Moderate hypothermia during aortic arch surgery is associated with reduced risk of early mortality

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Objective: Selective antegrade cerebral perfusion (ACP) during hypothermic circulatory arrest (HCA) provides cerebral protection during aortic arch surgery. However, the ideal temperature for HCA during ACP remains unknown. Clinical outcomes were compared in patients who underwent moderate (nasopharyngeal temperature, ≥20°C) versus deep (nasopharyngeal temperature, <20°C) HCA with ACP during aortic arch repair.

Methods: By using a prospectively maintained clinical database, we analyzed data from 221 consecutive patients who underwent aortic arch replacement with HCA and ACP between December 2006 and May 2009. Seventy-eight patients underwent deep hypothermia (mean lowest temperature, 16.8°C ± 1.7°C) and 143 patients underwent moderate hypothermia (mean, 22.9°C ± 1.4°C) before systemic circulatory arrest was initiated. Multivariate stepwise logistic and linear regressions were performed to determine whether depth of hypothermia independently predicted postoperative outcomes and blood-product use.

Results: Compared with moderate hypothermia, deep hypothermia was associated independently with a greater risk of in-hospital death (7.7% vs 0.7%; odds ratio [OR], 9.3; 95% confidence interval [CI], 1.1-81.6; *P* = .005) and 30-day all-cause mortality (9.0% vs 2.1%; OR, 4.7; 95% CI, 1.2-18.6; *P* = .02), and with longer cardiopulmonary bypass time (154 ± 62 vs 140 ± 46 min; *P* = .008). Deep hypothermia also was associated with a higher incidence of stroke, although this association was not statistically significant (7.6% vs 2.8%; *P* = .073; OR, 4.3; 95% CI, 0.9-12.5). No difference was seen in acute kidney injury, blood product transfusion, or need for surgical re-exploration.

Conclusions: Moderate hypothermia with ACP is associated with lower in-hospital and 30-day mortality, shorter cardiopulmonary bypass time, and fewer neurologic sequelae than deep hypothermia in patients who undergo aortic arch surgery with ACP. (J Thorac Cardiovasc Surg 2013;146:662-7)

Hypothermic circulatory arrest (HCA) has been used for decades for cerebral protection during aortic arch surgery. HCA creates a motionless, bloodless field; minimizes the need for aortic clamping; and provides neuroprotection by reducing the cerebral metabolic rate, excitatory transmitter release, ion influx, and vascular permeability.[1] However, the ideal temperature for HCA remains unknown. Prolonged deep HCA (DHCA) has been associated with increased coagulopathy, inflammatory response, vascular endothelial dysfunction, apoptosis, and stroke risk.[2-4] Interestingly, studies have suggested that deep hypothermia alone without circulatory arrest also may be associated with increased inflammatory response and neurologic damage.[5-7]

With the advent of antegrade cerebral perfusion (ACP) during HCA to provide some measure of uninterrupted cerebral perfusion during aortic arch repair, the desired temperature level for HCA has become even more unclear. Indeed, moderate HCA (MHCA) (nasopharyngeal temperature, ≥20°C) still may afford cerebral protection while minimizing the side effects of DHCA (nasopharyngeal temperature, <20°C). To address this question, we compared clinical outcomes in patients who underwent MHCA versus DHCA with selective ACP during aortic arch repair.

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MATERIALS AND METHODS

Study Design

Institutional review board approval and informed patient consent were obtained for the prospective collection and subsequent analysis of clinical data. We identified 243 consecutive patients who underwent aortic arch repair between December 2006 and May 2009 at the Texas Heart Institute at St. Luke's Episcopal Hospital (Houston, Tex). Both HCA and selective ACP were used in all patients. Patients who received aprotinin intraoperatively (n = 22) were excluded from further analysis because of this drug's

Abbreviations and Acronyms

ACP	= antegrade cerebral perfusion
AKI	= acute kidney injury
AKIN	= Acute Kidney Injury Network
CI	= confidence interval
CPB	= cardiopulmonary bypass
DHCA	= deep hypothermic circulatory arrest
HCA	= hypothermic circulatory arrest
LOS	= length of stay
MHCA	= moderate hypothermic circulatory arrest
MI	= myocardial infarction
OR	= odds ratio

adverse effects on renal function and mortality risk.[8] The 221 remaining patients were divided into 2 groups: DHCA (lowest nasopharyngeal temperature, <20°C; n = 78) and MHCA (lowest nasopharyngeal temperature, ≥20°C; n = 143).

