Risk of Central Nervous System Injury by Location of Arterial Cannulation and Age in Veno-Arterial ECLS

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Abstract

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Objective

The objective of this study was to determine whether the risk of central nervous system (CNS) injury is higher in carotid compared to femoral artery cannulation in veno-arterial extracorporeal life support (VA-ECLS) and to evaluate whether this differs by age.

Methods

We conducted a retrospective cohort study of patients 3-55 years old treated with VA-ECLS between 1989-2012 utilizing the Extracorporeal Life Support Organization Registry. We used logistic regression to estimate the association between site of cannulation and CNS injury adjusting for confounders and assessing for effect modification by age.

Results

We found a three fold increased odds of CNS infarction with carotid as opposed to femoral artery cannulation (OR 2.99, 95% CI 1.86 – 4.81), which was not appreciably different by age group.

Conclusion

In this study, carotid artery cannulation was associated with an increased likelihood of CNS injury as compared to femoral artery cannulation, which differed little by age.

INTRODUCTION

Extracorporeal life support (ECLS) is a modality of advanced, mechanical support used to treat acute, reversible cardiac, respiratory, or combined cardiorespiratory failure not responsive to standard treatments. There are two basic modes of ECLS: veno-venous (VV) and veno-arterial (VA). Veno-venous ECLS is used to support patients with respiratory failure; blood is removed from the body via a large cannula in a central vein, oxygenated in the ECLS circuit and then re-infused in a central vein. Veno-arterial ECLS can support patients with cardiac failure or respiratory failure; blood is removed via a large cannula in a central vein, is oxygenated in the ECLS circuit and then is re-infused into a large artery in order to provide circulatory support. There are multiple risks associated with ECLS, such as bleeding, infection, mechanical complications of the ECLS circuit and central nervous system (CNS) injury.[1]

Patients treated with ECLS are at risk for CNS injury from multiple etiologies, such as emboli from a thrombus in the ECLS circuit or from hemorrhage resulting from heparinization. However, one potentially modifiable risk factor for CNS injury is the site of arterial cannulation in VA ECLS, given that in many patients the carotid artery and femoral artery are both options. The concern with carotid artery cannulation is that there is acute, distal ligation of the common carotid artery which interrupts blood flow to the brain for the duration of ECLS support, potentially causing an ipsilateral ischemic stroke (depending on the adequacy of collateral circulation from the basilar artery and contralateral carotid artery via the circle of Willis). In adult patients with head and neck cancer or intracranial aneurysms, the risk of stroke from acute, unilateral carotid artery occlusion ranges 17-30%.[2] This could potentially mimic the scenario of an adult patient acutely being cannulated for ECLS with ligation of the distal aspect of the carotid artery.

There are no studies directly comparing the risk of stroke based on site of arterial cannulation in adults treated with VA ECLS. There are two published studies in children that investigate this question. Teele et al. studied patients ≤18 years old, including neonates, requiring ECLS for respiratory or cardiac indications or as rescue from cardiac arrest (extracorporeal cardiopulmonary resuscitation, ECPR) with cannulation via the femoral artery, carotid artery or aorta. After adjusting for confounding variables, carotid artery cannulation was associated with a 1.3 fold increased odds of CNS injury (infarction, hemorrhage or seizures) as compared to femoral and aortic cannulation sites, which did not differ significantly by age group.[3] Rollins et al. studied this same question in patients <18 years old treated with ECLS for a respiratory indication. They found that overall there was not a difference in infarction between the carotid and femoral groups (6% versus 5%). However, when stratified by age, in those patients greater than 10 years old there was a greater proportion with CNS infarct as compared to the femoral group.[4] However, this study did not account for potential confounders in the assessment of age as a modifier of the relationship between the outcome and arterial cannula location.

