Perioperative extracorporeal membrane oxygenation bridging in patients undergoing pulmonary endarterectomy

Patrick Nierlich[a],* and Robin Ristl[b]

[a] Division of Thoracic Surgery, Department of Surgery, Medical University of Vienna, Vienna General Hospital, Vienna, Austria
[b] Department of Medical Statistics, Medical University of Vienna, Vienna General Hospital, Vienna, Austria

* Corresponding author. Division of Thoracic Surgery, Department of Surgery, Vienna General Hospital, Medical University Vienna, Waehringer Guertel 18, 1090 Vienna, Austria. Tel: +43-664-1818007; fax: +43-40-4005644; e-mail: patrick.nierlich@meduniwien.ac.at (P. Nierlich).

Abstract

OBJECTIVES: Chronic thromboembolic pulmonary hypertension is the only curable form of pulmonary arterial hypertension. Pulmonary endarterectomy (PEA) has been established as the treatment of choice in these patients producing very satisfying results. Some patients develop severe cardiorespiratory decompensation before PEA or during weaning from cardiopulmonary bypass. This might be due to acute reperfusion oedema and/or right ventricular failure caused by residual hypertension. Extracorporeal membrane oxygenation (ECMO) support has been established as a bridging therapy in cardiorespiratory failure. At our department, we used peripheral veno-arterial ECMO in patients deteriorating before PEA and in patients where weaning from cardiopulmonary bypass was not possible.

METHODS: We conducted a retrospective analysis of all the patients undergoing PEA who needed pre- and/or postoperative veno-arterial ECMO support. Outcomes including survival, morbidity and haemodynamic improvement were compared between patients surviving and non-surviving after ECMO support. Further, we analysed survival and risk factors of patients requiring ECMO versus patients without ECMO support.

RESULTS: Between January 2001 and March 2013, a total of 161 patients underwent PEA at our institution. Thirty-one patients (19.3%) required support with peripheral veno-arterial ECMO, either both, pre- and postoperatively ($n = 2$), or only postoperatively ($n = 29$). Twenty-eight patients received ECMO directly in the theatre and 1 patient received ECMO at the ICU after successful weaning from cardiopulmonary bypass after PEA. Twenty-eight patients (90.3%) were successfully weaned from ECMO and 20 patients left the hospital alive giving a salvage rate of 64.5%. For those not requiring ECMO support, in-house mortality was 3.1% ($n = 4$). In the 3 patients where weaning from ECMO was not possible, lung transplantation was performed as a rescue therapy. Long-term survival in the patients requiring ECMO who survived was worse than survival in the non-ECMO patient group. The only significant risk factor for the use of ECMO was a pulmonary vascular resistance higher than 1000 dynes cm s^{-5}.

CONCLUSIONS: Pre- and postoperative ECMO bridging in patients undergoing PEA is a feasible option to stabilize patients in a critical pre- and/or postoperative situation and to improve outcome in these patients who would otherwise probably not survive the procedure.

Keywords: Chronic thromboembolic pulmonary hypertension • Pulmonary endarterectomy • Extracorporeal membrane oxygenation • Pulmonary hypertension

INTRODUCTION

Pulmonary endarterectomy (PEA) has been established as the treatment of choice for chronic thromboembolic pulmonary hypertension (CTEPH) with very satisfying haemodynamic results and low postoperative mortality and morbidity if performed in experienced centres [1–3].

If performed successfully, PEA produces right away a decrease in pulmonary vascular resistance leading to improved cardiac output (CO) and gas exchange and immediate recovery of the patient's general condition. Despite the careful selection of surgical candidates by experienced physicians, a small group of patients will suffer from residual pulmonary hypertension. This can remain limited to the postoperative period not only in patients with good surgical results but also permanently in patients with extensive peripheral disease. In the first subgroup, this might be due to local trauma from the operation and cardiopulmonary bypass (CPB) and reperfusion oedema leading to residual pulmonary hypertension causing transient right ventricle failure with cardiorespiratory deterioration. In the latter patient group, this is primarily caused by the presence of distal small vessel vasculopathy which is very difficult to assess preoperatively and is not removable by surgery but contributes notably to the vascular resistance. Together with the already mentioned surgical

trauma and reperfusion oedema, it can lead to acute deterioration of the respiratory and haemodynamic situation. This constellation can make weaning form CPB impossible and may lead to death if not treated aggressively.

Extensive residual pulmonary hypertension is often limited to the immediate postoperative phase but can lead to severe morbidity and postoperative death if not treated effectively. If these patients can be assisted over the postoperative period using veno-arterial (VA) extracorporeal membrane oxygenation (VA-ECMO), they can be stabilized and stepwisely weaned from haemodynamic and respiratory support. In patients without pressure reduction due to distal small vessel vasculopathy, postoperative VA-ECMO can prevent cardiorespiratory failure leading to almost certain postoperative death.

