Retrograde Cerebral Perfusion Is Effective for Prolonged Circulatory Arrest in Arch Aneurysm Repair

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Background. **The optimal brain protection strategy for prolonged periods of circulatory arrest is still controversial. This study evaluated whether retrograde cerebral perfusion (RCP) provides adequate brain protection for prolonged periods of deep hypothermic circulatory arrest (DHCA).**

Methods. **From January 1997 to December 2014, 1,043 patients underwent aortic arch operations using RCP and DHCA at 18°C. The DHCA time for 993 patients was 49 minutes or less and the DHCA time for the remaining 50 patients was 50 minutes or more. Propensity matching between the two groups was performed, taking into account the main preoperative and surgical variables and all the preoperative and intraoperative neurologic risk factors. Logistic regression analysis was performed to identify independent predictors of operative death and postoperative cerebral complications.**

Results. **In the unmatched population, mortality in the 50 minutes or more vs the 49 minutes or less group was 8% vs 3.8% ($p = 0.143$), and the stroke rate was 2% vs 1.2% ($p = 0.623$). Propensity matching resulted in 48 pairs. Operative death and incidence of transient and permanent neurologic deficit were similar and not statistically significant in the matched groups for all comparisons. No difference in the incidence of other major postoperative complications was found between the two groups. Midterm survival was similar. Regression analysis showed DHCA duration was not independently associated with operative death or postoperative neurologic deficits.**

Conclusions. **RCP is an effective adjunctive cerebral protection strategy for complex aortic arch aneurysm repair with prolonged DHCA and is not associated with increased death or neurologic complications.**

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Since the introduction of deep hypothermic circulatory arrest (DHCA) in the management of aortic arch pathology, controversy persists regarding the optimal strategy for cerebral protection. Current options include lone DHCA, unilateral or bilateral antegrade cerebral perfusion (ACP) with varying degrees of hypothermia, and DHCA with retrograde cerebral perfusion (RCP). Each strategy has advantages and disadvantages, but no single strategy has been endorsed by the surgical community.

ACP is currently the most commonly used adjunct owing to a perceived increase in safety, especially with prolonged periods of circulatory arrest (CA). Respondents to a survey in Europe preferred ACP in 91% of acute and 98% of chronic cases [1]. However, ACP has not been proven superior to RCP in randomized trials or in large meta-analyses [2–5]. The common perception that ACP provides superior protection and an added "safety net," especially in less experienced centers, has never been proven in the literature.

Even less is known about the optimal management during cases with prolonged periods of CA. DHCA without an adjunct has been shown to be safe for less than 30 minutes [6] and up to less than 40 minutes in more contemporary series [7, 8]. Beyond 50 minutes, the rates of neurologic dysfunction increase significantly, with stroke rates up to 16.7% [9]. RCP and ACP can both extend the maximal safe CA time [2]. However, data on either RCP or ACP specifically for prolonged CA times exceeding 50 minutes are severely lacking in the literature.

We previously showed that RCP with DHCA is an effective method of cerebral protection in hemiarch and total arch procedures. In that study we noted that patients requiring periods of CA of 50 minutes or longer did not have a greater risk of permanent neurologic deficits (PND) [10]. We sought to more formally examine the use of RCP in complex arch reconstruction requiring prolonged CA (≥50 minutes).

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Patients and Methods

The Weill Cornell Medicine Institutional Review Board approved the study and waived the need for individual patient consent.

Patients

A review of our aortic surgery database identified 1,043 patients who underwent aortic operations in which RCP and DHCA were used from 1997 to 2014. Of these, DHCA lasted 49 minutes or less in 993 patients and was 50 minutes or more in the remaining 50. Receiver operating characteristic curve analysis could not identify a useful statistical cutoff because of the low incidence of events. A cutoff of 50 minutes was chosen based on previous literature. Data were obtained up until the point of the last follow-up or death.

Techniques

Our technique has been previously described [10]. For patients with arch pathology, the procedures were performed through a median sternotomy. For those with descending aneurysms extending into the arch, the operation was performed through a fifth interspace thoracotomy.

