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Original Article

Hypothermic circulatory arrest with or without antegrade cerebral perfusion for aortic arch surgery in infants

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Abstract

Background: Antegrade cerebral perfusion (ACP) minimizes deep hypothermic circulatory arrest (DHCA) duration during arch surgery in infants, which may impact the outcomes of the repair. We aimed to evaluate the effect of adding antegrade cerebral perfusion to deep hypothermic circulatory arrest on DHCA duration and operative outcomes of different aortic arch operations in infants.

Methods: We retrospectively collected data from infants (<20 weeks old) who underwent aortic arch reconstruction (Norwood operation, arch reconstruction for the hypoplastic arch and interrupted aortic arch) using DHCA alone (n=88) or combined with ACP (n=26). We excluded patients who had concomitant procedures and those with preoperative neurological disability.

Results: There was no difference between groups as regards the age, gender, and the operation performed (p= 0.64; 0.87 and 0.50; respectively). Among the 114 patients, 11 (9.6%) had operative mortality, and 14 (12.3%) had cerebral infarction diagnosed with CT scanning. Adding ACP to DHCA significantly reduced DHCA duration from 50.7 ± 10.6 minutes to 22.4 ± 6.2 minutes (p<0.001) and lowered the mortality (11 vs. 0; p=0.066) and cerebral infarction (13 vs. 1; p=0.18). No statistically significant difference between the two groups in terms of ischemic time (p=0.63) or hospital stay duration (p=0.47).

Conclusion: Using ACP appears to reduce the DHCA duration and was associated with better survival and neurological outcomes of aortic arch surgery in infants. A study with longer follow-up to evaluate the long-term neurological sequelae is recommended.

KEYWORDS

Antegrade cerebral perfusion; Aortic arch; Hypothermia; Mortality

Article History

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Introduction

Deep hypothermic circulatory arrest (DHCA) is a surgical technique that aims to protect the brain during cardiac and aortic surgeries. It was established in the 1950s and promoted in the 1970s [1]. The main principle of this technique is to reduce brain metabolism by cooling the body below 18C, allowing for more extended periods of interrupted blood flow [2]. The metabolism rates decrease by about 7% for every 1°C drop below 37°C [3,4]. Moreover, when the body temperature reaches 20°C, oxygen consumption is reduced to 20% of normothermic values [5].

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Cooley and colleagues reported the first successful operation of aortic arch replacement with this strategy in 1955. However, the patient died after six days due to cerebral ischemia [6]. By the mid-1970s, Griepp reported the first successful experience of using DHCA to facilitate aortic arch replacement [7]. Most patients tolerate about 30 minutes of DHCA without significant neurological dysfunction. However, when extended beyond 40 minutes, the incidence of brain injury increases significantly [8]. Above 60 minutes, most patients will suffer an irreversible brain injury. Therefore, the adjunctive use of cerebral perfusion techniques was suggested.

Antegrade cerebral perfusion (ACP) is a cardiopulmonary bypass (CPB) technique that aims at continuous perfusion of the brain with oxygenated blood (also known as regional low-flow cerebral perfusion) [9]. This technique was developed as a perfusion process to minimize DHCA duration during aortic arch surgery. This is because intermittent cerebral perfusion for 10 minutes every 20 minutes is needed during DHCA to control the cerebral anaerobic metabolism during long periods of circulatory arrest [10]. This technique showed significant benefits in terms of prolonging the safe time and improving the cerebral cooling results [11,12].

In this study, we aimed to evaluate whether adding ACP to DHCA reduces DHCA duration and improves the neurological outcomes and mortality of different aortic arch operations in infants.

Patients and Methods:

Design and Patients:

We performed a retrospective cohort study on patients who had arch surgery from January 2011 to October 2015. We collected data from infants (age < 20 weeks), undergoing Norwood operation, arch reconstruction for the hypoplastic arch and interrupted aortic arch [IAA] with healthy preoperative neurological status (based on brain MRI). We excluded preterm babies, those aged more than 20 weeks, patients who underwent any procedure other than the three mentioned above, and those with preoperative neurological disability. The study was reported following the guidelines of the STROBE checklist.

