Diagnostic and therapeutic options for patients with congenital heart disease have improved over the past decades, and this has lead to a significant decrease in mortality rates. As a result, many patients survive into adulthood with adult congenital heart disease (ACHD). However, many of these patients are not truly “repaired” but are “palliated”, and face long-term effects of residual defects, such as deterioration of prosthetic valves and surgical conduits, dysrhythmia, heart failure, cardiogenic shock and other complications that may require mechanical circulatory support (MCS), further surgical intervention or both. Extracorporeal life support (ECLS) can be viewed as a spectrum of modalities that provide cardiac and respiratory support, which can be used for extended periods, from hours to several weeks. Extra-corporeal membrane oxygenation (ECMO) is a miniaturised modification of cardiopulmonary bypass (CPB) and is among the most frequently used forms of ECLS. It can be configured for venovenous (VV) blood flow, to provide adequate oxygenation and carbon dioxide removal in isolated refractory respiratory failure, or in a venoarterial (VA) configuration, when support is required for cardiac and/or respiratory failure. VA ECMO can also be initiated in urgent settings, including cardiogenic shock and imminent or actual cardiac arrest.

Said and colleagues recently indicated that ECMO may be used in patients with ACHD either in the pre- or postoperative periods. It can be used to optimise the patient’s haemodynamic status, overcome heart failure or treat cardiogenic shock after cardiomyotomy. A wide variety of ACHD diagnoses can result in heart failure requiring MCS. These include the conotruncal anomalies (eg, tetralogy of Fallot and pulmonary atresia) or Ebstein anomaly, that are most commonly associated with right-sided heart failure, or other ACHD lesions, such as atrioventricular septal defects and left-sided obstructed lesions that may be associated with left- or right-sided heart failure. However, strong data on survival of high-risk cardiac operations of patients with ACHD are lacking. We sought to review our institution’s experience with MCS in this patient population.

**ABSTRACT**

**Objective:** Extracorporeal membrane oxygenation (ECMO) can be used as rescue intervention for cardiac and/or respiratory failure. High-risk adult patients with adult congenital heart disease (ACHD) may require pre- and post-operative ECMO support.

**Design, setting and participants:** Retrospective data collection within a five-year time period from 2011 to 2016, at a single-centre study at a tertiary university hospital and regional unit for ACHD. Patients with ACHD in cardiogenic shock or failure to be separated from cardio-pulmonary bypass (CPB) were included.

**Intervention:** Venoarterial (VA) ECMO.

**Results:** Three patients had Ebstein anomaly and one patient had a double-outlet right ventricle transposition type and severe atrioventricular valve insufficiency. Three male patients and one female patient were aged ranging from 19 to 52 years. All received VA ECMO, two each with central or peripheral cannulation. The mean duration of ECMO support was 7 days (range, 3–13 days) and bleeding complications were the main complications observed, with a range of 12 to 104 blood products used. One patient required renal replacement therapy for acute kidney injury and also had leg ischaemia.

**Main outcome measures:** Two of four patients (50%) were successfully weaned off ECMO and survived to hospital discharge in this high-risk group of patients in severe heart failure. The patients are currently at 3 and 4 years follow-up, with improved mobility and exercise tolerance compared with pre-operatively.

**Conclusion:** ECMO is a promising temporary rescue intervention for patients with ACHD and cardiogenic shock. The extracorporeal cardiac support is a useful bridge to recovery.

**Methods**

We reviewed our clinical experience with VA ECMO for patients with ACHD over a 5-year period from 2011 to 2016. The data are safely stored in the hospital’s ACHD database. A retrospective chart review was performed for patients who received ECMO. This was an internal audit and service review that did not require ethics approval, as determined using the...
National Health Service health research authority decision tool (www.hra-decisiontools.org.uk/research).

The Manchester Heart Centre at the Manchester Royal Infirmary houses the regional ACHD unit for northwest England. Numerous patients with a wide range of conditions, from simple to severe ACHD, present at the Centre every year. An average of 100 patients per year require surgical procedures, with fewer than 1% of patients requiring ECMO support (an average of one patient with ACHD requiring ECMO support per year). Our institution is an adult cardiac ECMO centre and a registered member of the Extracorporeal Life Support Organization (ELSO).

VA ECMO care is provided in the 16-bed cardiac surgery intensive care unit (CSICU) (12 Level III and four Level II beds) by our multidisciplinary team of cardiac anaesthetists, surgeons, perfusionists, cardiologists, pharmacists and the nursing staff. Patients with respiratory failure for VV ECMO are usually referred to Wythenshawe Hospital in south Manchester.

