

# The Need for Extracorporeal Membrane Oxygenation in Adults Undergoing Congenital Heart Surgery: Impact and Trends of Utilization

Salvatore Aiello, Rohit S. Loomba<sup>1</sup>, Connor Kriz, Matthew Buelow<sup>1</sup>, Saurabh Aggarwal<sup>2</sup>, Rohit R. Arora

Division of Cardiology, Chicago Medical School, North Chicago, IL, <sup>1</sup>Division of Cardiology, Children's Hospital of Wisconsin/Medical College of Wisconsin, Milwaukee, WI, <sup>2</sup>Division of Cardiology, Creighton University School of Medicine, Omaha, NE, USA

## Abstract

**Introduction:** Adults with congenital heart disease (ACHD) represent a population with unique health-care needs. Many patients require cardiac surgery, with some requiring postoperative extracorporeal membrane oxygenation (ECMO). This study aimed to identify the risk factors for the need of postoperative ECMO and characterize the impact of ECMO on admission characteristics. **Methods:** Data from the 2005–2012 iterations of the Nationwide Inpatient Sample were used. ACHD admissions over 18 years with a documented cardiac surgery were included. Univariate analysis was conducted to compare the characteristics between those requiring ECMO and those who did not. Regression analysis was done to identify the independent risk factors associated with ECMO and to determine the impact of ECMO on length, cost, and mortality of the admission. **Results:** A total of 186,829 admissions were included. Of these, 446 (0.2%) admissions required ECMO. Those with acute kidney injury, double-outlet right ventricle, or total anomalous pulmonary venous connection were more likely to require ECMO. ECMO was also significantly more utilized in patients undergoing septal defect repair, complete repair of tetralogy of Fallot, atrial switch, and heart transplant. The use of ECMO significantly increased length, cost, and mortality of stay. Overall mortality was 62.6% in the ECMO group. **Conclusion:** ECMO is only needed in a small proportion of postoperative ACHD patients. The use of ECMO significantly increases cost, length of stay and mortality in these patients. Improved identification of postoperative ACHD patients who are more likely to survive ECMO may facilitate improved survival and decreased resource utilization.

**Keywords:** Adult congenital heart disease, extracorporeal membrane oxygenation, mechanical support

## INTRODUCTION

Patients with congenital heart disease (CHD) are living longer and increasingly surviving into adulthood.<sup>[1]</sup> Currently, nearly 60% of all CHD patients are adults and recent measurements of the adult CHD (ACHD) patient population range from 1.47 to 3 per thousand.<sup>[1-3]</sup> The ACHD patient population is expected to continue growing until 2050.<sup>[3]</sup> As the ACHD patients age, treatments increasingly require emergency department evaluation, hospitalization, and elective or emergent surgery.<sup>[4]</sup>

ACHD patients who undergo surgery require a disproportionate allocation of resources.<sup>[5]</sup> Increased resource utilization in the ACHD appears to coincide with an overall increased postoperative morbidity and mortality.<sup>[5,6]</sup>

While many ACHD patients' conditions require cardiac surgery, only a small percentage of these patients require

postoperative extracorporeal membrane oxygenation (ECMO) to support circulation while the heart recovers.<sup>[7]</sup> There is a paucity of data regarding postoperative ACHD patients and the need for ECMO as well as ECMO survival.<sup>[7,8]</sup> There are also limited data regarding the risk factors associated with the need for ECMO and quantification of the impact ECMO has on admission length and cost.

We conducted an analysis of the Nationwide Inpatient Sample (NIS), a national administrative discharge database, with a primary aim of identifying risk factors associated with

**Address for correspondence:** Dr. Salvatore Aiello,  
Chicago Medical School, 3333 North Chicago, IL, USA.  
E-mail: salvatore.aiello@my.rfums.org

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ECMO utilization in ACHD patients undergoing cardiac surgery. Secondary aims included assessing trends in utilization of ECMO over an 8-year period and determine the impact of ECMO on admission characteristics.

## METHODS

### Patient identification

A retrospective cohort study was conducted using the NIS. Data regarding hospital admissions were obtained from the 2005–2012 NIS iterations. Only admissions of patients over 18 years of age with CHD undergoing heart surgery were included. These were identified using ICD-9 diagnosis and procedure codes. Institutional review board approval was waived as the analyses utilized de-identified data from a national database.

