Published in final edited form as:

Perfusion. 2013 September ; 28(5): 424–432. doi:10.1177/0267659113485873.

The use of extracorporeal membrane oxygenation in pediatric patients with sickle cell disease

KW Kuo, TT Cornell, TP Shanley, FO Odetola, and GM Annich

Department of Pediatrics and Communicable Diseases, Division of Critical Care, C.S. Mott Children's Hospital, University of Michigan, Ann Arbor, MI, USA

Abstract

Previous reports have described the use of extracorporeal membrane oxygenation (ECMO) for acute chest syndrome of sickle cell disease (SCD). However, there have been no reports of venoarterial (VA) ECMO for cardiac dysfunction in patients with SCD. We describe a patient with SCD and life-threatening cardiogenic shock who was successfully treated with VA ECMO. Furthermore, SCD patients have unique comorbidities that warrant particular consideration when utilizing ECMO. We discuss these considerations and review the documented experience with ECMO for pediatric SCD patients from the Extracorporeal Life Support Organization (ELSO) registry. From 1990 until 2012, 52% of the 65 pediatric patients with SCD placed on ECMO survived, with 85% of those receiving venovenous (VV) ECMO surviving and 43% of those receiving VA ECMO surviving. However, significant complications, such as bleeding, neurological injury and kidney injury, also occurred with both VV and VA ECMO. Ten percent of SCD patients receiving VA ECMO experienced either a cerebral infarct or hemorrhage; our patient suffered a cerebrovascular accident while on ECMO, though she survived with good neurologic outcome. To our knowledge, this is the first report of a pediatric patient with SCD and cardiogenic shock successfully managed with VA ECMO. In conjunction with the ELSO registry review, this case report suggests that, while VA ECMO can be successfully used in patients with SCD and severe cardiovascular dysfunction, clinicians should also be aware of the potential for serious complications in this high-risk population.

Keywords

sickle cell disease; extracorporeal membrane oxygenation; acute chest syndrome; cardiogenic shock; sepsis

Introduction

Sickle cell disease (SCD) is an autosomal, recessive hemoglobinopathy that results in hemoglobin S polymerization and subsequent chronic anemia, pain crises and secondary

© The Author(s) 2013

Corresponding author: Kevin W Kuo Department of Pediatrics and Communicable Diseases Division of Critical Care University of Michigan 1500 East Medical Center Drive F6790 Ann Arbor MI 48109 USA. kkevin@med.umich.edu.

Conflict of interest statement

The authors declare that there are no conflicts of interest.

organ damage. SCD patients are at unique risk for conditions that may cause severe cardiorespiratory compromise, such as acute chest syndrome and sepsis caused by encapsulated organisms related to acquired, functional asplenia. In addition, respiratory illnesses such as pneumonia or ARDS present further challenges in SCD patients as hypoxia induces increased hemoglobin S polymerization and further end-organ damage. These challenges can sometimes be insurmountable despite medical management, with a death rate of 1.1% for children with acute chest syndrome and up to 20% from *Hemophilus influenza* bacteremia.^{1,2}

Extracorporeal membrane oxygenation (ECMO) is used routinely in the treatment of severe respiratory and cardiovascular failure in neonatal, pediatric and adult patients. In particular, venoarterial (VA) ECMO has been demonstrated to be successful in treating pediatric patients with cardiovascular failure, including post-cardiac arrest with extracorporeal cardiopulmonary resuscitation (ECPR).³ However, the role for ECMO in SCD patients is unclear. SCD patients' unique comorbidities, including hemolysis, vasoocclusion and increased risk for both pulmonary and cerebral thrombosis, present distinct challenges for ECMO management. Previous reports in pediatric patients undergoing ECPR have not demonstrated any difference in outcome based on cannulation site.⁴ However, it is possible that SCD-related, long-term cerebral vascular abnormalities may be aggravated following cannulation of the carotid artery for VA ECMO. These comorbidities likely confer additional risk to the use of ECMO in patients with sickle cell disease.

