

Cite this article as: Preventza O, Garcia A, Kashyap SA, Akvan S, Cooley DA, Simpson K *et al.* Moderate hypothermia ≥ 24 and $\leq 28^{\circ}\text{C}$ with hypothermic circulatory arrest for proximal aortic operations in patients with previous cardiac surgery. *Eur J Cardiothorac Surg* 2016;50:949–54.

Moderate hypothermia ≥ 24 and $\leq 28^{\circ}\text{C}$ with hypothermic circulatory arrest for proximal aortic operations in patients with previous cardiac surgery[†]

Ourania Preventza^{a,b,*}, Andrea Garcia^a, Sarang A. Kashyap^b, Shahab Akvan^a, Denton A. Cooley^b, Kiki Simpson^c, Athina Rammou^b, Matt D. Price^a, Shuab Omer^{a,c}, Faisal G. Bakaen^{a,b,c}, Lorraine D. Cornwell^{a,c} and Joseph S. Coselli^{a,b}

^a Division of Cardiothoracic Surgery, Michael E. DeBakey Department of Surgery, Baylor College of Medicine, Houston, TX, USA

^b Department of Cardiovascular Surgery, Texas Heart Institute, Houston, TX, USA

^c The Michael E. DeBakey Veterans Affairs Medical Center, Houston, TX, USA

* Corresponding author. Division of Cardiothoracic Surgery, Michael E. DeBakey Department of Surgery, Baylor College of Medicine, 6770 Bertner Street, C-330, Houston, TX 77030, USA. Tel: +1-832-3559910; fax: +1-832-3559920; e-mail: opsmile01@aol.com (O. Preventza).

Received 8 September 2015; received in revised form 4 April 2016; accepted 13 April 2016

Abstract

OBJECTIVES: To determine whether, in patients with previous cardiac operations, moderate hypothermia (between 24 and 28°C) for hypothermic circulatory arrest (HCA) during antegrade cerebral perfusion (ACP) is safe for use during surgery on the proximal aorta and transverse aortic arch.

METHODS: Over a 7-year period, 118 patients underwent ascending aortic and hemiarch repair ($n = 70$; 59.3%), total arch replacement ($n = 47$; 39.8%) or ascending aortic replacement to treat porcelain aorta ($n = 1$; 0.9%). Simultaneous procedures included aortic root repair or replacement ($n = 33$; 28.0%) and coronary artery bypass grafting ($n = 21$; 17.8%). All patients had previously undergone cardiac operations via a median sternotomy. Eighteen patients (15.3%) had more than 1 previous sternotomy, and 24 patients (20.3%) required emergent/urgent operation. Median cardiopulmonary bypass, cardiac ischaemic, circulatory arrest and ACP times (min) were 136.0 [118–180 interquartile range (IQR)], 91.0 (68–119 IQR), 34.0 (21–59 IQR) and 33.5 (20–59 IQR), respectively. The median temperature when HCA was initiated was 24.2°C (24.1–24.8°C IQR).

RESULTS: The operative mortality rate was 10.2% ($n = 12$). Six patients (5.1%) had a permanent stroke, and 16 patients (13.6%) had a composite adverse outcome (operative mortality and/or a permanent neurological event and/or permanent haemodialysis at discharge). Preoperative renal disease was significantly more prevalent ($P = 0.020$) and the median circulatory arrest time significantly longer (48.5 vs 33 min; $P = 0.058$) in patients with composite adverse outcomes. Multivariable analysis of the redo patients showed that age ($P = 0.025$), preoperative renal disease ($P = 0.024$) and ACP time ($P = 0.012$) were independent risk factors for a new postoperative renal injury.

CONCLUSIONS: Moderate hypothermia for HCA during ACP is being used with increasing frequency, but has not been thoroughly evaluated in patients undergoing cardiovascular reoperations. Our experience suggests that in patients with previous cardiac surgery who are undergoing hemiarch and total aortic arch operations, moderate hypothermia is safe and produces respectable results.

