Journal of Pediatric Surgery 53 (2018) 1301–1304

Contents lists available at ScienceDirect

Journal of Pediatric Surgery

journal homepage: www.elsevier.com/locate/jpedsurg

Is there a best approach for extracorporeal life support cannulation: a review of the extracorporeal life support organization

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ARTICLE INFO

Article history:
Received 7 May 2017
Received in revised form 15 January 2018
Accepted 23 January 2018

Key words:
ECLS
Cannulation
Stroke

ABSTRACT

Background: Neurologic complications are common, and amongst the most devastating complications in pediatric patients undergoing extracorporeal life support (ECLS). Carotid artery cannulation (CAN) has been associated with an increase in these complications, thereby shaping practices to avoid this approach in most pediatric patients in which other cannulation approaches are viable.
Methods: A retrospective review of children (0–18 years) in the ELSO database was undertaken from 1989 through 2013. Multivariate logistic regression analysis of rates of stroke and other neurologic complications based on cannulation technique was undertaken, adjusting for patient factors including age, underlying disease process, and severity of illness.
Results: A total of 30,282 ECLS runs were found in the database. CAN was associated with higher rates of stroke (5.15% vs 3.74%) and overall neurologic complications. However, when correcting for patient factors, including age, underlying disease process, and support type, CAN was not associated with an increased rate of neurologic complications or stroke ($p > 0.05$ for both).
Conclusion: When correcting for patient related factors CAN is not associated with an increase in stroke or neurologic compilcations. CAN should be re-examined as a cannulation technique for older pediatric patients.
Level of evidence: III.

Neurologic complications, such as bleeding, stroke or seizures, occur in about 20% of pediatric patients during veno-arterial (VA) extracorporeal life support (ECLS). Cannulation via the right common carotid artery (CAN) may result in higher rates of neurologic injury compared to other approaches for VA ECLS [1]. In older children with cardiac failure CAN is largely abandoned in favor of femoral artery cannulation, which is fraught with risks of limb ischemia and amputation [2]. In children on veno-venous (VV) ECLS for severe respiratory failure, the rate of stroke and neurologic complications are unclear. Finally, it is unclear whether delays in initiation of ECLS in order to establish alternative cannulation to the carotid artery is warranted in pediatric patients with profound shock.

The rates of neurologic injury and the use of CAN for VA ECLS are highest in neonates, and interestingly are higher in respiratory failure than in cardiac failure in this age group [1]. .However, the risk of ischemic stroke, intracranial hemorrhage, and seizure following CAN for VA ECLS for various age groups is unclear. The role of CAN in the genesis of neurologic injury when compared to VV ECLS is also unknown as previous studies only compare groups for VA ECLS [1].

The aim of this study is to understand the association that cannulation sites (CAN, aortic, femoral artery, and VV) and age have on rates of neurologic complications in children. We hypothesize that rates of neurologic injury and stroke will increase with CAN and increasing age. The goal is to determine a logical approach to cannulation with an understanding of the inherent risks for each age group and diagnosis.

1. Methods

Following an institutional review board waiver, we queried the Extracorporeal Life Support Organization (ELSO) registry from inception in 1989 through 2013. Only patients under 18 years of age who underwent a primary ECLS run were included in the analysis. The ELSO registry was used for analysis, as it includes clinical data from over 30 years, and from 160 US and 120 international centers [3].

Data abstracted included demographic information (gender, age at time of ECLS cannulation, weight, race), modifying factors [(oxygenation

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https://doi.org/10.1016/j.jpedsurg.2018.01.015
0022-3468/

index (OI), pre-ECLS arrest, support type (Respiratory, Cardiac, or ECPR), type of cannulation], and outcomes, specifically mortality and neurologic complications. Variables were chosen based on literature search for variables that affect neurologic outcome or stroke rates and expert opinion.

Patient age was stratified into clinical groups: neonates (age less than 30 days), infants (age 30 days to 1 year), toddlers (age 1–2 years of age), small children (age 2–5 years), large children (age 6–12 years), and teenagers (age 13–17 years). The clinical groups were chosen to prevent bias from a preponderance of neonatal and infant cannulations, as these groups are more likely to have neurologic complications while on ECLS and groin cannulation is extremely difficult, and generally not performed, on patients less than 5 years of age [4]. Additionally, age groups were compared with regard to many of the factors known to affect neurologic outcomes, including support type, cannulation site, and pre-ECLS factors.

Cannulation approaches included VV and VA ECLS as determined by the cannulation sites indicated in the registry data. Dual lumen and single lumen VV ECLS were included in the same group. Additional modes of cannulation, including conversions from VV to VA, or when multiple sites were used (VVA, VAV, etc.), were excluded to remove any bias. VA cannulations were further categorized by site as carotid artery (CAN), femoral (FEM), and aortic (AOR).