Limited literature exists regarding the use of ECMO in patients with SCD. A review of the Extracorporeal Life Support Organization (ELSO) registry in 1996 revealed a total of 15 cases of pediatric patients with SCD receiving ECMO, with only 26% (4 patients) surviving compared to an overall survival rate of approximately 65% for pediatric ECMO patients.^{5,6} Nonetheless, there have been case reports of successful utilization of both venovenous (VV) and VA ECMO for acute chest syndrome in patients with SCD, with no prior descriptions of the use of VA ECMO for cardiac dysfunction in pediatric patients with SCD.^{5,7,8}

We describe the use of VA ECMO in a child with SCD and cardiac dysfunction and also review the most recent data in the ELSO registry describing the use of ECMO for children with SCD, including patient demographics, type of ECMO use, ECMO-related complications and clinical outcomes.

Case history

A six-year-old, 17 kg girl with SCD (homozygous hemoglobin SS disease) was admitted to the pediatric intensive care unit of C.S. Mott Children's Hospital at the University of Michigan with a three-day history of nasal congestion, cough and fatigue and a one-day history of fever with chest and abdominal pain. She had a history of vasoocclusive pain crises, but no other complications from her SCD, such as acute chest syndrome or prior pediatric intensive care unit (PICU) admissions. Routine follow-up visits demonstrated elevated transcranial Doppler velocities (197 cm/s and 156 cm/s over the right and left internal carotid arteries, respectively), but she had no resultant neurologic manifestations.

Upon arrival into the PICU, initial physical exam revealed a girl in severe respiratory distress, with significant intercostal retractions, respiratory rate of 40 breaths/minute and an oxyhemoglobin saturation of 89% on room air. Her trachea was intubated for hypoxemic respiratory failure and mechanical ventilation was initiated. Chest radiograph demonstrated moderate cardiomegaly, bilateral patchy pulmonary opacities and a moderate-sized right pleural effusion (Figure 1). An arterial catheter was placed for invasive continuous blood pressure monitoring and serial measurement of blood gas tension. Her blood pressure quickly declined from 100/49 mmHg on admission to 80/40 mmHg, despite a 20 cc/kg normal saline bolus, a 20 cc/kg packed red blood cell transfusion, a 15 cc/kg 5% albumin bolus and titration of an epinephrine infusion up to 0.7 µg/kg/min. She had persistent tachycardia to 160–170 beats/minute. Physical examination at this time was consistent with marked peripheral vasoconstriction, with cool extremities, weak peripheral pulses and prolonged capillary refill time of 3–4 seconds.

Initial complete blood count revealed a white blood cell count of 59,300 with a differential count of 77% neutrophils, 18% bands and 1% lymphocytes. Her hemoglobin was 5.4 g/dL and the platelet count was 240,000/mm³ with sickle cell anaemia (HbSS) on electrophoresis of 29%, with the post-transfusion hemoglobin reaching a peak of 14.6 g/dL after the transfusion of 2 units of packed red blood cells. The arterial blood gas worsened with a nadir PaO₂/FiO₂ ratio of 65. Broad-spectrum antibiotics were started, including vancomycin, piperacillin/tazobactam and azithromycin. An echocardiogram obtained five hours after admission on 0.7 µg/kg/min of epinephrine and 0.5 µg/kg/min of milrinone revealed severely depressed biventricular function, with left ventricular fractional shortening of 12% and an estimated ejection fraction of 20%, as well as ½ to ⅔ systemic right ventricular systolic pressure, moderate mitral regurgitation and severe tricuspid regurgitation. Milrinone was initiated given the combination of severe cardiac dysfunction and marked peripheral vasoconstriction. The troponin level was significantly elevated at 14.7 ng/ml as was B-type natriuretic peptide (BNP) at 3802 pg/ml.

ECMO therapy was considered due to her worsening clinical condition and severe cardiac dysfunction despite significant medical support. There was considerable discussion of various cannulation options given the risks of cannulating either carotid artery to place her on ECMO given her SCD and known elevated transcranial Doppler velocities. Ultimately, the decision was made to place her on VA ECMO via her right neck vessels. A 17-French venous cannula was placed into the right internal jugular vein and a 15-French arterial cannula was placed into the right common carotid artery (RCCA) (Figure 2). The initial blood gas immediately prior to initiating ECMO was pH 6.96, PaCO₂ 134 mmHg, PaO₂ 95 mmHg, HCO₃ 28.5 mmol/L, lactate 2.2 mmol/L on 100% FiO₂, with a PaO₂/FiO₂ ratio of 95 and an oxygenation index of 20. Although high frequency oscillatory ventilation has been successfully utilized with acute chest syndrome, it was not used in this patient as her significant cardiac dysfunction necessitated emergent cannulation for VA ECMO.⁹ Nitric oxide at a peak dose of 20 parts per million was initially trialed pre-ECMO in an effort to decrease the elevated pulmonary vascular resistance and improve ventilation-perfusion matching. It was discontinued after 12 hours due to lack of demonstrable benefit.