Keywords: Moderate hypothermia • Hypothermic circulatory arrest • Aorta • Total aortic arch replacement • Hemiarch repair • Ascending aortic repair or replacement

INTRODUCTION

Cerebral protection strategies for proximal aortic and arch surgery have evolved over time. Deep hypothermic circulatory arrest (HCA) has been used extensively by experienced aortic surgical groups as the main strategy for protecting the brain by increasing

the safety of circulatory arrest and by decreasing the metabolic demands of the brain [1]. Owing to the increased rates of mortality and stroke, coagulopathy, re-exploration for bleeding and transfusion, as well as longer intensive care and hospital stays [2–5], there is a trend at experienced aortic centres towards the use of warmer temperatures. According to the expert consensus on the classification of hypothermia in circulatory arrest in aortic arch surgery [6], moderate hypothermia ranges from 20.1 to 28°C. An emerging European paradigm for conducting aortic arch repair with HCA in

[†]Presented at the 29th European Association of Cardiothoracic Surgery Meeting, Amsterdam, Netherlands, 3–7 October 2015.

moderate hypothermia was revealed in a recent questionnaire concerning HCA in adults [7, 8]. In patients with previous cardiac operations, proximal aortic or transverse arch surgery is a particularly complex procedure, in which increased time to complete the repair under circulatory arrest is often required and the safety of moderate hypothermia is not well established. To review our experience in using moderate hypothermia (≥ 24 and $\leq 28^\circ\text{C}$) for HCA during antegrade cerebral perfusion (ACP) in these cases, we studied the safety and outcomes of this approach in patients undergoing surgery on the proximal aorta and transverse aortic arch.

PATIENTS AND METHODS

Over a recent 7-year period, 118 patients [94 men and 24 women with a median age of 60.5 years; 25–75% interquartile range (IQR): 50–68 years] had proximal and total arch surgery with moderate hypothermia between 24 and 28°C . All the patients previously had cardiac surgery via a median sternotomy. Data were obtained from a prospectively maintained database, and the Institutional Review Board of Baylor College of Medicine approved the study. The median temperature when HCA was initiated was 24.2°C (25–75% IQR: 24.1 – 24.8°C). Preoperative patient characteristics and demographic variables are given in Table 1. The proximal arch and hemiarch operations, as well as concomitant procedures

and intraoperative times, are listed in Table 2. The Social Security Death Index, clinic visits and hospital records were used to obtain follow-up data.

We previously provided our definitions for pulmonary and renal disease, outcomes and intraoperative times [9]. Briefly, operative mortality was defined as death within 30 days after the index operation or death prior to hospital discharge; stroke was defined as a new brain injury evident clinically and/or radiographically after the procedure and renal injury was defined as the need to start dialysis or a doubling of the patient's serum creatinine level. Permanent neurological events included all strokes and/or spinal cord deficits evident at hospital discharge. A composite adverse outcome was defined as a life-changing event, i.e. operative mortality and/or permanent neurological injury at discharge and/or permanent dialysis at discharge. This review analyses the rates of mortality, overall postoperative stroke, overall postoperative renal injury and composite adverse outcomes.

Intraoperative procedure

We use the following surgical algorithm when operating on patients with previous cardiac surgery who are undergoing surgery on the proximal aorta or transverse aortic arch. Prior to the procedure, we obtain computed tomography (CT) images of the chest to evaluate the proximity of the different cardiac structures (right ventricle, aorta, innominate vein, bypass grafts) to the

Table 1: Demographic and other patient characteristics ($n = 118$)

Variable	Number	%
Age (years) [median (25–75% IQR)]	60.5	50–68
Male	94	79.7
Priority		
Elective	94	79.7
Urgent/emergent	24	20.3
Smoker	41	34.8
Hypertension	94	79.7
Chronic obstructive pulmonary disease	49	41.5
Prior cardiac history ^a	49	41.5
Congestive heart failure	55	46.6
Renal disease	24	20.3
More than one prior sternotomy	18	15.3
Diabetes	9	7.6
Atrial fibrillation	8	6.8
Endocarditis	6	5.1
Prior stroke or TIA	19	16.1
Prior proximal aortic dissection	37	31.4
Prior proximal aortic procedures		
Aortic root	37	31.4
Ascending aortic	9	7.6
Ascending and hemiarch	62	52.5
Ascending and arch	3	2.5
Prior CABG	26 ^b	22.0
Prior other cardiac operations (non-aortic)	4	3.4

Data are reported as median [interquartile range (25–75%)] for continuous variables and as number (percentage) for categorical variables.

TIA: transient ischaemic attack; CABG: coronary artery bypass grafting.

^aPrior myocardial infarction, prior percutaneous angioplasty and/or stent placement, prior coronary artery bypass, non-obstructive coronary artery disease, prior pacemaker placement.

^bThese 26 patients are included in the 49 patients with a prior cardiac history.