The ECMO circuit we used consisted of a Levitronix console (Levitronix), a CentriMag blood pump (Thoratec) with a Hilite 7000 LT oxygenator (Meds) in a Medos tubing pack, a mechanical gas blender (Schrist Industries) and a 3T Heater–Cooler System (Sorin).

Cannulation strategies in ACHD patients included femoral vessels, neck vessels, combined femoral and neck vessels or central cannulation.10 We used a combination of arterial and venous cannulae (EOPA, Medtronic) and long venous cannulae (Edwards Lifesciences). These were introduced either centrally or through the femoral artery and vein, depending on the individual situation and the surgeon’s decision. ECMO flows varied between 3 L/minute and 5 L/minute to adjust blood pressure and to maintain flow through the heart and lungs to avoid clot formation. All patients were treated with heparin as an anticoagulant, according to institutional standard operating procedures to achieve activated clotting times of 160–200 seconds.11 The circuit and console function were frequently checked by perfusionists. The standard monitoring also included a right radial arterial line or right-sided SpO2 measurement to detect potentially reduced blood flow to the right upper body.

Weaning of patients from ECMO depended on cardiovascular recovery. Patients were weaned off inotropes and vaspressors with increasing blood pressure and echocardiographic examination to visualise cardiac contractility and recovery. Flows were reduced to 1.5 L/min while maintaining adequate blood pressure, and were eventually circulated through the “bridge” to investigate if the patient could maintain their haemodynamic status without ECMO support, before ECMO was explanted.

We initially performed our literature search in PubMed by using the keywords “extracorporeal membrane oxygenation”, “ECMO”, “adult congenital heart disease” and “ACHD”. Based on the findings of our case series on patients with Ebstein anomaly, we extended our search to include the search term “Ebstein’s”. We screened the resulting literature, and publications that met our search criteria were included in our discussion.

Results

We identified four patients with ACHD who required ECMO support. The patient demographics are summarised in Table 1.

Patient 1

Patient 1 presented with severe Ebstein anomaly and atrial septal defect (ASD). He underwent a Da Silva-type repair of his Ebstein anomaly, received a bidirectional Glenn shunt and underwent partial closure of his secundum ASD. The patient had had no previous surgical procedure but was deeply cyanotic (oxygen saturation, 74%) and erythrocytotic (haemoglobin level, 24.5 g/dL). He had moderate-to-severe right ventricle (RV) dysfunction, small pulmonary arteries, a small aorta and a small left ventricle (LV). Pre-operatively, he was in New York Heart Association (NYHA) class III–IV. After two runs on CPB for a total of 198 minutes, the patient was vasoplegic and could not be weaned off CPB. Stress-dose hydrocortisone (200 mg) and high doses of norepinephrine were administered. VA ECMO was initiated using peripheral cannulation, because the chest could be closed without compromising the right heart, and the patient was transferred to the CSICU, where he remained on VA ECMO for 6 days for cardiovascular recovery. During that time, the patient required massive blood transfusion (Table 1). After the ECMO intervention, a clot in the right atrium was diagnosed and treated with warfarin. The patient remained on prolonged mechanical ventilation because he had pneumonia (due to Escherichia coli), treated with meropenem for 12 days. After a total of 35 days in the CSICU, the patient was discharged on Day 37 with normal neurological function.

The patient had a very favourable outcome, with frequent follow-up appointments, and he continued to improved. Currently (4 years later), the patient is doing well, is in NYHA Class I, regularly exercises in a gym and can manage to walk about one mile a day.

Patient 2

Patient 2 presented with a complex double-outlet RV of transposition type. He had previously been palliated with a pulmonary artery band. He underwent a debanding procedure, bidirectional Glenn shunt, atrial septectomy, then a completion of lateral tunnel fenestrated Fontan procedure, with repair of tricuspid valve (TV) and insertion...
of a pacemaker. He then presented with severe recurrence of TV regurgitation and significantly reduced ejection fraction (at 40%) with NYHA Class II–III symptoms. The patient was scheduled for a redo-TV replacement (TVR) and insertion of biventricular epicardial pacing leads. Preoperatively, he was treated with antibiotics for an upper respiratory tract infection. Intraoperatively, two attempts failed to wean the patient off CPB, and severe vasoplegia had occurred, requiring extremely high vasopressor doses of norepinephrine (90 µg/kg/min) and inotropic support with enoximone at 25 mg/h. Transoesophageal echocardiography (TEE) showed severe global hypokinesis. A stress dose of hydrocortisone 200 mg and calcium gluconate 2.25 mmol were administered. Central VA ECMO was initiated using the cannulae that had been used for CPB, and the patient’s chest remained open with the skin closed when he was transferred to the CSICU. VA ECMO was maintained for 6 days for cardiovascular support and recovery. After the long CPB time, the patient became coagulopathic and required massive transfusion. Repeated TEE in the CSICU showed severely impaired ventricular function. During the course of VA ECMO treatment, the patient also developed leg ischaemia and acute kidney injury (AKI) requiring renal replacement therapy (RRT), starting on postoperative Day 3. The patient’s chest was re-explored for pleural effusions and haemothorax on postoperative Days 3 and 4, respectively. On Day 6, because the patient had multiorgan failure and fixed and dilated pupils, care was withdrawn and he died.