The ECMO circuit utilized a Centrimag centrifugal pump system (Levitronix Technologies LLC, Waltham, MA) and a pediatric Quadrox-iD oxygenator (Maquet Cardiovascular LLC, Wayne, NJ) and was continually monitored and titrated by a dedicated ECMO technician, with goal parameters set daily by the critical care physicians. These goal parameters included a mean arterial blood pressure of greater than 55 mmHg, central venous oxygen saturation greater than 70% and a PaO₂ greater than 60 mmHg. Over the next 48 hours, with ECMO flows ranging from 1.8 L/min to 3 L/min (105–175 cc/kg/min), there was marked improvement in the patient's condition and she was able to be weaned off vasopressor infusions. While there was initial concern on day 1 about loss of pulsatility and ventricular dysfunction, despite the increased left ventricular afterload imposed by VA ECMO, she never required a left atrial drain. The initial blood culture grew micrococcus and viral studies were negative. Given her rapid clinical improvement, it was thought that her acute cardiovascular dysfunction was likely to be a result of micrococcus-induced sepsis and subsequent myocardial depression rather than primary viral myocarditis; nevertheless, she received intravenous immunoglobulin treatment. It is also possible that significant pulmonary hypertension, as evidenced by the echocardiogram, may have contributed to her global cardiovascular dysfunction. Patients with SCD are known to be at risk for pulmonary hypertension; 30% of screening echocardiography in SCD patients age 2–14 without concurrent respiratory disease demonstrated elevated pulmonary artery pressures (tricuspid regurgitant velocity >2.5 m/s).¹⁰ Bypassing the pulmonary circulation with VA ECMO may have allowed her heart to recover. Nonetheless, though she did not require significant cardiovascular support by day three of ECMO, she continued to have significant ventilator requirements, necessitating continued use of ECMO. Due to subsequent left-sided pulmonary opacification, flexible bronchoscopy was performed on day six of ECMO, which revealed a large mucus plug at the left mainstem bronchus. Chest x-ray following bronchoscopy with saline lavages demonstrated significantly improved aeration of the left hemithorax.

On day seven of ECMO, she was noted to acutely develop anisocoria, with the left pupil diameter much larger than the right pupil diameter, as well as hemiparesis of her right upper and right lower extremities. A head computed tomography (CT) scan revealed a large hemorrhage in the left frontoparietal region, with surrounding vasogenic edema and mass effect, with subfalcine shift and evidence of uncal herniation. After acute management of presumed intracranial hypertension with a temporary increase in ECMO sweep gas and boluses of 3% hypertonic saline and mannitol, she was emergently taken off VA ECMO. Heparin had been used for systemic anticoagulation, targeting activated clotting times of 210–230 seconds, our institutional standard for anticoagulation on ECMO. This systemic anticoagulation certainly may have contributed to her cerebral hemorrhage. Protamine was administered to reverse this systemic heparinization. She underwent emergent decompressive craniectomy and placement of an intracranial pressure monitor in the operating room. Intra-operatively, layering of the hemorrhage was found, which suggested the bleeding had been present for more than 24 hours. She was able to sustain her systemic perfusion on only a milrinone infusion at 0.7 µg/kg/min, with an echocardiogram demonstrating normal left ventricular systolic function and an estimated ejection fraction of

65%. A summary of her ventilator requirements, blood gas results and inotropic support over her clinical course is presented in Table 1.

Over the next week, the cerebral edema resolved and the intracranial pressure monitor was removed. Her trachea was subsequently extubated and oxygen supplementation weaned to room air. The following week, she was transferred to the general care ward, with rehabilitation and, as of August 30, 2012, she had regained most of her mobility on her right side. In addition, an initial expressive aphasia after the stroke has since significantly improved. A tunneled dialysis catheter was placed to provide stable access for future erythrocytapheresis and transfusion therapy to mitigate the patient's increased stroke risk.