Table 2: Intraoperative variables and associated procedures ($n = 118$)

Categorical variables (number, percentage)		
Ascending aortic and hemiarch replacement	70	59.3
Total aortic arch replacement	47	39.8
Ascending aortic replacement	1	0.9
Concomitant procedures		
Aortic root procedure	33	28.0
CABG	21	17.8
Aortic valve replacement	19	16.1
Aortic valve commissuroplasty \pm resuspension	5	4.2
Cannulation sites		
Direct aortic	1	0.9
Innominate artery	30	25.4
Axillary artery	84	71.2
Femoral artery	1	0.9
Carotid artery	2	1.7
Unilateral ACP	35	29.7
Bilateral ACP	83	70.3
Intraoperative blood products		
PRBCs	97	82.2
PLTs	108	91.5
FFP	98	83.1
Continuous variables (median, 25–75% IQR)		
Intraoperative times (min)		
CPB time	136	118–180
Cardiac ischaemia time	91	68–119
Circulatory arrest time	34	21–59
Circulatory arrest time with no ACP (10 patients)	4.5	1.0–7.0
ACP time	33.5	20–59

Data are reported as number (percentage) for categorical variables and as median [interquartile range ((25%–75%)] for continuous variables.

CABG: coronary artery bypass grafting; PRBCs: packed red blood cells; PLTs: platelets; FFP: fresh frozen plasma; IQR: interquartile range; CPB: cardiopulmonary bypass; ACP: antegrade cerebral perfusion.

sternum. Aortic inflow for cardiopulmonary bypass (CPB) is achieved via right axillary, innominate and/or femoral artery cannulation. Our first choice, depending on the CT chest images, is right axillary or innominate artery cannulation, which is performed with an 8-mm graft sutured end-to-side to the artery, as previously described [9, 10]. If the cardiac structures are in close proximity to the sternum, we establish arterial inflow before achieving sternal entry via the right axillary artery. In this series, femoral artery cannulation was used only in selected emergency cases. The wires from the prior sternotomy were removed before or after arterial inflow was established. The advantage of removing the wires immediately after making the median sternotomy skin incision is that this can be done without the 5000 U of heparin that is usually required when using a right axillary graft. Percutaneous access to either femoral vein (preferably the right one) with a wire parked in the right atrium is also obtained in case CPB needs to be established upon sternal entry. The femoral dual-stage venous cannula is not inserted via the femoral vein unless full heparinization and CPB are initiated prior to the sternotomy. Full CPB with hypothermia is required before sternal entry only in cases in which the aortic or arch aneurysm is attached or protruding via the sternum. Upon sternal entry, haemostasis is achieved. If arterial inflow is not yet established, the innominate artery is dissected and prepared for the 8-mm graft. Most of the dissections in the redo operations are performed before the patients are given any heparin. When a total arch operation is planned, the arch vessels [innominate artery, left common carotid artery (LCCA) and left sub-clavian artery if possible] are dissected and prepared prior to going on CPB. Once CPB is established, cooling is initiated by monitoring the nasopharyngeal temperature; in our study group, HCA was initiated when the temperature was $\geq 24^{\circ}\text{C}$. Brain protection is monitored with cerebral oximetry via near-infrared spectroscopy. ACP is initially established unilaterally via the right common carotid artery and then bilaterally via a 9F Pruitt catheter (LeMaitre Vascular, Inc., Burlington, MA, USA) in the LCCA. The technical aspects of the redo arch and hemiarch operation have previously been described [9, 10].

Statistical analysis

Descriptive statistics are reported as frequencies and percentages for categorical variables and as the median with a 25–75% IQR for continuous variables. In performing univariate analysis to test for significant differences between the group with a composite adverse outcome and the group without a composite adverse outcome, we used the χ^2 test or the Fisher's exact test when necessary for the categorical data. For the continuous variables, the Wilcoxon two-sample test was used. Significance was defined as $P < 0.05$. Potential risk factors for operative outcomes were assessed by using nominal logistic regression models. This multivariable analysis first limited the number of variables that were considered in the models by univariately determining which variables were significantly different for those with versus without the outcome being modelled. The following 22 preoperative and intraoperative variables were analysed initially in this manner: total arch replacement versus hemiarch repair, concomitant coronary artery bypass grafting, aortic root replacement, temperature at which circulatory arrest with ACP was initiated, cannulation type, dissection/aneurysm/endocarditis, age, male, surgical priority, current smoker, hypertension, chronic obstructive pulmonary disease, New York Heart Association (NYHA) Class III/IV status, preoperative coronary event, preoperative renal