Before the implementation of ECMO, these patients could not be treated and outcome was often lethal. Reports about the use of ECMO after PEA are rare [4–7]. Therefore, we want to present our experience with the use of peripheral VA-ECMO in PEA patients over the last 13 years.

PATIENTS AND METHODS

Patients

Since the introduction of ECMO treatment at our institution in 2000, 161 (62 female/99 male) patients have undergone PEA at our department from January 2001 until March 2013. Among these were 2 patients with angiosarcoma.

Over the last 5 years, an average of 18 patients per year was operated at our centre. All patients selected for PEA were discussed at a multidisciplinary board involving thoracic surgeons, cardiologists and radiologists. Patients were evaluated using ventilation–perfusion scan, computed tomography (CT) of the chest, right and left heart catheterization, angiography of the pulmonary artery system, heart ultrasound and functional tests (6MWD, Lung Function). Patients were considered eligible for the operation when the surgically accessible thromboembolic material could be detected. The correlation between thromboembolic material and pulmonary pressures made a sufficient pressure reduction likely. Comorbidities and resulting risk were evaluated on an individual basis. Extreme forms of haemodynamic disease were no reason to exclude a patient from surgery. All patients received effective treatment with oral warfarin for at least 3 months and were re-evaluated before they were accepted and scheduled for surgery.

The institutional review board of the Medical University Vienna approved this retrospective analysis and has waived requirements for individual patient consent.

Surgical technique

PEA was performed as described by the USCD [8, 9] group via median sternotomy with extracorporeal circulation and intermittent circulatory arrest in deep hypothermia (18°C). Transcranial cerebral oximetry was used for monitoring cerebral function. The operation was always performed bilaterally unless there were clear signs of unilateral disease preoperatively (CT, angiography). An inferior vena cava filter is not routinely placed at our institution. In this particular patient group, an inferior vena cava filter might also obstruct the correct placement of the venous cannula.

Bridging technique

The decision for installation of ECMO was made for each case individually. Deciding factors for initiation of ECMO support in the theatre were as follows: a difference between systemic mean arterial pressure and mean pulmonary arterial pressure less than 20 mmHg, severe partial pressure of oxygen and partial pressure of carbon dioxide derangement, failure of medical therapy to stabilize haemodynamic intravenous catecholamines, dobutamine and inhalative nitric oxide. ECMO bridging was performed using the Medtronic portable bypass system (Medtronic Bio-Console 560, Medtronic, Inc., Minneapolis, MN) with a hollow fibre oyxgenator (Medtronic COMPCB Affinity BPX-80 or Affinity NT, Medtronic, Inc.). For cannulation of the artery, a Bio-Medicus Cannula 15–19 French and for cannulation of the vein a Bio-Medicus Cannula 17–21 French were used. If clinically indicated, an additional limb cannula (8 or 10 French) was implanted. Cannulation was performed using the Seldinger technique. All patients received a combination of broad-spectrum antibiotic prophylaxis and piperacillin/tazobactam. Fungal prophylaxis with either fluconazole or voriconazole was only administered if clinically indicated.

Extracorporeal membrane oxygenation control and weaning from extracorporeal membrane oxygenation

ECMO blood flow was set at approximately 2–3 l/min to allow sufficient blood flow through the heart and lungs and to avoid pulmonary hypertension. The therapeutical goal was to keep mean pulmonary arterial pressures at least 20–30 mmHg below mean systemic arterial pressures. Pulmonary pressures were controlled using a Swan-Ganz Catheter that was usually removed 2–4 days after the operation. For postoperative measurement of pulmonary vascular pressures, a catheter was placed in the left atrium at the end of the operation. If a leg cannula was placed, the blood flow in the leg was supervised by pulse oximetry and hourly clinical controls.

Weaning could normally be started 24 h after the surgery but the decision was always made on an individual basis. For successful weaning from ECMO, the patient needs a negative to even fluid balance, stable haemoglobin values and normal coagulation parameters. Intravenous heparin was administered for the first 24 h to keep the partial thromboplastin time between 60 and 80 s. After stabilization of coagulation parameters, anticoagulative treatment was changed to subcutaneous heparin twice a day.

Under stepwise reduction of circulatory supportive drugs, ECMO flow was gradually reduced below 1 l/min. If haemodynamics and blood gas analysis remained stable, the ECMO was removed at the ICU.

After removal of all chest tubes, central intravenous lines and pacing wires, anticoagulation was switched to oral warfarin therapy with a target international normalized ratio of 2.0–3.0.

Statistical analysis

Perioperative and postoperative data were entered prospectively in our PEA Database. Analysis was performed using the SPSS statistical programme.

Metric variables were described by the mean and standard deviation, categorical variables by absolute and relative frequencies.

The metric baseline values were compared between all groups by analysis of variance for the symmetric distributions and by Kruskal–Wallis test for asymmetric ones. The distribution of categorical variables was compared by χ^2 tests, if the assumptions for this test were not met, by an exact test.