Discussion

ELSO registry review

Institutional review board approval was obtained for both the chart review and a query of the ELSO registry for the use of ECMO in pediatric patients with SCD. From 1990 to 2012, there were 65 reported cases of ECMO use in pediatric patients between the ages of 30 days to 18 years with SCD. ICD9 codes 282.6 and 517.3 were used to identify patients with sickle cell disease and/or acute chest syndrome, respectively. The most common indications included respiratory failure (69%) and sepsis (14%) (Table 2). Despite the fact that respiratory failure was the most common indication for ECMO, VA support was used in 80% of patients, with only 20% utilizing VV ECMO (Table 2). Of the patients who underwent VA ECMO, the common carotid artery was the most common site (71%) for cannulation while femoral and aortic cannulations accounted for 21% and 9%, respectively (Table 2).

The median (range) age of patients was 7.3 years (1 month-17 years) with a median weight of 23.5 kg (3.6–70 kg) (Table 2). At the time of ECMO initiation, the median $\text{PaO}_2/\text{FiO}_2$ ratio and Oxygenation Index ($[\text{Mean Airway Pressure} \times \text{FiO}_2]/\text{PaO}_2 \times 100$) were 59 (17–361) and 50 (3–173), respectively. The median duration of mechanical ventilation prior to the initiation of ECMO was 15.5 hours (0–859 hours) and the median duration of ECMO was 155 hours (5–689 hours) or approximately 6.5 days (Table 2).

The most common complication encountered during ECMO included acute kidney injury, defined as a creatinine value greater than 1.5 (45% of patients) and/or dialysis treatment (38% patients) (Table 3). Other common complications included bleeding (25%), inotrope requirement while on ECLS (40%) and oxygenator clotting (15%). Despite the predominant use of VA ECMO in these patients with an innate risk of compromised cerebral circulation, only 12% of the patients suffered a documented neurological complication, such as central nervous system (CNS) infarct, CNS hemorrhage or seizure. There were no reported cases of CNS infarct or hemorrhage in patients who underwent VV ECMO as compared to 5 (10%) of the patients who experienced CNS infarct or hemorrhage while on VA ECMO. One patient was reported to have had a seizure (8%) in the VV ECMO group as compared to 4 patients (8%) experiencing seizures in the VA supported group, though the percentage incidence was similar (Table 4). Overall survival for sickle cell patients undergoing ECLS

was 52%, with 43% of VA ECMO patients surviving and 85% of VV ECMO patients surviving.

Risk of stroke in sickle cell disease

While the decision to place any patient on VA ECMO requires careful consideration, the patient with sickle cell disease warrants even further deliberation due to their inherently increased risk of stroke. Children with sickle cell disease are at risk for cerebral infarction associated with occlusive vasculopathy involving the distal intracranial internal carotid artery (ICA) and the proximal middle and anterior cerebral arteries (MCA, ACA).¹¹ By age 20 years, approximately 11% of patients with homozygous sickle cell disease have developed stroke, with approximately 70% being ischemic and 30% hemorrhagic strokes.¹² The occurrence of both ischemic and hemorrhagic strokes makes anticoagulation on ECMO particularly challenging, as a fine balance must be achieved. Transcranial Doppler (TCD) ultrasonography is used to predict stroke risk in children with sickle cell anemia, with a rate of approximately 10%/year in children with ICA/MCA velocities of 200 cm/sec or greater compared to a rate of less than 0.5%/year in children with velocities less than 170 cm/sec.¹³

It is unclear why the majority of sickle cell patients are placed on VA vs. VV ECMO (80% vs. 20%, respectively) given that the primary indication in the majority of cases is respiratory failure. However, while the registry data seem to suggest that those undergoing VV vs. VA ECMO have lower mortality and less neurological morbidities, it may be that the patients undergoing VV ECMO represent a subset of patients with lower acuity and perhaps relatively better preserved cardiac function at the time of ECMO initiation relative to their VA ECMO counterparts.