disease, preoperative neurological deficit, diabetes mellitus, CPB time, cardiac ischaemic time, cardiac arrest time and ACP time. Owing to the low number of events for the outcomes being modelled, we reduced the number of variables considered in the models by including from the potential 22 variables only those that were significantly different univariately for the outcome being modelled. (e.g. variables with a P -value of < 0.1 for patients who had a stroke versus those who did not have a stroke). For stroke, we used two variables (ACP time and prior AVR); for mortality, three variables (current or previous smoker, congestive heart failure and preoperative renal disease); for postoperative renal injury, five variables (current or previous smoker, preoperative renal disease, ACP time, age and COPD); for the composite outcome, three variables (current or previous smoker, preoperative renal disease and ACP time). The logistic regression models were then run with a stepwise selection option. Owing to the close proximity of the circulatory arrest time and the ACP time (which differed by only 30 s in median value and 1 min in range), only the ACP time was used in the multivariate analysis.

The Kaplan–Meier method was used to estimate the survival function for all 118 patients. The time from the date of surgery until death was computed for patients who died before 30 April 2015. Patients who did not die before the end of the study were considered as censored. All statistical analyses were conducted by using SAS software, version 9.1 (SAS Institute, Inc., Cary, NC, USA).

RESULTS

Mortality, neurological events and composite adverse outcomes

The operative mortality rate was 10.2% ($n = 12$ patients). Four patients were unable to be weaned from the extracorporeal membrane oxygenator (ECMO) due to respiratory and heart failure. Three patients died of multiorgan failure on postoperative days 5, 15 and 26, respectively. Two patients had a fatal stroke. One patient developed profound coagulopathy and was placed on ECMO support, which was later withdrawn with the family's consent. Two other patients developed pulseless electromechanical dissociation while recovering in the intensive care unit (Day 12) and on the hospital floor (Day 43), respectively; despite aggressive cardiopulmonary resuscitation, they each had an anoxic brain injury, and life support was withdrawn.

A total of 7 patients (5.9%) had a stroke, which was permanent in 6 cases (5.1%). A composite adverse outcome (operative mortality and/or permanent neurological injury at discharge and/or permanent dialysis at discharge) occurred in 16 patients (13.6%). In these 16 patients, the incidence of preoperative renal disease was significantly higher ($P = 0.020$), and the history of current or prior smoking ($P = 0.013$), median ACP time ($P = 0.049$) and median circulatory arrest time were significantly longer ($P = 0.058$) than those in patients who did not have a composite adverse outcome (Table 3). None of the variables that were considered in the multivariable model appeared to be associated with mortality, stroke or a composite adverse outcome, except that being a current or prior smoker was associated with mortality and a composite adverse outcome (Table 4).

Other adverse events

Major and short-term adverse outcomes are listed in Table 5. Without accounting for censoring of the data, the median time

Table 3: Univariate analysis: composite versus non-composite adverse outcomes

Variable	All patients (n = 118)	Composite = yes (n = 16)	Composite = no (n = 102)	P-value
Categorical variables (number, %)				
Male	94 (79.7)	14 (87.5)	80 (78.4)	0.52
Priority				
Urgent/emergent	24 (20.3)	3 (18.8)	21 (20.6)	1.00
Elective	94 (79.7)	13 (81.3)	81 (79.4)	1.00
Smoker	41 (34.8)	10 (62.5)	31 (30.4)	0.013
Hypertension	94 (79.7)	14 (87.5)	80 (78.4)	0.52
COPD	49 (41.5)	7 (43.8)	42 (41.2)	0.85
Prior cardiac history ^a	49 (41.5)	8 (50.0)	41 (40.2)	0.46
Congestive heart failure	55 (46.6)	10 (62.5)	45 (44.1)	0.17
Preoperative renal disease	24 (20.3)	7 (43.8)	17 (16.7)	0.020
Diabetes	9 (7.6)	0 (0.0)	9 (8.8)	0.61
Atrial fibrillation	8 (6.8)	2 (12.5)	6 (5.9)	0.30
More than one prior sternotomy	18 (15.3)	2 (12.5)	16 (15.7)	1.00
Prior history of stroke/TIA	19 (16.1)	4 (25.0)	15 (14.7)	0.29
Prior proximal aortic procedures	75 (63.6)	12 (75.0)	63 (61.8)	0.31
Prior CABG ^b	26 (22.0)	6 (37.5)	20 (19.6)	0.12
Prior other cardiac procedures, non-aortic	4 (3.4)	1 (6.3)	3 (2.9)	0.45
Continuous variables [median (25–75% IQR)]				
Age (years)	60.5 (50–68)	63.5 (52–69.5)	58 (50–68)	0.27
CPB time (min)	136.0 (118–180)	149.5 (126–226.5)	135.5 (117–177)	0.19
Cardiac ischaemia time (min)	91 (68–119)	89 (62–121)	91 (68–119)	0.81
Circulatory arrest time (min)	34 (21–59)	48.5 (28.5–75.5)	33 (18–58)	0.058
ACP time (min)	33.5 (20–59)	48.5 (28.5–75.5)	32.5 (18–58)	0.049
ICU stay (days)	4.0 (2.0–12.0)	7.0 (3.0–13.0)	4.0 (2.0–12.0)	0.21
Hospital LOS (days)	13.0 (8.0–22.0)	11.5 (6.5–15.5)	13.5 (8.0–22.0)	0.12

