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Results of Proximal Arch Replacement Using Deep Hypothermia for Circulatory Arrest: Is Moderate Hypothermia Really Justifiable?

Brian Lima, M.D., **Judson B. Williams, M.D.**, **S. Dave Bhattacharya, M.D.**, **Asad A. Shah, M.D.**, **Nicholas Andersen, M.D.**, **Jeffrey G. Gaca, M.D.**, and **G. Chad Hughes, M.D.**
Division of Thoracic and Cardiovascular Surgery, Department of Surgery, Duke University Medical Center, Durham, NC 27710

Abstract

Objective—The use of selective cerebral perfusion with warmer temperatures during circulatory arrest has been increasingly utilized for arch replacement over concerns regarding the safety of deep hypothermic circulatory arrest (DHCA). However, little data actually exists on outcomes following arch replacement and DHCA. This study examines modern results with DHCA for proximal arch replacement to provide a benchmark for comparison against outcomes with lesser degrees of hypothermia.

Methods—Between 7/2005–6/2010, 245 proximal arch replacements (“hemi-arch”) were performed using deep hypothermia; mean minimum core and nasopharyngeal temperatures were 18.0±2.1°C and 14.1±1.6°C, respectively. Adjunctive cerebral perfusion was used in all cases. Concomitant ascending aortic replacement was performed in 41%, ascending plus aortic valve replacement in 23%, and aortic root replacement in 32%.

Results—Mean age was 58±14 years; 36% procedures were urgent/emergent. Mean duration of DHCA was 20.4±6.2 minutes. Thirty day/in-hospital mortality was 2.9%. Rates of stroke, renal failure, and respiratory failure were 4.1% (0.8% for elective cases), 1.2%, and 0.4%, respectively.

Conclusions—Deep hypothermia with adjunctive cerebral perfusion for circulatory arrest during proximal arch replacement affords excellent neurologic as well as non-neurologic outcomes. Centers utilizing lesser degrees of hypothermia for arch surgery, the safety of which remains unproven, should ensure comparable results.

Keywords

aortic surgery; hemi-arch; circulatory arrest; hypothermia; aortic arch

Introduction

Preventing cerebral injury and other end-organ dysfunction during aortic arch surgery remains a formidable challenge, which has led to the evolution of a number of circulatory management strategies over recent decades[1–17]. A unifying, central tenet of these various approaches is a perfusion algorithm encompassing some level of hypothermic circulatory arrest (HCA) to minimize cerebral metabolic consumption and simultaneously enable a bloodless operative field. Traditionally, HCA has been rendered in the setting of profound or deep hypothermia (DHCA), with core temperatures of ≤18°C. Further refinements in

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Address for correspondence: G. Chad Hughes, M.D., Box 3051 DUMC, Durham, NC 27710, Phone: (919) 668-0903, Fax: (919) 684-8563, gchad.hughes@duke.edu.

cerebral protection have included the advent of antegrade (ACP) and retrograde (RCP) cerebral perfusion adjuncts to attenuate cerebral injury during extended periods of HCA (beyond 30–45 minutes) often requisite in complex aortic arch operations [5, 9, 16].

Despite the modest diminution in adverse outcomes in more recent DHCA series, many investigators remain concerned over the potentially deleterious consequences of deep hypothermia[6, 7, 10, 18, 19]. Among these concerns is a heightened risk of postoperative bleeding secondary to the coagulopathy precipitated not only by the deep hypothermia itself, but also by the prolonged periods of cardiopulmonary bypass necessary for cooling and rewarming. Some evidence also suggests deep hypothermia may cause direct neuronal injury and lead to subtle neurocognitive deficits that may persist long-term[20–22].

Citing these theoretical and empirically based concerns as justification, an increasing number of aortic surgeons are utilizing warmer temperatures during HCA (25–28°C), in conjunction with selective cerebral perfusion. This paradigm shift, however, has been predicated largely on adverse outcome data derived from outmoded DHCA series. Contemporary outcomes of aortic arch replacement with DHCA remain sparsely reported in the literature. As such, the objective of the current study was to analyze modern results with DHCA for proximal arch replacement to establish a point of reference for comparison of outcomes with moderate hypothermia.

