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Original Research Article

Outcome of single-ventricle patients supported with extracorporeal membrane oxygenation

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ABSTRACT

Background: Single ventricle heart disease can be left or right ventricle dominant congenital heart disease mostly associated with other risk factors like low birth weight, Preterm, chromosomal abnormality and all these risk factor associated with increase mortality.

Methods: A retrospective chart review of paediatric patients from neonatal age to 14 years since 2012 to 2021, with supported by extracorporeal membrane oxygenation (ECMO) including both single ventricle heart physiology and biventricular heart, admitted in paediatric cardiac surgical intensive care unit in our hospital was conducted. All data were compared between single ventricle heart physiology and biventricular heart. Data was performed using commercially available software (SPSS), with statistical significance set $p<0.05$.

Results: We enrolled total 124 patients who underwent ECMO cannulation. 68 children had single ventricle, while 56 being biventricular heart. Most children acquired ECMO cannulation in CICU 63 (50.8%). Male to female ratio was 74:50. 70.2% children got the ECMO cannulation when they had already been operated for surgical repair.

Conclusions: Paediatric ECMO utilization in SV is valuable and recently its utilization has been increased in it with improve survival.

Keywords: Congenital heart diseases, Single ventricle heart, Paediatric extracorporeal membrane oxygenation, Complications, Outcome

INTRODUCTION

Single ventricle heart disease can be left or right ventricle dominant congenital heart disease, mostly associated with other risk factors like low birth weight, prematurity, chromosomal abnormalities, with prevalence to have risk of increase mortality.[1-4]

Extracorporeal membrane oxygenation (ECMO) is a rescue therapy, used to provide mechanical circulatory support, to maintain end organ oxygenation, in special circumstances like cardiopulmonary arrest, low cardiac output syndrome, hypoxia, unable to wean from cardiopulmonary bypass, hemodynamic instability, and severe pulmonary hypertension.[5]

The main goals of ECMO therapy are as rescue therapy prior to permanent organ dysfunction.[1,2] To investigate for reversible causes of cardiac dysfunction timely weaning from ECMO to minimize its the complications.[3] As per extracorporeal life support organization registry survival to discharge for single ventricle still remains poor at 41-50%.[6] Though, many studies are being conducted to see utility of ECMO in single ventricle heart physiology and its use has been rising with time. Across the literature reviewed, it has been observed an increase in volume of single ventricle heart disease supported with ECMO with no significant improvement in survival rate.[7-9] Several other studies have reported improved survival in single ventricle ECMO supported patients, but there is much variation in results in addition to other studies.[10]

The goal of this study is to see outcome of single ventricle patients supported ECMO and its comparison with biventricular heart supported with ECMO in form of mortality, length of stay on ECMO and complications. Our study showing our institutional experience of single ventricle heart physiology (SV) patients supported with ECMO.

Objectives of study

The aim of this study is to determine the outcome of patients with single ventricle supported with ECMO.

METHODS

This study was a retrospective chart review of paediatric patients from neonatal age to 14 years in 2012 to 2021, with supported by ECMO including both single ventricle heart physiology and biventricular heart, admitted in paediatric cardiac surgical intensive care unit in our hospital. Other data include admission and discharge status, primary and secondary outcome, patient demographics (e.g. age, and gender), length of intensive care unit (ICU) stay, length of hospital stay. Other comorbid factors or complications that were included in our study were arrhythmias, neuro/cerebral vascular disease, length of stay on mechanical ventilator, length of stay on ECMO, heart failure, acute liver failure, acute kidney failure, sepsis, need for gastrostomy tube, need for tracheostomy tube. All patients who required ECMO before or after surgery, age less than 14 years. We excluded the patients with Single ventricle patients who required ECMO after orthotropic heart transplant and All patients age more than 14 years.

Duration of mechanical ventilation was defined as duration before ECMO included duration on ventilation from tracheal intubation to initiation of ECMO and covered pre- and postoperative periods. Pre-ECMO arrest was defined as cardiac arrest at any time prior to initiation of ECMO and didn't include extracorporeal cardiopulmonary resuscitation (ECPR).