CHD was identified using ICD-9 codes: double-outlet right ventricle using 745.11, atrioventricular septal defect using 745.60, partial anomalous pulmonary venous connection using 747.42, total anomalous pulmonary venous connection using 747.41, transposition of the great arteries using 745.10, congenitally corrected transposition using 745.12, hypoplastic left heart syndrome using 746.7, atrial septal defect using 745.61, ventricular septal defect using 745.5, pulmonary atresia with ventricular septal defect using 746.01, tricuspid atresia using 746.1, Ebstein's anomaly using 746.2, truncus arteriosus using 745.0, and coronary artery anomaly using 746.85. Arrhythmias were identified using codes 427.0–427.42 as well as 426.0–426.13. It was not possible to distinguish between those with absence of a spleen or multiple spleens due to the ICD-9 coding strategy.

Cardiac surgery was identified using the following codes: codes 35.10 through 35.14 for valvuloplasty with no valve replacement, 35.20 through 35.28 for valvuloplasty with replacement, codes 35.50 through 35.73 for septal defect repair (including atrioventricular septal defect repair), 35.81 for complete repair of tetralogy of Fallot, 35.82 for pulmonary venous repair, 35.83 for complete repair of common arterial trunk, 35.84 for arterial switch operation for transposition, 35.91 for atrial switch operation for transposition, 35.92 for right ventricle to pulmonary artery conduit, 39.22 for Blalock-Tausig shunt, and 37.51 for heart transplant.

ECMO was identified using ICD-9 code 39.65.

### Data identification and collection

Demographic information including gender and race were collected for each admission. Comorbid conditions and admission characteristics such as admission month, length of stay, and cost of stay were collected and assessed.

### Statistical analysis

Continuous variables are reported using mean and standard deviation while categorical variables are reported using absolute frequency and percentages. Continuous variables were analyzed using a student *t*-test or Mann–Whitney U-test

as appropriate with categorical variables being analyzed using Chi-square analysis. Baseline characteristics such as age, gender, race, and comorbid conditions were compared between those with and without ECMO.

Next, the proportion of admissions requiring ECMO, length of ECMO admissions, cost of ECMO admissions, and mortality of ECMO admissions was compared by the years from which data were included using an analysis of variance.

Logistic regression was then conducted to determine factors associated with need for ECMO with ECMO as the dependent variable. Next, a logistic regression was done to determine risk factors for inpatient mortality with inpatient mortality as the dependent variable and ECMO included as an independent variable. Linear regression analyses with length of stay and cost of admission as independent variables to determine the effect were then conducted to determine the impact of ECMO on these variables.

All statistical analyses were done using SPSS version 20.0 (IBM, Chicago, IL, USA).

## RESULTS

### Admission characteristics in those with and without extracorporeal membrane oxygenation (univariate analysis)

A total of 186,929 admissions with ACHD and a documented cardiac surgery were included in the analysis. Of these, 446 (0.2%) admissions required ECMO. Those requiring ECMO were significantly more likely to be younger (56.1 years vs. 65.6 years,  $P < 0.001$ ) and of male gender (63.5% vs. 58.3%,  $P = 0.029$ ). Racial differences were also present with those requiring ECMO more likely to be African American, Hispanic, or Asian/Pacific Islander ( $P < 0.01$ ). Comorbidities more likely in those with ECMO included heart failure (odds ratio [OR] 2.4, 95% confidence interval [CI] 2.0–2.9,  $P < 0.001$ ) and acute kidney injury (OR 8.9, 95% CI 7.4–10.8,  $P < 0.001$ ) [Table 1].

Length of stay was significantly longer in those with ECMO (23.9 days vs. 11.5 days,  $P < 0.001$ ) as was cost of the admission (\$642,410 vs. \$174,424,  $P < 0.001$ ). Inpatient mortality was also greater in those with ECMO with a 62.6% mortality in those with ECMO compared to 4.5% in those without (OR 35.1, 95% CI 28.9–42.6,  $P < 0.001$ ) [Table 1].

### Cardiac morphology and surgery in those with and without extracorporeal membrane oxygenation

The following cardiac malformations were more likely in those with ECMO: double-outlet right ventricle (OR 26.3, 95% CI 8.1–84.8,  $P < 0.001$ ), total anomalous pulmonary venous connection (OR 20.9, 95% CI 2.8–156.5,  $P < 0.001$ ), ventricular septal defect (OR 2.3, 95% CI 1.1–5.7,  $P = 0.049$ ), pulmonary atresia (OR 9.7, 95% CI 1.3–70.9,  $P = 0.006$ ), and congenitally corrected transposition (OR 7.9, 95% CI 1.1–57.3,  $P = 0.015$ ) [Table 1].