Patients and Methods

Between July 2005 and June 2010, N=245 proximal arch replacement (“hemi-arch”) procedures (Figure 1) were performed at a single referral institution. Indications for hemi-arch replacement were as previously described[23]. Preoperative, intraoperative, and postoperative variables were abstracted from the Duke Thoracic Aortic Surgery Database, a prospectively maintained clinical registry of all patients who have undergone a thoracic aortic procedure at Duke University Medical Center (Durham, NC) since July, 2005. This study was reviewed and approved by the Institutional Review Board of Duke University and the need for individual patient consent was waived.

All cases were performed via median sternotomy with intraoperative transesophageal echocardiographic (TEE) and invasive hemodynamic monitoring. Solumedrol (1gm, IV) was administered for pharmacologic neuroprotection to all patients preoperatively. Cardiopulmonary bypass with deep systemic hypothermia was utilized for all hemi-arch repairs, with the duration of cooling guided by neurocerebral monitoring with intraoperative electroencephalography (EEG) as previously described[24] for all elective cases and when available for urgent/emergent cases for a total of n=201 cases (82%) monitored. In the unmonitored cases, patients were cooled for a minimum of 50 minutes or until the nasopharyngeal temperature was below 18 °C based on prior work by Stecker et al[25]. Mean minimum core and nasopharyngeal temperatures were 18.0 ± 2.1 °C and 14.1 ± 1.6 °C, respectively.

Upon completion of profound cooling and electrocerebral inactivity (ECI) by EEG, the circulation was halted, and the aortic arch was opened. Intraoperative assessment of aortic arch diameter was used to confirm preoperative imaging feasibility of proximal versus total arch replacement. Specifically, tapering of arch diameter to a normal caliber proximal to the left subclavian artery enabled hemi-arch replacement. This procedure was performed using the “peninsula” technique as described by Miller’s group at Stanford University[26]. Patients in whom the aortic arch remained dilated (≥ 40 mm) beyond the left subclavian artery required total arch replacement and are not included in this series.

Adjunctive ACP (n=218, 89%) or RCP (n=27, 11%) was used for cerebral protection in all circulatory arrest cases. ACP was the preferred adjunctive strategy with RCP being utilized in cases where the right axillary artery was not suitable for cannulation, generally because of a diameter <6 mm or dissection of the artery on preoperative computed tomography angiography (CTA). Dissection of the more proximal innominate artery was not a contraindication to right axillary cannulation. For ACP cases, the right axillary artery was cannulated using an 8 mm Dacron side graft technique. For RCP cases, the distal ascending aorta or, in cases of dissection involving the right axillary artery, the left axillary or femoral artery were chosen for arterial cannulation. If the distal ascending aorta or femoral artery were utilized, cannulation was switched to the hemi-arch graft after completion of this anastomosis. Perfusion data are summarized in Table 1.

For performance of ACP, the base of the innominate and left common carotid arteries was clamped and perfusion was via the right axillary graft at a target flow rate of 5–15 cc/kg/min and an inflow temperature of 12°C to a target right radial arterial line pressure of 50–70 mm Hg. For RCP, flow (12°C) was retrograde via a long angled #26-French single stage venous cannula in the superior vena cava (SVC) with the SVC snared. RCP flows averaged 150–450 cc/min to a target central venous pressure of 25 mm Hg. Following completion of the hemi-arch anastomosis, CPB was reinstituted, and the patient re-warmed following a 5-minute period of cold reperfusion for free radical washout. During the rewarming phase other concomitant cardiac procedures were completed (Table 2).