Data are reported as number (percentage) for categorical variables and as median [interquartile range (25–75%)] for continuous variables.

COPD: chronic obstructive pulmonary disease; TIA: transient ischaemic attack; CABG: coronary artery bypass grafting; CPB: cardiopulmonary bypass; ACP: antegrade cerebral perfusion; ICU: intensive care unit; LOS: length of stay.

^aPrior myocardial infarction, prior percutaneous angioplasty and/or stent placement, prior coronary artery bypass, non-obstructive coronary artery disease, prior pacemaker placement.

^bPrior CABG is also included in prior cardiac history.

Table 4: Multivariable analysis (n = 118 patients)

Variable	Significant variables with stepwise selection option	P-value	Odds ratio	95% odds ratio confidence limits
Mortality	Prior or current smoker	0.022	4.42	1.24–15.73
Renal failure	Prior or current smoker	0.026	3.16	1.15–8.70
	Preoperative renal disease	0.024	3.56	1.18–10.72
	Age	0.025	1.05	1.01–1.09
	ACP	0.012	1.02	1.01–1.04
Composite adverse outcome	Prior or current smoker	0.017	3.82	1.28–11.43

ACP: antegrade cerebral perfusion.

from surgery to operative death was 8.5 days (3.5–14.0 IQR). For the 106 patients who survived the operation, the median time from surgery to the end of the study (30 April 2015) or to the date of death (if applicable) was 3.0 years (1.3–6.0 IQR). Ninety-seven (91.5%) of the 106 operative survivors were alive at the end of the study. A Kaplan–Meier curve for all 118 redo patients is shown in Fig. 1.

DISCUSSION

Hypothermia, selective ACP and advances in techniques for proximal and total aortic arch surgery have changed the aortic surgery landscape. Modifications in temperature protocols with regard to

core and cerebral temperature during circulatory arrest have gained increased interest [4, 8, 11], and a trend towards mild and moderate hypothermia has been reported [7, 8]. The literature regarding proximal and aortic arch surgery contains very few reports that focus on redo cardiac surgery patients [10, 12, 13]. As a consequence, no specific outcomes data have been reported regarding procedures using the higher range of moderate hypothermia in this group. In this report, we concentrated only on patients who had previous cardiac surgery and underwent proximal or total arch surgery with moderate hypothermia in the range of 24–28°C (25–75% IQR: 24.1–24.8°C). Our short-term results showed that this range of hypothermia may be used safely, with respectable morbidity and mortality, in this cohort.

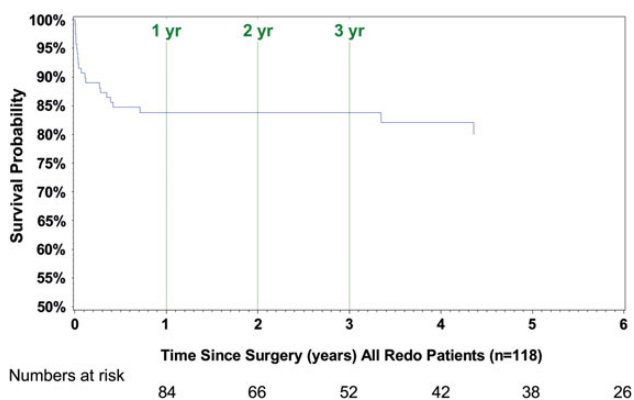
Table 5: Major and short-term adverse outcomes ($n = 118$)

Outcome	Number (%)
Mortality	12 (10.2)
Stroke	7 (5.9)
Permanent stroke	6 (5.1)
Composite adverse outcome ^a	16 (13.6)
Renal failure ^b	27 (22.9)
Permanent renal failure	0 (0.0)
Mechanical ventilation for >48 h	39 (33.3)
Tracheostomy	12 (10.3)
Reoperation for bleeding	12 (10.3)
Pericardial window	2 (1.7)
Pulmonary embolism	1 (0.9)
Deep vein thrombosis	9 (7.8)
Myocardial infarction	4 (3.5)

Data are reported as number (%).