ECPR is defined as V-A ECMO cannulation during refractory cardiac arrest. Arrhythmia is defined as irregularities in the heartbeat, including when it is too fast or too slow, evident on 12 lead ECG. Neuro/cerebral vasculature disease was taken into account who were evident by either clinically abnormal movements /altered level of conscious, any focal deficit or findings on radiological images (CT/MRI). Heart failure was defined by echo (i.e. LV dysfunction), or by requiring anti-failure medications (ACE inhibitors, diuretics, beta blockers) or clinically signs of failure, like pedal oedema, pulmonary oedema, persistent tachycardia, tachypnoea, hepatomegaly, and sweating on feeding.

Acute liver failure was defined as moderate coagulopathy (INR>1.5) with encephalopathy and severe coagulopathy (INR>2.0) without evidence of encephalopathy or transaminases (AST, and ALT) elevated 2 times of normal limit. While, Acute renal injury was defined if there was a decrease in kidney functions, evident by increase creatinine by 1.5 times of normal, decrease in urine 0.5 ml/kg/hour for 6 hour or oliguric or need for renal replacement therapy (PD/CRRT). We charted the sepsis if there was suspected or proven infection or clinical syndrome (high inflammatory markers, leucocytosis, fever), with high probability of infection.

Statistical analysis

All data were compared between single ventricle heart physiology and biventricular heart. Data was performed using commercially available software, statistical package for the social sciences (SPSS), with statistical significance set $p<0.05$. Continuous variables were analysed as mean, median and standard deviation and categorical variables was analysed as frequency.

Definitions

Duration of mechanical ventilation is duration before ECMO included duration on ventilation from tracheal intubation to initiation of ECMO and covered pre- and postoperative periods.

Pre-ECMO arrest is defined as cardiac arrest at any time prior to initiation of ECMO and didn't include extracorporeal cardiopulmonary resuscitation ECPR

ECPR is defined as V-A ECMO cannulation during refractory cardiac arrest.

Arrhythmia is defined as irregularities in the heartbeat, including when it is too fast or too slow, evident on 12 lead ECG.

Neuro/cerebral vasculature disease is evident by either clinically abnormal movements/altered level of conscious, any focal deficit or findings on radiological images (CT/MRI).

Heart failure is either evident by echo (i.e. LV dysfunction), or requiring anti-failure medications (ACE inhibitors, diuretics, beta blockers) or clinically signs of failure, like pedal oedema, pulmonary oedema, persistent tachycardia, tachypnoea, hepatomegaly, sweating on feeding.

Acute liver failure was defined as moderate coagulopathy (INR>1.5) with encephalopathy and severe coagulopathy (INR>2.0) without evidence of encephalopathy or transaminases (AST, and ALT) elevated 2 times of normal limit.

Acute renal injury is abrupt decrease in kidney functions, evident by increase creatinine by 1.5 times of normal, decrease in urine 0.5 ml/kg/hour for 6 hour or oliguric or need for renal replacement therapy (PD/CRRT).

Sepsis is suspected or proven infection or clinical syndrome (high inflammatory markers, leucocytosis, fever), with high probability of infection.

RESULTS

We enrolled total 124 patients who underwent ECMO cannulation. 68 children had single ventricle, while 56 being biventricular heart. Most children acquired ECMO cannulation in CICU 63 (50.8%).

Male to female ratio was 74:50. 70.2% children got the ECMO cannulation when they had already been operated for surgical repair. 27 children also had ECMO insertion before operation.

Most common indication was ECMO cannulation following the cardiopulmonary resuscitation. Although, hemodynamic deterioration also leads in 30 children comprising the 24.2% of all ECMO cases. Low cardiac output syndrome also contributing significantly, in 8.1% children as a leading cause for ECMO initiation.

Regarding the complications, children attain the neurological injuries, arrythmias, acute kidney injury (AKI), acute liver injury and sepsis (Tables 1 and 2).

Table 1: Features of all ECMO patients (n=124).

