Total arch replacement using moderate hypothermic circulatory arrest and unilateral selective antegrade cerebral perfusion

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Objective: To examine the clinical outcomes and impact of using moderate hypothermic circulatory arrest (MHCA) and unilateral selective antegrade cerebral perfusion (uSACP) in the setting of total aortic arch replacement (TOTAL).

Methods: From 2004 to 2012, 733 patients underwent open arch reconstruction with MHCA and SACP. Of these, 145 (20%) underwent TOTAL. Measured outcomes included death, stroke, temporary neurologic dysfunction (TND), and renal failure. Mean follow-up time was 33 months and ranged from 0 to 95 months.

Results: Core temperature at the onset of MHCA was 25.8°C. Cardiopulmonary bypass and myocardial ischemic times were 236 minutes and 181 minutes, respectively. Twenty-three patients (16%) underwent emergency repair of acute type A dissection. Fifty-four cases (37%) were reoperative and 52 (34%) were stage I elephant trunk procedures. Concomitant root replacement was performed in 50 (35%) patients, including 20 David V valve-sparing procedures. Mean duration of circulatory arrest was 55 minutes. Operative mortality was 9.7%. Overall incidence of stroke and TND was 2.8% and 5.6%, respectively. Four patients (2.8%) required postoperative dialysis. Seven-year survival was significantly reduced ($P = .04$) after repair of type A dissection (83.8%) compared with elective surgery (89.5%). Higher temperature during TOTAL was not found to be a significant risk factor for adverse events.

Conclusions: TOTAL using MHCA and uSACP can be accomplished with excellent early and late results. MHCA was not associated with adverse neurologic outcomes or higher operative risk, despite prolonged periods of circulatory arrest. (J Thorac Cardiovasc Surg 2014;147:1488-92)

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Griepp and colleagues'[1] original series of successful total arch replacements used deep hypothermic circulatory arrest (DHCA) alone for cerebral protection. Since that landmark publication, advances in surgical technique and methods of cerebral protection have improved outcomes after surgical therapy for diseases of the aortic arch. Contemporary methods of cerebral protection during aortic arch surgery include moderate (core temperature >22°C) rather than profound hypothermia and the addition of continuous cerebral perfusion (antegrade or retrograde) during the period of circulatory arrest.[2-6] The debate regarding the optimal method of cerebral protection for aortic arch surgery remains unsettled. However, there seems to be a current consensus that for the prolonged periods of circulatory arrest required for total arch replacement, antegrade cerebral perfusion is warranted.[7,8]

In 2004, a protocol of moderate hypothermic circulatory arrest (MHCA) with unilateral selective antegrade cerebral perfusion (uSACP) via right axillary artery cannulation was instituted at Emory for all cases involving arch replacement. This technique has produced acceptable outcomes with low rates of adverse neurologic events in both elective and emergency cases.[2,9] Our previous publications have focused primarily on the safety of the technique with hemiarch reconstruction alone. Total arch replacement with individual reimplantation of the great vessels (TOTAL) is a more complex and challenging procedure, which requires a prolonged period of circulatory arrest. This report examines the safety of MHCA/uSACP in both elective and emergency TOTAL.

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METHODS

This study was conducted with the approval of the Institutional Review Board at Emory University in compliance with Health Insurance Portability and Accountability Act regulations and the Declaration of Helsinki. The Institutional Review Board waived the need for individual patient consent. A review of the Emory Aortic Surgery Database from 2004 to 2012 identified 733 patients who underwent open arch reconstruction with MHCA and uSACP via right axillary artery cannulation; 145 (20%) of these patients underwent TOTAL and are the subject of this report. Twenty-three TOTAL patients (16%) underwent complete arch replacement during emergency repair of an acute type A aortic dissection. The remaining 122 patients underwent elective TOTAL.

Abbreviations and Acronyms

CABG = coronary artery bypass grafting
CI = confidence intervals
DHCA = deep hypothermic circulatory arrest
MHCA = moderate hypothermic circulatory arrest
PND = permanent neurologic dysfunction
TND = temporary neurologic dysfunction
uSACP = unilateral selective antegrade cerebral perfusion
TOTAL = total aortic arch replacement

Surgical Technique

The technical details of our operative technique have been published previously.[2] Core body temperature was measured via a temperature probe connected to a Foley catheter. Transcutaneous bilateral cerebral oximetry (INVOS 3100-SD, Troy, Mich) and continuous electroencephalogram monitoring were routinely performed. Intraoperative transesophageal echocardiography was used in all patients.