Total survival was analysed by Kaplan–Meier estimations of the survival functions. Survival curves were tested for homogeneity across strata using the log-rank test. Survival was estimated from the date of operation until 30 September 2013 or the date of death. A P-value of <0.05 was considered significant.

RESULTS

In total, 31 patients (19.3%) required pre- and/or postoperative support with VA-ECMO. The mean age was 53.29 years (13–84 years) including 13 female and 18 male patients. In the same time period, 130 (80.7%) patients underwent PEA that did not require ECMO support.

Two patients received VA-ECMO preoperatively and ECMO was continued after PEA. Twenty-eight patients received ECMO due to failed weaning from CPB in the theatre and 1 patient received ECMO at the ICU due to respiratory failure 4 days after the operation.

Of 31 patients, 28 (90.3%) were successfully weaned from ECMO support at the ICU. Average weaning time from ECMO was 3.65 days in the survivor group and 5 days in the non-survivor group.

Twenty-one patients left the hospital alive giving a salvage rate of 67.7%. For those who did not require ECMO support, in-hospital mortality was 3.1% ($n = 4$).

Ten patients died in the hospital after PEA and perioperative ECMO support. Causes for death were multiorgan failure in 4 patients, isolated right ventricular failure in 3 patients, severe stroke in 2 patients and bleeding from the trachea in 1 patient.

The 4 patients that could not be weaned from ECMO support were listed for lung transplantation. All of them underwent lung transplantation (2 double-lung transplantation, 1 single-lung transplantation). Three patients died shortly after transplantation due to multiorgan failure. One patient is alive with good organ function.

There were no significant differences in preoperative baseline parameters, operation times and preoperative and postoperative haemodynamics between ECMO survivors and non-survivors. Postoperative CTEPH classification was no predictor for fatal outcome after the use of ECMO either (see Table 1).

Operating times were significantly longer in the ECMO group: operation time was 8.21 h in the ECMO group versus 5.9 h in the

Table 1: Comparison of pre- and postoperative patient characteristics between survivors versus non-survivors in patients requiring ECMO bridging

Characteristics	ECMO survivors	ECMO non-survivors	P-value
Patient number	20	11	
Female	8 (40%)	5 (45%)	
Male	12 (60%)	6 (55%)	>0.05
Age (years)	51 ± 15.31	57.45 ± 16.54	0.2991
Initial NYHA functional class II	1 (5%)	0 (0%)	
Initial NYHA functional class III	14 (70%)	6 (55%)	
Initial NYHA functional class IV	5 (25%)	5 (45%)	0.6292
Extracorporeal circulation (min)	256.05 ± 92.74	303 ± 55.35	0.0951
Aortic-clamp time (min)	182.8 ± 51.75	187.4 ± 61.99	0.8425
Cardiac arrest (min)	40.6 ± 16.65	35.4 ± 10.81	0.2705 KW
Total operation time (h)	7.97 ± 1.65	8.64 ± 1.07	0.1377 KW
Time on ICU (days)	18.42 ± 10.47	18.2 ± 16.14	0.6457 KW
Ventilation time (days)	12.11 ± 8.29	15.7 ± 16.67	0.7648 KW
Time on ECMO (days)	3.65 ± 2.8	5 ± 2.24	0.1546
Systolic PAP preoperative (mmHg)	89.16 ± 28.63	85.25 ± 24.7	0.7255
Diastolic PAP preoperative (mmHg)	34.79 ± 15.21	33 ± 8.28	0.6981
Mean PAP preoperative (mmHg)	52.95 ± 15.13	51.62 ± 11.01	0.8026
PVR preoperative (dynes s cm^{-5})	870.28 ± 318.73	1052.46 ± 460.83	0.3057
CO preoperative (l/min)	4.4 ± 1.39	3.54 ± 1.26	0.233
CI preoperative (l/min/m^2)	2.25 ± 0.51	2.35 ± 0.71	0.7463
Systolic PAP postoperative (mmHg)	54.18 ± 18.26	56.5 ± 9.19	0.7942
Diastolic PAP postoperative (mmHg)	20.47 ± 6.65	28 ± 4.24	0.1836
Mean PAP postoperative (mmHg)	34.59 ± 10.15	42 ± 5.29	0.1156
PVR postoperative (dynes s·cm^{-5})	388.31 ± 192.81	423.28 ± 7.47	0.496
Cardiac output postoperative (l/min)	5.36 ± 1.72	4.49 ± 1.1	0.3226
Cardiac index postoperative (l/min/m^2)	2.92 ± 1.11	2.38 ± NA	0.6454 aov
CTEPH type I	11 (55%)	4 (36%)	
CTEPH type II	6 (30%)	2 (18%)	
CTEPH type III	2 (10%)	1 (9%)	
CTEPH type IV	1 (5%)	4 (36%)	0.1707

Data are shown as mean ± standard deviation or absolute numbers with percentages. P-values are calculated using the χ^2 (no indication), Kruskal–Wallis (KW) or analysis of variance (aov).
PAP: pulmonary arterial pressure; PVR: pulmonary vascular resistance; CTEPH: chronic thromboembolic pulmonary hypertension; ECMO: extracorporeal membrane oxygenation; NYHA: New York Heart Association.

