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5 6	Open Abdomen during Extracorporeal Membrane Oxygenation is a Safe and Effective Treatment for Abdominal Compartment Syndrome
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ABSTRACT

Background/Purpose

Decompressive laparotomy and open abdomen for abdominal compartment syndrome have been historically avoided during Extracorporeal Membrane Oxygenation (ECMO) due to seemingly elevated risks of bleeding and infection. Our goal was to evaluate a cohort of pediatric respiratory ECMO patients who underwent decompressive laparotomy with open abdomen at a single institution and to compare these patients to ECMO patients without open abdomen.

Methods

We reviewed all pediatric respiratory ECMO (30 days-18 years) patients treated with decompressive laparotomy with open abdomen at Riley Hospital for Children (1/2000-12/2019) and compared these patients to concurrent respiratory ECMO patients with closed abdomen. We excluded patients with surgical cardiac disease. We assessed demographics, ECMO data, and outcomes and defined significance as p=0.05.

Results

6 of 81 ECMO patients were treated with decompressive laparotomy and open abdomen. Open and closed abdomen groups had similar age (p=0.223) and weight (0.286) at cannulation, but the open abdomen group had a higher reliance on vasoactive medications (Vasoactive Inotropic Score, p=0.040). Open abdomen group survival was similar to closed abdomen patients (66.7%, vs 62.7%, p=1). Open abdomen patients had lower incidence of ECMO complications (33.3% vs 83.6%, p=0.014), but the groups had similar bleeding complications (p=0.412) and PRBC transfusion volume (p=0.941).

Conclusion/Impact

Pediatric ECMO patients with open abdomen after decompressive laparotomy had similar survival, blood products administered, and complications as those with a closed abdomen. An open abdomen is not a contra-indication to ECMO support in pediatric respiratory patients and should be considered in select patients.

KEYWORDS

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7	Extracorporeal membrane oxygenation
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14	Abdominal compartment syndrome
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LEVEL OF EVIDENCE

III

5 6 7

ABBREVIATIONS

- CNS: Central Nervous System
- DIC: Disseminated Intravascular Coagulation

ECMO: Extracorporeal Membrane Oxygenation

EMR: Electronic Medical Record

FFP: Fresh Frozen Plasma

ICU: Intensive Care Unit

IQR: Interquartile Range

LOS: Length of Stay

PRBCs: Packed Red Blood Cells

P-Prep: Pediatric Pulmonary Rescue with Extracorporeal Membrane Oxygenation

VA: Venoarterial

VIS: Vasoactive Inotropic Score

VV: Venovenous

1. INTRODUCTION:

Extracorporeal Membrane Oxygenation (ECMO) is a lung and/or heart bypass modality, which is used for respiratory and cardiovascular support in critically ill patients who have failed conventional therapy and have a possibility of recovery. The rare ECMO patient may suffer from abdominal catastrophy or abdominal compartment syndrome. Decompressive laparotomy and subsequent open abdomen may be required in order to relieve intra-abdominal pressure and restore blood flow to vital organs, preventing ischemia and necrosis [1]. However, performing a laparotomy or maintaining an open abdomen prior to or during ECMO support may lead to an elevated risk of bleeding and intra-abdominal infection, leading physicians to recommend against this treatment modality. There are documented examples of these complications [2, 3], but they are scant in the literature and do not conclusively demonstrate that these risks outweigh the potentially life-saving benefit of ECMO support. In adults, the use of laparotomy with open abdomen in ECMO patients was recently described by Schulz and colleagues [4]. This singlecenter retrospective study reported that laparotomy with open abdomen was a necessary treatment in adult ECMO patients with abdominal compartment syndrome but had an associated mortality of 50% in their 8-patient cohort [4].

Over the last decade at our institution, ECMO support has been increasingly utilized for patients who have an open abdomen and for those who require decompressive laparotomy. The primary aim of this study was to describe children on ECMO with an open abdomen. The secondary aim was to compare children with an open abdomen on ECMO to children without an open abdomen on ECMO. We hypothesize that open abdomen ECMO patients will have similar survival and ECMO related complications to other patients on ECMO.

2. METHODS:

2. 1. Study Design

After Indiana University IRB approval (IRB protocol# 2005722795) was received as a consent-exempt study, all pediatric (30 days-18 years) patients treated with a decompressive laparotomy with open abdomen either prior to or during ECMO support at Riley Hospital for Children from 2000 through 2019 were reviewed during June and July 2020. We compared this group to the total cohort of pediatric patients supported with ECMO at Riley during the same period. Exclusion criteria included pediatric ECMO patients with hemodynamically significant congenital heart disease, those who underwent multiple ECMO runs, and those treated with thoracotomy during their ECMO run.