Variables	Yes	No
Single ventricle	68 (54.8)	56 (45.2)
Male	74 (59.7)	50 (40.3)
ECMO before surgery	27 (21.8)	97 (78.2)
ECMO after surgery	87 (70.2)	37 (29.8)
Arrythmia	32 (25.8)	92 (74.2)
Neuro-injury	42 (33.9)	82 (66.1)
Heart failure	19 (15.3)	105 (84.7)
Acute kidney injury	41 (33.1)	83 (66.9)
Acute liver injury	18 (14.5)	106 (85.5)
Sepsis	40 (32.3)	84 (67.7)
Tracheostomy	09 (7.3)	115 (92.7)
Indications		
ECPR	49 (39.5)	
Hemodynamic instability	30 (24.2)	
LCOS	10 (8.1)	
Survival on de-cannulation	80 (64.5)	44 (35.5)
Survival on discharge	52 (41.9)	72 (58.1)

Children on ECMO with single ventricle had mean time of 15.24±31.44 while it was 12.07±16.64 days in bi-ventricle patients. Length of stay on ventilator and ICU has been also described in Table 3.

Multivariate analysis showed that the children having more ECMO time has increased risk of mortality, as demonstrated in Table 4.

Table 2: Features in single ventricle versus non-single ventricle.

Variables	Single ventricle (%)	Non-SV (%)	P value
ECMO before surgery (27)	07	20	0.15
ECMO after surgery (87)	54	33	0.02
Arrhythmias (32)	12	20	0.02
Neurological injury (42)	21	21	0.004
Heart failure (19)	01	18	0.01
Acute kidney injury (41)	18	23	0.05
Acute liver injury (18)	07	11	0.006
Sepsis (40)	20	20	0.003
Survival at decannulation (80)	47	33	0.02
Survival at discharge (52)	31	21	0.004
Death (72)	40 (32.3)	32 (25.8)	0.02

Table 3: Descriptive analysis of the length of stay on ECMO, on ventilator and in ICU.

Variables	SV	Non SV	P value
LOS ECMO (days)	15.24±31.44 (0–153)	12.07±16.64 (0–91)	0.04
LOS VENT (days)	33.88±60.47 (1–334)	35.91±55.42 (1–309)	0.51
LOS ICU (day)	50.12±109.90 (2–830)	58.14±130 (1–833)	0.72

Table 4: Multivariate analysis of variables related to SV and mortality (p values).

Variables	SV	Death
LOS ECMO	0.47	0.03
LOS VENT	0.84	0.82
LOS ICU	0.72	0.11
Arrhythmia	0.02	0.53
Neuro	0.41	0.03
Acute renal failure	0.06	0.01

DISCUSSION

The data in our study not only represent outcome of patients with single ventricle heart on ECMO but also represents outcome in biventricular heart with ECMO supported. Previous studies suggested that outcome for single ventricle heart physiology is less than those with BV physiology, therefore, in many centres single ventricle physiology heart was considered to be contraindication to ECMO utilization.[10,11] However recently several centres have demonstrated improved outcome of children with single ventricle heart (SV) with ECMO supported even though single ventricle heart physiology (SV) continues to be a risk factor for higher ECMO mortality. Therefore, use of ECMO in patients with single ventricle heart physiology is increasing nowadays.

We enrolled total 124 patients who underwent ECMO cannulation. 68 children had single ventricle heart (SV) physiology, while 56 children had biventricular heart and male to female ratio was 59:40. Average length of stay on ECMO in our study for single ventricle heart physiology was 15.24±31.44 (0–153) and for biventricular heart was 12.07±16.64 (0–91) and we found that length of stay on ECMO for single ventricle heart has direct relationship on mortality.

Average length of stay on mechanical ventilator for single ventricle heart physiology was 33.88±60.47 (1–334) and for biventricular heart was 35.91±55.42 (1–309), length of stay of mechanical ventilator has no relation with mortality both in single ventricle heart or biventricular heart. Average length of stay in cardiac intensive care unit for single ventricle heart physiology was 50.12±109.90 (2–830) and for biventricular heart was 58.14±130 (1–833).

In our study survival on discharge for single ventricle heart physiology (SV) 45.5% which is consistent with previous studies, and survival to discharge for biventricular physiology is 37.5% which is slightly lower than single ventricle heart physiology likely related to complications that occurred during long course of stay (ECMO) for biventricular heart specifically dilated cardiomyopathy (DCM).[12-17]

The timing of initiation of ECMO was 21.8% before surgery and 70.2% after the surgery, and those with before surgery it was more common in biventricular heart mostly due to low cardiac output (LCO) and high lactate in dilated cardiomyopathy patients. After surgery it is more common in single ventricle physiology patients and most common causes were unable to wean from bypass, hemodynamic instability and ECPR in cardiac intensive care unit. The timing of initiation doesn’t have any effects on overall mortality.