Table 2: Haemodynamic characteristics of the total patient collective, of the ECMO and non-ECMO group

Characteristics	Total patients (n = 161)	ECMO group (n = 31)	Non-ECMO group (n = 130)	P-value
Pre systolic PAP (mmHg)	84 ± 23.05	88 ± 27.11	82.42 ± 21.78	0.2734 aov
Post systolic PAP (mmHg)	48.54 ± 16.63	54.42 ± 17.37	45.27 ± 15.78	*0.0487 aov*
Mean decrease sys PAP (mmHg)	42.02 ± 28.91	38.47 ± 35.79	43.74 ± 26.02	0.5291 aov
Pre diastolic PAP (mmHg)	29.22 ± 10.24	34.26 ± 13.39	27.45 ± 8.51	*0.0022 aov*
Post diastolic PAP (mmHg)	19.05 ± 6.08	21.26 ± 6.78	17.75 ± 5.34	0.0348 aov
Mean decrease dia PAP (mmHg)	12.53 ± 12.74	13.74 ± 17.1	11.79 ± 10.52	0.5973 aov
Pre mean PAP (mmHg)	49.72 ± 13.05	52.56 ± 13.84	48.83 ± 12.85	0.1868 aov
Post mean PAP (mmHg)	31.72 ± 10.27	35.7 ± 9.85	30.93 ± 10.27	0.0569 aov
Mean decrease mean PAP (mmHg)	17.9 ± 15.5	19.37 ± 19.65	17.49 ± 14.83	0.6313 aov
Pre PVR (dynes/s/cm^{-5})	793.67 ± 359.12	928.84 ± 371.69	757.2 ± 352	*0.0248 aov*
Post PVR (dynes/s/cm^{-5})	302.66 ± 170.95	392.43 ± 180.74	287.71 ± 167.28	*0.0194 aov*
Mean decrease PVR (dynes/s/cm^{-5})	472.54 ± 344.11	472.77 ± 370.56	471.55 ± 344.5	0.9894 aov
Pre cardiac output (l/min)	4.49 ± 1.1	4.2 ± 1.39	4.55 ± 1.03	0.1946 aov
Post cardiac output (l/min)	5.41 ± 1.37	5.21 ± 1.64	5.44 ± 1.34	0.5211 aov
Mean improvement CO (l/min)	0.99 ± 1.31	1.15 ± 1.58	0.97 ± 1.27	0.6174 aov
Pre cardiac index (l/min/m^2)	2.36 ± 0.51	2.28 ± 0.56	2.38 ± 0.5	0.3553 aov
Post cardiac index (l/min/m^2)	2.77 ± 0.81	2.88 ± 1.08	2.75 ± 0.77	0.5628 aov
Mean improvement cardiac index (l/min/m^2)	0.45 ± 0.74	0.69 ± 1.31	0.4 ± 0.58	0.1863 aov

P-values were calculated by using an analysis of variance (aov).
sys PAP: systolic pulmonary arterial pressure; dia PAP: diastolic pulmonary arterial pressure; mean PAP: mean pulmonary arterial pressure; PAP: pulmonary arterial pressure; PVR: pulmonary vascular resistance; ECMO: extracorporeal membrane oxygenation.

non-ECMO group ($P < 0.05$), mean duration of extracorporeal circulation was 271 vs 211 min ($P < 0.05$), aortic-clamp time was 184 vs 141 min ($P < 0.05$) and cardiac arrest 38 vs 34 ($P > 0.05$) min.

Time at the ICU (18.34 days in the ECMO group vs 6.45 days in the non-ECMO; $P < 0.05$) and intubation time (13.34 vs 3.14 days; $P < 0.05$) were also significantly longer than in patients who did not require ECMO support.

PVR was significantly higher in the ECMO group (92 884 vs 757.2 dynes cm s^{-5} in the non-ECMO group; $P < 0.05$). Diastolic PAP (34 vs 27 mmHg) was also significantly higher in the ECMO than in the non-ECMO group. Systolic (88 vs 82 mmHg) and mean PAP (52 vs 48 mmHg) were higher in the ECMO group but these were statistically not significant ($P = 0.27$ and 0.18, respectively). CO and cardiac index were not significantly different.

Postoperative haemodynamic outcome was significantly better in the non-ECMO group than in the ECMO group (see Table 2 and Fig. 1).

Increased morbidity was observed in the ECMO group in comparison with the non-ECMO group. Tracheostomy was performed in 6 patients due to prolonged respiratory weaning. There were no limb complications such as ischaemia or peripheral emboli. Eight patients required continuous haemofiltration. All survivors regained normal kidney function. Lymph fistula occurred in 1 patient at the cannulation site in the groin. Local infection at the cannulation site was not observed. Infection of the sternotomy wound occurred in 1 patient. This was successfully treated by vacuum assisted closure therapy.

