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Extracorporeal membrane oxygenation for the support of infants, children, and young adults with acute myocarditis: A review of the Extracorporeal Life Support Organization registry*

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Abstract

Objective—To describe survival outcomes for pediatric patients supported with extracorporeal membrane oxygenation for severe myocarditis and identify risk factors for in-hospital mortality.

Design—Retrospective review of Extracorporeal Life Support Organization registry database.

Setting—Data reported to Extracorporeal Life Support Organization from 116 extracorporeal membrane oxygenation centers.

Patients—Patients ≤ 18 yrs of age supported with extracorporeal membrane oxygenation for myocarditis during 1995 to 2006.

Interventions—None.

Measurements and Main Results—Of 19,348 reported pediatric extracorporeal membrane oxygenation uses from 1995 to 2006, 260 runs were for 255 patients with a diagnosis of myocarditis (1.3%). Survival to hospital discharge was 61%. Seven patients (3%) underwent heart transplantation and six patients survived to discharge. Of 100 patients not surviving to hospital discharge, extracorporeal membrane oxygenation support was withdrawn in 70 (70%) with multiple organ failure as the indication in 58 (83%) patients. In a multivariable model, female gender (adjusted odds ratio, 2.3, 95% confidence interval, 1.3–4.2), arrhythmia on extracorporeal membrane oxygenation (adjusted odds ratio, 2.7, 95% confidence interval, 1.5–5.1), and renal failure requiring dialysis (adjusted odds ratio, 5.1, 95% confidence interval, 2.3–11.4) were associated with increased odds of in-hospital mortality.

Conclusion—Extracorporeal membrane oxygenation is a valuable tool to rescue children with severe cardiorespiratory compromise related to myocarditis. Female gender, arrhythmia on extracorporeal membrane oxygenation, and need for dialysis during extracorporeal membrane oxygenation were associated with increased mortality.

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Keywords

myocarditis; pediatrics; extracorporeal membrane oxygenation

The clinical course of acute myocarditis in children is highly variable. Patients with the acute fulminant form of viral myocarditis may present with severe cardiovascular dysfunction and cardiovascular collapse necessitating mechanical circulatory support (1–8). Such support is most commonly provided with extracorporeal membrane oxygenation (ECMO) with a goal of bridging these patients to recovery or to orthotopic heart transplantation. The few published reports describing outcomes for infants, children, and young adults with myocarditis needing mechanical support with ECMO for cardiogenic shock suggested encouraging results with reported survival rates of 50% to 83%. However, these studies were limited by small sample size and single institutional experience, rendering analysis of risk factors for mortality difficult and generalizability of outcomes impossible (9–13).

The goals of this study are to describe survival outcomes, trends in ECMO utilization, and complications for pediatric patients with myocarditis requiring ECMO support using multi-institutional data reported to the Extracorporeal Life Support Organization's (ELSO) data registry. We hypothesized that we could identify patient and ECMO support-related factors that could help to define those children who are unlikely to survive to hospital discharge so that they can be considered for early listing for heart transplantation or transitioned to a longer-term mechanical circulatory support device.

MATERIALS AND METHODS

Data Collection and Study Population

The data for purposes of this study were obtained from the ELSO registry. The registry was founded in 1989 and collects data on the use of ECMO for mechanical circulatory and respiratory support in children and adults. Data are reported to ELSO by 116 member centers including 14 international centers. ECMO-related data are collected at the reporting center and submitted to the ELSO registry, using a standardized data collection form. Data reporting to ELSO is approved by each site's Institutional Review Board. The data reported contain patient demographic information, diagnosis and procedure codes, pre-ECMO support details, ECMO indication, ECMO support details, complications, and patient outcomes.

