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Comparison of Unilateral Antegrade Cerebral Perfusion at 16°C and 22°C Systemic Temperature

Soner Sanioglu, Onur Sokullu, I. Yucesin Arslan, Murat Sargin, Mehmet Yilmaz, Batuhan Ozay, Hamdi Tokoz, Fuat Bilgen

Department of Cardiovascular Surgery, Dr Siyami Ersek Thoracic and Cardiovascular Surgery Training and Research Hospital, Istanbul, Turkey

ABSTRACT

Objectives: Unilateral antegrade cerebral perfusion can be performed with minimal manipulations to arch arteries, but whether it provides adequate brain perfusion remains unclear. Some authors believe that this technique can be inadequate without deep hypothermia. We investigated the reliability of unilateral cerebral perfusion at 22°C hypothermia and the advantages of avoiding deep hypothermia.

Methods: Study participants were 55 patients who underwent surgery with unilateral cerebral perfusion. Patients were divided into 2 groups; 18 patients underwent surgery at 16°C hypothermia (group I) and 37 patients at 22°C hypothermia (group II). The mean age of the patients was 59 ± 10 years in group I and 55 ± 14 years in group II. Supracoronary ascending aorta replacement was performed in 25 and hemiarch replacement in 15 patients. Nine patients underwent surgery for a Bentall procedure. Total arch replacement was performed in 4 patients and total thoracic aorta replacement in 2 patients.

Results: The hospital mortality was 11% in group I and 5.4% in group II (*P* = .59). Transient neurologic deficits were not detected in any of the patients. The rate of permanent neurologic deficits was 5.9% in group I and 2.8% in group II (*P* = .54). Although mean aortic cross-clamp and antegrade cerebral perfusion times were not significantly different, mean cardiopulmonary bypass time was longer in group I than group II (174 ± 38 vs 142 ± 37 minutes, *P* = .005). Postoperative bleeding, blood product usage, serum creatinine and hepatic enzyme level changes, inotrope usage, and arrhythmia occurrence were not different between the 2 groups. Mean mechanical ventilation time was longer in group I than group II (24 ± 17 vs 16 ± 6 hours, *P* = .02).

Conclusions: Unilateral antegrade cerebral perfusion at 22°C systemic hypothermia appears to be safe and reliable for brain protection. Advantages of this technique are avoidance of deep hypothermia and reduced cardiopulmonary bypass and mechanical ventilation times in patients undergoing aortic surgery.

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Correspondence: Soner Sanioglu, Fenerbahce Mah, Fenerli Reis Sk. No. 5/2, Selamicesme 34030, Kadikoy/Istanbul; +90 216 3695940/gsm: +90 532 7151533; fax: +90 216 3698811 (e-mail: sanioglu@gmail.com).

INTRODUCTION

Successful performance of aortic surgical procedures is directly related to cerebral protection techniques, especially during hypothermic circulatory arrest. Recent studies have shown that neurologic complications are decreased with antegrade cerebral perfusion (ACP) [Hagl 2001; Kazui 2002]. Although the superiority of ACP is widely accepted, debate continues regarding perfusion characteristics. Bilateral ACP has been reported to increase the risk of thromboembolic events or air embolism due to manipulations of the supraaortic vessels [Immer 2008]. On the other hand, unilateral ACP can be performed with minimal manipulation, but whether it provides adequate brain perfusion remains unclear [Tasdemir 2002].

Optimal systemic temperature during the ACP is also a subject of debate. Excellent clinical results have been reported with moderate hypothermia [Kazui 2002; Tasdemir 2002; Zierer 2005], but many investigators still prefer lower systemic temperatures to ensure cerebral metabolic suppression [Harrington 2007]. The aim of our study was to establish the reliability of unilateral cerebral perfusion at 22°C systemic hypothermia and investigate the advantages of avoiding deep hypothermia.

MATERIALS AND METHODS

Between January 2005 and March 2008, 55 consecutive patients who underwent aortic surgery with unilateral ACP were included in this study. The study protocol was approved by the local ethics committee. Data were collected from medical records of the patients and were analyzed retrospectively. According to the systemic temperature during ACP, patients were divided into 2 groups: 18 patients (33%) underwent surgery at 16°C hypothermia (group I) and 37 patients (67%) at 22°C hypothermia (group II).