2. 2. Data Extraction and Analysis

We identified patients through an institutional pediatric ECMO database and supplemented the database with a comprehensive review of the Electronic Medical Record (EMR). From this data, we recorded demographics, ECMO modality (Venovenous [VV], Venoarterial [VA]) and flow, lactate trends, blood gases, ventilator settings, Vasoactive Inotropic Score (VIS), Pediatric Pulmonary Rescue with Extracorporeal Membrane Oxygenation (P-Prep) score, leukocyte count, volume of blood products administered, complications, length of stay, and survival. VIS is a validated aggregate of vasoactive medications used in a patient's care that has been demonstrated to be a predictor of morbidity and mortality in children after cardiopulmonary bypass [5]. The P-Prep score is a validated score used to predict mortality in children treated with ECMO for respiratory failure, based on ECMO modality, PaO₂/FiO₂, pH, primary pulmonary diagnosis, and comorbidities [6].

2. 3. Statistics

After recording these data points for each patient, we compared each datapoint from the open abdomen group to the closed abdomen group, using Fisher's exact test and Wilcoxon's rank-sum test for categorical and continuous variables, respectively. We defined significance as p<0.05. Additionally, we used ROC analysis to determine the optimal cutoff points to predict mortality for P-Prep score and VIS in the entire group of patients, as the open abdomen group included too few patients to be analyzed separately. The optimal cutoff points were defined as those that maximized Cohen's kappa, indicating agreement between the predicted outcome and the actual outcome. The primary outcome for this study was defined as survival to hospital discharge and the secondary outcomes as bleeding complications and volume of blood products administered.

The decision to perform a decompressive laparotomy followed by open abdomen in an ECMO patient in our center is an interdisciplinary one involving the pediatric surgery service, the pediatric intensive care team, and the multidisciplinary ECMO rounding team. These teams collaboratively weigh the benefits and risks for patients with reversible abdominal catastrophe and/or abdominal compartment syndrome to make the decision whether decompressive laparotomy and open abdomen during ECMO will most likely provide benefit and minimize harm. Our institution does not yet have a codified algorithm for care of this select group of highly morbid patients.

Our center utilizes unfractionated heparin as the primary anticoagulant during ECMO support. Patients are placed on a standard risk or high risk bleeding protocol with goal anti-Xa level of 0.5-0.7U/mL and 0.3-0.5U/mL, respectively, based on bleeding risk, as determined by

the daily ECMO rounding team. All open abdomen patients were maintained on the high risk bleeding protocol.

3. RESULTS:

3. 1. Study Population

Our study group included 6 patients who received decompressive laparotomy and had an open abdomen during ECMO support.

- Patient 1, a 6-year-old male, was transported to Riley after cold water drowning in
 respiratory failure and full cardiac arrest. He developed abdominal compartment
 syndrome and was treated with decompressive laparotomy and open abdomen followed
 by VA ECMO cannulation. His ECMO course was complicated by ECMO raceway
 rupture, chest tube bleeding, abdominal bleeding, and disseminated intravascular
 coagulation (DIC). He died after 33 hours on ECMO due to brain death and multiple
 organ failure secondary to drowning.
- Patient 2, a 5-year-old female, was admitted to Riley for obstructive sleep apnea and was placed on ECMO support after 9 days in intensive care due to refractory hypoxia on increasing ventilator settings. She was initially cannulated for VV ECMO but was converted to VA intraoperatively after cardiac arrest secondary to pericardial effusion. Her ECMO course was complicated by cannula site bleeding, chest tube site bleeding, and cardiac tamponade. After 75 hours on ECMO, she died from brain herniation secondary to cytotoxic cerebral edema.

Patient 3, a 13-month-old female, was transported to Riley in septic shock and abdominal compartment syndrome secondary to ruptured appendicitis with abscess formation. After an exploratory laparotomy with abdominal washout, appendectomy, and open abdomen, she was placed on VA ECMO for severe septic shock. Her ECMO course was uncomplicated, and after 237 hours her condition improved sufficiently to allow weaning from ECMO support. Her abdomen was closed 2 days later. She was discharged to home 39 days after admission.