Data from all patients ≤ 18 yrs old who were assigned a primary or secondary International Statistical Classification of Diseases and Related Health Problems, 9th Revision (ICD-9) diagnosis code for any type of myocarditis from January 1, 1995 to December 31, 2006 were extracted from the registry and included in this analysis. The ICD-9 codes used included 032.82 (Diphtheritic myocarditis), 036.43 (Meningococcal myocarditis), 074.23 (Cocksackie myocarditis), 093.82 (Syphilitic myocarditis), 130.3 (Myocarditis due to Toxoplasmosis), 391.2 (Acute rheumatic myocarditis), 398.0 (Rheumatic myocarditis), 422 (Acute myocarditis), 422.0 (Acute myocarditis in diseases classified elsewhere), 422.9

(Other and unspecified myocarditis), 422.90 (Acute myocarditis, unspecified), 422.91 (Idiopathic myocarditis), 422.92 (Septic myocarditis), 422.93 (Toxic myocarditis), and 429.0 (Myocarditis, unspecified).

Variables used for purposes of these analyses included patient demographic details, procedure and diagnosis codes, time from admission to ECMO center to ECMO cannulation (hrs), pre-ECMO respiratory and hemodynamic support information, ECMO cannulation technique, details of respiratory and hemodynamic support and patient management during ECMO, requirement for heart transplantation, reason for ECMO discontinuation, ECMO-related complications, survival to hospital discharge or transfer to another facility, and time to death or discharge after decannulation from ECMO (hrs). The indication for ECMO use (cardiac failure, as an extension of cardiopulmonary resuscitation [E-CPR], or combined cardiac and pulmonary failure) was also analyzed.

Data Categorization

Venous cannulation sites for ECMO were categorized as jugular vein, right atrium, or femoral vein, and arterial cannulation sites were categorized as aorta, carotid, or femoral artery. If either the venous or arterial cannula was placed in the right atrium or the aorta respectively, the cannulation was considered to be transthoracic (regardless of the report of other cannulation sites). When more than one venous or arterial cannulation site was recorded, then the second arterial or venous site was coded as a secondary cannulation site. To account for age-related changes, blood pressure data were categorized as hypo-, normo-, or hypertensive, using age-appropriate cutoffs.

Statistical Analysis

Only the first myocarditis-related ECMO run for each patient was included in the analysis. Five patients (2%) had >1 ECMO runs reported. Survival to hospital discharge was defined as discharge home or to another facility. Demographic, pre-ECMO, and ECMO support details were compared between survivors and nonsurvivors, using Wilcoxon rank sum tests for continuous variables and Fisher's exact tests for categorical variables. The Mantel-Haenszel chi-square test for trend was used to analyze the change in left atrial decompression rate by era.

We created a logistic regression model to evaluate risk factors for mortality before hospital discharge for patients supported on ECMO for myocarditis. A second model was created to evaluate risk factors for mortality before hospital discharge for those patients who were separated from ECMO after their end organ function was judged to have recovered. Candidate variables for inclusion in the logistic regression models were selected from the bivariate analyses. The criterion for candidate variable selection was a $p \leq .1$ and criterion for variable inclusion in the model was set at a $p \leq .05$. Candidate variables that had >25% missing data were not considered for inclusion in the logistic regression regardless of the bivariate analysis to prevent loss of information. A forward selection technique was used for building the logistic regression models. SPSS version 15.0 software (SPSS, Chicago, IL) was used for the data analysis.

RESULTS

Study Population and Survival

From 1995 to 2006, a total of 19,348 pediatric ECMO runs were reported to the ELSO registry. Of these, 260 (1.3%) ECMO runs in 255 patients were for severe cardiorespiratory failure associated with a diagnosis of myocarditis. These 255 patients are the subject of this analysis. All 255 patients were supported with venoarterial ECMO. The median age of the study group was 17 mos (interquartile range = 3–96 mos) and the median weight was 11 kg (interquartile range = 6–25 kg). Males (n = 131) accounted for 52% of the patients and 46% were white. Fifty-three patients (21%) had a documented infection (viral, bacterial, or fungal). Common infectious agents identified in this cohort included enterovirus (n = 16), influenza A and B (n = 6 and n = 1, respectively), respiratory syncytial virus (n = 4), adenovirus (n = 3), *Neisseria meningitidis* (n = 3), *Cytomegalovirus* (n = 2), parainfluenza (n = 2), and other (n = 16).