The mean age of the patients was 59 ± 10 years in group I and 55 ± 14 years in group II. Ten patients in group I (56%) and 24 (65%) in group II were male. Preoperative characteristics of the patients and etiology of their aortic pathologies are listed in Table 1.

Anesthetic and Operative Protocol

Standard anesthetic management was used in all patients and included intravenous fentanyl (50 μg/kg), pancuronium,

Table 1. Preoperative Characteristics of the Study Patients*

Variable	Group I (n = 18; 33%)	Group II (n = 37; 67%)	Significance
Age, y	59 ± 10	55 ± 14	NS
Male	10 (56%)	24 (65%)	NS
CAD†	2/10 (20%)	5/20 (25%)	NS
COPD	—	4 (11%)	NS
DM type II	—	4 (11%)	NS
Hypertension	14 (78%)	20 (54%)	NS
Redo operation	—	4 (11%)	NS
Urgent operation	8 (44%)	19 (51%)	NS
Etiology			
Degenerative	3 (17%)	10 (27%)	NS
Chronic dissection	6 (33%)	8 (22%)	NS
Acute dissection	8 (44%)	16 (43%)	NS
Others‡	1 (6%)	3 (8%)	NS
Dissection complication			
Malperfusion	—	—	
Cardiac tamponade	2/8 (25%)	4/16 (25%)	NS
Preoperative Cr, mg/dL	1.2 ± 0.5	1.2 ± 0.4	NS

*CAD indicates coronary artery disease; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; Cr, creatinine; NS, not significant.

†Preoperative coronary angiography was not performed in patients with acute dissection and intramural hematoma.

‡Others indicates intramural hematoma, Marfan, Takayasu disease, and porcelain aorta.

and etomidate for induction and isoflurane or enflurane inhalation for maintenance. All procedures were performed by the same surgical team. In the majority of the patients (n = 53, 96%), surgery was performed via median sternotomy. A clamshell type of incision was used in the other 2 patients (4%) to replace the descending aorta. Standard right axillary artery and right atrial cannulation were performed for cardiopulmonary bypass (CPB) in all patients. The axillary artery was cannulated as described in one of our previous reports [Sanioglu 2007]. Direct cannulation was used frequently, and side-graft cannulation was used in patients with small axillary arteries (n = 4, 7%). Myocardial protection was achieved via antegrade and retrograde cold-blood cardioplegia at 20-minute intervals. Topical head cooling was used, and cooling and rewarming gradients of up to 10°C between arterial inflow and rectal temperature were allowed. Intravenous penthotal, methylprednisolone 500 mg, and mannitol 1 g/kg were administered in all cases before circulatory arrest. When rectal heat reached the target temperature (16°C in group I, 22°C in group II) during the cooling period, the pump flow rate was decreased to 10 mL/kg per minute, the patient was placed in trendelenburg position, and the innominate artery was clamped. The retrograde blood flow from the left carotid artery was evaluated following the aortotomy, and when an adequate retrograde blood flow was observed, the left carotid artery was also clamped. The left subclavian artery was clamped only in patients who underwent total arch replacement. Pressure monitoring was performed through a side hole of the arterial cannula during ACP, and the pressure was maintained at 40-60 mmHg. The blood pH was adjusted during CPB by means of an α-stat strategy. All distal aortic anastomoses were performed with an open distal technique. In patients with acute type A aortic dissection, dissected layers of the aortic wall were reconstructed with inner and outer Teflon felt with monofilament sutures, as described for the sandwich technique. An arch-first technique and branched grafts were used in patients who underwent total arch replacement.

All patients underwent detailed neurological evaluations after they awakened from anesthesia and daily during their hospital stay. A neurological consultation was performed for each patient with an evident neurologic deficit, and a cranial computed tomographic (CT) scan was performed to rule out stroke or bleeding. All stroke cases were documented clinically and radiologically.