All procedures began with an 8-mm Gelweave (Vascutek Terumo, Inchinnan, United Kingdom) graft sewn end to side to the right axillary artery. After median sternotomy, the right atrium was cannulated and the patient was placed on cardiopulmonary bypass. Systemic cooling was initiated and a left ventricular vent was placed via the right superior pulmonary vein. The goal core body temperature at the initiation of circulatory arrest was determined by multiple factors including age, renal function, and complexity of the planned total arch reconstruction. Once the goal temperature was reached, the innominate artery was occluded at the initiation of the lower body circulatory arrest period. Unilateral selective antegrade cerebral perfusion was initiated at 16°C-18°C at 10 mL/kg/min. Flow was adjusted to maintain a cerebral perfusion pressure of 60-70 mm Hg, which was measured off a side port from the axillary cannula.

After initiation of the circulatory arrest period, resection of all aortic arch pathology was performed. Indications for TOTAL in the emergency setting were complete destruction of the arch tissue from the dissection process or aneurysmal arch disease more than 5.0 cm. The innominate, left carotid, and left subclavian arteries were all clamped and then separated off the arch as individual vessels. Total arch replacement was defined as separate reimplantation of all supraaortic vessels and was performed using a 4-branch modified arch Gelweave graft. Once the distal aortic and left subclavian anastomoses were complete, a perfusion limb of the graft was cannulated with a separate 22-Fr elongated arterial cannula (Medtronic, Inc, Minneapolis, Minn) to restore full cardiopulmonary bypass and end the circulatory arrest period to the lower body. On completion of the circulatory arrest period, vigorous deairing maneuvers were performed before reinstitution of full flow cardiopulmonary bypass and rewarming was initiated. The left common carotid branch anastomosis was performed next, followed by all proximal aortic procedures (root, valve, coronary, and so forth). Once the neo-sinotubular junction anastomosis was complete, the crossclamp was removed. The innominate artery anastomosis was performed after the crossclamp was removed during the period of cardiac reperfusion.

Statistical Analysis

All patients undergoing total arch reconstruction were subdivided into 2 groups by their elective or emergency status. Variable distributions were compared across groups using 2-sample *t* tests for numerical variables and χ^2 tests for categorical variables. Kaplan-Meier product-limit estimation, in conjunction with Social Security Death Index dates, was used to calculate long-term survival in these patients. Kaplan-Meier curves were generated to compare the survival of elective versus emergency patients. Survival was compared using log-rank tests.

Multivariable logistic regression analysis was used to estimate the effect of temperature and circulatory arrest time of clinical end points: death, permanent neurologic dysfunction (PND), temporary neurologic dysfunction (TND), new renal failure, and prolonged mechanical ventilation (>48 hours). Adjustments were made for several preoperative variables: age, renal failure, redo surgery, diabetes, and chronic lung disease. Adjusted odds ratios and 95% confidence intervals (CI) were estimated. All analyses were performed using SAS version 9.3 (SAS Institute, Inc, Cary, NC). All tests were evaluated at the 0.05 alpha level.

RESULTS

Preoperative demographics for elective and emergency TOTAL patients are listed in Table 1. The mean age of all patients was 59 ± 14 years. The 2 groups were equivalent with regard to gender, stroke, diabetes, hypertension, chronic obstructive pulmonary disease, and renal failure. Elective patients had a significantly higher incidence of previous myocardial infarction ($P < .05$). Both groups had normal ventricular function (ejection fraction >55%). A higher percentage of elective patients underwent TOTAL in the setting of reoperative cardioaortic surgery (elective 43% vs emergency 4.4%, $P < .01$).