Of the 255 patients supported with ECMO for myocarditis, 73% (n = 185) were decannulated from ECMO and 61% (n = 155) survived to hospital discharge. Survival rates did not change over the 12-yr study period. The indication for decannulation for all 185 patients who were weaned off ECMO was recorded as adequate recovery of end organ function. The 30 patients (12%) who were weaned from ECMO, but subsequently died before discharge, accounted for 30% of all deaths. Of the remaining 70 patients who died on ECMO or had ECMO support withdrawn, irreversible organ failure was recorded as the reason in 83%. Seven patients underwent heart transplantation and six of these survived to hospital discharge, representing 3% of the study population and 4% of the group surviving to discharge.

Survivors Versus Nonsurvivors

Patient demographic differences between survivors and nonsurvivors are shown in Table 1. Patient age, weight, race, year of ECMO support, and myocarditis subtype (by ICD9 code) were not significantly different among survivors and nonsurvivors. Males were more likely to survive to discharge.

Pre-ECMO Cannulation Factors and ECMO Support Technique

Severity of illness and pre-ECMO support details for survivors and nonsurvivors are shown in Table 2. Pre-ECMO arterial blood gas pH and standardized bicarbonate concentration were significantly higher in survivors. Pre-ECMO blood pressure category was also associated with survival to discharge. The proportion of patients treated with sodium bicarbonate and/or tris-hydroxymethyl aminomethane (THAM) before ECMO was significantly lower among survivors.

There was no difference in the proportion of survivors and nonsurvivors who had a documented viral, bacterial, or fungal infection. However, a greater proportion of nonsurvivors were infected with enterovirus compared with survivors (12% vs. 3%, $p = .003$). Primary diagnosis, time to institution of ECMO post admission, pre-ECMO ventilatory settings, use of high-frequency oscillatory ventilatory modes, and the use of

inhaled nitric oxide were not significantly different between survivors and nonsurvivors. Although not reaching statistical significance, there was a trend toward greater mortality in those who suffered a pre-ECMO cardiac arrest.

Differences in ECMO techniques and related variables among survivors and nonsurvivors are shown in Table 3. The two groups did not differ by ECMO flow rates at 4 hrs after ECMO initiation, cannulation technique (peripheral or transthoracic), or blood vessels used for cannulation. A greater percentage of patients survived to hospital discharge if the indication for ECMO was isolated cardiac failure vs. other indications (E-CPR or combined cardiac and pulmonary failure) (65% vs. 48%, $p = .03$). The survival to hospital discharge rate after E-CPR was 49%, compared with 63% for those not undergoing E-CPR. The difference did not reach statistical significance.

The left side of the heart was decompressed with catheter-based techniques or surgery in 18% of patients ($n = 47$). A venting cannula was used to provide ongoing left atrial decompression in 16 of these patients. There was an increase in the percentage of patients who underwent left atrial decompression over the study period from 4% in 1995 to 1998 to 11% in 1999 to 2002 to 30% in 2003 to 2006 (Mantel-Haenszel chi-square $p < .001$). There was no association between left heart decompression and overall survival or survival within different era (data not shown).

The median duration of ECMO did not differ between survivors and nonsurvivors. Fifteen percent of the patients ($n = 38$) were supported for >2 wks with 47% of them surviving to hospital discharge. Six percent of the patients ($n = 15$) were supported for >3 wks with 33% surviving to hospital discharge. The longest ECMO run in a patient surviving to hospital discharge was 29 days.

ECMO Complications

Complications occurring while on ECMO for survivors and nonsurvivors are shown in Table 4. The proportions of patients with cardiac arrhythmias requiring treatment, renal failure (serum creatinine >1.5 mg/dL), renal failure requiring dialysis, seizures, metabolic acidosis with pH <7.2 , pulmonary hemorrhage, disseminated intravascular coagulation, and hyperglycemia were significantly higher among nonsurvivors compared with survivors. Brain death occurred in 6% of patients ($n = 16$) resulting in withdrawal of ECMO support. The prevalence of neurologic injury (seizure, infarction, hemorrhage, and brain death) was similar in patients cannulated for ECMO during active CPR compared with all other patients (19% vs. 14%; $p = .37$).