Supracoronary ascending aorta replacement was performed in 25 (45%) of patients and hemiarch replacement in 15 (27%). Nine patients (17%) underwent surgery for a Bentall procedure. Four patients (7%) underwent total arch replacement and 2 (4%) underwent total thoracic aorta replacement. Operations and additional procedures performed in both groups are listed in Table 2.

Statistical Analysis

We performed statistical analysis with SPSS statistical software (version11.0, SPSS, Chicago, IL, USA). Continuous variables were expressed as mean ± SD and compared with the Mann-Whitney *U* test because the sample size was small. Categorical variables were expressed as frequencies and analyzed with either Pearson χ^2 test or Fisher exact test, as appropriate. A *P* value less than .05 was considered significant.

RESULTS

ACP was set up successfully in all patients with no technical difficulty. A transient injury of the brachial plexus was observed as a complication of axillary artery cannulation in 1 patient (1.8%).

When preoperative parameters, type of surgery, and additional procedures were considered, both groups were similar (Tables 1 and 2). Hospital mortality was 11% (n = 2) in group I and 5.4% (n = 2) in group II ($P = .59$). In group I, 1 patient who underwent total thoracic aorta replacement died on the first postoperative day because of low cardiac output syndrome. The other death in the group I patients occurred in a patient who underwent total arch replacement and coronary artery bypass graft. This patient's condition was complicated by a stroke occurring after surgery, and the patient died because of multiorgan failure 25 days after the operation. In both of the group I patients who died the aortic pathology was degenerative aneurysm. In group II, 2 patients died; 1 patient, who underwent surgery for acute type A dissection and was treated with total arch replacement, died during the surgical procedure; in this patient weaning from CPB was not successful. The second patient, who was scheduled for aortic

Table 2. Number of Performed Operations and Additional Procedures

	Group I (n = 18; 33%)	Group II (n = 37; 67%)	Significance
Operations, n			
Supracoronary ascending aorta replacement	9 (50%)	16 (43%)	NS
Hemiarch replacement	4 (22%)	11 (29%)	NS
Bentall	3 (17%)	6 (16%)	NS
Total arch replacement	1 (5.5%)	3 (8%)	NS
Total thoracic aorta replacement	1 (5.5%)	1 (3%)	NS
Additional procedures, n	5 (28%)	10 (27%)	NS
CABG + AVR	—	2 (5%)	
CABG	3 (17%)	2 (5%)	
AVR + mitral valve repair	—	1 (3%)	
AVR	2 (11%)	3 (8%)	
Aortic valve repair	—	2 (5%)	

CABG, coronary artery bypass graft; AVR, aortic valve replacement; NS: not significant

valve replacement, underwent supracoronary ascending aorta replacement for "porcelain aorta." In this patient, permanent neurologic deficit occurred after the surgery and he died because of septicemia.

Transient neurologic deficit was not detected in any of the patients. Permanent neurologic deficit was seen in 1 patient in each group (5.9% in group I and 2.8% in group II; $P = .54$), and both of these patients died after the surgery.

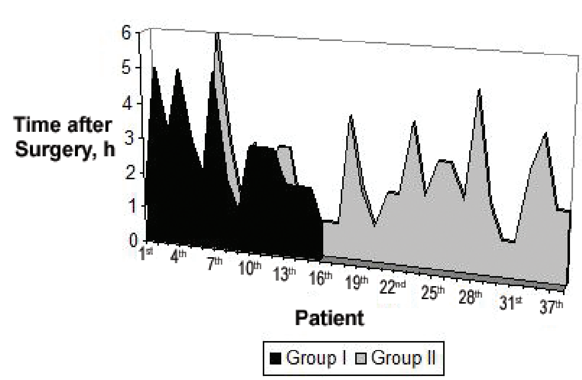
None of the patients required repeat surgery for excessive bleeding, and cardiac tamponade did not occur in any of the patients. None of the patients required hemodialysis for acute renal failure.