The risk factors for mortality in our study, like poor perfusion, high lactate, and prolong duration of ECMO are similar to other studies and have been associated with increased risk of mortality.[18,19]

Complications

Most common complication overall which was identified in our study was neuro-injury 33.9%, followed by acute kidney injury 33.1% and sepsis 32.3% and other complications were arrythmias 25.8%, heart failure 15.3%, acute liver injury 14.5% and need for tracheostomy tube 7.3%.

Neuro-injury

Neuro-injury was most common complication and it accounts 33.9%. Its incidence in single ventricle heart physiology (SV) was 30.8% and while in biventricular heart was 37%. Most common neuro-injury in single ventricle physiology was subdural haemorrhage 45% and haemorrhagic stroke 17% was most common neuro-injury in biventricular heart.

Risk factors in our study were long ECMO stay, prolong anticoagulation usage and biventricular heart specifically dilated cardiomyopathy (DCM).

Acute kidney injury

Acute kidney injury was the second most common complication 33.0%. It was more common in biventricular heart physiology 41% then single ventricle heart 26.4%. In this study acute renal failure was associated with higher mortality which is consistent with some other studies.[18] Based upon these results we can predict poor prognosis for survival on ECMO supported patients. Risk factors identified in our study were long ECMO stay, poor perfusion and long ventilator stay. Out of 41 patients with acute kidney injury 12 (29.2%) patients required renal replacement therapy inform of peritoneal dialysis and continues renal replacement therapy (CRRT).

Sepsis

Sepsis is the third most common complications (40) 32.2% and it was more common in biventricular heart 35.7% then single ventricle physiology heart (SV) 29.5%. Blood cultures proven cases were 30% overall.

Arrythmias

Incidence of arrythmias in our study was 25.8% (32) patients out of 124 totals. It was more common in biventricular heart 39.3% specifically in DCM and in single ventricle physiology heart (SV) it was 17.6%. Incidence of arrythmias is almost double in biventricular heart. Most common type of arrythmias in single heart physiology (SV) was junctional ectopic tachycardia (JET), while in biventricular heart is ventricular tachycardia (Vtech).

Heart failure

Heart failure was present in 15.3% in all patients and it was more common in biventricular heart 32.1% and mostly present in DCM, and it was only 1.5% in single ventricle heart that occurred in post-operative patients and related to residual lesion.

All the complications including arrythmias, neuro-injury, heart failure, acute kidney injury, acute liver injury, sepsis and need for tracheostomy tube are more common in biventricular heart than single ventricle heart physiology, likely it is associated with longer stay on ECMO.

Extracorporeal cardiopulmonary resuscitation

The use of ECPR with ECMO support provide rapid cardiovascular support to patients who are not responding to conventional cardiopulmonary resuscitation. In single ventricle patients, it is challenging considering its physiology and adequate resuscitation during CPR. In our study, most common indication for usage of ECMO is ECPR. The success of ECPR depends upon rapidity of ECMO deployment, presence of cannulation snares in high-risk patients, adequacy of CPR and presence of a structured ECPR protocol in institution. Indication to apply ECPR in our institution is full code and not responding to conventional CPR within five minutes. In our study patients with SV 49 (39.5%) underwent ECPR and have higher survival. We didn't find any co-relationship with duration of CPR before placement of ECMO with increase mortality.

Our study has many limitations including the retrospective nature of the study. We had included all possible data considering the confounders in list. Still, we believe the active nature of complications including the true nature of arrythmias, type of sepsis, and response to treatment could be better manifested with prospective study. We have planned to conduct another study in this regard with inclusion of other centre.

CONCLUSION

Paediatric ECMO utilization in SV is valuable and recently its utilization has been increased in it with improve survival. Acute kidney injury, prolong ECMO duration, and end organ injury associated with increase mortality. Whereas early utilization of ECMO, expedite weaning of ECMO to prevent its complications and optimization of end organ perfusion can improve outcome.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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