Multivariable Analysis of Factors Associated With Mortality

A multivariable logistic regression model was created, demonstrating that female gender, arrhythmia while on ECMO, and renal failure requiring dialysis were independently associated with in-hospital mortality (Table 5). Variables not retained in the model were: age, blood pressure category, pre-ECMO arterial blood pH, arterial blood bicarbonate concentration, administration of sodium bicarbonate or THAM before ECMO, ECMO indication, arterial blood gas pH <7.2 on ECMO, infection with enterovirus, pre-ECMO high-frequency ventilation, pre-ECMO cardiorespiratory arrest, pulmonary hemorrhage,

hyperglycemia, renal failure, leukopenia, seizures, and disseminated intravascular coagulation.

Analysis of Patients Who Died After Successful ECMO Decannulation

We analyzed the subgroup of patients ($n = 30$) who were separated from ECMO after adequate recovery of end organ function, but died before hospital discharge. The median time to death after decannulation was 15 days (interquartile range = 5–19 days) for the 25 patients for whom data were available. Among these 30 patients, bivariate analyses demonstrated that duration of ECMO, gender, renal failure, need for dialysis, pulmonary hemorrhage, and infection with enterovirus differed between survivors and nonsurvivors (Table 6). The need for dialysis while on ECMO (odds ratio, 6.6; 95% confidence interval, 2.5–17.4) was the only factor that independently predicted mortality in a logistic regression model.

DISCUSSION

To our knowledge, this is the first multicentered study to report survival to hospital discharge from a large cohort of children with myocarditis requiring ECMO. We found an encouraging survival-to-hospital-discharge rate of 61% ($n = 155$). Six of the survivors (4%) were discharged from the hospital only after successful heart transplantation. We found that survival post institution of mechanical support for acute myocarditis was influenced by patient factors and the occurrence of ECMO-related complications. Female gender was independently associated with mortality before hospital discharge. As expected, complications that developed during ECMO support increased the risk of mortality; these included the presence of cardiac arrhythmias on ECMO and renal failure requiring dialysis.

The survival rate of 61% found in this cohort of patients is higher than the 48% survival rate reported by Bowles et al in the largest multicentered study to date of children ($n = 480$) with myocarditis (14). This retrospective study included all patients with biopsy-proven myocarditis and was not restricted to those with the more fulminant presentations of those in our study. In a study comparing outcomes of adults with fulminant vs. nonfulminant myocarditis, McCarthy et al demonstrated that a fulminant presentation was paradoxically associated with better survival (1).

The authors of several smaller case series involving children requiring mechanical support for myocarditis have reported survival rates of 67% to 83% (10–12, 15, 16). The lower survival rate in our study may reflect the multi-institutional nature of our data, the presence of better developed ECMO deployment and management programs in some institutions, and the variability in clinical practice regarding the timing of ECMO initiation post presentation. The survival rate for children with myocarditis supported with ECMO is comparable to the 61% overall survival for children supported with ECMO of all indications and is better than the outcomes for postcardiotomy ECMO after repair or palliation of congenital heart disease (37%–42%) (16–19). Thus, of pediatric patients with heart disease, those with myocarditis may be particularly well suited for ECMO support.

The survival disadvantage for female gender is surprising and difficult to explain. We speculate that this association may be due to gender-based differences in the inflammatory response to the primary disease, or to ECMO, analogous to those seen in studies of children and adults undergoing cardiopulmonary bypass (20–22).

Complications that arise while on ECMO support are associated with poor outcomes for all ECMO indications (17, 23–26). We found that the presence of cardiac arrhythmia requiring therapy while on extracorporeal support was associated with a nearly three-fold increase in the odds of death. Lee et al reported a 29% frequency of arrhythmia in children with myocarditis and that the prevalence of arrhythmia was lower in survivors compared with nonsurvivors and those requiring heart transplantation (11). It is possible that patients with rhythm disturbances have more severe myocardial injury than those without, resulting in worse outcomes. Whether prophylactic anti-arrhythmic therapy can alter the disease course for these patients, and whether patients with cardiac arrhythmias should be considered for early listing for transplantation could be studied in the future.

Similar to other reports on ECMO use, we found a strong association between renal injury severe enough to require dialysis and increased mortality (10, 17, 19). Renal failure may have resulted from inadequate end-organ perfusion before or during ECMO support. Careful attention to maintaining good end-organ perfusion during ECMO, minimizing patient exposure to nephrotoxic medications, avoiding the induction of severe prerenal azotemia, and promptly recognizing and relieving abdominal compartment syndrome may help preserve renal function and improve outcomes. Whether prophylactic renal protective therapies, such as infusions of fenoldopam or N-acetylcysteine, can alter outcomes needs to be studied prospectively.