Patient 3

Patient 3 presented with Ebstein anomaly and ASD. She underwent an Ebstein repair combined with ASD closure, right atrial reduction, and insertion of a bidirectional Glenn shunt and epicardial pacing leads. She was chronically cyanosed and erythrocytotic, had some residual neurological weakness and was asthmatic and, in the past, had had a sagittal sinus thrombosis, two embolic myocardial infarcts and one paradoxical stroke. She had impaired RV function and a very dilated right heart with mildly impaired LV function. In the past, she had undergone a device closure of the ASD and her RV function had deteriorated. After failure of attempts to wean her from CPB, central VA ECMO was instituted and she was transferred to the CSICU with an open chest, on inotropic and vasopressor support. The patient was maintained on ECMO for 13 days. Attempts at decannulation and conversion to an RV assist device failed, and therefore she had to be reconverted to VA ECMO. After 13 days, the patient’s RV function deteriorated, with inflow problems of the atrial cannula requiring repositioning. The patient had multiorgan failure, did not respond to aggressive supportive treatment and died on postoperative Day 13.

Patient 4

Patient 4 presented with a history of Duane syndrome, Ebstein anomaly, ASD and ventricular septal defect (VSD). He had previously undergone pulmonary artery banding, followed by debanding and ASD and VSD closure. This was followed by two successive TVRs with mechanical valves at the ages of 10 and 15 years. The patient was transferred from a referring hospital with severe low-output cardiac failure and multiorgan dysfunction caused by TVR.
dysfunction from an acute-on-chronic thrombotic event. A TEE revealed thick pannus on the mechanical TV, causing severe anatomical narrowing. After initial treatment with epinephrine, enoximone and norepinephrine in the CSICU, VA ECMO was initiated using peripheral cannulation with the patient awake. He remained on VA ECMO for 3 days for cardiac recovery before he underwent cardiac surgery, and his tricuspid prosthesis was replaced with a bioprosthetic valve. The patient was considered for VA ECMO as bridge to insertion of a ventricular assist device (VAD) and a bridge to heart transplantation, but he recovered after the TVR. After 5 days in the CSICU, the patient was discharged to the ward without sequelae.

Discussion
VA ECMO is frequently used as bridging tool for cardiogenic shock to recovery, VAD or cardiac transplantation. For patients with ACHD in cardiogenic shock, it may serve as bridge to surgery, but also to provide circulatory and respiratory support for post-cardiotomy complications. VA ECMO can be particularly useful for patients with ACHD, who often have diminished RV function, or even for Fontan circulation, given that the RV can be fully bypassed.8 The available experience and literature in ACHD patients is extremely limited.

Uilkema and Otterspoor described their experience of ECMO in two patients with ACHD in shock.8 Their first patient, a 33-year-old woman, presented with acute rightsided heart failure caused by severe outflow tract stenosis on a background of tetralogy of Fallot with closure of the VSD and correction of the RV outflow tract. This patient was peripherally cannulated and stabilised to allow careful planning of valve surgery. However, the patient developed bleeding complications and a low-flow state with subsequent multigraft failure. Due to new-onset LV failure (likely due to myocardial stunning), the patient remained ECMO-dependent. Six days after correction of the pulmonary stenosis, the ECMO system could be removed. Shortly before discharge to the ward, arterial bleeding occurred from the old femoral cannula insertion site and the patient died from haemorrhagic shock. In this case, ECMO was used as a bridge to surgery and, even though the patient died, this represents a useful modality to rescue patients with failing circulation and complex heart defects, as previously described by Bautista-Hernandez and colleagues in paediatric patients.12 Three patients in our series received post-cardiotomy VA ECMO for difficult weaning from CPB as bridge to recovery, and one received it for cardiogenic shock as a bridge to surgery. Despite all the patients we studied clearly being in high-risk situations due to their compromised ventricular function, they had a 50% survival rate. Direct comparison to the patient reported by Uilkema and Otterspoor is difficult, since all patients had individually different baselines. However, there were similarities relating to bleeding complications and high transfusion requirements.