Neurologic complications were abstracted from the database. Seizures were diagnosed clinically or with electroencephalogram, and brain death is decided based on the reporting institution's criteria. Additionally, ischemic stroke was defined as a CNS infarct confirmed by ultrasound or CT.

We compared the rates of neurologic injury (seizures, brain death, intracranial hemorrhage) and ischemic stroke across the various age groups.

1.1. Statistical analysis

We matched the population of patients with the various cannulations using age, weight, gender, race, oxygenation index, pre-ECLS arrest, and support type to create a homogenous population to compare neurologic complications for each cannulation site. Finally, we performed multivariate logistic regression analysis of neurologic complications and stroke after correcting for the factors listed above.

2. Results

Of a total of 30,282 runs of ECLS, 1334 non-primary runs were excluded to avoid changes in complication rates or cannulation strategies associated with multiple ECLS runs. Of VA cannulations carotid cannulation was performed in 14,517 of the runs that were performed (64%), aortic in 7237 patients (32%), and femoral cannulation in 917 patients (4%) (See Fig. 1). VV cannulations were performed in 5881 patients. Demographic data showed that there was a male predominance, with 56% of patients undergoing a primary run of either VV or VA ECLS being male, and 56% being Caucasian. All cannulation groups were similar when comparing gender, age, weight, and ethnicity between groups (Table 1). Additionally, pre-ECLS factors including oxygenation index and rates of pre-ECLS arrest were similar between groups, as was the etiology of underlying physiologic derangement requiring ECLS (Table 1). The type of cannulation technique when compared between age groups (Table 2) shows a preponderance of neonatal patients in the carotid cannulation group ($p < 0.001$).

Carotid ligation was associated with a higher rate of stroke (OR 1.37), and all types of neurologic complications (OR 1.32) when compared with other sites of arterial cannulation. However, when multivariate analysis was performed to adjust for age, gender, weight, race, in addition to factors affecting the severity of illness (oxygenation index, pre-ECLS arrest, and support type) amongst patients undergoing primary ECLS runs, there was no significant difference in the rates of neurologic complications ($p > 0.05$ for all groups), or stroke ($p > 0.05$ for all groups) by cannulation site. Adjusted rates of neurologic injury and stroke were 19.4% and 4.35% in CAN, respectively, compared with 19.5% and 4.5% overall (Table 3).

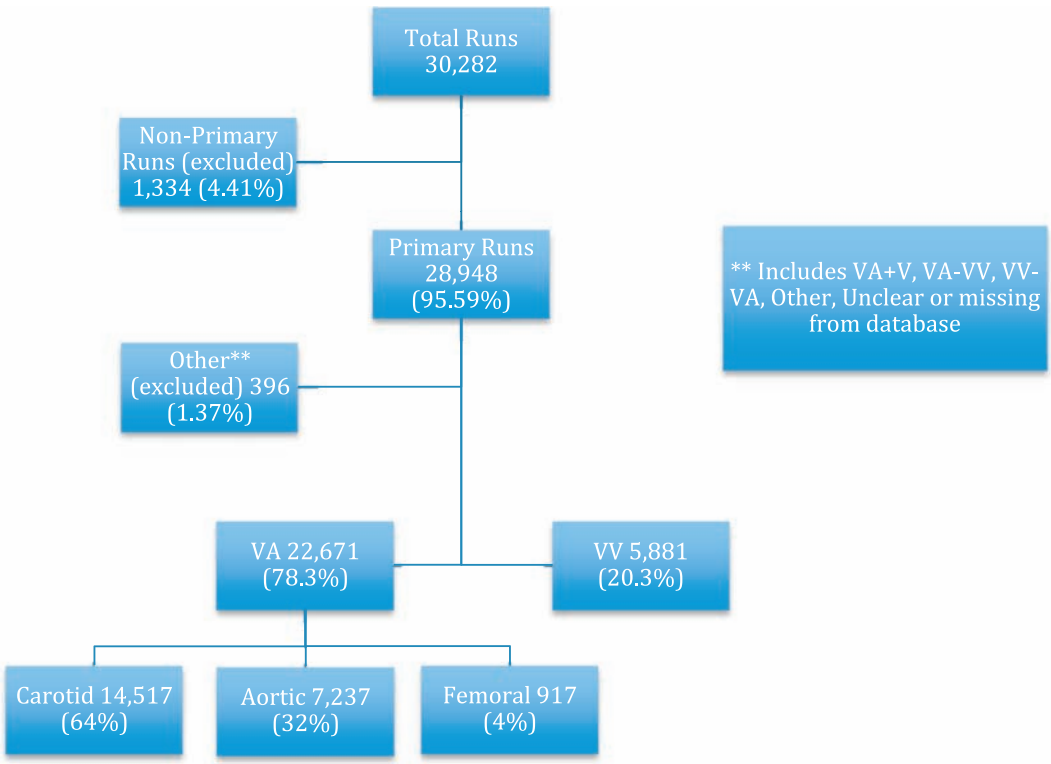

Fig. 1. Flow Chart.