Fifteen percent of the patients in this study required ECMO for failed conventional CPR. Although the overall number is small, we demonstrate a nearly 50% survival rate for a group of patients whose risk of mortality approaches 100%. This reflects the reversible nature of both the specific events leading to the arrest (i.e., malignant rhythm disturbance) and of severe myocarditis itself. Children with nonmyopathic, structural heart disease, a group well known to benefit from E-CPR, have a survival rate of 42%, comparable with the rate in our study (27). Thus, ECMO must be considered in the pediatric patient with myocarditis and cardiorespiratory arrest refractory to conventional CPR.

The importance of adequate left heart decompression for maximizing the chance of myocardial recovery for patients requiring ECMO including those with myocarditis has been extrapolated from myocardial protection strategies related to cardiopulmonary bypass. We were unable to identify an association between left heart decompression and survival. The relatively small number of patients reported to have undergone left heart decompression in this cohort made it difficult to draw conclusions regarding this therapy. It is unclear if the low rate of left heart decompression in the present study accurately reflects clinical practice or is an artifact of underreporting. Thus, the decision to decompress the left heart to promote myocardial rest and recovery should be based on the clinical situation and should be studied carefully in the future.

With the increasing availability of ventricular assist devices (VADs) for mechanical circulatory support in children with refractory cardiac failure, it is important to compare outcomes of ECMO and VADs (28, 29). Of the five devices that have been used in children, the largest recent experience has been with the Berlin Heart Excor device. Hetzer and Stiller reported that, of 21 children supported with the Berlin Heart Excor device for myocarditis or cardiomyopathy, 90% survived to hospital discharge (30). Although encouraging, the total number of children supported with VADs is small and the experience is limited to a handful of centers. There is also the concern that the ventriculotomy required for VAD placement could lead to the future development of arrhythmias and ventricular dysfunction in those who are bridged to recovery. In addition, it is important to consider the risk of neurologic complications associated with VADs. Rockett et al recently reported a 40% prevalence of cerebrovascular accidents in their single center study of 17 children undergoing Berlin Heart Excor implantation (31). This is significantly higher than the 13% frequency of neurologic complications reported for all ECMO uses (23).

This report has several important limitations. Data collected by the ELSO registry are not specific for studying ECMO support of children with myocarditis and thus important variables, such as hemodynamic parameters, etiological agents, histologic information from endomyocardial biopsy, and use of steroids or immunoglobulin therapy, are not available; therefore, important variables that influence survival outcomes may have been missed. In addition, missing data limited the choice of covariates for inclusion in the multivariable models. In addition, data on the amount and type of support required after decannulation from ECMO were not collected. The number of patients listed for transplantation cannot be accurately evaluated as these data are not collected by ELSO. Furthermore, longer-term outcomes, such as functional, neurocognitive status, and quality-of-life measures, are not available for analysis. The retrospective nature of the data limits deriving conclusive information on risk factors for mortality based on this report. However, this report is the largest epidemiologic study to describe outcomes for children with myocarditis supported with ECMO and can serve as a guide for future studies comparing survival and complications for children with myocarditis supported with ECMO and other mechanical support devices.

In conclusion, we found that ECMO can be used effectively to support children with cardiorespiratory collapse in children and young adults with myocarditis. However, despite its use, mortality remains nearly 40%. We have identified three independent risk factors for death in this study including female gender, the need for dialysis on ECMO, and the presence of arrhythmias requiring treatment on ECMO. It will be important to test prospectively whether medical interventions that target these variables, such as early renal protective therapies and prophylaxis with antiarrhythmic medications, can alter the disease course for these critically ill children. The identification of these risk factors can help clinicians make difficult decisions regarding early listing for transplantation and transition to VAD therapy when the probability of mortality is high.