The concern is that adults may not have as robust collateral circulation to accommodate acute ligation of the carotid artery as infants and children, given the increased prevalence of atherosclerosis with age.[5-7] In addition to atherosclerosis, there is also evidence of other mechanisms for impaired collateral circulation associated with aging.[8] There have been informal recommendations that adults and even older children be preferentially cannulated via the femoral artery as opposed to the carotid artery in order to reduce risk of CNS injury, although without a consensus among ECLS providers.[4,9] However, cannulation of the femoral artery is also not without risk, with reports of acute limb-threatening ischemia in both children and adults and even late vascular complications.[9-13] Additionally, in femoral artery cannulation the oxygenated blood must flow retrograde up the aorta to perfuse the brain. If native heart function is good and pulmonary venous saturation is low, then the brain may be perfused with relatively de-oxygenated blood which could potentially cause global CNS injury.[14]

By undertaking this study our goal was to better clarify the risk of CNS injury with carotid artery cannulation as compared to femoral artery cannulation in different age groups. This study has a larger number of patients than the two prior pediatric studies and includes adults. Our objective was to determine whether the risk of CNS injury is higher in carotid artery cannulation compared to femoral artery cannulation in VA ECLS and, more specifically, to evaluate whether this risk is modified by age.

METHODS

Study Design & Data Source

We conducted a retrospective cohort study of patients treated with VA ECLS utilizing the Extracorporeal Life Support Organization (ELSO) Registry. The ELSO Registry was created in 1989 by a group of centers using ECLS. There are over 170 domestic and international ECLS centers contributing data to the ELSO Registry with greater than 30,000 neonatal, 11,000 pediatric and 5,000 adult cases with respiratory and/or cardiac failure.[15] Data are collected and voluntarily submitted by member ECLS centers to the ELSO Registry for purposes of quality improvement and research. Until 2012, each center collected data using standard, handwritten data collection forms which were subsequently entered into the database at ELSO. Currently, ELSO utilizes a secure, encrypted web-based data entry system which has data integrity monitoring. The data for this study were not collected specifically for this research project. The registry includes patient demographic information, diagnoses, procedures, pre-ECLS clinical characteristics, ECLS technique and equipment, complications and outcomes. This study has been reviewed by the institutional review board (IRB) at Seattle Children's Hospital which determined it to be exempt from IRB review (#14564).

Population

We included all patients >30 days of age undergoing any form of VA ECLS (VA, VA+V, VA-VV, VV-VA, VVA) with either carotid or femoral artery cannulation between 1989 and 2012. We excluded patients without a designation of the site of arterial cannulation, patients with more than one ECLS run, patients with multiple arterial cannulation sites during the run (i.e., carotid and femoral, femoral and aorta, carotid and aorta, or bilateral carotid arteries, but did not exclude those with bilateral femoral artery cannulation) and those whose indication was ECPR. We then limited the population to ages 3 to 55 years in order to have at least 5% of the patients in each age stratum with the alternate cannulation strategy for the comparative analyses.

Variables

The exposure of interest was site of arterial cannulation. The outcome of interest was CNS injury, which we defined three ways. The primary definition was CNS infarction, which is a binary variable in the ELSO Registry. We also defined it more broadly: 1) CNS infarct or hemorrhage; and 2) global CNS injury, which includes CNS infarction, CNS hemorrhage, brain death, or death due to irreversible CNS organ failure. All of the individual components of these composite outcomes are binary variables in the ELSO Registry.

Covariates included in descriptive and analytic statistics were patient demographics, pre-ECLS support, characteristics of the ECLS run and complications. We created six categories of age (3-5 years, 6-10 years, 11-15 years, 16-20 years, 21-40 years, and 41-55 years). Year of treatment was categorized as 1989-1999, 2000-2006, and 2007-2012. We grouped similar pre-ECLS support modalities together. We included pre-ECLS use of a Berlin heart, biventricular assist device, intra-aortic balloon, and left or right ventricular assist device as pre-ECLS mechanical cardiac support (MCS). Pre-ECLS inotrope or vasopressor use included treatment with dobutamine, dopamine, epinephrine, inamrinone, milrinone, norepinephrine, or other vasoactive/inotropic drugs. Pre-ECLS vasodilator use includes nitroprusside, tolazoline, or other vasodilator drugs. Administration of sodium bicarbonate or Tris(hydroxymethyl)aminomethane (THAM) prior to ECLS was also grouped together. Related ECLS complication variables were also grouped together. Cardiac tamponade by air, serous fluid and blood were grouped as tamponade. Clots anywhere in the ECLS circuit (bladder, bridge, hemofilter, oxygenator, or other sites) were combined as circuit thrombosis. Raceway rupture and tubing rupture were labelled circuit rupture. We defined dialysis on ECLS as use of hemofiltration, dialysis or continuous arteriovenous hemodialysis, which are three separate complication codes in the ELSO Registry.