- Patient 4, a 1-month-old male, was placed on VA ECMO support on the day after his admission to Riley due to septic shock leading to cardiac arrest. The next day, he was treated with a decompressive laparotomy and open abdomen due to abdominal compartment syndrome likely due to Clostridium difficile peritonitis. His abdomen was closed after 4 days while still on ECMO support. After an uncomplicated ECMO course of 240 hours, his improved condition warranted decannulation and he was discharged 44 days after admission.
- Patient 5, a 6-month-old male, was admitted to Riley due to a bowel perforation from idiopathic colonic necrosis. He was treated with an exploratory laparotomy and total abdominal colectomy with end ileostomy and open abdomen. He was placed on VA ECMO support due to refractory septic shock on postoperative day 1. The ECMO course was otherwise uncomplicated, and his abdomen was closed on post-operative day 7. The next day, he was decannulated after 172 hours on ECMO support, and he was discharged home 29 days after admission.
- Patient 6, a 2-year-old male, was transferred to Riley due to intestinal perforation with septic shock. He was treated with an exploratory laparotomy and bowel resection, and

during that operation, he experienced PEA cardiac arrest, from which he attained return of spontaneous circulation. His abdomen was left open after the operation. The following day, he was placed on VA ECMO support due to severe septic shock refractory to conventional therapy. His ECMO course was uncomplicated, and he was decannulated after 111 hours on ECMO support. His abdomen was closed the following day, and he was eventually discharged to home 27 days after admission.

3. 2. Patient Demographics and ECMO Support:

The demographics of both study and comparison groups and ECMO course characteristics of each group are outlined in Table 1; the groups had no significant differences in any demographic category. The open abdomen group contained 6 patients, while the comparison group contained 75 patients. The open abdomen patients trended toward greater age, but likely due to the small sample size this difference did not reach statistical significance. The weight of the two groups, however, was clearly not significantly different. The patients who were treated with decompressive laparotomy were more likely to require ECMO for cardiovascular collapse related to septic shock, while the closed abdomen patients were disproportionally weighted toward purely respiratory indications.

3. 3. Serum Lactate Trends:

The median serum lactate trends pre-ECMO and during ECMO are shown in Figure 1. Note that while the lactate values were not statistically different at any time point, the serum lactate in the open abdomen group showed a consistent downward trend and normalized by 72 hrs. The closed abdomen group, however, remained relatively constant.

3. 4. ECMO Pump Flow:

The median pump flow rates over the first 24hrs of ECMO support were compared between the open abdomen and closed abdomen groups. The open abdomen group had higher median flow rates at each time point, although the difference between the open abdomen and closed abdomen groups was only significant at 24hrs of ECMO support (p=0.022). At 1 hour on ECMO support, the open abdomen group required a median flow rate of 108.7 mL/kg/min (IQR 99.4-118.1), while the closed abdomen group required a median of 61.8 mL/kg/min (IQR 48.4-89), p=0.080. At 4 hours on ECMO support, the median flow rate was 99.5 mL/kg/min for open abdomen (IQR 96.8-109) and 77.1 mL/kg/min for closed abdomen (IQR 53.7-97.2), p=0.056. At 24 hours on ECMO support, the median flow rate was 108 mL/kg/min for open abdomen (IQR 101.8-165.2) and 88.1 mL/kg/min for closed abdomen (IQR 67.4-100.3), p=0.022. Additionally, we compared pump flow between the open abdomen group, all of whom received VA ECMO support, and only those patients in the closed abdomen group who received VA ECMO support. This comparison is valuable because higher flow rates are often required in VA ECMO compared to VV ECMO to support circulatory function, and thus isolating VA ECMO allows a more direct comparison. At 1 hour on ECMO support, the median pump flow rate for VA ECMO closed abdomen patients was 58.8 mL/kg/min (IQR 48.2-88.3, p=0.113). At 4 hours, it was 79.4 mL/kg/min (IQR 53.5-100, p=0.173), and at 24hrs it was 88.5 mL/kg/min (IQR 67.8-100.7). In this comparison, while the open abdomen group once again had higher median flow rates at each time point, the difference was not significant at any point.

3. 5. Complications and Outcomes:

The overall outcomes for the study participants in terms of complications, length of treatment and stay, and survival are shown in Table 2. Of note, there was a significantly lower incidence of ECMO complications overall in the open abdomen group compared to the closed abdomen group. In all other measures of outcome, there were no significant differences found between the two groups.