**Table 1: Characteristics of admissions with and without extracorporeal membrane oxygenation**

	No ECMO (n=186,483)	ECMO (n=446)	OR (95% CI)	P
Age (years)	65.5±14.3	56.1±15.8	-	<0.001
Female	77,717 (41.7)	163 (36.5)	0.8 (0.6-0.9)	0.029
Race				
Caucasian	123,246 (80.7)	259 (71.3)	-	<0.001
African American	10,192 (6.7)	45 (12.4)		
Hispanic	9964 (6.5)	27 (7.4)		
Asian or Pacific Islander	3093 (2.0)	12 (3.3)		
Native American	971 (0.6)	*** (***)		
Other	5177 (3.4)	18 (5.0)		
Heart failure	63,897 (34.2)	249 (55.8)	2.4 (2.0-2.9)	<0.001
Tachyarrhythmia	80,584 (43.2)	141 (31.6)	0.6 (0.4-0.7)	<0.001
Atrioventricular block	5823 (3.1)	*** (***)	0.2 (0.1-0.6)	0.003
Acute kidney injury	29,532 (15.8)	280 (62.8)	8.9 (7.4-10.8)	<0.001
Cardiac lesion				
Double outlet right ventricle	48 (0.1)	*** (***)	26.3 (8.1-84.8)	<0.001
Atrioventricular septal defect	200 (0.1)	0	-	0.489
Partial anomalous pulmonary venous connection	183 (0.1)	*** (***)	2.3 (0.3-16.4)	0.393
Total anomalous pulmonary venous connection	20 (0.1)	*** (***)	20.9 (2.8-156.5)	<0.001
Coronary artery anomaly	431 (0.2)	*** (***)	2.9 (0.9-9.1)	0.053
Atrial septal defect	16,634 (8.9)	30 (6.7)	0.7 (0.5-1.1)	0.105
Tetralogy of Fallot	252 (0.1)	*** (***)	3.3 (0.8-13.4)	0.073
Ventricular septal defect	890 (0.5)	*** (***)	2.3 (1.1-5.7)	0.049
Pulmonary atresia	43 (0.1)	*** (***)	9.7 (1.3-70.9)	0.006
Tricuspid atresia	51 (0.1)	0	-	0.727
Ebstein anomaly	140 (0.1)	*** (***)	2.9 (0.4-21.4)	0.251
Hypoplastic left heart syndrome	*** (***)	0	-	0.905
Transposition	37 (0.1)	0	-	0.766
Congenitally corrected transposition	53 (0.1)	*** (***)	7.9 (1.1-57.3)	0.015
Common arterial trunk	32 (0.1)	0	-	0.782
Valvar stenosis or insufficiency	167,463 (89.8)	398 (89.2)	-	0.841
Cardiac surgery				
Valvuloplasty, no valve replacement	34,615 (18.5)	85 (19.1)	1.0 (0.8-1.3)	0.782
Valvuloplasty with valve replacement	139,088 (74.5)	269 (60.3)	0.5 (0.4-0.6)	<0.001
Septal defect repair	18,902 (10.1)	58 (13.0)	1.3 (1.1-1.7)	0.044
Tetralogy of Fallot repair	66 (0.1)	*** (***)	12.7 (3.1-52.1)	<0.001
Total anomalous pulmonary venous connection repair	127 (0.1)	*** (***)	3.3 (0.4-23.6)	0.208
Right ventricle to pulmonary artery conduit	151 (0.1)	*** (***)	2.7 (0.3-10.8)	0.289
Blalock-atausig shunt	4619 (2.5)	*** (***)	0.2 (0.1-0.8)	0.014
Common arterial trunk repair	*** (***)	0	-	0.945
Arterial switch	13 (0.1)	0	-	0.860
Atrial switch	106 (0.1)	*** (***)	7.9 (1.9-32.2)	0.001
Heart transplant	2834 (1.5)	90 (20.2)	16.4 (12.9-20.7)	<0.001
Length of hospital stay (days)	11.5±6.2	23.9±11.9	-	<0.001
Cost of hospitalization (US dollars)	174,424	642,410	-	<0.001
Inpatient mortality	8459 (4.5)	279 (62.6)	35.1 (28.9-42.6)	<0.001

\*\*\*Represents an absolute frequency <10 which per database policies cannot be explicitly reported. CI: Confidence interval; ECMO: Extracorporeal membrane oxygenation; OR: Odds ratio

The following cardiac surgeries were more likely in those with ECMO: septal defect repair (OR 1.3, 95% CI 1.1–1.7,  $P = 0.044$ ), complete repair of tetralogy of Fallot (OR 12.7, 95% CI 3.1–52.1,  $P < 0.001$ ), atrial switch (OR 7.9, 95% CI 1.9–32.2), and heart transplant (OR 16.4, 95% CI 12.9–20.7) [Table 1].