Data Analysis

Demographic data, pre-ECLS support, ECLS characteristics and complications are summarized by site of arterial cannulation, using frequencies and proportions for categorical variables and median and interquartile range (IQR) for continuous variables. We used multivariable logistic regression to estimate the association between site of arterial cannulation and CNS injury adjusting for confounding variables. Based on a priori hypothesis, we also included age category, modeled as a dummy variable, and an interaction term between the age categories and site of arterial cannulation to assess whether the relationship between CNS injury and cannulation site was modified by age, which was determined using the likelihood ratio test. Additional variables that were considered as potential confounders were demographic data, pre-ECLS support modalities, ECLS characteristics and complications. We adjusted for those variables that were significantly associated in univariate analysis both with cannulation site and CNS infarct or CNS infarct and/or hemorrhage, which included duration of ECLS run, era, use of inotropes on ECLS, cannula problems, oxygenator failure, hyperbilirubinemia, pre-ECLS MCS, and dialysis on ECLS. We excluded the occurrence of seizures from this list as these may fall in the causal pathway of interest. We also excluded any binary variable that was present in less than 5% of the study population. We additionally chose a priori to adjust for indication for ECLS (respiratory versus cardiac), pre-ECLS cardiopulmonary arrest (not ECPR), and CPR required while on ECLS. All analyses were performed using Stata software, version 12 (College Station, TX).

RESULTS

There were 3,022 unique patient runs that met inclusion and exclusion criteria (Figure 1). The youngest patients were cannulated almost exclusively via the carotid artery, with a steady trend of increasing prevalence of femoral artery cannulation with advancing age. In more recent years there has been increased prevalence of femoral artery cannulation as compared to the earliest era in each age group (Figure 2). In addition to being older, those patients who underwent femoral artery cannulation were more likely to be male, Asian, have a cardiac indication for ECLS, and have a shorter run (Table 1). Patients with carotid cannulation had worse blood gas results, higher ventilator support, utilized adjunctive respiratory support more frequently, and were treated more often with narcotics and neuromuscular blocking agents than those cannulated via the femoral artery. Mechanical circulatory support and cardiopulmonary bypass were used prior to ECLS more often in the femoral artery group (Table 2). In terms of complications, carotid artery patients more frequently had hypertension requiring treatment, cannula problems, seizures, pneumothorax requiring treatment, and dialysis on ECLS. The femoral group had a greater prevalence of oxygenator failure, hyperbilirubinemia, elevated pH, and creatinine ≥1.5 (Table 3).

Ninety-two of 1,253 (7.3%) carotid patients experienced an infarct as compared to 76 of 1,744 (4.4%) femoral patients. After adjusting for multiple confounders including age, there was approximately a three fold increased odds of infarct with carotid as opposed to femoral cannulation (OR 2.99, 95% CI 1.86 – 4.81). Twelve percent of the carotid patients had an infarct or hemorrhage (150/1,253) as compared to 7.1 % of the femoral patients (124/1,744) with an adjusted odds ratio of 2.23 (95% CI 1.55 – 3.22). In terms of global CNS injury, 23.0% (288/1,253) of the carotid group was affected as compared to 18.8% (328/1,744) of the femoral group with an adjusted odds ratio of 1.47 (95% CI 1.14 – 1.91). These relationships between cannulation site and outcome were not appreciably different by age group, either in relative (interaction p-value=0.6821, 0.5104, and 0.7791 respectively) or in absolute terms (Table 4).

DISCUSSION

In this study we observed that younger patients were cannulated preferentially via the carotid artery with a steady trend with advancing age to femoral artery cannulation in older individuals. After adjusting for age and a host of confounding variables, we found that there was an almost 3 fold increased odds of CNS infarction, 2.2 fold increased odds of CNS infarct or hemorrhage and 1.5 fold increased odds of global CNS injury with carotid versus femoral artery cannulation. However, although we hypothesized that these estimates would be modified by age, with a greater hazard for CNS injury in the oldest age groups comparing carotid to femoral cannulation, this was not the case.