Choice of arterial cannulation site

The decision to cannulate and potentially ligate the carotid artery would presumably compromise flow to an already vulnerable cerebral circulation and perhaps increase the risk of ischemic stroke. This is in addition to the known baseline risk of CNS infarct (1.5%) or hemorrhage (4%) while on ECMO.¹⁴ Our review of the ELSO registry revealed a 6% rate (n=4) of CNS infarct and 5% rate (n=3) of CNS hemorrhage in SCD patients on ECMO. Overall, as two patients had both CNS infarct and hemorrhage, 8% (n=5) of SCD patients on ECMO experienced CNS infarct and/or hemorrhage. However, a prior review of the ELSO registry from 1990 to 1996 did not reveal complications associated with carotid artery ligation in patients with sickle cell disease.⁵ Informal recommendations have been made for the use of the femoral artery as the preferred cannulation site in children requiring VA ECMO if they are >15 kg in order to reduce the risk of CNS injury by avoiding carotid cannulation.¹⁵ Our patient was 17 kg and our institutional guidelines reference >20 kg as a threshold for femoral cannulation, consistent with recently published recommendations.¹⁶ ELSO registry data reveal a median weight of 22 kg (5.1–41.5 kg) for patients cannulated via the common carotid artery as compared to a median weight of 45 kg (21.5–70 kg) for patients cannulated via the femoral artery. Nonetheless, femoral arterial cannulation confers its own risks, including limb ischemia and the frequent need for a dedicated lower extremity reperfusion cannula. In addition, given our patient's poor cardiovascular function, there were significant concerns about achieving ECMO flows necessary to provide adequate oxygen

delivery if femoral arterial cannulation was pursued. Another option for arterial cannulation involves direct central cannulation. Central cannulation is often the preferred route in children with congenital heart disease requiring postoperative VA ECMO support as this involves a median sternotomy. While central cannulation has been used successfully for children with refractory septic shock, no prospective trial comparing outcomes after central versus peripheral VA ECMO cannulation exists.¹⁷ In the absence of a prior sternotomy and given the associated risks, notably surgical bleeding and wound infection, this option was not favored and, hence, the RCCA was cannulated in this patient.

Carotid artery reconstruction after ECMO

After ECMO discontinuation, the arterial and venous cannulae are removed and both the RCCA and right internal jugular vein are often permanently ligated. While there is no clear evidence of adverse effects attributable to permanent RCCA ligation, there have been reports of right cerebral hemispheric ischemic abnormalities or contralateral hyperperfusion of the left hemisphere on brain imaging in patients after decannulation from VA ECMO.¹⁸ This complication would be of particular concern in a patient with sickle cell disease and known intracranial vasculopathy and raises the issue of carotid artery reconstruction following decannulation. While some reports have suggested re-occlusion rates of up to 72% following RCCA repair in infants, these have largely involved neonates.¹⁹ In addition, other studies have shown lower restenosis rates (24% with stenosis >50%) and fewer brain scan abnormalities in children who have undergone RCCA repair when compared to patients who have not undergone repair.²⁰ Currently, there is no formal recommendation regarding RCCA reconstruction following carotid cannulation. Our patient had experienced a left-sided infarct with no evidence of right-sided cerebral injury nor left-sided motor deficits, suggesting that collateral flow via the left common carotid artery and the circle of Willis was sufficient to perfuse her right cerebral hemisphere. Given her neurological status as well as the risk of reperfusion injury, the decision was made to forgo RCCA reconstruction.

Management of post-ECMO carotid ligation stroke risk

Patients with SCD and elevated TCD velocities are at increased risk of stroke. It is unclear whether carotid vessel ligation further increases this risk. It seems physiologically plausible to draw such a conclusion given the known pathological changes in the ICA, MCA and ACA of such patients. Hence, it also seems reasonable to attempt to mitigate this increased stroke risk. Clinical series have demonstrated that regular blood transfusions are associated with a reduced risk of stroke.²¹ The Stroke Prevention Trial in Sickle Cell Anemia (STOP) study demonstrated that, in sickle cell patients with TCD velocities greater than 200 cm/s, a transfusion protocol to reduce the Hb S concentration to less than 30% of total hemoglobin, with subsequent transfusions every three to four weeks, resulted in a 92% reduction in stroke risk compared to the standard care group.¹³ Thus, while our patient had a TCD velocity of 196 cm/s, less than the cutoff of 200 cm/s, given her history of stroke as well as concern for the overall increased risk of stroke after carotid ligation, she received a permanent indwelling vascular catheter and now undergoes regular transfusion therapy to maintain the Hb S concentration less than 30%.