### Trends in extracorporeal membrane oxygenation utilization and burden over the study period

Overall, ECMO was utilized in 0.2% of included admissions. The percentage of admissions in which ECMO was utilized increased significantly across years (0.1% in 2005–0.6% in 2012,  $P < 0.001$ ). Cost of admissions with ECMO also

increased significantly over the study period with mean total charges of \$470,491 in 2005 compared to \$804,046 in 2012 ( $P = 0.001$ ). Inpatient mortality and length of stay did not significantly change over this time period [Table 2].

### Independent risk factors associated with extracorporeal membrane oxygenation (regression analysis)

The following risk factors were associated with ECMO: acute kidney injury (OR 7.3, 95% CI 5.7–9.3), double-outlet right ventricle (OR 8.0, 95% CI 1.5–42.6), total anomalous pulmonary venous connection (OR 18.0, 95%CI 1.6–203.1), septal defect repair (OR 3.9, 95%CI 2.4–6.1), complete repair of tetralogy of Fallot (OR 19.0, 95% CI 1.7–208.6), atrial switch (OR 14.2, 95% CI 2.2–89.3), heart transplant (OR 10.5, 95% CI 6.6–16.6), and later year in the study period (OR 4.6, 95% CI 2.6–8.0) [Table 3].

### Effect of extracorporeal membrane oxygenation on admission characteristics (regression analysis)

After multivariate analysis, the use of ECMO was associated with significant increases in the length, cost, and mortality of admissions. ECMO increased the length of admission by 3.2 days, increased the cost of admission by approximately \$343,694, and increased inpatient mortality approximately 24-fold [Table 4].

## DISCUSSION

Our analysis of the NIS database demonstrated that only 0.2% of ACHD patients undergoing cardiac surgery require postoperative ECMO. However, during the study period, we found there to be an overall increasing proportion of ACHD admissions requiring postoperative ECMO with the most recent year having a 0.6% frequency. Particular subsets of patients were more likely to require postoperative ECMO: those with acute kidney injury, double-outlet right ventricle, or total anomalous pulmonary venous connection. Those undergoing septal defect repair, complete repair of tetralogy of Fallot, atrial switch, and heart transplant were also more likely to require postoperative ECMO.

The frequency of postoperative ECMO in our study was lower than that found in a previous study by Acheampong *et al.* who reported that 1.1% of ACHD patients required postoperative ECMO. While the overall frequency in our study was 0.2%, it should be noted that this percentage was 0.6% when only the final study year is considered. This suggests a trend toward the values documented by Acheampong *et al.* Nonetheless, both studies highlight the low frequency of postoperative ECMO in this population.<sup>[7]</sup>

Furthermore, our study revealed that the use of ECMO increased the cost of admission by approximately \$343,694. Increased cost of admission may be attributed to the need for specialized care as well as increased length of stay required for ACHD patients.<sup>[5]</sup> Our study demonstrates that the use of ECMO in ACHD patients increased the length of stay by over 3 days. Previous data of the impact of postoperative ECMO in ACHD patients are not available for comparison.

Our study also demonstrated that ACHD patients requiring postoperative ECMO have significantly increased mortality. In our study, only 62.6% of those requiring ECMO experience inpatient mortality. This high rate of mortality may be due to the degree of illness and number of comorbidities present in those who are placed on ECMO. ECMO-related complications are also likely to contribute to this high rate of mortality. It remains unclear at this time what the particular mechanisms of mortality are in those with ACHD requiring postoperative ECMO. A better delineation of these factors will perhaps allow for better prediction of those who have an increased likelihood of surviving to discharge after postoperative ECMO.<sup>[8,9]</sup>

Our mortality data are similar to that of previous studies. Paden *et al.* reported a 60% mortality rate in an analysis of Extracorporeal Life Support Organization data from ACHD patients requiring ECMO.<sup>[10]</sup> In another study examining ACHD patients receiving ECMO after cardiogenic shock, Schmidt *et al.* reported a mortality of 68%, although it should be noted that this study did not exclusively include operative patients.<sup>[8]</sup>