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Table 1

Demographic features of survivors and nonsurvivors of extracorporeal membrane oxygenation initiated for myocarditis

Variable	Survivors (n = 155)	Nonsurvivors (n = 100)	p
Age, mos	21 (7–106)	14 (0.5–84)	.07
Gender			.002
Female	62 (40)	60 (61)	
Male	92 (60)	39 (39)	
Weight, kg	12 (7–26)	10 (4–22)	.13
Race ^d			.49
White	59 (44)	42 (49)	
Other	75 (56)	43 (51)	
Era			.23
1994–1998	31 (20)	22 (22)	
1999–2002	44 (28)	37 (37)	
2003–2006	80 (52)	41 (41)	
Myocarditis			.09
ICD9 code			
422 ^b	105 (68)	65 (65)	
422.91 ^c	17 (11)	22 (22)	
422.9 ^d	17 (11)	5 (5)	
422.90 ^e	10 (6)	4 (4)	
422.0 ^f	6 (4)	4 (4)	

ICD9, *International Statistical Classification of Diseases and Related Health Problems, 9th Revision*.

^a 14% missing data;

^b acute myocarditis;

^c idiopathic myocarditis;

^d other and unspecified myocarditis;

^e acute myocarditis, unspecified;

f acute myocarditis in diseases classified elsewhere.

Data are presented as median (interquartile range) or n (%).

Table 2

Precannulation variables in patients requiring ECMO for myocarditis

Variable	Survivors (n = 155)	Nonsurvivors (n = 100)	p
Time to ECMO cannulation (hrs) ^a	14 (6–38)	12 (3–4)	.11
Arterial blood gas analysis ^b			
pH	7.34 (7.21–7.41)	7.26 (7.13–7.40)	.01
P _{CO2} , torr	40 (32–51)	38 (30–49)	.41
P _{O2} , torr	72 (45–152)	77.5 (52–163)	.47
HCO ₃ , mmol/L	20 (17–25)	18 (13–23)	.006
Pre-ECMO factors			
Blood pressure ^c			.04
Hypotensive	56 (47)	50 (65)	
Normotensive	45 (38)	22 (29)	
Hypertensive	17 (14)	5 (6)	
Bicarbonate or THAM administered	55 (36)	49 (49)	.04
Cardiac arrest (excluding E-CPR)	68 (44)	55 (55)	.08
Pre-ECMO mechanical support	6 (4)	2 (2)	.49
Vasodilators	34 (22)	27 (27)	.37
Inotropes	124 (80)	82 (82)	.69
Infection	31 (20)	22 (22)	.70
Enterovirus positive	4 (3)	12 (12)	.003
Duration of mechanical ventilation, hrs ^d	20 (6–49)	13 (4–47)	.28
Ventilator parameters ^e			
Rate	23 (18–30)	24 (17–30)	.53
F _{IO2} , %	100 (60–100)	100 (80–100)	.13
PIP, cm H ₂ O	26 (22–31)	27 (23–32)	.51
PEEP, cmH ₂ O	6 (5–8)	6 (5–8)	.98
MAP, mmHg	14 (10–20)	12 (10–14)	.07

Variable	Survivors (n = 155)	Nonsurvivors (n = 100)	p
High-frequency ventilation	17 (11)	5 (5)	.10
Inhaled nitric oxide	17 (11)	8 (8)	.44

ECMO, extracorporeal membrane oxygenation; THAM, tris-hydroxymethyl aminomethane; E-CPR, extension of cardiopulmonary resuscitation; PIP, peak inspiratory pressure; PEEP, positive end-expiratory pressure; MAP, mean arterial pressure.

Missing values

^a 17%;

^b 11%–18%;

^c 23%;

^d 6%;

^e 11%–56%.

Data are presented as median (interquartile range) or n (%).