Our results are not dissimilar from the findings of Teele, but do differ from those of Rollins. Teele et al. studied 2,977 children ranging in age from neonates to 18 years old who were treated with VA ECLS for pulmonary or cardiac indications or for ECPR between 2007 and 2008 using the ELSO registry. They found that patients with carotid artery cannulation had 30% increased odds of CNS injury (defined as seizure, infarction or hemorrhage) as compared to those cannulated via the femoral artery or aorta in adjusted analysis (OR 1.30, 95% CI 1.01 – 1.69);

the odds of CNS injury with carotid artery cannulation was not significantly different among pediatric age groups.[3] Rollins et al. studied 1,632 children in the ELSO registry ages 1 month to 17 years treated with VA ECLS for pulmonary indications between 1993 and 2007. They found that overall the carotid artery group had CNS hemorrhage more often than those with femoral cannulation (7% versus 2%), but that there was not a significant difference in infarction (6% versus 5%). However, when stratified by age there was a statistically significantly higher proportion of infarcts in patients with carotid artery cannulation as compared to femoral in those >10 years old, which was not seen in the <1 year, 1-5 years, and 5-10 years age groups.[4] However, this study did not account for potential confounders in the assessment of age as a modifier of the relationship between the outcome and arterial cannula location.

The question of CNS injury directly attributable to carotid artery cannulation in ECLS has been long standing. As neonates have been the predominant age group utilizing ECLS, most of whom undergo arterial cannulation via the carotid artery for VA ECLS, most of the research on lateralization of CNS injury associated with carotid cannulation has occurred in this population. However, the results have been inconsistent with several studies finding increased right sided CNS injury[16-20] and multiple other studies finding no lateralization.[21-27] However, alternative arterial cannulation sites are not realistic options for most neonatal patients; the femoral approach is technically challenging due to the small size of the vessel at this age, and aortic cannulation is typically reserved for patients undergoing cardiac surgery who have had a sternotomy.

There have been several studies assessing cerebral blood flow in patients on VA ECLS, again predominantly in the neonatal population. Mitchell et al. studied 10 neonates on ECLS after cannulation of the right carotid artery and found that all had antegrade flow in bilateral middle cerebral arteries (MCA), but the velocity was not quantified.[28] Taylor's work corroborated these results with the finding of antegrade flow in bilateral MCAs in all patients.[29] Matsumoto et al. studied the cerebral blood flow velocity (CBFV) in the right MCA in 15 neonates with duplex ultrasonography (US) during cannulation of the right common carotid artery for ECLS prior to initiating pump flow. Peak systolic flow decreased to 47% of baseline at the time of ligation, although end diastolic velocity remained basically unchanged at 96% of baseline. Over the next 5 minutes, systolic velocity increased to 70% of baseline and end diastolic velocity increased to 121% of baseline.[30] Liem et al. studied 18 neonates with Doppler US prior to carotid artery cannulation to 60 minutes after initiation of ECLS flow. Bilateral MCAs had similar pre-cannulation CBFV. Sixty minutes after starting ECLS flow, the right MCA CBFV increased 19% as compared to 29% in the left MCA.[31] Fukuda et al. compared CBFV in neonatal patients on VA ECLS with those on VV ECLS. Although the VA group had higher CBFV in the left internal carotid artery and basilar artery, CBFV was similar in the left MCA and was lower in the right MCA in the VA group compared to the VV group.[32] More recently, van Heijst studied 10 neonates with near infrared spectrophotometry (NIRS) and Doppler US. After right common carotid artery ligation, there was a significant decrease in oxyhemoglobin and increase in deoxyhemoglobin in bilateral hemispheres. Sixty minutes after initiating ECLS flow this reversed and was not significantly different between hemispheres. There was a significant increase in CBFV in bilateral MCAs compared to pre-cannulation values that was not significantly different between the hemispheres.[33] Lastly, Ejike et al. studied 11 predominantly neonatal patients on VA ECLS using NIRS. Three patients were studied during the process of cannulation, whereas the remainder had NIRS monitoring initiated within 24 hours of cannulation. Prior to cannulation regional cerebral oxygenation index was similar in bilateral cerebral hemispheres. At the time of cannulation of the right carotid artery, the right sided cerebral oxygenation index decreased significantly as compared to the left. With initiation of pump flow, bilateral cerebral oxygenation indices increased immediately up to the maximum value measured by the cerebral oximeter (95%) before decreasing back to near baseline level. There was no significant difference between right and left cerebral oxygenation index for the remainder of the observation period.[34]