Bleeding complications during ECMO are displayed in Figure 2. Some patients had bleeding from multiple sites; to clarify this, the last entry in the table is an aggregate value representing any of the reported bleeding complications. No significant differences in bleeding complications were found between the open abdomen and closed abdomen groups. 32% of closed abdomen patients had cannula site bleeding, compared to 16% of open abdomen patients. CNS bleeding was found in 14.7% of closed abdomen patients, vs 0% open abdomen. Chest bleeding occurred in 9.3% of closed abdomen patients, vs 33.3% open abdomen. Abdominal bleeding occurred in 4% of closed abdomen patients, vs 16.7% open abdomen. Other site bleeding occurred in 6.7% of closed abdomen patients, vs 0% open abdomen. Any one or more of the above bleeding complications occurred in 54.7% of closed abdomen patients, vs 33.3% of open abdomen patients.

3. 7. Blood Product Transfusions:

The median volume of Packed Red Blood Cells (PRBCs), Fresh Frozen Plasma (FFP), platelets, and cryoprecipitate administered over the course of treatment is shown in Figure 3. There was no significant difference in blood products administered between the two groups. Open abdomen patients required a median of 70mL/kg of PRBCs (Interquartile range [IQR] 64.2-105), while closed abdomen patients required a median of 64.2mL/kg (IQR 26.7-226.4). For FFP, the open abdomen median was 54.2mL/kg (IQR 49-61.6), while the closed abdomen median was 22mL/kg (IQR 9.9-66.9). Platelet volume median was 82.9mL/kg for open abdomen (IQR 40.1-164.5), and 66mL/kg for closed abdomen (IQR 19.4-220.1). Finally, cryoprecipitate volume median was 19.7mL/kg for open abdomen (IQR 11.7-154.8) and 8.2mL/kg for closed abdomen (IQR 5.4-17).

4. DISCUSSION:

In this study, we reviewed ECMO patients with respiratory and/or cardiac failure who underwent a decompressive laparotomy followed by open abdomen therapy. We compared these patients to a group of similar ECMO patients who did not require an open abdomen. Despite the small size of our series, this is one of the largest such series in the pediatric ECMO literature. Our main findings showed no significant difference in mortality, length of stay, blood products administered, or bleeding complications between the two groups. The overall incidence of ECMO complications was lower in the open abdomen group. Schulz and colleagues recently reported similar findings to ours in an adult cohort of ECMO patients requiring decompressive laparotomy for abdominal compartment syndrome [4]. They reported a slightly lower survival rate and a considerably longer median LOS, but the methods and findings were otherwise quite similar, providing encouraging corroboration from an adult population to our findings in a pediatric one. Interestingly, they described age as a risk factor for mortality in populations with this treatment, as did Glowka in a similar adult study, providing one possible explanation for our higher survival rate [4, 7]. The pediatric series published in 2013 by Rollins described a similar treatment course in the same age group as ours [3]. While none of their 7 patients survived to discharge, they argued that decompressive laparotomy for abdominal compartment syndrome in children treated with ECMO, while controversial, should not be ruled out, as none of their patients developed significant bleeding complications, and 3 of their 7 patients were able to be stabilized for organ donation. As our own open abdomen cohort did not have a significant increase in bleeding complications compared with our closed abdomen patients, these findings are consistent with ours.

Various operations during pediatric ECMO support have been described in the literature. While all small series, these studies show that many operations are reasonable to consider in the appropriate clinical scenario. Schwartz and colleagues published a small series describing bedside tracheostomy on pediatric ECMO patients in the ICU, with a 67% survival rate and no deaths associated with the tracheostomy procedure [9]. Jackson, on the other hand, reported less optimistic findings for chest tube placement in pediatric ECMO patients, with major bleeding complications occurring in 22% of their 27-patient cohort. However, overall mortality was similar to other pediatric respiratory ECMO studies (26.5%) [10]. Finally, Houmes and colleagues published a series of 25 patients who underwent open lung biopsy during ECMO support, reporting rare hemorrhagic complications (245mL was the maximum reported blood loss) and 100% operation survival rate [11].