Operative technique:

We included patients who underwent aortic arch surgery under DHCA or DHCA plus ACP. In the latter group, the ACP procedure was performed as described by Pigula and associates [12]. Briefly, after starting CPB and gradual cooling of the patient over 40 minutes to 20°C using the alpha-stat strategy, the systemic circulation was arrested. We sewed a 3.5 mm polytetrafluoroethylene (PTFE) graft into the right innominate artery with fine Prolene sutures (by side occlusion with a vascular clamp during full flow). The brachiocephalic vessels and descending thoracic aorta were snared, and blood flow was sustained to the brain via the right innominate and right vertebral arteries (mean ACP flow rate: 37 ± 4.2 mL/kg/min). All infants were operated by a single surgical consultant to remove inter-operator variability.

*Table **1**: Data are presented as number (%) or mean ± standard deviation. The preoperative characteristics and operative outcomes in the enrolled patients*

	DHCA (N= 88)	DHCA + ACP (N= 26)	Total (N = 114)	p-value
Age (weeks)	9.3 ± 5.6	10.4 ± 6	9.5 ± 5.7	0.64
Gender				
Male	49 (55.7%)	15 (57.7%)	64 (56.1%)	0.87
Female	39 (44.3%)	11 (42.3%)	50 (43.9%)	
Procedure				
Hypoplastic arch reconstruction	44 (50%)	15 (57.7%)	59 (51.8%)	0.497
Norwood operation	32 (36.4%)	8 (30.7%)	40 (35.5%)	
Interrupted aortic arch surgery	12 (13.6%)	3 (11.5%)	15 (13.2%)	
Duration of circulatory arrest (minutes)	48.6±13.7	22.1±6.24	42.6 ± 16.7	<0.001
Ischemic time (minutes)	120.8±30.5	118.1±37.5	120.2 ± 32.1	0.63
Hospital stay duration (days)	36.2±53.6	29.6±34.2	34.7 ± 49.8	0.47
Hospital mortality	11 (12.5%)	0	11 (9.65%)	0.066

DHCA: deep hypothermic circulatory arrest; ACP: antegrade cerebral perfusion

Data collection:

The collected data included (I) Preoperative data: patient's diagnosis, age at time of operation and gender (II) Operative data: type of the operation, DHCA duration, ischemic time and flow rates during ACP perfusion and (III) Postoperative data: outcomes [mortality, seizures, cerebral infarction and bleeding] and length of hospital stay. All patients underwent postoperative CT scanning and electroencephalogram (EEG) monitoring for 48 hours. These data were collected from the hospital registry records, and patients with missing data were excluded from the analysis. The study was approved by the Institutional Review Board, and patients' consent was waived.

Statistical analysis

Categorical data were expressed as frequencies and percentages, while numerical data were expressed as means ± standard deviations. Shapiro- Wilk normality test was used to test the distribution of the continuous variables, and we used the Student's t or Mann-Whitney tests accordingly. Chi-Square or Fisher exact (if the expected frequency is less than 5) tests were used to compare both groups in terms of categorical data. A p value of < 0.05 was considered statistically significant. All analyses were performed using the Statistical Package for Social Sciences (SPSS, version 22, IBM Corp, Chicago, IL, USA).

Results

Preoperative details:

We included 114 infants who had aortic arch surgery with DHCA alone (88 patients) or DHCA plus ACP (26 patients). The patients' age ranged from 5 to 20 weeks (9.5 ± 5.7 weeks), and 64 patients were males (56.1%). The most frequent surgery was hypoplastic arch reconstruction (n= 59; 51.8%), followed by Norwood operation (n= 40; 35.5%). No significant differences were found between the DHCA and DHCA + ACP groups in terms of age, gender, and type of procedure (Table 1)

Operative outcomes:

Among the 114 patients, 11 (9.6%) had operative mortality. Cerebral infarction was detected by postoperative CT scanning in 14 (12.3%) patients, and major bleeding occurred in two patients (1.7%). Seizures occurred in six patients (5.2%), and EEG detected an epileptic focus in three patients (2.6%). The mean ischemic time in all patients was 120.2 (±32.1) minutes, and the mean DHCA and hospital stay durations were 36.2 ± 53.6 minutes and 29.6 ± 34.2 days, respectively.