The temperature at the initiation of MHCA for the entire cohort was 25.8°C ± 2.7°C, and was slightly warmer in the emergency group (elective 25.6°C ± 2.7°C vs emergency 27.2°C ± 2.4°C; $P < .01$). Cardiopulmonary bypass and crossclamp times were 237 ± 71 minutes and 182 ± 63 minutes, respectively, and did not differ between elective and emergency cases. The mean duration of circulatory arrest was longer in the emergency group (elective 53 ± 16 minutes vs emergency 61 ± 19 minutes; $P = .06$). There was no difference in the incidence of concomitant root replacement or coronary artery bypass procedures between the groups (Table 2). Bilateral cerebral oximetry data were available for analysis for 101 (70%) patients. After 5 minutes of circulatory arrest, the right and left cerebral oximetry had changed by +1.7% and −5.9% from baseline, respectively. After 15 minutes of circulatory arrest, the right and left cerebral oximetry had changed by +6.1% and −1.2% from baseline, respectively.

Operative mortality for the entire series was 9.7% (elective 10.7% vs emergency 4.3%; $P = .34$). The causes of death included multisystem organ failure (n = 6), right ventricular failure (n = 3), intractable hemorrhage (n = 2), ruptured abdominal aortic aneurysm (n = 1), hypoxic brain injury (n = 1), and colonic perforation (n = 1). The overall incidence of PND and TND was 2.8% and 5.6%. PND occurred more commonly in emergency patients and TND was more frequent in elective patients. The overall incidence of dialysis-dependent renal failure was 2.8% and there was no difference between

TABLE 1. Preoperative demographics: total arch

Risk factor	Elective (n = 122)	Emergency (n = 23)	P value
Age, y ± SD	58.5 ± 13.4	58.4 ± 15.7	.99
BMI, kg/m^2 ± SD	27.9 ± 6.9	29.3 ± 5.2	.51
Male gender, n (%)	78 (63.9)	15 (65.2)	.91
History of CVA, n (%)	15 (12.3)	1 (4.4)	.26
Diabetes mellitus, n (%)	16 (13.1)	1 (4.4)	.23
Hypertension, n (%)	100 (82.0)	21 (91.3)	.27
Renal failure, n (%)	4 (3.3)	2 (8.7)	.23
Myocardial infarction, n (%)	23 (18.9)	0 (0.0)	.023
COPD, n (%)	38 (31.2)	4 (17.4)	.18
Redo, n (%)	53 (43.4)	1 (4.4)	<.001
Previous CABG, n (%)	9 (7.4)	0 (0.0)	.18
Previous valve surgery, n (%)	31 (25.4)	1 (4.4)	.026
Previous proximal aortic surgery, n (%)	22 (18.0)	1 (4.4)	.10
Mean ejection fraction, % ± SD	56.7 ± 7.6	58.7 ± 9.1	.34
Mean aneurysm size, mm ± SD	6.3 ± 1.5	5.7 ± 1.1	.17

SD, Standard deviation; *BMI*, body mass index; *CVA*, cerebrovascular accident; *COPD*, chronic obstructive pulmonary disease; *CABG*, coronary artery bypass grafting.

preoperative and postoperative creatinine levels (1.20 mg/dL vs 1.23 mg/dL, respectively; $P = .45$). There were no cases of postoperative paraplegia.

An adjusted multivariate analysis was conducted to determine whether the temperature at the initiation of circulatory arrest or the duration of the circulatory arrest period contributed to adverse outcomes. Table 3 demonstrates that temperature did not represent an adverse risk factor for mortality, PND, TND, dialysis-dependent renal failure, or prolonged ventilation for more than 48 hours. Table 4 demonstrates that the duration of the circulatory arrest period was not an adverse risk factor for operative death, PND, TND, renal failure requiring dialysis, or prolonged ventilation (Table 4).

DISCUSSION

Complete replacement of the transverse arch is a complex procedure that requires expert surgical technique and sophisticated knowledge of circulation management and cerebral protection strategies. These operations necessitate prolonged periods of circulatory arrest to adequately

TABLE 3. Multivariable covariates for the effect on temperature on adverse outcomes: total arch (elective + emergency)

Outcome	Temperature adjusted odds ratio (95% CI)	P value
Mortality	0.81 (0.65-1.00)	.05
PND	0.90 (0.62-1.30)	.57
TND	0.91 (0.70-1.19)	.50
Renal failure dialysis	0.81 (0.55-1.18)	.27
Mechanical ventilation >48 h	0.87 (0.74-1.03)	.10

CI, Confidence interval; *PND*, permanent neurologic dysfunction; *TND*, temporary neurologic dysfunction.

reconstruct the aortic arch and great vessels in a hemostatic fashion. Total arch replacement was originally described with the use of DHCA alone and island reimplantation of the great vessels.[1] This technique ushered in the modern era of aortic arch surgery. Contemporary series describe total arch replacement with low morbidity and mortality performed with a myriad of different cerebral protection and surgical techniques.[2,3,5,10-12] In this report, we analyze the outcomes of elective and emergency TOTAL using a technique of MHCA with unilateral selective antegrade cerebral perfusion via right axillary artery cannulation.