Limitations

This study has several potential limitations. While the ELSO registry represents the largest ECLS database and has over twenty years of data, reporting of information is limited and neither guaranteed to be complete or accurate. For example, diagnostic information may not be accurately or consistently reported and, hence, not all patients with SCD who have received ECMO may be represented. Also, while the ELSO registry provides pre-ECMO data, such as ventilator settings and blood gas results that may help characterize the degree of respiratory compromise, it lacks information, such as echocardiography results and dosages of vasoactive or inotropic infusions, that may reflect the degree of cardiovascular dysfunction prior to the initiation of ECMO. The small number of patients and infrequent occurrence of specific complications in the registry review also poses a significant limitation, making meaningful statistics difficult to perform. For example, while it is plausible that VA ECMO may be associated with a higher risk of cerebrovascular accident compared to VV ECMO, this conclusion cannot be made from this study's limited data. For this reason, descriptive rather than comparative statistics are presented. Finally, the data in the ELSO registry review spans 22 years and, hence, likely reflects significant heterogeneity in medical technology, practices and management strategies for both SCD and ECMO that may affect outcomes. Our review does not account for this potential heterogeneity.

Conclusion

Our experience with this patient highlights both the potential benefits and associated risks of VA ECMO in patients with SCD. While without ECMO, it is unlikely our patient would have survived, ECMO also likely contributed to her CNS injury. Fortunately, she has steadily regained neurological function with intensive rehabilitation. In conjunction with the ELSO registry data, our case demonstrates that VA ECMO can be utilized in patients with sickle cell disease, with approximately 43% of patients surviving. Nonetheless, the significant risk of complications such as neurological injury and kidney injury emphasizes the need to cautiously consider the need for VA vs. VV ECMO and to regularly evaluate the need for continued ECMO support. While it remains unclear whether carotid artery ligation worsens neurological outcome in patients with SCD, the choice of arterial cannulation site, the potential benefit of carotid artery reconstruction and post-ECMO transfusion protocols to limit stroke risk also warrant careful consideration.

Acknowledgments

Funding This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

References

1. Vichinsky EP, Styles LA, Colangelo LH, et al. Acute chest syndrome in sickle cell disease: clinical presentation and course. *Blood*. 1997; 89:1787–1792. [PubMed: 9057664]
2. Gill FM, Sleeper LA, Weiner SJ, et al. Clinical events in the first decade in a cohort of infants with sickle cell disease. *Blood*. 1995; 86:776–783. [PubMed: 7606007]
3. Wolf MJ, Kanter KR, Kirshbom PM, et al. Extracorporeal cardiopulmonary resuscitation for pediatric cardiac patients. *Ann Thorac Surg*. 2012; 94:874–880. [PubMed: 22698774]