The second case described by Uilkema and Otterspoor was a 38-year-old man who presented with Fontan circulation after previous correction of a congenital tricuspid atresia, and had recurrent atrial tachyarrhythmias. He was admitted for a maze operation and partial resection of the atria. Due to an increase in intrathoracic pressure caused by mechanical ventilation, the passive pulmonary blood flow of the Fontan circuit was postoperatively impaired, after which he became hypoxic and hypotensive. He was treated with sedatives, inodilators and nitric oxide ventilation. Progressive shock and multigraft failure developed. Eight days after ICU admission an ECMO support system was implanted, which stabilised his haemodynamic condition, although he was still in need of high-dose vasopressors and fluid therapy. Due to progressive multigraft failure, care was withdrawn. In this patient, ECMO was used as bridge to decision after multigraft failure was established. It remains unclear if early ECMO initiation could have been beneficial for this patient or if it should have been avoided at this late time point. Ko and colleagues stated that ECMO provided a satisfactory partial cardiopulmonary support to patients with post-cardiotomy cardiogenic shock, and allowed time for clinicians to assess the patients and make appropriate decisions.13 In their study, they report multiple different cardiac procedures, with 20 out of 76 adult patients surviving post-cardiotomy ECMO to discharge. Of these 76 patients, three had ACHD; one was successfully weaned off ECMO and survived, one was successfully weaned off ECMO but died, and one patient could not be weaned off ECMO and eventually died, resulting in a 33% survival rate for patients with ACHD in this study.

Belohlavek and colleagues published the case of a 42-year-old woman with an uncorrected ASD with Eisenmenger physiology, who suffered two episodes of cardiac arrest with successful cardiopulmonary resuscitation.9 Several days later, she developed bronchial bleeding with further progression of respiratory insufficiency and intermittent resuscitation. After 12 days and by mutual consensus, the ECMO support was terminated and the patient died.

It appears that right heart conditions such as Eisenmenger syndrome or Fontan circulation have a significant impact on outcome. Two survivors and one non-survivor in our study suffered from Ebstein anomaly, in which the septal and posterior leaflets of the TV are displaced towards the apex of the RV with subsequent atrialisation of the morphological RV. This causes the right atrium to be large and the anatomical RV to be small. Correction of this anomaly may lead to more ventricular filling and work for the RV. However, in case of initial RV failure, ECMO may
provide RV recovery and volume adjustment in patients after repair of Ebstein anomaly.

Luo and colleagues also reported their experience with adult patients having right-sided heart failure after Ebstein anomaly correction.14 The authors applied various approaches to prevent heart failure but two patients required MCS. Both their patients suffered severe postoperative hypotension, the first with atrial and the second with ventricular tachycardia, both with high inotropic and vasopressor requirements and needing MCS. Three days later, after achieving haemodynamic stability in the first patient, the patient was taken off ECMO but again experienced severe hypotension 1 hour later. The patient again underwent ECMO implantation and a thoracotomy, followed by an emergency bidirectional Glenn procedure. One day later, care was withdrawn by request of the family, and the patient died immediately after discharge. The second case was a patient who had presented with Ebstein anomaly involving severe tricuspid regurgitation, patent foramen ovale (PFO) with bidirectional shunts and a dilated RV and left atrium and right bundle branch block. The patient underwent TVR, PFO closure and pacemaker insertion and was weaned off CPB without problems. Thirteen hours later, the patient experienced ventricular tachycardia and hypotension and required defibrillation, without success. She subsequently needed significant inotropic and vasopressor support and ECMO was initiated. With progressing cardiac recovery and stabilised haemodynamics, the patient was weaned from ECMO at Day 7 and was discharged from the ICU at Day 31. A telephone follow-up call 300 days after weaning from ECMO at Day 7 and was discharged from the ICU at Day 31. A telephone follow-up call 300 days after weaning revealed that she did not develop any complications from right heart failure. These two cases were similar to and comparable with ours and suggest that ECMO may allow RV recovery and time for volume adjustment of the previously small RV in patients after Ebstein repair.