Antifibrinolytic therapy was routinely administered intraoperatively; prior to withdrawal from the U.S. market, aprotinin (Bayer Corporation, West Haven, CT) was used (2MU bolus and 0.5Mu/hr infusion until bleeding cessation). Subsequently, epsilon aminocaproic acid was administered as a 10g bolus followed by a 1g/hr infusion with an additional 5g bolus prior to separation from cardiopulmonary bypass. The return of washed, shed red blood cells (BRAT II cell saver, Cobe, Arvada, CO) to the patient was routine. Transfusion decisions in the perioperative period were aided by local guidelines and use of chest tube output, activated clotting time, platelet count, fibrinogen level, thromboelastogram, prothrombin, and partial thromboplastin time tests as recommended by the American Society of Anesthesiologists published guidelines[27]. Clopidogrel or other P2Y12 inhibitors, regardless of dose, were held 7 days prior to operation. Aspirin 325mg (but not 81mg) was held 5 days prior to operation. All antiplatelet agents were restarted at preoperative dose on postoperative day 1 unless active bleeding was noted.

Adverse perioperative events were prospectively documented and analyzed according to previously published guidelines for reporting morbidity and mortality after cardiac valvular operations[28]. All patients were re-examined with either gated MRA or CTA with transthoracic echocardiography at serial follow-up visits, 6–9 months post-surgery and then annually thereafter. The present report includes all data collected through the patients' most recent follow-up visit. Deaths from all causes were included in the analysis. In addition, the social security death index was queried (http://ssdi.rootsweb.com/) to confirm all patient deaths.

Patient characteristics were reported as percentages for discrete variables. Means and standard deviations were provided for continuous variables. For comparisons, the Wilcoxon Rank Sum test was used for continuous variables, and the Chi-squared test for categorical variables, with an alternative hypothesis that the rates between groups were not different. All statistical analyses were computed using SAS version 9.1.3.

Results

A summary of pertinent preoperative patient variables is provided in Table 3. Mean patient age was 58 with a range of 19 to 87. Most of the patients were male (71%) and 37% presented with symptoms attributable to aortic pathology, including back pain, anterior chest pain, malperfusion, and syncope. A number of patients presented with acute aortic syndromes necessitating urgent/emergent operation (36%) including acute type A dissection (22%), aortic rupture (7%), and cardiac tamponade (2%). A sizeable proportion of patients (16%) had undergone previous cardiac operation via sternotomy. The maximal aortic diameter ranged from 4.5 cm to 9.5 cm with a mean of 5.6±0.9 cm.

Procedures performed varied according to the extent of thoracic aortic and cardiac pathology and are summarized in Table 2. In addition to hemi-arch replacement, the majority of patients (>60%) required ascending aortic replacement either alone (45%) or in conjunction with aortic valve replacement (Wheat procedure, 23%). A significant proportion of patients also presented with disease of the aortic root meeting criteria for surgical repair (N=78, 32%). Aortic root replacement with performed with mechanical (N=30, 12%) or stented bovine pericardial (N=15, 6%) composite prostheses, commercially available stentless porcine full aortic roots (N=33, 13%), or with a valve-sparing David approach (N=15, 6%). Other concomitant cardiac procedures included coronary artery bypass grafting (N=52, 21%), Maze procedure for atrial fibrillation (N=6, 2%), atrial septal defect repair (N=6, 2%), aortic valve repair (N=9, 4%), mitral valve procedures (N=4, 2%), as well as other procedures (N=17, 7%).

Following hemi-arch replacement, the median postoperative length of stay was six days (Table 4). 30-day/in-hospital mortality was 2.9% (3.2% and 2.2% for elective and urgent/emergency cases, respectively); 365-day mortality was 3.3%. The overall rate of postoperative stroke was 4.1%; among elective cases (N=156), only one stroke occurred (0.8%). Seven patients (2.9%) required operative re-exploration for hemorrhage. Only one patient (0.4%) suffered postoperative respiratory failure necessitating tracheostomy. Renal failure requiring hemodialysis occurred in three patients (1.2%). During the median follow-up period of 21 months, 2 deaths occurred beyond hospitalization, yielding an actuarial survival rate of 99%.