In our cohort, the majority of the open abdomen patients exhibited hemodynamic compromise, particularly septic shock, and required a much more extensive compensatory vasopressor regimen than the closed abdomen patients, as shown in their higher median Vasoactive Inotropic Score. The respiratory status of the two groups, on the other hand, was similar, as evidenced by the groups' similar P-PREP scores. Serum lactate reflects the degree of tissue perfusion and oxygenation: proper perfusion allows cellular respiration to proceed normally, while hypoxia leads to anaerobic metabolism, increasing serum lactate levels. One would expect patients with a high VIS to have higher lactate levels due to poor end organ perfusion. Because of this relationship between serum lactate and perfusion, lactate clearance is an important indicator of a patient's status on ECMO support and has been recently described as predictive of survival in children on ECMO by Amodeo [8]. In our study, the open abdomen patients began ECMO treatment with a high mean serum lactate, and their lactate levels normalized by 72 hours after ECMO initiation: this ability to clear lactate provides support for the relatively high survival rate in our open abdomen group. Our closed abdomen group showed no such trend. While there was no significant difference between our open abdomen and control groups in regards to lactate clearance, we feel that the ability of the open abdomen group to clear lactate so quickly on ECMO support is an important observation.

As described above under Methods, our high-risk bleeding protocol is employed for all ECMO patients who have an open abdomen. Based on our center's experience and the encouraging results of this series, we recommend that patients who experience abdominal catastrophe or otherwise require decompressive laparotomy followed by open abdomen be treated surgically before ECMO cannulation. They can then be placed on ECMO support with a high-risk bleeding protocol, aiming for a lower anticoagulation target. With proper surveillance of coagulation parameters and tight control of anticoagulation, these patients with an open abdomen can be maintained with limited hemorrhagic complications, as shown by open abdomen patients having equivalent bleeding complications and blood product transfusions to control ECMO patients. This recommended treatment algorithm stands in contrast to the method described by Schultz and Glowka in adults and by Rollins in children, all of whom performed decompressive laparotomy after ECMO initiation. We believe that our method of opening the abdomen before initiating ECMO support is superior and may lead to better outcomes, particularly compared to Rollins' pediatric series, none of whom survived to discharge [3, 4, 6].

As a single institution review, this study is inherently limited in scope. Additionally, the small size of the study population, 6 patients with differing presentations and diagnoses, makes the results difficult to generalize. Our findings would ideally be confirmed with a larger, multi-center study, but such a study is inherently difficult when dealing with such a rare condition.

5. CONCLUSION:

Decompressive laparotomy followed by open abdomen in pediatric patients supported with ECMO is associated with similar outcomes as closed abdomen ECMO patients, particularly regarding mortality, volume of blood products administered, and overall complications. The importance of these conclusions lies in the finding that concurrent ECMO treatment with decompressive laparotomy and open abdomen likely does not present significantly elevated risk and therefore should be considered as an option for pediatric patients with abdominal catastrophe and severe respiratory and/or cardiac failure.

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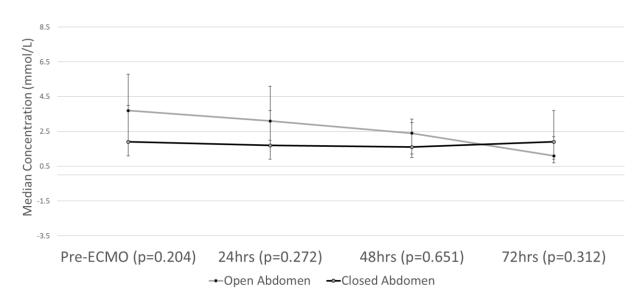


Figure 1: Serum Lactate Trends Pre-ECMO and During ECMO

Results reported as a median value with lower and upper error bars representing the associated 1st and 3rd quartiles, respectively