4. Alsoufi B, Al-Radi OO, Nazer RI, et al. Survival outcomes after rescue extracorporeal cardiopulmonary resuscitation in pediatric patients with refractory cardiac arrest. *J Thorac Cardiovasc Surg.* 2007; 134:952–959. [PubMed: 17903513]
5. Trant CA, Casey JR, Hansell D, et al. Successful use of extracorporeal membrane oxygenation in the treatment of acute chest syndrome in a child with severe sickle cell anemia. *ASAIO Journal.* 1996; 42:236–239. [PubMed: 8725698]
6. ECMO Registry report of the Extracorporeal Life Support Organization. University of Michigan; Ann Arbor, Michigan: Jul. 2012
7. Gillet DS, Guinning KJ, Sawicka EH, et al. Life threatening sickle chest syndrome treated with extracorporeal membrane oxygenation. *BMJ.* 1987; 294:81–82. [PubMed: 3105665]
8. Pelidis MA, Kato GJ, Resar LMS, et al. Successful treatment of life-threatening acute chest syndrome of sickle cell disease with venovenous extracorporeal membrane oxygenation. *J Pediatr Hematol Oncol.* 1997; 19:459–461.
9. Wratney AT, Gentile MA, Hamel DS, et al. Successful treatment of acute chest syndrome with high-frequency oscillatory ventilation in pediatric patients. *Respiratory Care.* 2004; 49:263–269. [PubMed: 14982646]
10. Pashankar FD, Carbonella J, Bazy-Asaad A, et al. Prevalence and risk factors of elevated pulmonary artery pressures in children with sickle cell disease. *Pediatrics.* 2008; 121:777–782. [PubMed: 18381543]
11. Bridgers WH. Cerebral vascular disease accompanying sickle cell anemia. *Am J Pathol.* 1939; 15:353–362. [PubMed: 19970453]
12. Ohene-Frempong K, Weiner SJ, Sleeper LA, et al. Cerebrovascular accidents in sickle cell disease: rates and risk factors. *Blood.* 1998; 91:288–294. [PubMed: 9414296]
13. Adams RJ, McKie VC, Hsu L, et al. Prevention of a first stroke by transfusions in children with sickle cell anemia and abnormal results on transcranial Doppler ultrasonography. *N Engl J Med.* 1998; 339:5–11. [PubMed: 9647873]
14. Dalton, H.; Fortenberry, JD.; Frenckner, B., et al. ECMO for pediatric respiratory failure. In: Annich, GM., editor. *ECMO Extracorporeal Cardiopulmonary Support in Critical Care.* Extracorporeal Life Support Organization; Ann Arbor: 2012. p. 283
15. Bartlett, R. JPS lecture. American Pediatric Surgical Association 41st Annual meeting; 2010.
16. Rollins MD, Hubbard A, Zabrocki L, et al. Extracorporeal membrane oxygenation cannulation trends for pediatric respiratory failure and central nervous system injury. *J Pediatr Surg.* 2012; 47:68–75. [PubMed: 22244395]
17. MacLaren G, Butt W, Best D, et al. Central extracorporeal membrane oxygenation for refractory pediatric septic shock. *Pediatr Crit Care Med.* 2011; 12:133–136. [PubMed: 20453704]
18. Mendoza JC, Shearer LL, Cook LN. Lateralization of brain lesions following extracorporeal membrane oxygenation. *Pediatrics.* 1991; 88:1004–1009. [PubMed: 1945603]
19. Buesing KA, Kilian AK, Schaible T, et al. Extracorporeal membrane oxygenation in infants with congenital diaphragmatic hernia: follow-up MRI evaluating carotid artery reocclusion and neurologic outcome. *AJR Am J Roentgenol.* 2007; 188:1636–1642. [PubMed: 17515387]
20. Desai SA, Stanley C, Gringlas M, et al. Five-year follow-up of neonates with reconstructed right common carotid arteries after extracorporeal membrane oxygenation. *J Pediatrics.* 1999; 134:428–433.
21. Pegelow CH, Adams RJ, McKie V, et al. Risk of recurrent stroke in patients with sickle cell disease treated with erythrocyte transfusions. *J Pediatrics.* 1995; 126:896–899.

Figure 1.
Chest X-ray on day 1 of hospitalization demonstrating cardiomegaly and bilateral pulmonary infiltrates and right-sided pleural effusion.

Figure 2. Chest X-ray on day 1 of hospitalization following venoarterial ECMO cannulation with cannulae in the right internal jugular vein and right common carotid artery.

Table 1

Summary of cardiopulmonary support and status.

Hour	Intervention	FiO ₂ (%)	PIP (cm H ₂ O)	PEEP (cm H ₂ O)	Paw (cm H ₂ O)	Vt/kg (cc/kg)	pH	PaCO ₂	PaO ₂	OI	VIS
2	Post-Intubation	70	28	7	14	7	7.20	48	209	4.7	20
14	Pre-ECMO	100	31	10	19	4.6	6.96	134	95	20	105
159	Post-ECMO	55	34	8	21	6.7	7.40	46	77	15	7

Hour: hour after admission; FiO₂: inspired oxygen concentration; PIP: peak inspiratory pressure; PEEP: positive end expiratory pressure; Paw: mean airway pressure; Vt: tidal volume; PaCO₂: arterial carbon dioxide tension; PaO₂: arterial oxygen tension; OI: oxygenation index; VIS: vasoactive-inotropic score = dopamine dose (µg/kg/min) + dobutamine dose (µg/kg/min) + 100 * epinephrine dose (µg/kg/min) + 10 * milrinone dose (µg/kg/min) + 10,000 * vasopressin dose (U/kg/min) + 100 * norepinephrine dose (µg/kg/min).

Table 2

Patient characteristics and ECLS use in patients with sickle cell disease.