Discussion

Central to the debate over the temperature nadir of HCA is the contention that deep hypothermia potentiates bleeding risk, is directly injurious to the brain and other organ systems, and therefore poses significant perioperative morbidity and mortality. The results from the present study would appear to refute these notions, however. With a rate of postoperative hemorrhage requiring re-exploration of only 2.9%, the reputed bleeding hazard imparted by DHCA may be overstated. The validity of this assertion is substantiated by a recent report by Kamiya and colleagues of HCA cases performed at moderate temperatures, where the rate of re-sternotomy was more than four times greater (14.1%)[7] than the current series. This comparison is not entirely fair, however, as total arch replacements accounted for 25% of cases in the moderate hypothermia series, whereas only proximal arch replacements are included in this current analysis. Regardless, even with propensity matching, the study by Kamiya failed to demonstrate any discernible difference in bleeding or duration of cardiopulmonary bypass in moderate versus deep HCA cases[7]. These findings underscore the fact that other factors beside profound hypothermia, such as emergency surgery or preoperative hemoglobin, figure more prominently as predictors of hemorrhage following HCA[29].

Considering the high acuity (36% non-elective) and procedural complexity of the patients in the present series, the operative mortality was quite low (2.9%) and compares very favorably with other large published series of DHCA for aortic arch replacement[4, 8, 9, 15, 16, 30–32]. More specifically, in a review of 20 published series including over 2000 patients and spanning the time period 1989–2007, Elefteriades calculated an overall operative mortality of 9.6% following aortic arch surgery with DHCA[17]. Unpublished work from the authors' institution evaluating outcomes for ascending/arch replacement in North America (N = 45,894) using the Society of Thoracic Surgeons Adult Cardiac Surgery Database (STS ACSD) demonstrate an overall operative mortality of 8.9%, including 3.4% and 15.4% for elective and non-elective cases, respectively. Finally, the 15–30% operative mortality reported by studies from the International Registry for Acute Aortic Dissection (IRAD) for acute Type A dissection repair was nearly 5–10 times that observed in the present study[33, 34].

Relative to that reported in recent series of moderate hypothermia[5, 7, 18, 19], the significantly reduced operative mortality and morbidity presented here further supports the safety and efficacy of DHCA approaches. For example, in a retrospective comparison of moderate HCA with selective ACP (N=205) versus DHCA alone (N=66) at Emory University, the operative mortality in the moderate HCA group was 8.8% (and 22.7% in the DHCA alone group)[5], which is significantly higher than the 2.9% reported herein. Further, the results of the Emory study, if taken at face value, are misleading given that a significantly greater proportion of the DHCA patients were emergencies (61% versus 32% in the moderate hypothermia group). In addition, no adjunctive cerebral perfusion was utilized in the DHCA group, an adjunct we deem to be a key facet of an optimal neuroprotective strategy. In one of the largest series ever published of aortic arch reconstruction with DHCA and RCP (N=682) and moderate HCA with ACP (N=94), Bavaria's group from the University of Pennsylvania reported uniformly excellent outcomes with operative mortalities of 2.8% and 3.2%, respectively[12]. An important caveat to consider when comparing the Penn results to those of the current study, however, is that all of the cases in the Penn series were elective. Last year, the Emory group published an update on their outcomes with moderate hypothermia and unilateral selective ACP in N=412 patients[19]. The operative mortality in that study, which included a very similar patient cohort to that in the present report, was 7.7% with a 4.6% incidence of renal failure requiring dialysis and a postoperative length of stay averaging 10 days.

The relatively high rate of postoperative renal failure in this latter study raises important concerns about the susceptibility to visceral ischemia and other end-organ dysfunction implicit in HCA performed with warmer temperatures. This effect becomes especially pronounced during more complex cases when aortic arch reconstruction times extend beyond thirty minutes[12]. Therefore, profound hypothermia may be an indispensable modality during such aortic cases where the anticipated duration of HCA may be prolonged, and preservation of end-organ viability beyond the brain is at a premium. As demonstrated by the current results, proximal arch replacement under deep hypothermia can minimize ischemic insult to the periphery with resultant low rates of renal (1.2%) and respiratory failure (0.4%), along with 0% rate of paraplegia. To date, published data[5, 7, 12, 19] do not support moderate hypothermia approaches utilizing selective ACP as providing an equal degree of protection to non-brain organs. On the contrary, in vivo studies in large animal models of moderate HCA have revealed that the spinal cord may be particularly susceptible to ischemic injury under such conditions with an alarmingly high incidence of irreversible paraplegia at 60 minutes[35]. The enhanced cytoprotective effects ascribed to deep versus moderate HCA may, at the molecular level, entail upregulation of the small-ubiquitin-like modifier (SUMO) conjugation pathway[36]. Further delineation of these molecular mechanisms are hopefully forthcoming, but these and other data already available provide a compelling argument for deep hypothermia as the preferred perfusion strategy for HCA.