^aDefined as operative mortality and/or permanent neurological injury at discharge and/or permanent dialysis at discharge.

^bDefined as the need to start dialysis or a doubling of the patient's serum creatinine level.

**Figure 1:** Kaplan-Meier survival curves for all 118 redo patients.

Our composite end-point was 13.6%. In a previous report [10], our group described all of our redo total aortic arch procedures. In those cases, we used a wide range of hypothermia (21–25°C), not only 24–28°C, and the composite end-point was 13.5%, which is almost identical to the current result.

Our current mortality rate was 10.2% and permanent stroke rate was 5.1%. In another recent report from our group [14], describing 274 patients who had total arch surgery (154 were redo cases) using a wide range of hypothermia (21–25°C), our mortality and stroke rates were 10.3 and 5.5%, respectively, and therefore also similar to our current results [14]. These outcomes are comparable with those of other surgeons [12, 15]. In a cohort of 168 patients studied over a 14-year period, Quintana *et al.* [12] observed an 8.3% 30-day mortality rate and a 5.4% permanent stroke rate. Deep HCA was used in all cases, ACP in 39.3%, retrograde cerebral perfusion in 13.7% and no adjunct cerebral perfusion in 47%. The authors mention an increasing use of selective ACP during the study period [12]. Univariate analysis showed age, NYHA class III or IV status, and extracorporeal circulation time as predictors of perioperative mortality [12].

Etz *et al.* [15], of Mount Sinai Hospital, reported a mortality rate of 10% for their redo transverse arch repairs; this result was almost

similar to that for their primary open arch operations (9% mortality). Additionally, they reported a mortality rate of 3% for primary operations on the ascending aorta and aortic root versus 7% for reoperations [15]. When circulatory arrest was required, these surgeons used an oesophageal temperature of 12–15°C and selective ACP [15].

We observed the same mortality rate (10.2%) in our redo patients, but our procedures were performed with the aid of moderate hypothermia (25–75% IQR: 24.1–24.8°C). We did not compare our redo patients with the non-redo ones, as the Mount Sinai group did. Although redo and non-redo patients can undergo the same total arch, hemiarch or root operation, the two groups are inherently different. Because of unclear surgical planes, redo operations necessitate lengthy dissection, which involves potential risks and increases the operative time; such dissection is not necessary in a primary operation. Moreover, primary operations involve no removal of a prior ascending aortic Dacron graft due to infection or pseudoaneurysm formation, sternal re-entry in a patient with a patent left internal mammary artery after coronary artery bypass or sternal re-entry after a prior proximal arch operation, all of which entail significant risks.

In a cohort of 523 patients ($n = 53$ redo operations) described by Czerny *et al.* [16], multivariable logistic regression analysis showed that the mortality rate was 26% for redo surgery versus 9% for non-redo procedures ($P = 0.01$). For cerebral perfusion, these authors used a blood temperature of 20°C in treating both acute type A aortic dissection and chronic ascending aortic aneurysms. The patients with chronic ascending aneurysms were cooled to a bilateral tympanic temperature of 26°C and a bladder temperature of 30°.

In our cohort of redo cardiac surgery patients who underwent aortic surgery at the higher range of moderate hypothermia, univariate regression analysis showed that preoperative renal disease ($P = 0.020$), circulatory arrest time ($P = 0.058$), ACP time ($P = 0.049$) and smoking (current or prior) ($P = 0.013$) were associated with an adverse composite outcome (Table 3). In the multivariable model, we did not identify any independent predictors of a composite outcome, mortality or stroke except that being a current smoker raised the risk for mortality and a composite adverse outcome. With regard to postoperative renal injury, we identified age, preoperative renal disease, ACP time and current or prior smoking as independent predictors.

In redo patients who underwent thoracic aortic surgery with moderate hypothermia and ACP, Pacini *et al.* [17] observed a 19.7% rate of postoperative kidney injury. This result is close to ours (22.9%). Similarly, they also showed that preoperative renal status is an independent predictor of postoperative kidney injury [17]. That age and preoperative renal status are predictors for postoperative renal injury has also been shown by others [18], signifying the importance of optimizing preoperative renal function and hydration in these patients. In our study, we found that the ACP time was also associated with postoperative renal failure. During the circulatory arrest period, ACP provides energy substrates to the brain, but the rest of the body is subjected to total ischaemia. Apoptosis, vascular endothelial dysfunction and an ischaemia-reperfusion mechanism have been implicated in multiorgan dysfunction after HCA [19]. As a result, even more pronounced postoperative renal injury may be expected to result from deep hypothermia. A more complex and lengthy operation associated with prolonged circulatory arrest time and increased CPB time in patients undergoing aortic root repair or replacement can lead to low cardiac output syndrome and acute kidney injury postoperatively.