DISCUSSION

Despite good surgical results with the removal of large amounts of thromboembolic material, residual pulmonary hypertension remains the main cause of postoperative death after PEA [10]. In some patients suffering from residual postoperative pulmonary hypertension,
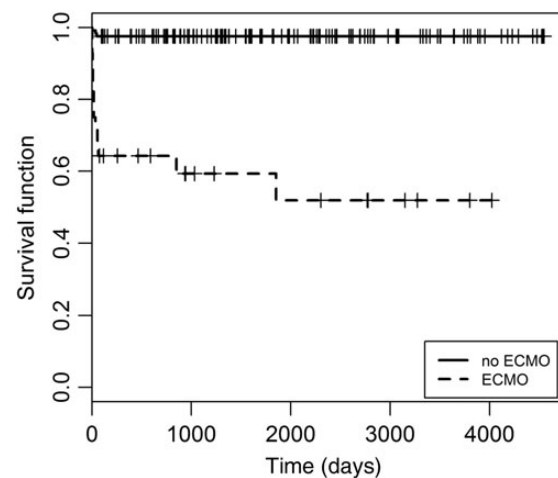

Figure 1: Survival curves of the non-ECMO group (n = 130; continuous line) versus the ECMO group (n = 31; dotted line). Thirty-day survival was significantly lower in the ECMO group (P < 0.05). Long-term survival was also significantly reduced in ECMO survivors. ECMO: extracorporeal membrane oxygenation.

conventional medical and respiratory support is not sufficient to stabilize haemodynamic and respiratory body functions. These patients require full cardiorespiratory support using VA-ECMO to breach the vicious circle of increasing pulmonary vascular resistance, hypoxia, right ventricle failure and as an inevitable consequence multiorgan failure and death. ECMO is an established therapy in respiratory failure [11]. Further, it is successfully used after lung transplantation in patients with graft failure [12, 13] or post-transplant pulmonary hypertension but also as a bridging therapy for deteriorated patients awaiting heart [14] and lung transplantation [15] and as an intra- and postoperative support in lung transplantation [16].

Our case series demonstrates three different therapeutical approaches for the use of peripheral VA-ECMO in patients

suffering from CTEPH: Firstly, bridging to PEA in patients with acute cardiorespiratory failure; secondly, support after PEA if weaning from CPB is not possible; thirdly, support at the ICU in patients with oxygenation problems due to reperfusion injury.

In our series, most patients requiring ECMO support developed persisting pulmonary hypertension with transiently deteriorating cardiopulmonary function immediately after separation from CPB. According to our observations, there are three different types of patients requiring postoperative ECMO support: firstly, patients with centrally located occlusions (CTEPH type I), good surgical result and massive haemodynamic improvement; secondly, patients with centrally located occlusions, good surgical result, but only moderate haemodynamic improvement and thirdly, patients with occlusions located more peripherally (CTEPH type III and IV) and with unsatisfactory surgical and haemodynamic results. In the two latter groups, postoperative deterioration might be mainly caused by the presence of peripheral disease while, in the first group, it is caused by extensive reperfusion oedema. Table 3 gives an outline of this patient collective.

Two patients received VA-ECMO before PEA surgery and were successfully bridged to PEA. Both had extensive bilateral occlusions with severe cardiorespiratory deterioration. One of them received ECMO in another hospital where his haemodynamic situation deteriorated massively and was transferred by helicopter to our clinic and underwent PEA. Intraoperative findings showed angiosarcoma extending in both pulmonary arteries. The operation was successful, the patient could be weaned from ECMO after 7 days and left the hospital in good general condition. Unfortunately, he died 4 months after the operation due to his underlying malignant disease. Another patient, a young woman, was admitted in a very poor general condition. Owing to cardiorespiratory failure on the ward 1 day prior to scheduled surgery, an ECMO was implanted under resuscitation at the ICU. The young woman underwent surgery on the next day with an excellent surgical result. ECMO was removed on the 3rd postoperative day. She had no neurological deficit and left the hospital 2 months after the operation. Six months after the operation, she went on her suspended honeymoon with her husband.

One patient was successfully weaned from CPB after PEA with good surgical result and was transferred in a haemodynamic and respiratory stable condition to the ICU. After 4 days at the ICU, his cardiorespiratory condition worsened probably due to a combination of reperfusion oedema and fluid overload. He was reintubated and put on peripheral VA-ECMO support. Under extracorporeal support, he was stabilized. ECMO could be removed after 4 days.