Formal assessment for subtle neurocognitive deficits following DHCA was not performed in this study. Notwithstanding, the rates of permanent neurologic dysfunction such as stroke were relatively low and virtually nonexistent among electively performed cases (0.8%). In the previously mentioned large series of electively performed arch procedures reported by Milewski[12] and colleagues from the University of Pennsylvania, the rate of permanent neurologic dysfunction was approximately 3% for both DHCA and moderate HCA approaches. Proponents of moderate hypothermia have cited a higher incidence of postoperative delirium in procedures utilizing DHCA[18], along with other more subtle indices of neurocognitive impairment[20–22]. An in-depth psychometric analysis of DHCA patients recently performed at Yale discounts these claims, however, documenting complete preservation of cognitive capacity, even among high-cognitive patients[37].

Study Limitations

The authors acknowledge that even slight neurocognitive deficits following any cardiac operation have important prognostic implications[38]. Consequently, one criticism of the current study is the lack of comprehensive neurocognitive evaluation both in the perioperative period and in long-term follow-up. Future studies will therefore need to incorporate such formal evaluations. Moreover, the current study was retrospective in design and did not include a comparison group, such as a patient cohort in whom moderate HCA was utilized. Prospective, randomized studies directly comparing deep and moderate HCA, in conjunction with selective cerebral perfusion techniques, would undoubtedly provide valuable and accurate insight into which circulatory management strategy maximizes neuroprotective effects while preserving peripheral organ function.

Conclusions

In summary, the use of deep hypothermia with adjunctive cerebral perfusion for circulatory arrest during proximal arch replacement affords excellent neurologic as well as non-neurologic outcomes. Centers utilizing lesser degrees of hypothermia for arch surgery, the safety of which remains unproven, should ensure comparable results.

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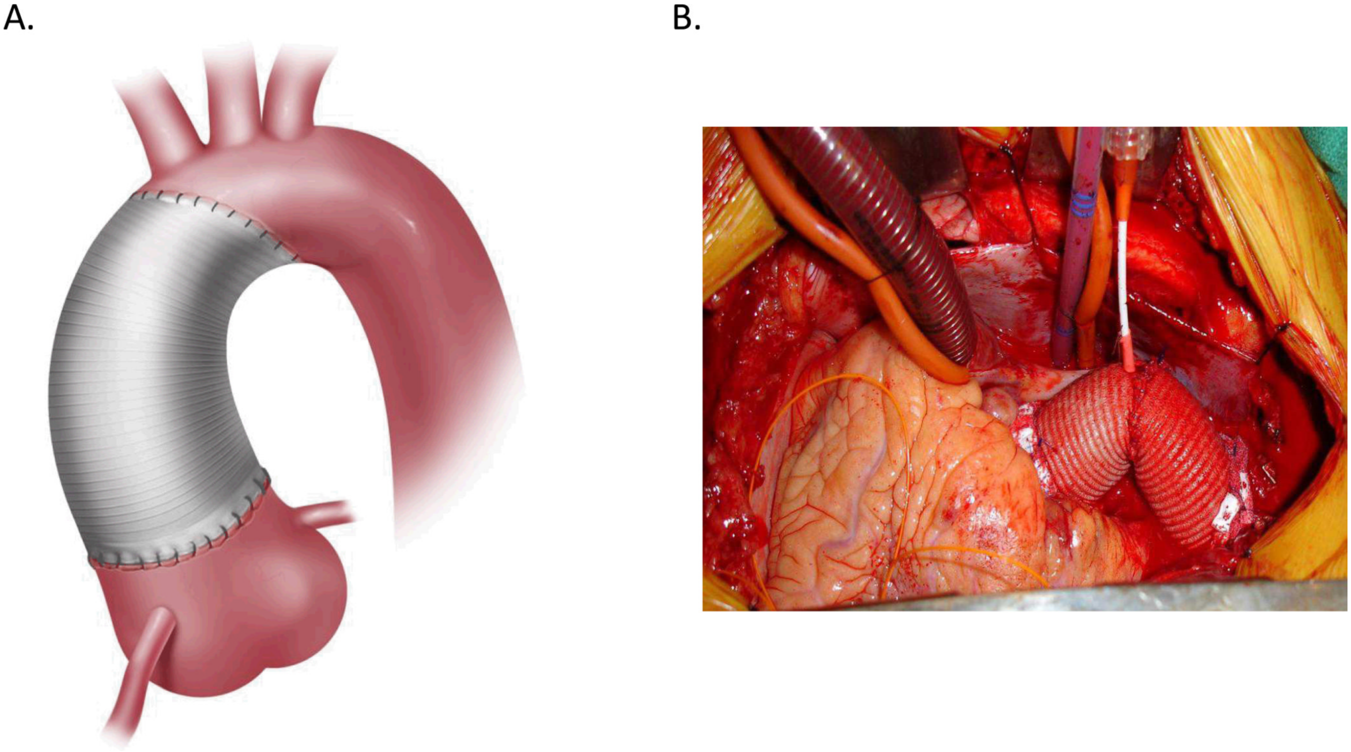