With regard to age as a risk factor for an adverse outcome in patients who undergo aortic surgery under moderate hypothermia, the data are sparse and inconsistent. Age is associated with mortality in patients undergoing atherosclerotic arch aneurysm procedures using ACP [20], as well as patients with prior cardiac surgery undergoing proximal aortic procedures [15]. In our study, age was not an independent risk factor for operative mortality or a composite outcome, but it was an independent risk factor for postoperative renal injury ($P = 0.025$; odds ratio = 1.0; 95% CI 1.0–1.1). Czerny *et al.* [21] emphasize that the critical preoperative status of the patient, more than the age itself, is associated with operative mortality, which was 13% in their series. They used a bilateral 20°C tympanic temperature and 26°C bladder temperature (for more complex repair of the aortic arch) or a bilateral 26°C tympanic temperature and 30° bladder temperature (for hemi-arch repair) [21].

Limitations

The main limitation of our study is its retrospective nature, with its inherent bias. In addition, this study focused only on patients with prior cardiac surgery in whom the proximal aortic procedure was performed under moderate hypothermia. Owing to the inherent risks that a redo versus a primary operation entails, as previously explained, we did not compare the redo patients with non-redo ones. For a control group, we used reports regarding our own group of patients who had redo cardiac, redo aortic or non-redo cardiac surgery performed in various temperature ranges; we also used reports from the existing literature concerning patients requiring circulatory arrest with ACP. Owing to the small number of operative deaths, neurological events and composite adverse outcomes, the multivariable analysis failed to identify meaningful outcome predictors for this patient population. Nevertheless, to our knowledge, this is one of the few studies, if not the only one, to analyse this group of patients.

CONCLUSION

Moderate hypothermia in redo cardiac surgery patients undergoing proximal aortic procedures has not been thoroughly evaluated. We have demonstrated that moderate hypothermia for proximal aortic and total arch reoperations is safe and has respectable results in this challenging patient population.

Conflict of interest: Dr Preventza consults for Medtronic, Inc., and participates in clinical trials for WL Gore & Associates. In the past, she has received travel expenses from both Cook, Inc., and Gore. Dr Coselli participates in clinical research trials conducted by Glaxo Smith Kline, Edwards Lifesciences, and Bolton Medical; he consults for, receives royalties and a departmental educational grant from, and participates in clinical trials for Vascutek Terumo; he consults and participates in clinical trials for Medtronic, Inc., and WL Gore & Associates; and he participates in clinical research for Cook, Inc. None of the other authors has any potential conflict of interest with regard to the work described in this manuscript, and this work was not funded by a grant or any other source of external funding.