DHCA versus DHCA plus ACP comparison:

Adding ACP to DHCA significantly reduced DHCA duration from 50.7 ± 10.6 minutes to 22.4 ± 6.2 minutes (p<0.001) and lowered the mortality (11 vs. 0 for DHCA alone and DHCA plus ACP groups; p=0.066) and cerebral infarction (13 vs. 1 for DHCA alone and DHCA plus ACP groups; p=0.18). We detected no statistically significant difference between the two groups in terms of ischemic time (p=0.63) or length of hospital stay (p=0.47) (Table 1).

Table 2: Comparison between DHCA alone versus DHCA + ACP groups in terms of ischemic time, DHCA and hospital stay durations. Data are presented as number (%) or mean ± standard deviation.

	DHCA	DHCA plus ACP	p value
Ach Repair Operation			
DHCA Duration (minutes)	46.9±16.2	24.7±3.87	**<0.001**
Ischemic Time (minutes)	101.2±16.9	100.9±21.5	0.93
Hospital Stay Duration (Day)	27.6±19.3	18.3±6.6	0.18
Norwood Operation			
DHCA Duration (minutes)	50.7±10.6	22.4±6.2	**<0.001**
Ischemic Time (minutes)	154.5±16.4	127.2±40.1	0.16
Hospital Stay Duration (Day)	41±64	21.3±9.8	0.39

DHCA: deep hypothermic circulatory arrest; ACP: antegrade cerebral perfusion

Subgroup analysis

Operation Type: Fifty-nine patients underwent reconstruction for hypoplastic aortic arch. The mean ischemic time in these patients was 101.2±16.9 minutes, and the DHCA and hospital stay duration were 46.9±16.2 minutes and 27.6±19.3 days, respectively. Subgroup analysis showed significantly shorter DHCA ($p<0.001$) and non-significant hospital stay durations ($p=0.18$) in patients who underwent DHCA and ACP.

Forty patients underwent the Norwood operation. The mean ischemic time in these patients was 154.5±16.4 minutes, and the DHCA and hospital stay duration were 50.7±10.6 minutes and 41±64 days, respectively. There were significant decreases in DHCA duration ($p<0.001$), as well as a non-significant reduction in DHCA plus ACP group, compared to DHCA alone group in terms of ischemic time ($p=0.16$) and hospital stay duration ($p=0.39$) (Table 2).

Operative mortality:

In subgroup analysis, the mean DHCA duration was significantly longer ($p=0.017$) in non-survivor patients, compared to survivors. We detected no significant difference ($p=0.21$) between both groups in terms of ischemic time (Figure 1).

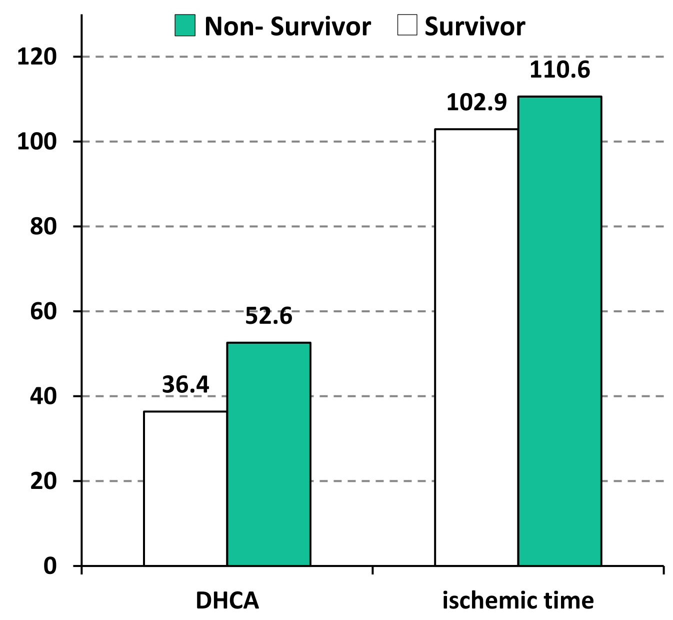

Figure 1: shows the differences between survivors and non-survivors in terms of DHCA duration and ischemic time.