In the reported case series, different cannulation procedures were reported: while the San Diego group used veno-venous (VV) access [5], the Papworth group [4], the Japanese group [6] and the Istanbul group [7] chose a VA approach either centrally or peripherally. We believe that in the intraoperative situation when weaning from CPB is despite all medical therapies not possible, VA is superior to VV-ECMO support. In this situation, the weaning problem is probably caused by persisting pulmonary hypertension due to operative trauma leading to acute deterioration of the right ventricle. Bypassing the heart allows the right ventricle to recover and adapt to the new haemodynamic situation and gives the opportunity to extract excessive fluids from circulation using aggressive diuresis or, if needed, dialysis. Normally, ECMO support can be withdrawn within a few days. This should be aspired implicitly because we did experience more severe problems in patients with longer periods of ECMO use. VV-ECMO is a good option in patients who suffer only from poor oxygenation

(due to reperfusion oedema) directly after PEA and who have no signs of right ventricular overload. Besides being less invasive, one further advantage of VV-ECMO is that it is also possible to use a single cannula technique. If such a patient's cardiac function should deteriorate on the ICU, it is easy to switch him to VA-ECMO. In the one patient with deteriorating oxygenation 4 days after PEA, we decided against VV-ECMO because of the poor cardiac function verified by heart ultrasound on the ICU and the very poor general condition of the patient (generalized oedema, renal insufficiency).

With regard to the type of VA-ECMO, we prefer a peripheral cannulation strategy. This can be easily done in the operating theatre under stable conditions while still on CPB. The sternotomy can be closed reducing the risk for infections and allowing the heart to recover under regular circumstances. The cannulas can be removed at the ICU. There is no need to transfer the patient back in the operating theatre and put him under deep anaesthesia.

The Papworth group based their choice for the use of a central VA cannulation on a higher complication rate using peripheral VA-ECMO [17]. In our collective, we did not encounter any complications like limb ischaemia or peripheral emboli associated with the use of peripheral ECMO. Stroke with brain death in one patient and pulmonary bleeding in another patient after ECMO removal were the most severe complications that could be linked to the use of ECMO.

Morbidity was significantly higher in the ECMO versus the non-ECMO group which can be explained by the more severe disease and complicated course in patients needing ECMO support. Lymph fistula in the groin occurred in one patient who received ECMO under resuscitation at the ICU before PEA. The lymph fistula could be managed conservatively. Infection of sternotomy wound was observed in one patient in the non-ECMO group. Deterioration of coagulation due to haemolysis and thrombocytolysis has been observed in a few patients. In our experience, this can be a distressing problem in patients with prolonged ECMO therapy and must be managed early and vigorously.

Operation times were longer in the ECMO group than in the non-ECMO group mainly because operations were prolonged by the prolonged weaning procedure and implantation of ECMO.

In our patients, we have used this strategy in a rather high frequency (19.3%). Some might argue that this is disproportionally high in comparison with other centres. The majority of the patients treated with ECMO after PEA were referred to our centre at a very late and advanced stage of their disease with extensive centrally located occlusion, high pulmonary vascular resistance and very poor cardiac function. As mentioned above, most of these patients had centrally located CTEPH (type I and II, $n = 23$, 74.2%) with no clear sign of peripheral disease. So it was not really predictable that the cardiac function of these patients would deteriorate so extremely after a successful operation. All the 14 patients with type I disease had very centrally located occlusion with almost complete obstruction of the pulmonary trunk. From our observations, we can only postulate that massive central obstruction might be a potential predictive factor for ECMO use in the postoperative period. So there were clear signs of thromboembolic material and the indication was verified at surgery. In all the patients classified as type I or II after the operation, large amounts of thromboembolic material were removed from the pulmonary arteries. In most patients, finally (after bridging with VA-ECMO) a very good surgical result with very satisfying improvement of haemodynamics was obtained. In those patients with a good surgical result but only limited reduction of PVR, extensive small vessels might be the main underlying reason. This

Table 3: An overview of the individual characteristics and clinical courses of all 31 patients requiring ECMO support