There has been much less investigation of cerebral blood flow in children and adults on VA ECLS. Using daily transcranial Doppler US, O'Brien and Hall evaluated 18 pediatric patients (mean age 3.8 years, predominantly aged ≤18 months old) on ECLS, 8 on VA and 10 on VV ECLS. They found that there was not a significant difference between the CBFV in bilateral MCAs in those patients cannulated via the neck vessels for VA or VV ECLS.[35] Finally, in adults (mean age 48 years), Wong et al. report a series of 20 adults on ECLS, 17 on VA and 3 on VV, in whom they routinely used NIRS to monitor adequacy of cerebral perfusion with a protocol to improve cerebral oxygen delivery if cerebral saturation was low. All VA patients were cannulated via the femoral artery. All 20 patients had a bilateral transient drop in cerebral saturation at least once that resolved with resolution of mechanical issues with the ECLS equipment or with interventions to increase oxygen delivery overall. Two patients had persistent bilateral decrease in cerebral saturation; they were diagnosed with diffuse anoxic brain injury and subsequently were declared brain dead. Two other patients had persistent unilateral decrease in cerebral saturations and were found to have large unilateral infarcts.[14]

The present study has several limitations that should be discussed. One of the main limitations is the possibility of under-ascertainment of the outcome of interest using the database. Although this is likely non-differential based on carotid versus femoral location of cannulation in general, it could potentially be differential if there are different practices of evaluating pediatric versus adult patients. The ELSO registry does not provide information on the laterality of the CNS injury to be able to attribute the injury to the cannulation site. We have no information regarding ischemic leg injury with femoral artery cannulation such as use of a distal perfusion catheter, or need for fasciotomy or amputation. The small number of patients in the femoral group at the younger ages, and small number of carotid patients at the older ages, means that we had limited ability to examine the relative CNS safety of different cannulation sites for these age groups. Although we adjusted for multiple confounding variables, there may be residual confounding that we are unable to account for. Lastly, we were unable to account for the potential independent effect of the ECLS center where patients were treated, as treatment center is not available in the dataset. This information may be important given that treatment protocols for ECLS patients can be specific to each individual ECLS center, such as preferred site of cannulation, and outcomes may not be uniform across all ECLS centers.

CONCLUSION

In this study, carotid artery cannulation in pediatric and adult patients between 3 and 55 years of age was associated with an increased likelihood of CNS injury as compared to cannulation of the femoral artery. The size of the association differed little by age. We believe that in older children and adults undergoing VA ECLS, the choice of cannulation site should take into account an increased risk of CNS injury related to carotid artery cannulation.