Table 1
Demographics, Pre-ECLS Factors, Support Type.

	VA CAN	VA Aor	VA Fem	VV	p-value
Female	44.2%	43.4%	44.0%	44.3%	0.58
Age (days)	564 ± 1394	573 ± 1409	581 ± 1455	567 ± 1403	0.81
Weight (kg)	8.82	9.08	9.40	8.94	0.48
Caucasian	56.4%	56.3%	57.6%	58.1%	0.09
Oxygenation Index	47.6	48.6	51.9	47.0	0.18
Pre-ECLS Arrest	22.8%	22.5%	24.8%	23.1%	0.46
Primary Dx					
Pulmonary	58.9%	59.1%	59.5%	59.3%	0.90
Cardiac	31.8%	31.3%	30.3%	31.3%	
ECPR	9.3%	9.6%	10.1%	9.3%	

Table 3
Adjusted Rates of Neurologic Complication and Stroke.

	VA Carotid	OR	p-value	CI
*Neuro Complications				
VA Carotid	19.4%	Ref Value	–	–
VA Aortic	19.6%	0.98	0.67	0.89–1.07
VA Femoral	20.1%	1.09	0.42	0.88–1.35
VV	19.7%	1.04	0.37	0.94–1.15
*Stroke Rate				
VA Carotid	4.35%	Ref Value	–	–
VA Aortic	4.98%	1.09	0.30	0.92–1.30
VA Femoral	5.13%	1.33	0.12	0.92–1.92
VV	4.28%	1.08	0.35	0.90–1.30

* Adjusted for Age, Gender, Weight, Race, Oxygenation Index, PreECLS Arrest, Support Type.

3. Discussion

Neurologic complications in patients on ECLS are associated with increased mortality, longer length of stay, and higher need for long-term care after discharge [5]. Studies analyzing rates of neurologic complications as a function of cannulation site have shown varied results, with some demonstrating carotid artery cannulation being associated with higher rates of neurologic complications and stroke, and others showing no difference [1,5,6]. Similarly, rates of neurologic complication and stroke in patients undergoing CAN have been shown to increase with age in some studies, while others have not demonstrated this trend [1,7]. Despite the lack of formal guidelines or recommendations regarding cannulation site, the use the use of alternate cannulation sites in older children and adults has become standard practice at many centers [7].

Historically carotid artery cannulation has been avoided in most patients because of the presumed increased risk of stroke associated with this technique [1]. . The exception to this is with neonates, in whom prohibitively small femoral vessels preclude femoral cannulation. In this study the relative risk of neurologic complications and stroke did increase with carotid artery cannulation (OR 1.32 and 1.37 respectively). Similarly, previous studies have shown higher rates of neurologic complications across all age groups, with an odds ratio of stroke being higher amongst patients undergoing carotid cannulation [1]. This increased risk was believed to be related to derangement of cerebral autoregulation, impairment of cerebral venous drainage related to the venous cannula being placed within the internal jugular vein, and increased risk of embolic phenomena to the brain [1].

In our study, we found that rates of neurologic complications and stroke were similar irrespective of cannulation site when correcting for other factors. Addtionally, after correcting for other factors rates of these complications did not increase with age as well. This differs from our hypothesis that rates of neurologic complications and stroke would increase with CAN and increasing age. By adjusting for other factors, including age, severity of illness, and support type, differences in rates of neurologic complications and stroke related to age or cannulation site were eliminated.

Known risk factors for intracerebral hemorrhage (ICH) in neonates include small size (kg <3, OR 1.3), and early gestational age [4,8,9]. This increased risk of neurologic complications within the neonatal group, along with a disproportionate number of CAN in the neonatal population may have skewed outcomes seen in previous analyses [1]. Correcting for these factors, in addition to other contributing factors including underlying disease process and age, may explain the difference in outcomes found in this analysis when compared to previously performed studies. Our analysis found similarly increased rates of neurologic complications and stroke in pediatric patients (OR 1.32 and 1.37, respectively) undergoing CAN prior to correcting for these factors, but with similar rates of neurologic complications and stroke across age ranges following correction (See Fig. 2).