Although mean aortic cross-clamp and ACP times did not differ significantly in the 2 groups, mean CPB time was longer in group I than group II patients (174 ± 38 vs 142 ± 37 minutes, $P = .005$). Postoperative bleeding, blood product usage, serum creatinine and hepatic enzyme level changes, inotrope usage, and arrhythmia occurrence did not differ between the 2 groups. Mean mechanical ventilation time was longer in group I than group II (24 ± 17 versus 16 ± 6 hours, $P = .02$). Mean length of intensive care unit stay was 2 ± 1 days in both groups. Mean hospital stay was 11 ± 3 days in group I and 12 ± 6 days in group II (Table 3).

DISCUSSION

When compared with bilateral ACP, unilateral ACP has the advantages of minimizing the manipulation of aortic arch vessels, providing an easy setup and allowing fewer cannulas in the surgical field. Controversy still exists, however, regarding whether unilateral ACP is as protective as bilateral perfusion for cerebral protection. Good results with unilateral ACP have been reported for several studies [Kucuker 2005; Panos 2006; Bakhtiary 2008]. Immer et al stated that results for early survival and permanent neurologic events in their comparative study were better with unilateral ACP than bilateral ACP [Immer 2008]. However, Dossche et al. and Olsson et al. reported larger numbers of permanent neurologic events and increased mortality with unilateral ACP than with bilateral ACP [Dossche 1999; Olsson 2006]. Malvindi et al. documented that the number of complex aortic arch procedures in the studies supporting unilateral ACP are very small, with mean ACP times usually not exceeding 30-50 minutes [Malvindi 2008]. Resolution of this issue requires prospective randomized clinical studies which unfortunately have not yet been established. The results of the present study are encouraging for the safety of unilateral ACP. The overall major neurologic event ratio was 3.8% (n = 2), even with arrest times longer than 30 minutes (n = 13) and 40 minutes (n = 8). But we have to point out that our series also includes few cases of complex aortic arch procedures.

The most important concern regarding unilateral ACP is circle of Willis variations, such as hypoplasia of both anterior and left posterior communicating arteries, which may lead to high-risk contralateral lobe hypoperfusion [Tasdemir 2002; Papantchev 2007]. Although these anomalies are very rare, testing of the adequacy of collateral flow in the circle of Willis can be useful to identify high-risk patients. Invasive angiographic methods have not been reported to increase the risk of stroke [Tasdemir 2002], but minimally invasive techniques such as CT scan were favored for this indication by Merkkola et al [2006] and Papantchev et al [2007]. However, Urbanski et al stated that the anatomical status of the circle of Willis assessed with cranial CT imaging does not correlate with functional and intraoperative tests examining cerebral cross-perfusion, and they do not recommend cranial CT angiography as a preoperative standard examination before open arch surgery in which unilateral cerebral perfusion is scheduled [Urbanski 2008]. We believe that an intraoperative assessment of the left carotid artery's retrograde blood flow at the beginning of ACP reflects the adequacy of the collateral flow, and such information is valuable for evaluating contralateral hemispheric perfusion. In cases of acute obstruction of



Time interval during which the extubation criteria were achieved on arterial blood gas analysis for each patient.

Table 3. Operative and Postoperative Clinical Variables of the Patients*

Variable	Group I (n = 18; 33%)	Group II (n = 37; 67%)	Significance
ACP time, min	35 ± 23	30 ± 13	NS
CC time, min	87 ± 28	83 ± 27	NS
CPB time, min	174 ± 39	142 ± 37	.005
Postop blood drainage, mL	889 ± 313	964 ± 301	NS
Blood transfusion, units	1.9 ± 0.9	2.1 ± 0.8	NS
Postop peak Cr, mg/dL	1.7 ± 0.6	1.6 ± 0.5	NS
Postoperative peak CK-MB, U/L	49 ± 13	53 ± 11	NS
Postoperative peak SGOT, U/L	108 ± 80	102 ± 70	NS
Postoperative peak SGPT, U/L	84 ± 76	74 ± 57	NS
Atrial fibrillation, n	2 (11%)	6 (17%)	NS
Inotrope usage	10 (56%)	22 (61%)	NS
IABP	1 (5.6%)	2 (5.6%)	NS
Mechanical ventilation time, h	24 ± 17	16 ± 6	.02
Transient neurologic deficit	—	—	
Permanent neurologic deficit	1 (5.9%)	1 (2.8%)	NS
ICU time, d	2 ± 1	2 ± 1	NS
Hospitalization time, d	11 ± 3	12 ± 6	NS
Hospital mortality	2 (11%)	2 (5.4%)	NS