Figure 1. Patient flowchart per inclusion and exclusion criteria

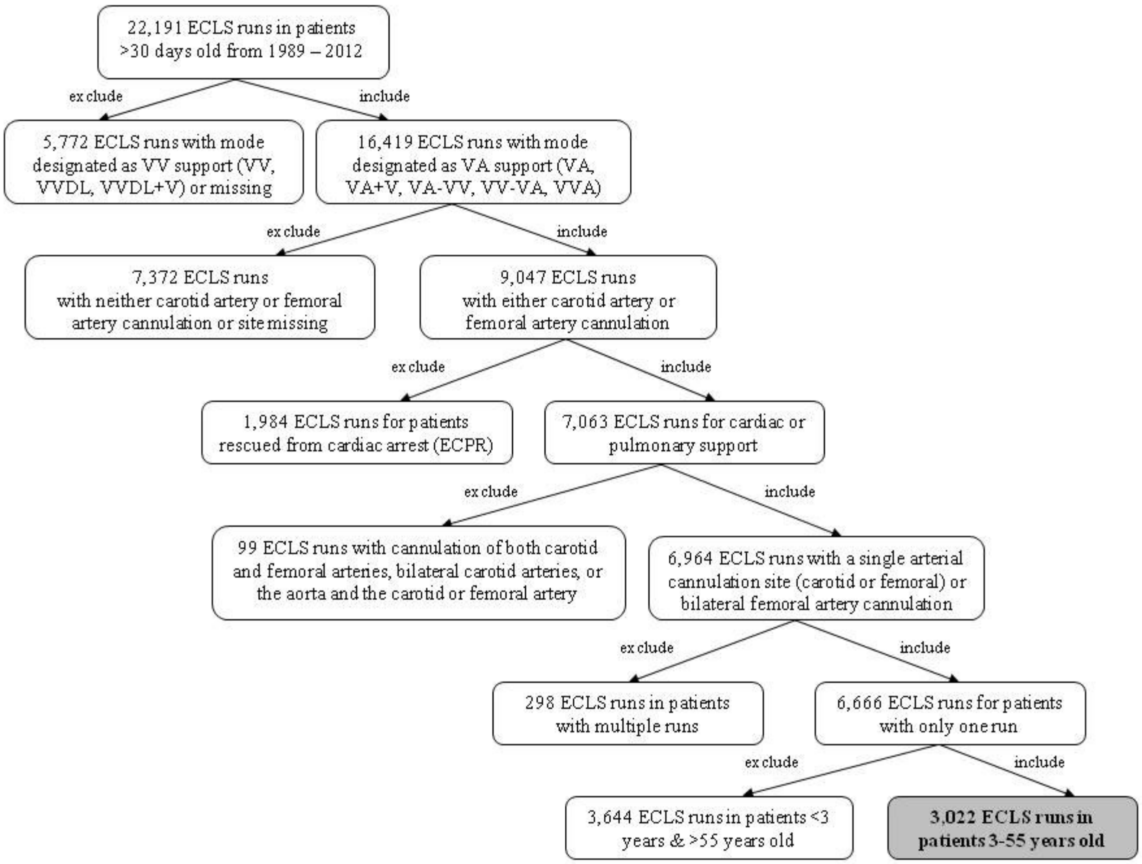

Figure 2. Proportion of patients with carotid artery as compared to femoral artery cannulation by age group and era

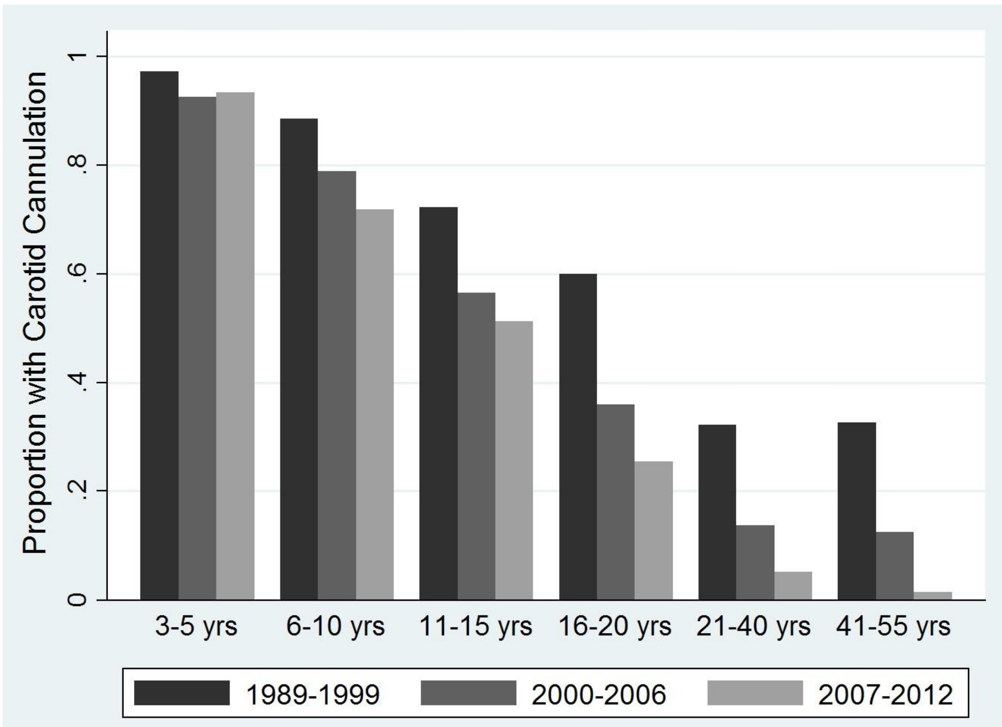

Table 1. Characteristics of patients 3 to 55 years old with carotid or femoral artery cannulation for VA ECLS