Pat	Gender	Age	CTEPH type	PVR pre	PVR post	Initial NYHA	Outcome NYHA	Outcome	Causes of death	ECMO (days)	ECMO (time-point)
1	F	49	1	585.9	489.5	3	2	Dead after 5 years	Cardiac failure	2	Post
2	F	22	4	x	x	4	x	Dead after 19 days	RVF	2	Post
3	M	33	4	653.9	373.3	3	2	Alive 11 years		3	Post
4	F	61	1	1273	175	4	1	Alive 11 years after PEA		3	Post
5	M	61	4	914	428.57	4	3	Dead on the 7th po day	RVF	7	Post
6	F	64	2	558	560	3	3	Alive 7 years after PEA		3	Post
7	F	55	1	725	145	3	2	Alive 7 years after PEA		2	Post
8	M	71	1	376.5	x	4	x	Dead on the 20th po day	MOF	6	Post
9	M	41	1	x	370	3	x	Dead 4 months after PEA	Angiosarcoma	7	Pre+post
10	M	75	1	800	350	3	2	Alive 8 years		1	Post
11	M	38	3	1080	920	3	2	Alive 7 years		3	Post
12	F	27	1	1066.7	248	4	2	Dead 16 months	Angiosarcoma	1	Post
13	F	49	4	1755.4	x	3	2	Dead 64 days after OP	Bleeding after TX	4	Post
14	M	65	2	592	320	3	2	Alive 6 years		5	Post
15	M	67	1	x	x	3	x	Dead 4 days after PEA	Bleeding, RVF	3	Post
16	F	64	4	960	x	4	x	Dead 35 days after PEA	Bleeding after TX	8	Post
17	M	62	1	1499	405	4	2	Alive 3 years		3	Post
18	M	77	3	905	x	3	x	Dead 54 days after PEA	MOF	4	Post
19	F	71	2	777	600	3	2	Alive 3 years		3	Post
20	M	44	2	1257	248.65	3	1	Alive 3 years		3	Post
21	M	57	3	764	x	3	1	Alive 2 years		13	Post
22	F	47	1	1364.71	x	3	x	Dead 3 days after PEA	Bleeding	3	Post
23	M	57	1	1500	x	3	x	Dead 3 days after PEA	MOF after TX	3	Post
24	M	53	2	1187.8	392.45	3	2	Alive 2 years		4	Post
25	F	38	2	461.3	433.3	2	2	Alive 1.5 years		1	Post
26	F	74	2	1246.5	x	4	x	Dead 10 days after PEA	Sepsis	8	Post
27	M	69	2	450	418	3	x	Dead 11 days after PEA	Stroke	3	Post
28	M	41	1	656.7	286	3	2	Alive 1 year		4	Post on ICU
29	M	51	1	928	380.4	3	1	Alive 1 year		2	Post
30	F	22	1	1344	380.1	4	1	Alive 10 months		3	Pre+post
31	M	36	1	497	x	4	3	Alive 6 months		9	Post

M: male; F: female; RVF: right heart failure; MOF: multiorgan failure; ECMO: extracorporeal membrane oxygenation; PEA: pulmonary endarterectomy; time-point of ECMO implantation: post: patient received ECMO in OR; pre+post: preoperative bridging with VA-ECMO which was continued after PEA, postoperative ICU: patient was successfully weaned from cardio pulmonary bypass in OR but required ECMO support on ICU; x: values indeterminate; NYHA: New York Heart Association; OR: operating room; TX: transplantation.

might have been caused by the secondary pulmonary arteriopathy with irreversible damage to the obstructed areas. But even for the experienced physician, the detection of peripheral disease remains a very challenging task when central occlusions are present.

There were only a few patients with rather poor surgical results. In these patients, the insufficient clearing of the pulmonary vascular bed due to peripheral disease in combination with the trauma caused by the operation led to complete deterioration of the right ventricular function and made weaning from CPB support impossible. Unfortunately, it is not possible to exclude all patients with peripheral disease even by meticulous preoperative evaluation. Even the largest and most experienced centre in San Diego classified around 8% of their PEA patients as unilateral and around 2% as bilateral type IV disease [2]. It is still very difficult to rule out small vessel disease either in patients with proximal lesions or in patients with only peripheral disease. New imaging techniques to reliably detect peripheral disease are strongly needed.

We did perform lung transplantation in 4 patients immediately after PEA. Three of them were bridged to transplantation using VA-ECMO. All of them died within 2 months after transplantation. In the other case, it was possible to get a suitable organ within a few hours so the patient was bridged with CPB. The patient recovered well from the operation and is now alive with a functioning graft for more than 4 years. Transplantation is a potential option but is connected with increased mortality in these already compromised patients and should therefore only be performed in very fit patients that fulfil general criteria for lung transplantation.

The only risk factor for postoperative use of ECMO we could identify was preoperative PVR. All other parameters were not significant. From our observations, cardiac function and particular right ventricular function might be a critical factor for survival in these patients. Maybe there is a critical limit in right heart dimensions and functions that can predict outcome. The N-terminal prohormone of brain natriuretic peptide (NT-pro BNP or proBNP) is a marker to prognose heart failure. Since 2009, we have routinely assessed proBNP values in CTEPH patients. We have observed that preoperative proBNP levels were significantly higher in patients requiring ECMO. Heart ultrasound using SPECKLE tracking and cardiac MRI are promising new techniques to assess right ventricular function. Longer operation times in patients receiving ECMO and peripheral location of thromboembolic occlusion (CTEPH type IV) were no significant risk factors either. From our observations, we do believe that the combination of very centrally located occlusions and poor right ventricular function predisposes for the need for postoperative ECMO support.

To the best of our knowledge, this is one of the largest series of the perioperative use of peripheral VA-ECMO in patients undergoing

PEA. As shown by Mydin et al. [18] before, we have demonstrated that peripheral VA-ECMO can be successfully used as a bridging in patients with deteriorating function awaiting PEA. The concept of peripheral VA extracorporeal cardiorespiratory support immediately following CPB has been employed at our department for >10 years now. It has proved to be feasible, safe and highly effective in stabilizing patients leading to increased survival in patients who would otherwise die.