REFERENCES

- [1] Ziganshin BA, Rajbanshi BG, Tranquilli M, Fang H, Rizzo JA, Elefteriades JA. Straight deep hypothermic circulatory arrest for cerebral protection during aortic arch surgery: safe and effective. *J Thorac Cardiovasc Surg* 2014;148:888–98; discussion 898–900.
- [2] Kamiya H, Hagl C, Kropivnitskaya I, Bothig D, Kallenbach K, Khaladj N *et al.* The safety of moderate hypothermic lower body circulatory arrest with selective cerebral perfusion: a propensity score analysis. *J Thorac Cardiovasc Surg* 2007;133:501–9.
- [3] Rastan AJ, Walther T, Alam NA, Daehnert I, Borger MA, Mohr FW *et al.* Moderate vs deep hypothermia for the arterial switch operation—experience with 100 consecutive patients. *Eur J Cardiothorac Surg* 2008;33:619–25.
- [4] Tsai JY, Pan W, Lemaire SA, Pisklak P, Lee VV, Bracey AW *et al.* Moderate hypothermia during aortic arch surgery is associated with reduced risk of early mortality. *J Thorac Cardiovasc Surg* 2013;146:662–7.
- [5] Vallabhajosyula P, Jassar AS, Menon RS, Komlo C, Gutsche J, Desai ND *et al.* Moderate versus deep hypothermic circulatory arrest for elective aortic transverse hemiarch reconstruction. *Ann Thorac Surg* 2015;99:1511–7.
- [6] Yan TD, Bannon PG, Bavaria J, Coselli JS, Elefteriades JA, Griep RB *et al.* Consensus on hypothermia in aortic arch surgery. *Ann Cardiothorac Surg* 2013;2:163–8.
- [7] Gutsche JT, Feinman J, Silvey G, Patel PP, Ghadimi K, Landoni G *et al.* Practice variations in the conduct of hypothermic circulatory arrest for adult aortic arch repair: focus on an emerging European paradigm. *Heart Lung Vessel* 2014;6:43–51.
- [8] Urbanski PP, Lenos A, Bougioukakis P, Neophytou I, Zacher M, Diegeler A. Mild-to-moderate hypothermia in aortic arch surgery using circulatory arrest: a change of paradigm. *Eur J Cardiothorac Surg* 2012;41:185–91.
- [9] Preventza O, Garcia A, Tuluca A, Henry M, Cooley DA, Simpson K *et al.* Innominate artery cannulation for proximal aortic surgery: outcomes and neurological events in 263 patients. *Eur J Cardiothorac Surg* 2015;48:937–42.
- [10] Preventza O, Garcia A, Cooley DA, Tuluca A, Simpson KH, Bakaeen FG *et al.* Reoperations on the total aortic arch in 119 patients: short- and mid-term outcomes, focusing on composite adverse outcomes and survival analysis. *J Thorac Cardiovasc Surg* 2014;148:2967–72.
- [11] Leshnowar BG, Myung RJ, Chen EP. Aortic arch surgery using moderate hypothermia and unilateral selective antegrade cerebral perfusion. *Ann Cardiothorac Surg* 2013;2:288–95.
- [12] Quintana E, Bajona P, Schaff HV, Dearani JA, Daly RC, Greason KL *et al.* Open aortic arch reconstruction after previous cardiac surgery: outcomes of 168 consecutive operations. *J Thorac Cardiovasc Surg* 2014;148:2944–50.
- [13] Moz M, Misfeld M, Leontyev S, Borger MA, Davierwala P, Mohr FW. Aortic arch reoperation in a single centre: early and late results in 57 consecutive patients. *Eur J Cardiothorac Surg* 2013;44:82–6.
- [14] Preventza O, Garcia A, Cooley DA, Haywood-Watson RJ, Simpson K, Bakaeen FG *et al.* Total aortic arch replacement: a comparative study of zone 0 hybrid arch exclusion versus traditional open repair. *J Thorac Cardiovasc Surg* 2015;150:1591–8; discussion 1598–600.
- [15] Etz CD, Plestis KA, Homann TM, Bodian CA, Di Luzzo G, Spielvogel D *et al.* Reoperative aortic root and transverse arch procedures: a comparison with contemporaneous primary operations. *J Thorac Cardiovasc Surg* 2008;136:860–7.
- [16] Czerny M, Krähenbühl E, Reineke D, Sodeck G, Englberger L, Weber A *et al.* Mortality and neurologic injury after surgical repair with hypothermic circulatory arrest in acute and chronic proximal thoracic aortic pathology: effect of age on outcome. *Circulation* 2011;124:1407–13.
- [17] Pacini D, Pantaleo A, Di Marco L, Leone A, Barberio G, Parolari A *et al.* Risk factors for acute kidney injury after surgery of the thoracic aorta using antegrade selective cerebral perfusion and moderate hypothermia. *J Thorac Cardiovasc Surg* 2015;150:127–33 e1.
- [18] Kim WH, Lee SM, Choi JW, Kim EH, Lee JH, Jung JW *et al.* Simplified clinical risk score to predict acute kidney injury after aortic surgery. *J Cardiothorac Vasc Anesth* 2013;27:1158–66.
- [19] Cooper WA, Duarte IG, Thourani VH, Nakamura M, Wang NP, Brown WM III *et al.* Hypothermic circulatory arrest causes multisystem vascular endothelial dysfunction and apoptosis. *Ann Thorac Surg* 2000;69:696–703.
- [20] Motomura N, Miyata H, Tsukihara H, Takamoto S, Japan Cardiovascular Surgery Database Organization. Risk model of thoracic aortic surgery in 4707 cases from a nationwide single-race population through a web-based data entry system: the first report of 30-day and 30-day operative outcome risk models for thoracic aortic surgery. *Circulation* 2008;118: S153–9.
- [21] Czerny M, Barchichat I, Meszaros K, Sodeck GH, Weber A, Reineke D *et al.* Long-term results after proximal thoracic aortic redo surgery. *PLoS ONE* 2013;8:e57713.