Central aortic cannulation was the primary cannulation method. Near-infrared spectroscopy was used to confirm symmetric cerebral protection (Somanetics, Troy, MI). The head was packed in ice. Patients were cooled to 18°C by bladder or tympanic temperature measurements for a minimum of 30 minutes, without exception. Three minutes before CA, 500 mg of methohexital was administered. The patient was placed into steep Trendelenburg position and the circulation arrested.

During DHCA, RCP was administered through the superior vena cava cannula at 150 to 300 mL/min at 14°C, keeping central venous pressure at 25 to 30 mm Hg. Arch reconstruction was performed with Hemashield grafts (Maquet, Oakland, NJ), using hemiarch replacement or total arch replacement with island reimplantation of great vessels, elephant trunk, or debranching. Inaccessible suture lines were reinforced with mattressed felt pledgets. Cardiopulmonary bypass was resumed through a prefabricated side branch. RCP was maintained until full flow was reestablished. Once suture lines were confirmed to be hemostatic, systemic warming ensued, keeping a gradient of 10°C between the blood and core temperature. Cardiopulmonary bypass was discontinued at 35°C.

Statistical Analysis

The aortic surgery database is constantly updated and maintained by clinical information analysts, and data collection is validated regularly by external and internal control. Preoperative and perioperative variables are entered prospectively during the patient's in-hospital stay. Postoperatively, data are entered at the time of follow-up.

Primary end points were operative death and death during follow-up from any cause. Secondary end points were the incidence of major postoperative complications (myocardial infarction, stroke, new renal insufficiency requiring dialysis, need for tracheostomy) and a composite of major postoperative adverse events (MAEs), comprising operative death and the previously listed major postoperative complications.

Operative death was defined as death within 30 days of the operation or during the initial hospitalization. PND was defined as stroke, coma, or new focal neurologic deficit persisting more than 48 hours, accompanied by imaging confirming a new brain injury. Transient neurologic dysfunction (TND) was defined as delirium, encephalopathy, seizure, or a focal motor deficit lasting 72 hours or less, without evidence of new cerebral injury on imaging.

Data were stored using Access 2010 software (Microsoft Corp, Redmond, WA) and analyzed using IBM SPSS Statistics 22 software (IBM, Armonk, NY), R 3.2.0 software (R Foundation for Statistical Computing, Vienna, Austria), IBM SPSS Statistics–Essentials for R 22.0, cmprsk package, and MatchIt package. Data were compared using the χ^2 test for categoric variables and the Student *t* test for continuous variables. Multivariate and univariate analyses for MAEs and long-term survival were computed to assess for significant demographic and preoperative predictors of such events.

Propensity score matching was used to adjust for baseline differences and reduce confounding. Propensity scores were generated to be semisaturated. Selected variables were age, previous myocardial infarction, previous stroke, peripheral vascular disease, urgent/emergency status, previous cardiac operation, and aortic dissection. These covariates were used to compare the groups by logistic regression algorithm in 1-to-1 matching. Nearest neighbor matching algorithm without replacement and a caliper size of 0.05 was used. Propensity matching models were assessed using balance diagnostics and standardized differences and were confirmed by propensity score histograms with kernel density estimates.

The Kaplan-Meier method was used to assess postoperative survival. Censoring of patients occurred at the time of their last follow-up.

Results

Aortic arch reconstruction with DHCA/RCP was performed in 1,043 patients. Patient demographics are summarized in Table 1. The mean age was 65.7 ± 13.3 years. Most were hypertensive (95.1%), 374 (35.9%) had aortic dissection, and 151 (14.5%) had a previous stroke. CA times were 50 minutes or more (≥50 group) in 50 patients (4.8%) and were 49 minutes or less (≤49 group) in 993 (95.2%). The ≥50 group was more likely to have aortic dissection (60% vs 34.6%; $p < 0.001$), previous cardiac operation (46% vs 21.2%; $p < 0.001$), and previous cerebrovascular accident (CVA; 30% vs 13.7%; $p = 0.005$).

Intraoperative data are provided in Table 2. Mean CA time of the overall population was 25.8 ± 11.4 minutes, and RCP was administered during most of the CA period.