Since 6% of patients will have an incomplete circle of Willis, ligation of the carotid artery should cause stroke in a small but perceptible portion of patients [10]. Interestingly, previous studies have shown that the side of cannulation for CAN does not correlate with the side of the brain lesion for patients with ICH or ischemic stroke, suggesting that physiologic changes associated with ECLS are more important than cannulation site when determining risk of neurologic complications [11,12]. Indeed, sepsis, coagulopathy, and poor perfusion, as evidenced by the need for epinephrine and bicarbonate infusions, and resultant persistent acidosis, are all known risk factors for stroke [5,13,14]. Reconstruction of the carotid artery following decannulation can be performed, but studies have not been able to demonstrate a benefit in neurologic function or complication rates despite reasonable patency rates following reconstruction [15,16].

The use of femoral cannulation has potential limitations in addition to increases in some types of complications as well. Femoral cannulation is associated with lower oxygenation of the brain and coronary vessels due to perfusion of these vital organs primarily by hypoxic blood ejected from the left ventricle, occasionally known as “North–South syndrome” [7]. Additionally, complications including pulmonary and gastrointestinal bleeding, limb ischemia, and amputation are more frequent in patients cannulated through the femoral vessels [2,7,17].

Limitations of this study include that the data are retrospective. As a result, selection bias leads to populations that are potentially heterogeneous when assessing the underlying disease process, patient age, and other factors. Therefore there are many factors that must be corrected for in order to obtain meaningful data. Additionally, the definitions and assessment modalities for neurologic complications evolve over time (ex: improvements in EEG sensitivity may increase the number of seizures diagnosed over time), so that this may not be comparing identical entities in all cases. Also, this database does not contain any data regarding the long-term neurologic outcomes of these patients, making the overall significance of these neurologic complications difficult to assess. Registries are also subject to underreporting, as disclosure of data is dependent on the centers included, and may result in a portion of complications not being reported.

The clinical implications of this study are that in pediatric patients in whom VA ECLS is needed CAN should be considered as a viable cannulation technique in all age groups, and not just in neonates. Despite these findings, we cannot recommend carotid cannulaion as the best option for all patients, as each clinical scenario is different,

Table 2
Cannulation Site by Age.

Mode and Site	0–30 days	30 days – 1 year	1–2 years	2–5 years	5–12 years	12–18 years
VA CAN	9008	2624	612	746	721	806
VA Aorta	4468	1298	327	380	364	400
VA Fem	559	182	45	31	46	54
VV	3693	1015	251	299	290	333

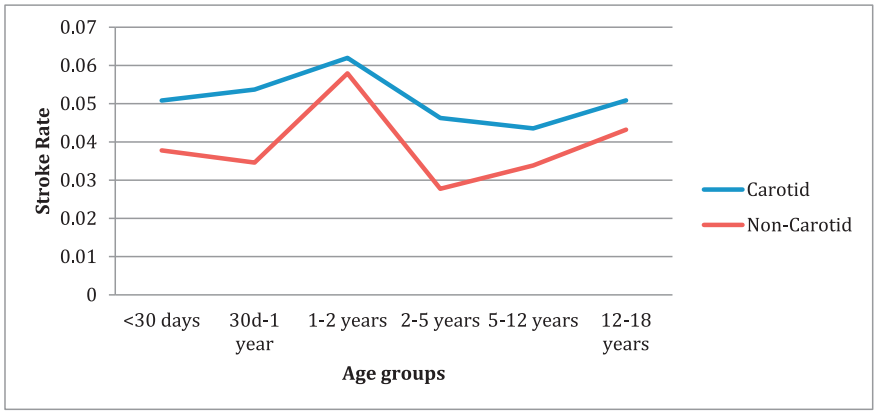

Fig. 2. Adjusted Stroke Rates by Age Group Raw stroke rate 3.74% for non-carotid, 5.15% for carotid, adjusted rates of 4.35% for non-carotid and 4.5%, $p > 0.05$ for all age ranges when compared to reference value (age < 30 days) following adjustment.

with the risks and benefits of each cannulation technique that need to be weighed. Scenarios in which CAN may be most appropriate may include unstable patients that require support as quickly as possible, and patients with significant cardiac dysfunction that would have less coronary blood flow with femoral cannulation. Further studies may show similar outcomes in the adult population, in which risks of neurologic complications and stroke are lower overall [4].

An additional implication of our study is that one could predict outcomes amongst patients based on multiple factors, including age, pre-ECLS factors including sepsis and poor perfusion, and type of support. Furthermore, rates of complications over the patient's course evolve and modeling these factors may allow providers and caregivers to predict the outcome. Additionally, creation of a prognostic model for various age groups may help determine the best site for cannulation based on patient and disease related factors.

4. Conclusion

The rates of neurologic complications and stroke are similar despite cannulation type amongst pediatric patients when one corrects for demographics, underlying disease process, and support type. There is no increase in stroke rate with increase in age, but rather a higher rate in neonates compared to other populations. Based on these results, we believe that the trend toward avoiding carotid artery ligation for VA ECLS in pediatric patients of all ages should be reconsidered.

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