The decision to utilize ECMO in ACHD patients is often complicated by their underlying cardiac anatomy and existing comorbidities.<sup>[4,9]</sup> For patients undergoing elective surgery, it is important to counsel them regarding the possibility, albeit low, of postoperative ECMO. Clinicians should work with patients and their families to determine the patient's desires in regard to the use of ECMO if the need arises. These efforts could help optimize resource allocation and the overall emotional burden of such admissions.<sup>[11]</sup>

Clinicians must also use current data to help guide the decision to utilize ECMO. The SAVE score, a novel predictive mortality model, incorporates 13 pre-ECMO variables for patients requiring ECMO after cardiogenic shock. An internal validation of this scoring method resulted in greater hospital survival (67% vs. 42%).<sup>[8,10]</sup> Such

**Table 2: Trends of extracorporeal membrane oxygenation admissions by year**

	2005	2006	2007	2008	2009	2010	2011	2012	P
Requiring ECMO	19 (0.1)	19 (0.1)	13 (0.1)	44 (0.2)	66 (0.2)	68 (0.3)	83 (0.3)	134 (0.6)	<0.001
ECMO mortality	12 (63.2)	14 (73.7)	7 (53.8)	33 (75.0)	35 (53.0)	46 (67.6)	56 (67.5)	76 (56.7)	0.164
ECMO length of stay (days)	33.1	11.1	24.1	20.2	27.2	19.1	21.2	28.0	0.113
ECMO cost of stay	470,491	299,912	474,843	580,106	611,984	552,376	635,340	804,046	0.001

ECMO: Extracorporeal membrane oxygenation

**Table 3: Regression results identifying factors independently associated with increased need for extracorporeal membrane oxygenation**

Factors associated with ECMO

Acute kidney injury (OR 7.3, 95% CI 5.7-9.3)
Double outlet right ventricle (OR 8.0, 95% CI 1.5-42.6)
Total anomalous pulmonary venous connection (OR 18.0, 95% CI 1.5-203.1)
Septal defect repair (OR 3.9, 95% CI 2.4-6.1)
Tetralogy of Fallot complete repair (OR 19.0, 95% CI 1.7-208.6)
Atrial switch (OR 14.2, 95% CI 2.2-89.3)
Heart transplant (OR 10.5, 95% CI 6.6-16.6)
Later year (OR 4.6, 95% CI 2.6-8.0)

ECMO: Extracorporeal membrane oxygenation; OR: Odds ratio; CI: Confidence interval

**Table 4: Regression results identifying impact of extracorporeal membrane oxygenation on admission characteristics**

Admission characteristic	Impact of ECMO
Cost of admission	Increased by \$343,694; $P < 0.001$
Length of admission	Increased by 3.2 days; $P < 0.001$
Inpatient mortality	Increased (OR 23.7, 95% CI 18.5-30.4)

OR: Odds ratio; CI: Confidence interval

predictive models, specific to the ACHD population, may also be particularly helpful.

What must also be considered is the quality of life of those who survive to discharge. While patients may experience some decrease in physical and psychological aspects of their daily life, many of those who survive to discharge have been able to return to work or school and report good quality of life with the help of rehabilitation programs.<sup>[12-15]</sup> It should be noted that this data does not come from the ACHD population.

A strength of this analysis is that it has a large number of patients as it utilizes data from a large national database. In addition, robust data regarding length and cost of admission are available from the NIS database. Despite the strengths of this analysis, there are also limitations. Several of the CHD ICD9 codes have not been validated. The coding for various congenital malformations of the heart may not be accurate. It is also possible that the numbers in this study represent an underrepresentation although this should not impact the presence and degree of overall relation to the overall outcome of interest. In addition, this study is limited by data available in the database. Specifics regarding ECMO cannulation and duration are among data not available for inclusion in the analysis. Temporal associations cannot be made from these data and except for the CHD these are all associations.

Acknowledging the limitations, we feel that the findings of these analyses provide novel and valuable data regarding ECMO utilization and burden in adults with CHD during admissions for cardiac surgery.

## CONCLUSION

Specific congenital heart malformations, cardiac surgeries, and comorbidities are associated with increased need for ECMO. Although needed in <1% of ACHD admissions during which cardiac surgery is required, ECMO is associated with a significant increase in resource utilization and mortality.

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## Conflicts of interest

There are no conflicts of interest.

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