Data Collection

Patient demographics, perioperative risk factors, and the incidence of adverse clinical outcomes were abstracted from a prospectively maintained clinical database. Preoperative renal function was assessed by using the abbreviated Modification of Diet in Renal Disease study equation to calculate each patient's estimated glomerular filtration rate.[9] Patient temperature was defined as the lowest recorded intraoperative nasopharyngeal temperature, which generally coincided with HCA initiation. Measured adverse outcomes included in-hospital mortality, 30-day all-cause mortality, stroke, myocardial infarction (MI), acute kidney injury (AKI), and postoperative bleeding that necessitated reoperation. A diagnosis of MI was made if the records showed new Q waves (Minnesota code, 1-1-1 to 1-2-7), new persistent ST-segment or T-wave changes (Minnesota code, 4-1, 4-2, 5-1, 5-2, or 9-2), increased levels of the muscle-brain isoenzyme of creatine kinase, or evidence of acute MI on autopsy. Stroke was diagnosed if there was clinical evidence of it or if a new focal or global defect was observed on computed tomography, magnetic resonance imaging, or autopsy. Postoperative AKI was defined according to Risk, Injury, Failure, Loss, and End-stage kidney diseases criteria[10] and Acute Kidney Injury Network (AKIN) classification.[11] Survivors' hospital length of stay (LOS) was computed as the number of days between procedure and discharge, including any time patients spent at hospitals or long-term acute care facilities after transfer from our institution. The number of units of packed red blood cells, fresh-frozen plasma, pooled platelets, platelet apheresis, and cryoprecipitate administered within 48 hours of surgery was collected from blood bank records.

Surgical and Anesthetic Technique

All patients underwent aortic arch replacement to treat aortic arch aneurysm or dissection. Before general anesthesia was induced, 2-channel near-infrared spectroscopy (INVOS System; Somanetics, Troy, Mich) noninvasive probes were placed on the forehead, approximating the frontal lobes bilaterally. The near-infrared spectroscopy then was monitored throughout surgery. General anesthesia was performed in a standardized fashion with etomidate, midazolam, fentanyl, and isoflurane. Before incision, patients received either aminocaproic acid or tranexamic acid as an antifibrinolytic.

All surgeries involved the use of HCA with selective ACP. Ninety-four percent of patients had either axillary artery cannulation or direct innominate artery cannulation to establish cardiopulmonary bypass (CPB). This was the case in 95% of elective procedures and 91% of urgent or emergent procedures. After systemic heparinization (300 IU/kg), CPB and systemic cooling were initiated. For CPB, pH-stat principles of acid-base management were used. Repeated administration of cold cardioplegia solution and topical cooling were used for myocardial protection. During cooling, 100 mg lidocaine, 100 mg esmolol, 150 mg amiodarone, and 2 mg magnesium were administered routinely through the central line. In the DHCA group, cooling continued until electrocerebral silence was seen on multichannel electroencephalography (mean nasopharyngeal temperature, 16.8°C ± 1.7°C). Starting in January 2008, the target temperature for HCA was increased to 23°C; all patients treated after this change was made were included in the MHCA group.

In patients undergoing total aortic arch repair, the Y-graft technique (ie, arch replacement with bifurcated or trifurcated grafts) was used.[12] Briefly, 2 of the branches of the Y-graft were sutured to the left subclavian artery and the left common carotid artery during the cooling phase. Upon reaching the target temperature, 500 mg of thiopental was administered, the patient's head was packed in ice, and HCA was initiated with ACP (target flow, 10-20 mL/kg/min) via the right axillary artery (by clamping the innominate artery) and, sometimes, 1 or more branches of the Y-graft (Figure 1). The innominate artery then was divided and sewn to the distal end of the Y-graft. After the branch artery anastomoses were completed, the innominate artery clamp was removed and a clamp was placed on the proximal aspect of the Y-graft, restoring flow from the axillary artery to the attached brachiocephalic arteries. Graft replacement of the ascending aorta and transverse aortic arch then was performed.

After the distal aortic anastomosis was completed, CPB flow to the lower body was restarted through the axillary artery (in partial arch replacement cases) or a side branch of the arch graft (in total arch replacement cases). After the repair was completed, the patient was warmed to 36.5°C (avoiding blood-bath gradients of >10°C) and weaned from CPB. Perioperative blood products were transfused according to the attending physician's judgment, taking into account the patient's clinical status and available laboratory values.

Statistical Analysis

All statistical analyses were performed with SAS statistical software (version 9.1; SAS Institute, Cary, NC) in the Division of Biostatistics and Epidemiology at the Texas Heart Institute (Houston, Tex). Continuous variables were expressed as the mean ± standard deviation, and categoric (frequency) variables were expressed as percentages. Univariate logistic regression analyses initially were conducted to test for between-group differences in patient preoperative demographics, risk factors, and preoperative medications (Table 1). Categoric variables were analyzed with the χ^2 or Fisher exact tests. Continuous variables first were examined for normality of distribution: the *t* test was used for those variables with normal distributions, and the nonparametric Wilcoxon rank-sum test was applied for the variables with skewed distributions. In all tests, 2-tailed *P* values were calculated.

To control for demographic factors, medications, and perioperative risk factors, multivariate stepwise logistic regression was performed on all patient data to determine whether DHCA was associated independently with worse postoperative outcomes than MHCA. Linear regression was used to determine whether DHCA was associated independently with prolonged CPB time, LOS, and increased blood product use.

RESULTS

Patient demographics and perioperative risk factors are presented in Table 1. Patients in the MHCA group had a marginally higher preoperative prevalence of pulmonary disease ($P = .07$) and were more likely to undergo total arch repair ($P = .07$) than patients in the DHCA group. Of note, the groups did not significantly differ with respect to age, gender distribution, diabetes, history of smoking, renal insufficiency,