*Mean cardiopulmonay bypass (CPB) time and mechanical ventilation time were longer in group I than group II. ACP indicates antegrade cerebral perfusion; CC, cross-clamp; Cr, creatinine; CK-MB, creatine kinase muscle-brain fraction; SGOT, serum glutamic oxaloacetic transaminase; SGPT, serum glutamic pyruvate transaminase; IABP, intraaortic baloon pump; ICU, intensive care unit.

major cranial vessels, such as internal carotid and vertebral arteries, perfusion of the contralateral hemisphere totally depends on the circle of Willis. The secondary collaterals, such as the ophthalmic, leptomeningeal, deep collateral, and extracranial arteries, supply blood during chronic hypoperfusion [Papantchev 2007]. Therefore, observation of decreased retrograde blood flow in the left carotid artery during unilateral ACP is a safe method for considering critical circle of Willis anomalies; however, such an assessment depends on the experience of the surgeon, and no clear threshold level has yet been established.

The usual monitoring during ACP includes serial internal jugular bulb venous oxygen saturation, electroencephalogram, bilateral transcranial doppler, and pressure measurement of perfusion [Apostolakis 2008]. Serial internal jugular bulb venous oxygen saturation and electroencephalogram are used to confirm maximal metabolic suppression of the brain. These techniques are not suitable for operations performed at moderate hypothermia, because maximal metabolic suppression cannot be provided at these temperature. Bilateral transcranial Doppler is a useful tool for blood velocity measurement of the middle cerebral artery, especially in cases of unilateral ACP [Apostolakis 2008]. Demonstration of the flow in the middle cerebral artery can indicate sufficient contralateral flow of the brain, but this technique must be performed by an experienced anesthesiologist and generally is not available at most of the clinics where aortic surgery is performed. Perfusion pressure measurement is the classical monitoring technique for ACP. During our surgical procedures, we use 10 mL/kg per minute cerebral perfusion flow and keep the pressure at 40-60 mmHg during ACP.

The use of ACP eliminates the need for deep hypothermia, which is associated with significant complications such as perioperative hemorrhage and postoperative pulmonary and renal dysfunction. Many studies have shown that the use of ACP avoids the adverse effects of hypothermia without an increased rate of neurologic complications. Kaneda et al reported that ACP with mild hypothermic arrest allows decreased transfusion volume and reduced duration of intubation and intensive care unit stay [Kaneda 2005]. Kamiya et al [2005] and Zierer et al [2007] stated that deep lower-body circulatory arrest is a strong risk factor for perioperative bleeding. But Harrington et al showed that the primary determinant of postoperative bleeding is the procedure extent, not profound hypothermia, and profoundly hypothermic CPB does not appear to be a risk factor for renal or early pulmonary dysfunction or intensive care unit length of stay [Harrington 2004]. The present study supports the results of the latter study. There was no difference between groups regarding postoperative clinical variables except mechanical ventilation time (Table 3). Medical records of the patients were reevaluated to find out the reasons for different mean intubation times in the 2 groups, and we hypothesized that this difference cannot be attributed to pulmonary dysfunction, because the time intervals in which the extubation criteria were achieved on arterial blood gas analysis were similar in both groups (2.8 ± 1.3 hours in group I and 2.3 ± 13 hours in group II, $P = .2$) (Figure). This difference seems to be associated with the duration of conscious awakening. ACP at 22°C systemic hypothermia can be more protective than 16°C hypothermia because cooling leads to uncoupling of cerebral flow and metabolism and loss of cerebral autoregulation. This uncoupling occurs at approximately 22°C [Harrington 2007]. Thus, 22°C systemic hypothermia may provide maximal cerebral protection by decreasing cerebral metabolism and maintaining cerebral autoregulation.

In conclusion, unilateral ACP at 22°C systemic hypothermia appears to be safe and reliable for brain protection and has the advantages of avoiding deep hypothermia and reducing CPB and mechanical ventilation times in patients undergoing aortic surgery.

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