Evaluation of outcomes after aortic arch surgery typically focuses on 2 main parameters: mortality and neurologic injury. Adverse neurologic outcomes are defined as permanent (PND) or temporary (TND) neurologic dysfunction. It is well agreed that PND is related to embolic phenomena related to the site of arterial cannulation, and TND is related to the adequacy and type of cerebral protection during the period of circulatory arrest.[6,13-16]

The incidence of PND in the current report was 2.8%, with 3 of the 4 strokes occurring in emergency type A repairs. This rate compares favorably with other large published series focusing solely on patients undergoing total arch replacement in which the reported PND rate ranged from 3.3% to 4%.[10-12] The low stroke rate in the present series is likely multifactorial in origin.

At Emory, arterial cannulation for emergency or elective aortic arch surgery is via an 8-mm Dacron graft sewn to the right axillary artery. Axillary artery cannulation results in lower embolic stroke rates compared with alternative sites

TABLE 2. Operative characteristics: total arch

Variable	Elective (n = 122)	Emergency (n = 23)	P value
Mean HCA temperature, °C ± SD	25.6 ± 2.7	27.2 ± 2.4	.006
Mean CA time, min ± SD	53.4 ± 15.6	60.5 ± 18.7	.06
Mean crossclamp time, min ± SD	181 ± 60	182 ± 81	.97
Mean CPB time, min ± SD	234 ± 64	245 ± 99	.61
Aortic root replacement, n (%)	45 (36.9)	5 (21.7)	.16
CABG, n (%)	22 (18.0)	2 (8.7)	.27

SD, Standard deviation; *HCA*, hypothermic circulatory arrest; *CA*, circulatory arrest; *CABG*, coronary artery bypass grafting; *CPB*, cardiopulmonary bypass.

TABLE 4. Multivariable covariates for the effect on duration of circulatory arrest on adverse outcomes: total arch (elective + emergency)

Outcome	Adjusted odds ratio (95% CI)	P value
Mortality	1.016 (0.979-1.055)	.39
PND	1.042 (0.978-1.110)	.21
TND	1.018 (0.975-1.062)	.43
Renal failure dialysis	1.01 (0.948-1.076)	.75
Mechanical ventilation >48 h	1.027 (0.998-1.056)	.07

CI, Confidence interval; *PND*, permanent neurologic dysfunction; *TND*, temporary neurologic dysfunction.

of cannulation and enables easy conversion to unilateral selective antegrade cerebral perfusion with occlusion of the innominate artery at the initiation of circulatory arrest.[16] Arterial inflow via the right axillary artery results in high-velocity retrograde blood flow entering the aortic arch from the orifice of the innominate artery, which may protect against embolic phenomena from the proximal aorta at the time of aortic manipulation or crossclamping.

Great care is also taken during the operation to minimize manipulation of the great vessels until the period of circulatory arrest. After initiation of circulatory arrest, individual clamps are applied to the innominate, left common carotid, and left subclavian arteries. In this manner, embolic events to both the right and left carotid systems as well as the posterior circulation via the left subclavian artery are minimized. Aortic crossclamping is only performed if minimal disease is demonstrated on epiaortic ultrasonography, performed at the beginning of the procedure before initiating cardiopulmonary bypass.

A third important technical factor contributing to the low stroke rate is the technique of individual reimplantation of the great vessels, as opposed to an en bloc or island reimplantation. Atherosclerotic plaques typically develop at the ostia of the branches of the arterial tree. These plaques become a source of embolic stroke with great vessel manipulation. After the individual great vessels are clamped, all the aortic tissue around the ostia are excised. In this way, most of the plaque burden and the greatest risk factor for embolic stroke are eliminated. The great vessels are subsequently anastomosed individually to a multibranched arch graft. Although this may be more tedious and time consuming compared with the island reimplantation technique, it reduces the time of MHCA because only the distal aortic anastomosis is performed under circulatory arrest. Furthermore, reperfusion of the lower body and subsequent rewarming can occur earlier and concurrently with great vessel reimplantation. We believe that all these factors contribute to the low incidence of PND observed in this series.