Table 3

ECMO-related variables in patients with myocarditis requiring extracorporeal support

Variable	Survivors (n = 155)	Nonsurvivors (n = 100)	p
Indication for ECMO			.03
Cardiac failure	126 (81)	69 (69)	
Other	29 (19)	31 (31)	
E-CPR	18 (12)	19 (19)	
Cardiac and pulmonary failure	11 (7)	12 (12)	
ECMO flow at 4 hrs, mL/kg/min ^a	89 (69–111)	97 (75–110)	.22
ECMO duration, hrs	168 (118–226)	172 (70–289)	.71
Cannula variables ^b			
Perfuser site			.45
Carotid artery	105 (80)	63 (76)	
Femoral artery	19 (14)	11 (13)	
Aorta	8 (6)	9 (11)	
Not recorded	23	17	
1° Drainage site			.28
Internal jugular vein	108 (82)	63 (72)	
Femoral vein	11 (13)	15 (17)	
Right atrium	8 (6)	10 (11)	
Not recorded	28	12	
Percutaneous cannulation	13 (10)	7 (8)	.66
Trans thoracic cannulation	9 (7)	10 (12)	.20
Left atrial decompression (any method)	31 (20)	16 (16)	.51
2 nd Drainage cannula	19 (12)	15 (15)	.58

ECMO, extracorporeal membrane oxygenation; E-CPR, extension of cardiopulmonary resuscitation.

Missing values

^a 15%;^b 8–16%.

Data are presented as median (interquartile range) or n (%).

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Table 4

Complications during ECMO for patient with myocarditis

Variable	Survivors (n = 155)	Nonsurvivors (n = 100)	p
ECMO support			
Mechanical failure ^a	19 (12)	21 (21)	.06
pH <7.2 on ECMO	5 (3)	12 (12)	.006
Circuit thrombus	31 (20)	24 (24)	.45
Bleeding ^b	42 (27)	28 (28)	.88
Inotrope requirement	108 (70)	66 (66)	.54
Brain injury			
Brain death	0 (0)	16 (16)	<.001
Seizures (EEG or clinical)	6 (4)	10 (10)	.05
CNS infarction or hemorrhage	12 (8)	9 (9)	.72
Renal injury			
Renal failure, Cr >1.5 mg/dL	18 (12)	32 (32)	<.001
Dialysis ^c	12 (8)	30 (30)	<.001
Cardiac			
Arrhythmia (requiring therapy)	44 (28)	48 (48)	.001
CPR done on ECMO	5 (3)	6 (6)	.35
Hematologic			
Leukopenia, WBC <1500 cells/uL	0 (0)	3 (3)	.06
DIC	4 (2.6)	9 (9)	.02
Endocrine			
Hyperglycemia, glucose >240 mg/dL	18 (12)	25 (25)	.005
Hypoglycemia, glucose <40 mg/dL	2 (1)	2 (2)	.65
Infectious			
Culture proven infection	20 (13)	17 (17)	.36
Respiratory			
Pulmonary hemorrhage	11 (7)	16 (16)	.02

ECMO, extracorporeal membrane oxygenation; EEG, electroencephalographic; CNS, central nervous system; CPR, cardiopulmonary resuscitation; WBC, white blood cell; DIC, disseminated intravascular coagulation.

^aOxygenator failure, tubing rupture, pump malfunction, heat exchanger malfunction, air in circuit and cracks in Luer lock connectors;

^bcannulation or surgical site;

^cintermittent or continuous arteriovenous hemodialysis (not intrafiltration).

Data are presented as median (interquartile range) or n (%).

Table 5

Logistic regression analysis of predictors of in-hospital mortality for pediatric patients requiring ECMO for myocarditis (n = 225)

Variable	Adjusted Odds Ratio (95% CI)	p
Female gender	2.3 (1.3–4.2)	.007
Arrhythmia on ECMO	2.7 (1.5–5.1)	.001
Dialysis on ECMO	5.1 (2.3–11.4)	<.001

ECMO, extracorporeal membrane oxygenation; CI, confidence interval

Table 6
Pre-ECMO and ECMO-related variables associated with survival after successful decannulation

Variable	Survivors to Hospital Discharge (n=155)	Nonsurvivors After Decannulation (n=30)	p
Duration of ECMO (hrs)	168 (145–226)	245 (145–347)	.03
Male gender	92 (60)	12 (40)	.04
Renal failure on ECMO, Cr > 1.5 mg/dL	18 (12)	9 (30)	.02
Dialysis on ECMO	12 (8)	11 (37)	<.001
Pulmonary hemorrhage on ECMO	11 (7)	6 (20)	.04
Infection with enterovirus	4 (3)	4 (13)	.03

ECMO, extracorporeal membrane oxygenation.

Data are presented as median (interquartile range) or n (%)