Discussion

We found that antegrade cerebral perfusion was associated with shorter DHCA duration and lower mortality. Therefore, a combination of DHCA and ACP is recommended for cerebral protection during aortic arch operations in infants. ACP reduced DHCA duration in patients who underwent arch and Norwood procedures but did not affect the ischemic time. Only 15 patients had IAA surgery; therefore, independent subgroup analysis for outcomes with this operation was not powered.

Infants with critical arch hypoplasia and hypoplastic left heart structures have a high incidence of pre-existing structural brain lesions, which predispose them to brain injury following cardiac surgery. Chau and associates suggested that the reported worse neurological outcomes after 40 minutes of DHCA in the literature may be related to the more complex pathology in these patients, not the inadequacy of cerebral protection [2]. Therefore, in our practice, all patients undergo brain MRI before the operation, and we included only infants with normal preoperative neurological condition in this study.

Turkoz and colleagues enrolled 37 neonates and infants to arch construction in the presence of selective cerebral and myocardial perfusion and short-term total circulatory arrest. They concluded that continuous perfusion every 10 minutes was safe and practical in these patients [13]. In a randomized trial on neonates, Newburger and coworkers compared deep hypothermia with total circulatory arrest to deep hypothermia with low-flow cardiopulmonary bypass. They reported that the low-flow group was associated with the less ictal activity, clinical seizures, and shorter recovery time. Moreover, they observed that all cases of clinical seizures were associated with prolonged circulatory arrest above 35 minutes [14].

Regarding the degree of cooling, we opted for gradual cooling to 20°C over 40 minutes. Folkerth and colleagues recommended cooling to 20°C for 30 minutes of total cardiac arrest [15]. Similarly, Treasure and associates showed that surface cooling should not exceed 18°C to avoid the occurrence of neurological depressions [16]. On the other hand, Wolin and coworkers reported that the cooling should be between 10 and 15°C to achieve optimal protection against brain damage [17]. Therefore, the average cooling temperature in the published literature ranges between 15 and 20°C to cover up to 40 minutes of circulatory arrest [14].

Neurological deficits that occur after DHCA are difficult to be elicited according to the affected brain center. It may appear in the form of seizures, cerebral infarction with or without focal affection in EEG, and CT scan. Ischemic cerebral changes may appear in the form of intellectual impairment, which will appear in the school period [18] and need close long-term follow up for these infants. The rate of postoperative bleeding in our study was very low due to the availability of the cell saver machine and re-transfusion of shed blood.

Our study has some limitations. First, the retrospective nature of the study does not allow controlling the type of collected data; therefore, we could not report data on cerebral oximetry results and the doses of cerebral protecting medications, for example. We only studied the major neurologic dysfunctions like infarctions and seizures, not including minor or asymptomatic dysfunctions. To ensure a comprehensive evaluation of ACP, additional studies should measure the tissue oxygenation in multiple brain regions under varying conditions of flow, pressure, temperature, hematocrit, and different cannulation strategies. Further measures should include functional neurological testing in the recovering infant.

Conclusion

Using ACP appears to reduce the DHCA duration and was associated with better survival and neurological outcomes of aortic arch surgery in infants. Therefore, a combination of DHCA and ACP is recommended for cerebral protection during aortic arch operations in infants. Future studies should employ more extended follow-up periods to evaluate the long-term neurological sequelae in these patients.

Conflict of interest: Authors declare no conflict of interest.

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