Conflict of interest: none declared.

REFERENCES

[1] Jamieson SW, Kapelanski DP, Sakakibara N, Manecke GR, Thistlethwaite PA, Kerr KM et al. Pulmonary endarterectomy: experience and lessons learned in 1,500 cases. Ann Thorac Surg 2003;76:1457–62; discussion 62–4.

[2] Madani MM, Auger WR, Pretorius V, Sakakibara N, Kerr KM, Kim NH et al. Pulmonary endarterectomy: recent changes in a single institution's experience of more than 2,700 patients. Ann Thorac Surg 2012;94:97–103; discussion.

[3] Mayer E, Jenkins D, Lindner J, D'Armini A, Kloek J, Meyns B et al. Surgical management and outcome of patients with chronic thromboembolic pulmonary hypertension: results from an international prospective registry. J Thorac Cardiovasc Surg 2011;141:702–10.

[4] Berman M, Tsui S, Vuylsteke A, Snell A, Colah S, Latimer R et al. Successful extracorporeal membrane oxygenation support after pulmonary thromboendarterectomy. Ann Thorac Surg 2008;86:1261–7.

[5] Thistlethwaite PA, Madani MM, Kemp AD, Hartley M, Auger WR, Jamieson SW. Venovenous extracorporeal life support after pulmonary endarterectomy: indications, techniques, and outcomes. Ann Thorac Surg 2006;82:2139–45.

[6] Ogino H, Ando M, Matsuda H, Minatoya K, Sasaki H, Nakanishi N et al. Japanese single-center experience of surgery for chronic thromboembolic pulmonary hypertension. Ann Thorac Surg 2006;82:630–6.

[7] Yildizeli B, Tas S, Yanartas M, Kaymaz C, Mutlu B, Karakurt S et al. Pulmonary endarterectomy for chronic thrombo-embolic pulmonary hypertension: an institutional experience. Eur J Cardiothorac Surg 2013; 44:e219–27.

[8] Moser KM, Auger WR, Fedullo PF, Jamieson SW. Chronic thromboembolic pulmonary hypertension: clinical picture and surgical treatment. Eur Respir J 1992;5:334–42.

[9] Thistlethwaite PA, Kaneko K, Madani MM, Jamieson SW. Technique and outcomes of pulmonary endarterectomy surgery. Ann Thorac Cardiovasc Surg 2008;14:274–82.

[10] Thistlethwaite PA, Kemp A, Du L, Madani MM, Jamieson SW. Outcomes of pulmonary endarterectomy for treatment of extreme thromboembolic pulmonary hypertension. J Thorac Cardiovasc Surg 2006;131:307–13.

[11] Peek GJ, Mugford M, Tiruvoipati R, Wilson A, Allen E, Thalanany MM et al. Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomised controlled trial. Lancet 2009; 374:1351–63.

[12] Fischer S, Bohn D, Rycus P, Pierre AF, de Perrot M, Waddell TK et al. Extracorporeal membrane oxygenation for primary graft dysfunction after lung transplantation: analysis of the Extracorporeal Life Support Organization (ELSO) registry. J Heart Lung Transplant 2007;26:472–7.

[13] Choquet S, Leblond V, Herbrecht R, Socié G, Stoppa AM, Vandenberghe P et al. Efficacy and safety of rituximab in B-cell post-transplantation lymphoproliferative disorders: results of a prospective multicenter phase 2 study. Blood 2006;107:3053–7.

[14] Almond CS, Singh TP, Gauvreau K, Piercey GE, Fynn-Thompson F, Rycus PT et al. Extracorporeal membrane oxygenation for bridge to heart transplantation among children in the United States: analysis of data from the Organ Procurement and Transplant Network and Extracorporeal Life Support Organization Registry. Circulation 2011; 123:2975–84.

[15] Lang G, Taghavi S, Aigner C, Rényi-Vámos F, Jaksch P, Augustin V et al. Primary lung transplantation after bridge with extracorporeal membrane oxygenation: a plea for a shift in our paradigms for indications. Transplantation 2012;93:729–36.

[16] Aigner C, Wisser W, Taghavi S, Lang G, Jaksch P, Czyzewski D et al. Institutional experience with extracorporeal membrane oxygenation in lung transplantation. Eur J Cardiothorac Surg 2007;31:468–73; discussion 73–4.

[17] Zimpfer D, Heinisch B, Czerny M, Hoelzenbein T, Taghavi S, Wolner E et al. Late vascular complications after extracorporeal membrane oxygenation support. Ann Thorac Surg 2006;81:892–5.

[18] Mydin M, Berman M, Klein A, Tsui S, Dunning J, Valchanov K et al. Extracorporeal membrane oxygenation as a bridge to pulmonary endarterectomy. Ann Thorac Surg 2011;92:e101–3.