TND is a reversible brain injury and is characterized by postoperative confusion, delirium, obtundation, or transient focal deficits (resolution within 24 hours) with negative brain computed tomography or magnetic resonance imaging scans. TND after arch surgery with DHCA alone occurs in approximately 25% of cases, and a linear relationship has been demonstrated between the incidence of TND and the duration of DHCA.[17-19] Compared with retrograde cerebral perfusion, antegrade cerebral perfusion has been shown to reduce the incidence of TND in both retrospective[13,14] and prospective studies.[6] The low rate of TND observed in this report is most likely to be because uSACP was used as part of the overall cerebral protection strategy. The cerebral oximetry data demonstrated minimal changes bilaterally during the period of MHCA. These data serve as an indirect measure of cerebral perfusion and oxygen delivery, indicating that uSACP provided adequate blood flow to both cerebral hemispheres during the period of circulatory arrest, which accounts for the low observed incidence of TND. In this study, the TND rate was 5.6%, which is comparable to the 4.7% to 6.0% range observed in other large series of TOTAL using DHCA + SACP.[10-12] The major modification in the circulation management strategy used in the current series of total arch replacements compared with previous series is the use of more moderate levels of hypothermia (>22°C).

Based on our experience and outcomes with the use of MHCA/uSACP for hemiarch replacement, we applied this circulation management strategy to TOTAL.[2,9] Our rationale was that the use of moderate levels of hypothermia would ameliorate the adverse effects observed with deep hypothermia including prolonged cardiopulmonary bypass times, coagulopathy, endothelial dysfunction, and renal dysfunction.[22,23] The risk in eliminating the use of profound hypothermia for TOTAL is an increase in cerebral and visceral organ ischemic injury. Profound hypothermia suppresses cellular metabolism and provides protection during periods of ischemia. It is well accepted that the addition of continuous cold antegrade cerebral perfusion improves cerebral protection and safely allows for longer periods of circulatory arrest.[7,8]

The prolonged period of MHCA (≈55 minutes) did not result in a significant degree of visceral organ injury in the current series. Five patients (3.4%) sustained postoperative renal dysfunction requiring dialysis, which is also in the 3.4% to 5.9% range in other large series of TOTAL using DHCA + SACP.[10-12] Furthermore, there was no difference between preoperative and postoperative creatinine levels (1.20 mg/dL vs 1.23 mg/dL, respectively; P = .45). There was also no significant incidence of clinically relevant mesenteric, liver, or spinal cord ischemia observed in this study. Thus, despite the use of MHCA for extended periods of time, we believe that visceral organ protection is adequate.

Limitations of the current study include its retrospective nature and the lack of a control group. We acknowledge the difficulty in evaluating a new technique without a direct comparison with the gold standard. However, application of MHCA/uSACP at our institution has gradually become the preferred circulation management technique for hemiarch and total arch replacement, and other methods (DHCA ± retrograde cerebral perfusion) have been abandoned. Therefore, a sizable control group of TOTAL performed under deep hypothermia does not exist at Emory.

This report contributes to a growing body of literature demonstrating that the strategy of moderate hypothermia with antegrade cerebral perfusion provides safe cerebral

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and visceral organ protection for the prolonged periods of circulatory arrest required for total arch replacement.[5,20,21] In this study, despite the prolonged periods of circulatory arrest, moderate hypothermia allowed for adequate cerebral and visceral organ protection during the period of circulatory arrest, and was not a predictor of adverse outcomes after elective or emergency TOTAL (Table 3). These data suggest that with the addition of antegrade cerebral perfusion, profound (<22°C) hypothermia may no longer be mandatory for total arch replacement. The use of moderate hypothermia does not result in an increase in end-organ ischemic dysfunction and represents an acceptable and safe alternative to the traditional use of deep hypothermia in total arch replacement. Ultimately, a randomized controlled trial of deep versus moderate hypothermia in aortic arch surgery is warranted to further evaluate and compare the safety and efficacy of these 2 circulation management strategies.

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