In a recent Mayo Clinic publication, the authors reported that, out of 2264 operations performed in patients with ACHD over a 12-year period, they had 24 patients (1.1%) who required MCS with either ECMO or combination of ECMO and intra-aortic balloon pump (IABP).10 In their study, 13 patients (54%) died and 11 (46%) survived. Interestingly, there was no difference in outcome between the ECMO and ECMO/IABP group that received IABP initially, and required ECMO additionally. The lack of statistical difference may have been because of the small number of patients in each group. The overall outcome at Mayo Clinic and at our institution is similar and slightly better than the 40% survival rate of the ELSO registry for adults with cardiac disease who received MCS.15 Therefore, MCS with ECMO appears to be a reasonable approach in this patient population. Even though VA ECMO is most commonly used in these patients for MCS, occasional VV ECMO for respiratory support may be used as well. Chimot and colleagues described the case of a 52-year-old man with Ebstein anomaly who was admitted with severe hypoxaemia, pleural and pericardial effusions, moderate RV dilation, good LV function and a PFO.16 During hospitalisation, the patient developed cardiac tamponade and worsening hypoxaemia, which required surgical pericardiocentesis. After tracheal intubation and mechanical ventilation, the patient had persistent severe hypoxaemia which necessitated the use of VV ECMO. Despite evacuation of the pleuropерicardial serous exudation effusions, hypoxaemia and circulatory failure persisted. In addition, the patient developed liver and kidney failure. TEE revealed severe RV and auricular dilatation associated with an intracardiac shunt caused by a large PFO. The authors discontinued mechanical ventilation, limited ECMO to minimal blood flow, and added inhaled nitric oxide. As a result, decreased flow across the PFO and an improvement in respiratory, circulatory, liver and kidney function was observed. The patient was weaned from ECMO and discharged from hospital 28 days after the surgery. At 6 months, the patient was healthy with resumption of his normal activities.

The high requirements for blood products in our patients, and as described in the other studies, are in line with the literature.17 Bleeding may not strictly be secondary to coagulopathy or anticoagulation. Transfusion requirements have been reported to average 45 units of packed red blood cells transfused per adult ECMO patient. Hypertension increases daily FFP requirements. Recent antiplatelet agents, a larger decline in haemoglobin level, and longer ECMO duration increase daily platelet requirements. Patients with sepsis or receiving ECMO for medical reasons have longer ECMO durations, which is associated with total transfusion requirements. Some of these factors may be identified early to optimise blood product support.17

The limitation of this case series is the small group of patients and the retrospective nature of our analysis. Comparison with other cases is difficult due to the small number of publications relating to this patient population and the different congenital conditions described.

Conclusions

The survival rate in the ELSO registry for adults with cardiac disease who received MCS averages 40%. ECMO in patients with ACHD is a rare intervention with a comparable or slightly better outcome than the general cardiac population, which is a promising result, given the overall complexity and high risk of procedures in patients with ACHD. Patients with Ebstein disease seem to benefit from MCS by slowly adapting to the post-operatively increasing RV volume load over a short supported period. Transfusion requirements appear high, but are in line with previous literature. We encourage readers to share and publish their experiences with patients with ACHD who require ECMO support,
whether the outcome is positive or negative, so we can gain more collective experience and knowledge in the management of this patient population.

Finally, this article must be seen in the context of a dedicated issue that explores multiple aspects of extracorporeal life support in the critically ill.18-21

Competing interests
None declared.

Acknowledgement
We thank all staff at Manchester Royal Infirmary involved in the care of these patients.

Author details
Marc O Maybauer1,2,3
Akbar Vohra3
Niall J O’Keeffe3
Ourania E Prodromou1
Wael Maher3
Hoeda Haravi4
Katrina Mountney4
Johann A Hoschtitzky5
1 Department of Anaesthesiology and Intensive Care Medicine, Philippus University, Marburg, Germany.
2 Critical Care Research Group, Prince Charles Hospital and University of Queensland, Brisbane, QLD, Australia.
3 Cardiothoracic Anaesthesia and Intensive Care, Manchester Royal Infirmary, Central Manchester University Hospitals, NHS Foundation Trust; Manchester Academic Health Science Centre, University of Manchester, Manchester, United Kingdom.
4 Manchester Perfusion Practice, Manchester Royal Infirmary, Central Manchester University Hospitals, NHS Foundation Trust, Manchester, United Kingdom.
5 Department of Cardiac Surgery, Regional Adult Congenital Heart Disease Unit, Manchester Royal Infirmary, Central Manchester University Hospitals, NHS Foundation Trust; Manchester Academic Health Science Centre, University of Manchester, Manchester, United Kingdom.

Correspondence: marc.maybauer@cmft.nhs.uk

References