	Total	% of Total	Total Survived	% Survived
Patients	64	100%	34	52%
Mode of ECMO				
VA	51	80%	22	43%
VV	13	20%	11	85%
Cannulation Site (VA)				
Common Carotid Artery	24	71%	11	46%
Femoral Artery	7	21%	4	71%
Aorta	3	9%	0	0%
Primary Diagnosis				
Respiratory Failure/Acute Chest	45	69%	29	64%
Sepsis	9	14%	1	11%
Cardiac Arrest/Cardiomyopathy	4	6%	1	25%
Other (none listed)	7	11%	3	43%

	Median	Mean	Range
Patient Characteristics			
Age (years)	7.3	8	(1 mo-17 yrs 3 mo)
Weight (kg)	23.5	29	(3.6–70)
Gender (% male, female)	60% male/40% female		
Pre-ECMO Characteristics			
Intubation to ECMO (hours)	27	84	(0–859)
pH at ECMO initiation	7.27	7.22	(6.76–7.63)
PIP at ECMO initiation (mmHg)	40	45	(23–81)
PEEP at ECMO initiation (mmHg)	12	12	(4–30)
Mean Airway Pressure at ECMO initiation (mmHg)	28	29	(11–50)
P/F ratio at ECMO initiation	63	86	(17–361)
Oxygenation Index at ECMO initiation	40	50	(3–173)
Time on ECMO (hours)	155	186	(5–689)

PIP: peak inspiratory pressure; PEEP: positive end expiratory pressure; P/F: PaO₂/FiO₂.

Table 3

Complications of ECLS and subsequent outcomes in patients with sickle cell disease.

Complications	Number	% of Patients	Number Survived	% Survived
Hematologic				
GI Bleeding	5	8%	1	20%
Pulmonary Hemorrhage	3	5%	1	33%
Cannula/Surgical Site Bleeding	16	25%	7	44%
Hemolysis	5	8%	1	20%
Neurological				
CNS Infarct and/or Hemorrhage	5	8%	1	20%
Seizure	5	8%	1	20%
Renal				
Acute Kidney Injury	29	45%	11	38%
Dialysis	25	38%	10	40%
Cardiovascular				
CPR	5	8%	1	20%
Inotrope requirement on ECLS	26	40%	9	35%
Arrhythmia	9	14%	4	44%
Hypertension requiring Vasodilator	10	15%	9	90%
Tamponade	1	2%	0	0%
Pulmonary				
Pneumothorax	9	14%	6	67%
Infectious				
Documented Infection	8	12%	3	38%
White blood cell count <1500	3	5%	1	33%
Metabolic				
pH<7.2	5	8%	2	40%
Hyperglycemia (glucose >240)	11	17%	6	55%
Hypoglycemia (glucose <40)	1	2%	0	0%
Hyperbilirubinemia	3	5%	2	67%
Mechanical				
Oxygenator (i.e. clot)	10	15%	8	80%
Pump/Tubing	6	9%	2	33%
Cannula	6	9%	4	67%

GI: gastrointestinal; CNS: central nervous system; CPR: cardiopulmonary resuscitation; ECLS: extracorporeal life support.

Table 4

Complications by type of ECLS (VA versus VV).

Complications	VA (51)	% of VA	VV (13)	% of VV
Hematologic				
GI Bleeding	4	8%	1	8%
Pulmonary Hemorrhage	3	6%	0	0%
Cannula/Surgical Site Bleeding	13	25%	3	23%
Hemolysis	5	10%	0	0%
Neurological				
CNS Infarct and/or Hemorrhage	5	10%	0	0%
Seizure	4	8%	1	8%
Renal				
Acute Kidney Injury	26	51%	3	23%
Dialysis	23	45%	2	15%
Cardiovascular				
CPR	5	10%	0	0%
Inotrope requirement on ECLS	22	43%	4	31%
Arrhythmia	7	14%	2	15%
Hypertension requiring vasodilator	6	12%	4	31%
Tamponade	1	2%	0	0%
Pulmonary				
Pneumothorax	7	14%	2	15%
Infectious				
Documented Infection	6	12%	2	15%
White blood cell count <1500	3	6%	0	0%
Metabolic				
pH<7.2	5	10%	0	0%
Hyperglycemia (glucose >240)	10	20%	1	8%
Hypoglycemia (glucose <40)	1	2%	0	0%
Hyperbilirubinemia	2	4%	1	8%
Mechanical				
Oxygenator (i.e. clot)	7	14%	2	15%
Pump/Tubing	5	10%	1	8%
Cannula	4	8%	2	15%

ECLS: extracorporeal life support; GI: gastrointestinal; CNS: central nervous system; CPR: cardiopulmonary resuscitation.