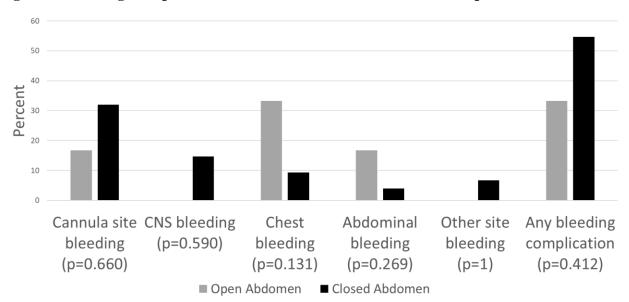


Figure 2: Bleeding Complications in Pediatric ECMO Patients with Open Abdomen

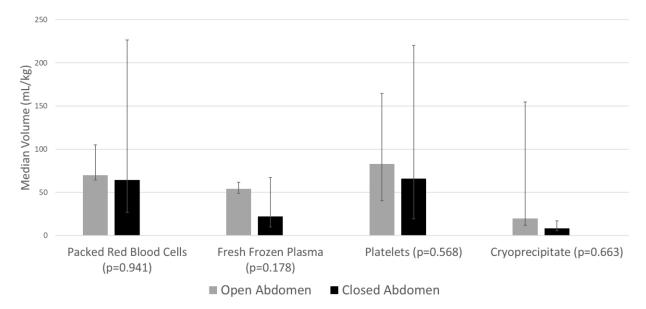


Figure 3. Blood Products Administered to Pediatric ECMO Patients with Open Abdomen

Results reported as a median value with lower and upper error bars representing the associated 1st and 3rd quartiles, respectively

	Open Abdomen (n=6)	Closed Abdomen (n=75)	Р	
Female patients	2 (33.3%)	39 (52%)	0.432	
Age at cannulation (months)	22.5 (7.8, 58.2)	49 (11.5, 103)	0.223	
Weight at cannulation (kg)	18.1 (15, 20)	21.5 (10.5, 43.9)	0.286	
Race, white	5 (83.3%)	41 (55%)	0.220	
Race, black	0 (0%)	23 (31%)		
Race, other	1 (20%)	11 (15%)		
Pre-ECMO VI Score	2020 (23, 3126)	10 (4.2, 34.6)	0.040	
P-PREP score	4 (2, 7)	7 (3, 15)	0.246	
ECMO Indication				
Respiratory	4 (66.6%)	67 (89.3%)	0.083	
Hemodynamic Compromise	3 (50%)	15 (20%)		
Post Cardiac Arrest	2 (33.3%)	7 (9.3%)		
ECMO modality (VA)	6 (100%)	35 (46.7%)	0.026	
ECMO modality (VV)	0	40 (53.3%)		
Pump type: centrifugal	3 (50%)	39 (52%)	1	
Pump type: roller	3 (50%)	36 (48%)	_	

Table 1: Pediatric ECMO Patient Demographics and Run Characteristics.

Results indicated as n (%) or Median with interquartile range (Q1, Q3). Abbreviations: VI Score (Vasoactive Inotropic Score), P-PREP (Pediatric Pulmonary Rescue with Extracorporeal Membrane Oxygenation) score.

	Open Abdomen (n=6)	Closed Abdomen (n=75)	Р
Any ECMO complication(s)	2 (33.3%)	61 (83.6%)	0.014
Cannula bleeding	1 (16.7%)	24 (32%)	0.660
Other site bleeding	0	5 (6.7%)	1
CNS bleeding	0	11 (14.7%)	0.590
Mechanical complication	1 (16.7%)	12 (16%)	1
CNS ischemic stroke	0	3 (4%)	1
Chest bleeding	2 (33.3%)	7 (9.3%)	0.131
Abdominal bleeding	1 (16.7%)	3 (4%)	0.269
Renal failure	0	22 (29.3%)	0.182
Hemodialysis on ECMO	0	12 (16%)	0.584
DIC	1 (16.7%)	6 (8%)	0.429
Cannula complication	0	6 (8%)	1
Other complication	1 (16.7%)	22 (29.3%)	0.669
Any complication(s) that required intervention	1 (16.7%)	24 (55.8%)	0.330
Any complication(s) that led to death	1 (16.7%)	22 (31%)	0.663
Median time on ECMO (hrs)	141.5 (84, 220.8)	177 (97, 293)	0.418
Length of ICU stay (days)	21 (19, 27)	29 (15, 39)	0.502
Hospital LOS (days)	29 (27, 39)	31.5 (20, 78.5)	0.417
Survival to discharge (number of patients)	4 (66.7%)	47 (62.7%)	1

Table 2: Complications and Outcomes in Pediatric ECMO Patients with Open Abdomen

Results indicated as n(%) or Median with interquartile range (Q1,Q3). Abbreviations: CNS (Central Nervous System), DIC (Disseminated Intravascular Coagulation), ICU (Intensive Care Unit), LOS (Length of Stay).

HIGHLIGHTS

- Laparotomy and/or open abdomen during ECMO may elevate risk of bleeding and infection. The literature is inconclusive regarding whether risks outweigh benefits.
- Decompressive laparotomy and open abdomen in children on ECMO correlated with lower complications and no difference in mortality or bleeding compared to ECMO without open abdomen.