Figure1.

(A) Schematic illustration and (B) intraoperative photograph depicting ascending and hemi-arch aortic reconstruction.

Table 1

Perfusion Data

	No. of Patients (%) N=245
Cardiopulmonary Bypass Time, min (Mean±SD)	212±50
Aortic Cross-Clamp Time, min (Mean±SD)	143±43
DHCA Time, min (Mean±SD)	20.4±6.2
Antegrade Cerebral Perfusion	218 (89)
- Duration, min (Mean±SD)	16.3±6.3
Retrograde Cerebral Perfusion	27 (11)
- Duration, min (Mean±SD)	18.1±5.1

DHCA, deep hypothermic circulatory arrest.

Table 2

Operative Details on N=245 Hemi-Arch Replacements

	No. of Patients (%)
Ascending Aortic (AA) Replacement	110 (45)
Wheat Procedure (AA + AVR)	57 (23)
Aortic Root Replacement	78 (32)
- Mechanical Composite	25 (10)
- Pericardial Composite	10 (4)
- Stentless Bioprosthetic	28 (11)
- David Procedure (Valve-Sparing)	15 (6)
Concomitant Cardiac Procedures	
- CABG	52 (21)
- Maze Procedure	6 (2)
- ASD Repair	6 (2)
- Aortic Valve Repair	9 (4)
- Mitral Valve Repair/Replacement	4 (2)
- Other	17 (7)

AA, ascending aortic; AVR, aortic valve replacement

Table 3

Preoperative Patient Characteristics

	No. of Patients (%) N=245
Age, y (mean+SD)	58±14
- Range	19–87
Females	70 (29)
Presenting Aortic Symptoms	91 (37)
- Back Pain	18 (7)
- Anterior Chest Pain	73 (30)
- Malperfusion	6 (2)
- Syncope	9 (4)
Maximal Aortic Diameter, cm (Mean±SD)	5.6±0.9
- Range	4.5–9.5
Urgent/Emergency Operation	89 (36)
- Acute Type A Dissection	54 (22)
- Aortic Rupture	16 (7)
- Cardiac Tamponade	4 (2)
Redo Sternotomy	39 (16)

Table 4

Postoperative Outcomes

	No. (%) **N=245**
Hospital Length of Stay, days (Median)	6
- 25th, 75th percentile	5, 8
30-Day Mortality	7 (2.9)
30-Day Morbidity	
- Stroke	10 (4.1)
- Elective Cases (N=156)	1 (0.8)
- Re-Exploration for Bleeding	7 (2.9)
- Renal Failure Requiring Dialysis	3 (1.2)
- Respiratory Failure	1 (0.4)