Variable	Femoral Artery n=1,765	Carotid Artery n=1,257
Age		
3-5 years	28 (1.6)	419 (33.3)
6-10 years	101 (5.7)	332 (26.4)
11-15 years	249 (14.1)	313 (24.9)
16-20 years	216 (12.2)	100 (8.0)
21-40 years	509 (28.8)	50 (4.0)
41-55 years	662 (37.5)	43 (3.4)
Gender		
Female	700 (39.7)	618 (49.2)
Male	1,049 (59.4)	622 (49.5)
Race		
Asian	552 (31.3)	67 (5.3)
Black	204 (11.6)	206 (16.4)
Hispanic	121 (6.9)	127 (10.1)
Other	91 (5.2)	66 (5.3)
White	765 (43.3)	703 (55.9)
Year of Treatment		
1989 – 1999	87 (4.9)	210 (16.7)
2000 – 2006	476 (27.0)	465 (37.0)
2007 – 2012	1,202 (68.1)	582 (46.3)
Indication for ECLS		
Pulmonary	558 (31.6)	698 (55.5)
Cardiac	1,207 (68.4)	559 (44.5)
Duration of ECLS run, hours*	111 (53, 192)	148 (80, 266)

Numbers may not add to total because of missing data.
Data are presented as n (%) or median (interquartile range).
*<1% missing data

Table 2. Pre-ECLS support in patients 3 to 55 years old with carotid or femoral artery cannulation for VA ECLS

Variable	Femoral Artery n=1,765	Carotid Artery n=1,257
Arterial Blood Gases$^{\Delta}$		
pH*	7.29 (7.17, 7.39)	7.25 (7.13, 7.35)
$paCO_2$, mm Hg*	42 (32, 56)	49 (39, 66)
paO_2, mm Hg*	72 (50, 126)	58 (46, 85)
Ventilator Settings		
FiO_2 (%)†	100 (80, 100)	100 (93, 100)
Mean Airway Pressure, cm H_2O‡	16 (11, 25)	22 (14, 30)
Positive End Expiratory Pressure, cm H_2Oˆ	8 (5, 12)	10 (6, 12)
Peak Inspiratory Pressure, cm H_2Oˆ	30 (24, 38)	36 (27, 48)
Adjunctive Respiratory Support		
Surfactant	4 (0.2)	22 (1.8)
Nitric oxide	231 (13.1)	337 (26.8)
High frequency oscillatory ventilation	107 (6.1)	306 (24.3)
Cardiovascular Support		
Mechanical Circulatory Support	324 (18.4)	32 (2.6)
Cardiac Pacemaker	64 (3.6)	25 (2.0)
Cardio-pulmonary Bypass	161 (9.1)	29 (2.3)
Inotrope or Vasopressor	1,489 (84.4)	1,110 (88.3)
Vasodilator	222 (12.6)	199 (15.8)
Other Medications		
Bicarbonate or THAM	441 (25.0)	377 (30.0)
Narcotics	712 (40.3)	878 (69.9)
Neuromuscular blockers	592 (33.5)	721 (57.4)
Steroids	61 (3.5)	35 (2.8)
Continuous Renal Replacement Therapy	40 (2.3)	5 (0.4)
Pre ECLS Cardiac Arrest	553 (31.3)	384 (30.6)

Data are presented as n (%) or median (interquartile range)
$^{\Delta}$ Worst blood gas results in the 6 hours preceding initiation of ECLS.
*11-12% missing data, †16% missing data, ‡48% missing data, ˆ34% missing data

Table 3. Complications occurring during ECLS run in patients 3 to 55 years old with carotid or femoral artery cannulation for VA ECLS

