and close monitoring of the coagulation profile in the postoperative course has limited the risk of major bleeding in our experience.

Overall, the use of central VA-ECMO in patients with difficulties coming off CPB allowed us to significantly decrease the mortality in this high-risk group of patients with DRHF undergoing PEA. This also translated in an improvement of the hospital mortality for patients with TPR >1,200 dynes.s.cm^{-5} from 13.2% in 2005-2013 to 1.7% in 2014-2019. More importantly, the benefit gained in the immediate postoperative recovery translated to long-term survival.

The recovery of patients with DRHF takes longer, especially for patients bridged to recovery with central VA-ECMO, leading to prolonged intensive care and hospital length of stay. This observation is explained by the more complicated care needed in the immediate postoperative period and by the degree of deconditioning that these patients experience before surgery. Nevertheless, these patients can achieve excellent recovery after PEA as demonstrated by their improvement at one year after surgery. Both functional class and 6-minute walk distance tests were similar when comparing the DRHF group to the elective group at one year after surgery.

The long-term survival was also excellent in patients who survived the surgery with 5-year survival of 84% in the DRHF group compared to 90% in the remaining patients. Patients with a preoperative diagnosis of DRHF, however, more frequently required PH targeted medical therapy for pulmonary hypertension after surgery, suggesting that their more advanced condition led to residual pulmonary vascular disease. Hence, even though these patients experienced benefit from PEA, their condition does not normalize to the same degree as patients undergoing PEA early in the course of their disease.

All patients requiring VA-ECMO after PEA in the DRHF group were female. The reasons are speculative, but could reflect a higher prevalence of segmental and subsegmental disease in female patients compared to males.[20] The right ventricle is known to be more resilient in female than male and therefore female patients may present at a later stage in the course of their disease.[21] Recent evidence has also shown that endothelial cell proliferation and overgrowth may be linked to the X chromosome, and female patients may thus have more vasculopathy than male and be at greater risk of residual PH after PEA.[22,23]

We recognize several limitations inherent to the retrospective nature of the analysis and the relatively small numbers of patients with DRHF. However, this is a single center comprehensive experience with early and long-term outcomes. Also, although better survival after 2014 could have been biased by better operative techniques or increased experience in the post-operative management of these patients, the use of VA-ECMO provided additional benefit by slowly weaning circulatory support over several days, which was particularly helpful for the sickest patients.

This study demonstrates the potential benefit of central VA-ECMO as a bridging strategy for CTEPH patients encountering difficulty weaning CBP. The risks associated with VA-ECMO, however, have to be kept in mind when deciding whether to use this strategy or not. This option should therefore be limited to patients with high risks of immediate postoperative complications related to right heart failure after coming off CPB.

Author contributions

Each named author has substantially contributed to conducting the underlying research and drafting this manuscript. Etienne Abdelnour Berchtold and Marc de Perrot elaborated the study design and wrote the manuscript. All the remaining authors equally participated in running the program, gathering consents and helping for both data acquisition and the analysis. All authors reviewed and made substantial contributions to the editing.

Disclosure statement

Dr. de Perrot reports personal fees from Bayer, Merck, Roche, AstraZeneca, and Actelion, outside the submitted work. Dr. Granton received unrestricted financial support provided to his institution, from Bayer and Janssen Pharmaceuticals for research in pulmonary hypertension and chronic thromboembolic disease, outside the submitted work. Dr. Thenganatt reports an advisor role from Bayer, Janssen Pharmaceuticals, and Pfizer, outside the submitted work. Dr Moric reports an advisor role from Johnson & Johnson,

outside the submitted work. The other authors report no competitive or financial conflict of interests in this study.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.healun.2022.02.022.

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