Variable	Femoral Artery n=1,765	Carotid Artery n=1,257
Bleeding		
Cannulation site bleeding	441 (25.0)	285 (22.7)
GI hemorrhage	77 (4.4)	70 (5.6)
Surgical site bleeding	300 (17.0)	186 (14.8)
Cardiovascular		
CPR required	108 (6.1)	70 (5.6)
Cardiac arrhythmia	314 (17.8)	196 (15.6)
Hypertension requiring treatment	102 (5.8)	236 (18.8)
Inotrope on ECLS	1,169 (66.2)	744 (59.2)
Myocardial stun by echocardiogram	100 (5.7)	66 (5.3)
Tamponade (air, blood, or serous)	76 (4.3)	40 (3.2)
Hematologic		
DIC	116 (6.6)	73 (5.8)
Hemolysis	205 (11.6)	122 (9.7)
Mechanical Complications		
Air in circuit	49 (2.8)	47 (3.7)
Cannula problems	137 (7.8)	139 (11.1)
Clots anywhere in circuit	399 (22.6)	303 (24.1)
Circuit Rupture	17 (1.0)	31 (2.5)
Oxygenator failure	299 (16.9)	128 (10.2)
Pump malfunction	26 (1.5)	24 (1.9)
Metabolic Complications		
Glucose<40	35 (2.0)	13 (1.0)
Glucose>240	383 (21.7)	217 (17.3)
Hyperbilirubinemia	226 (12.8)	86 (6.8)
pH<7.2	222 (12.6)	131 (10.4)
pH>7.6	145 (8.2)	27 (2.2)
Neurologic		
Seizures (clinical or EEG)	41 (2.3)	52 (4.1)
Pulmonary		
Pulmonary hemorrhage	159 (9.0)	153 (12.2)
Pneumothorax requiring treatment	85 (4.8)	133 (10.6)
Renal		
Creatinine ≥1.5	633 (35.9)	329 (26.2)
Dialysis	713 (40.4)	585 (46.5)
Infection, culture proven	293 (16.6)	181 (14.4)

Data presented as n (%).

Table 4. Adjusted logistic regression models with results presented as odds of outcome in carotid group as compared to odds of outcome in femoral group

	Total N	Carotid N (%)	Femoral N (%)	OR*	95% CI	p
INFARCT						
All ages	2997	92/1253 (7.3)	76/1744 (4.4)	2.99	1.86 – 4.81	<0.001
3 – 5 yrs	444	29/416 (7.0)	2/28 (7.1)	1.16	0.26 – 5.25	
6 – 10 yrs	432	21/331 (6.3)	3/101 (3.0)	2.36	0.68 – 8.16	
11 – 15 yrs	562	24/313 (7.7)	6/249 (2.4)	3.74	1.49 – 9.41	
16 – 20 yrs	313	9/100 (9.0)	5/213 (2.4)	4.98	1.59 – 15.53	
21 – 40 yrs	548	4/50 (8.0)	26/498 (5.2)	1.93	0.62 – 5.99	
41 – 55 yrs	698	5/43 (11.6)	34/655 (5.2)	3.47	1.23 – 9.83	
interaction						0.6821
INFARCT OR HEMORRHAGE						
All ages	2997	150/1253 (12.0)	124/1744 (7.1)	2.23	1.55 – 3.22	<0.001
3 – 5 yrs	444	45/416 (10.8)	2/28 (7.1)	1.76	0.39 – 7.81	
6 – 10 yrs	432	38/331 (11.5)	9/101 (8.9)	1.31	0.60 – 2.84	
11 – 15 yrs	562	43/313 (13.7)	11/249 (4.4)	3.57	1.78 – 7.16	
16 – 20 yrs	313	11/100 (11.0)	14/213 (6.6)	1.84	0.79 – 4.28	
21 – 40 yrs	548	7/50 (14.0)	41/498 (8.2)	1.91	0.78 – 4.68	
41 – 55 yrs	698	6/43 (14.0)	47/655 (7.2)	2.89	1.12 – 7.44	
interaction						0.5104
GLOBAL CNS INJURY						
All ages	2997	288/1253 (23.0)	328/1744 (18.8)	1.47	1.14 – 1.91	0.003
3 – 5 yrs	444	93/416 (22.4)	7/28 (25.0)	1.25	0.49 – 3.17	
6 – 10 yrs	432	77/331 (23.3)	18/101 (17.8)	1.47	0.81 – 2.65	
11 – 15 yrs	562	70/313 (22.4)	42/249 (16.9)	1.56	1.00 – 2.42	
16 – 20 yrs	313	29/100 (29.0)	40/213 (18.8)	1.97	1.11 – 3.52	
21 – 40 yrs	548	9/50 (18.0)	97/498 (19.5)	0.97	0.44 – 2.13	
41 – 55 yrs	698	10/43 (23.3)	124/655 (18.9)	1.28	0.59 – 2.76	
interaction						0.7791

*Adjusted for age, indication (respiratory versus cardiac), duration of ECLS run, era, use of inotropes on ECLS, cannula problems, oxygenator failure, hyperbilirubinemia, mechanical cardiac support prior to ECLS, dialysis on ECLS, pre-ECLS arrest (not E-CPR), and CPR on ECLS

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