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(Citation)
The Kobe journal of the medical sciences,43(1):25-35

(Issue Date)
1997-02

(Resource Type)
departmental bulletin paper

(Version)
Version of Record

(URL)
https://hdl.handle.net/20.500.14094/E0000977

Kobe J. Med. Sci. 43, 25/35, February 1997

# RETROGRADE CEREBRAL PERFUSION WITH PHARMACOLOGICAL CEREBRAL PROTECTION IN THE REPAIR OF AORTIC ARCH ANEURYSM

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INDEXING WORDS

retrograde cerebral perfusion; pharmacological cerebral protection; aortic arch aneurysm

## SYNOPSIS

Twenty-six patients underwent resection and graft replacement of an aortic arch aneurysm (proximal arch,5; transverse arch:2, distal arch,8; and type A dissecting aneurysm. Retrograde cerebral perfusion with pharmacological cerebral protection was carried out during aortic arch aneurysm surgery. Prostaglandin E1, thiopental and methylpredonisolone were administered for cerebral protection during core cooling. D-Mannitol and deferoxamine mesylate (radical scavengers) were administered for prevention of reperfusion injury. Retrograde cerebral perfusion time was 48± 16 minutes (range 20-80 minutes). Perfusion flow was 288±93 mL/min (range 150-500 mL/min). Since retrograde cerebral perfusion requires no arterial cannulation or aortic cross clamp, the operative field is simplified, and the risks of air and debris emboli to the brain were minimized. Reconstruction was designed to minimize the circulatory arrest time. Eleven cases underwent emergency surgery due to rupture and acute dissection. Five patients (19.2%) died (three from bleeding from the distal

Recieved for publication: February 26, 1997

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anastomosis, one from postoperative DIC and, one from intraoperative dissection). The remaining 21 patients survived neurologically intact. Retrograde cerebral perfusion with pharmacological cerebral protection is a very simple method to prevent air embolism or thromboembolism in aortic arch aneurysm surgery and allows aortic arch replacement in a bloodless field. In spite of the extended circulatory arrest time, recovery of consciousness was complete.

## INTRODUCTION

Circulatory arrest and profound hypothermia have frequently been used for aortic arch surgery. This method does not necessitate carotid or brachiocephalic cannulation, and can be applied easily after typical cardiopulmonary bypass. With this technique, open bloodless replacement of the aortic arch without cross clamping is possible. However, the safe period of circulatory arrest has not been well established in adults. Previous reports have shown that cerebral ischemic time greater than 45 minutes is associated with an increased risk of stroke. Morbidity and mortality increase significantly when circulatory arrest time exceeds 60 minutes [1]. Since 1990 we have caried out retrograde cerebral perfusion (RCP) during surgery to repair twenty six cases of aneurysm of the aortic arch. In this report, the results of this method are assessed.

## PATIENTS AND METHODS

Betweeen November 1990 and September 1994, 26 patients (12 male and 14 female) underwent resection and graft replacement of proximal arch, transverse arch, and distal arch aneurysms using RCP with pharmacological cerebral protection. Ages ranged from 28 to 78 years, with a mean age of 62.0 years. Arch aneurysms included the proximal arch in 5, the transverse arch in 2, and the distal arch (2 ruptured) in 8 patients. Stanford type A dissection was present in 11 patients (acute in 9, chronic in 2). Emergency surgery was performed in 11 patients (Table I).

Table I. Sites of aortic arch aneurysm.
DIC: disseminated intravascular coagulation.

| | type of aneurysm | case | surgical death | cause of death |
|---|---|---|---|---|
| TRUE | ascending arch | 5 (1) | 0 | |
| | transverse arch | 2 (o) | 1 | bleeding |
| | distal arch | 8 (2) | 3 | bleeding, dissection, DIC |
| Dissection | acute type A | 9 (o) | 1 | bleeding |
| | chronic type A | 2 (o) | 0 | |
| | | 26 (3) | 5 (19.2%) | |

*Techniques and principles*

Nineteen patients were in the supine position while 7 patients were placed in a 45° left lateral position. Tympanic and rectal temperatures were monitored. Arterial cannulation was accomplished through the ascending aorta or left femoral artery. The right atrium was cannulated with two venous cannulae. Cardiopulmonary bypass was initiated at the same time core cooling was begun.

Prostaglandin E1 (0.5 g/kg), methylpredonisolone 30 mg/kg, and thiopental 5 mg/kg were administered intravenously for cerebral protection. The body temperature was reduced gradually to 20℃ (rectal temperature). The heart was arrested 5 minutes prior to circulatory arrest by aortic cross clamping and antegrade or retrograde blood cardioplegia with topical cooling. Pump perfusion was then discontinued to achieve circulatory arrest. Both the right atrial cannulae were clamped, and perfusion was slowly restarted until the central venous pressure was 15 mmHg. The bypass circulation was then opened and RCP (oxygenated, at a rate of 150-500 mL/min and blood temperature of 20℃) through the superior vena cava cannula was instituted. D-Mannitol (300 mL) and deferoxamine mesylate (radical scavengers) 30 mg/kg were administered to prevent brain edema caused by reperfusion injury (Fig. 1)

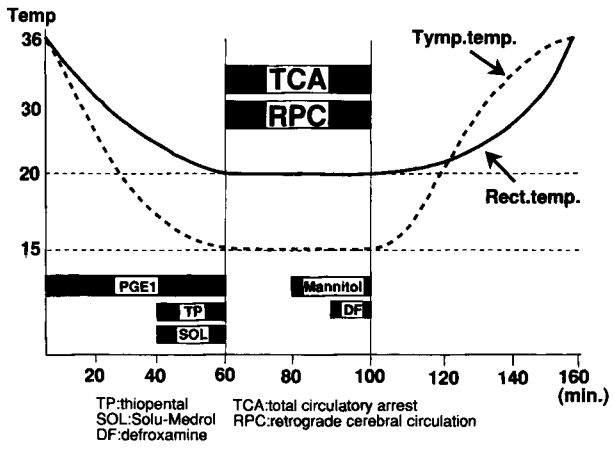


Fig. 1. Rectal and tympanic temperature monitoring and pharmacological cerebral protection with Prostaglandin E1, thiopental, D-mannitol, and deferoxamine mesylate.

*Reconstructive procedure*

1) Replacement of the proximal arch: Arterial perfusion and core cooling were carried out via the femoral artery. Circulatory arrest was induced and RCP was initiated, and the aneurysm was incised obliquely from the origin of the brachiocephalic artery to the inside of the aortic arch. The distal side of the graft was anastomosed. Air and small thrombi in the graft were completely evacuated and the proximal side of the graft was clamped. Retrograde cerebral perfusion was stopped and the typical cardiopulmonary bypass with rewarming was reinstituted. During the rewarming, the proximal side of the graft was anastomosed. Throughout the operation, aortic cross clamping was not necessary (Fig. 2).

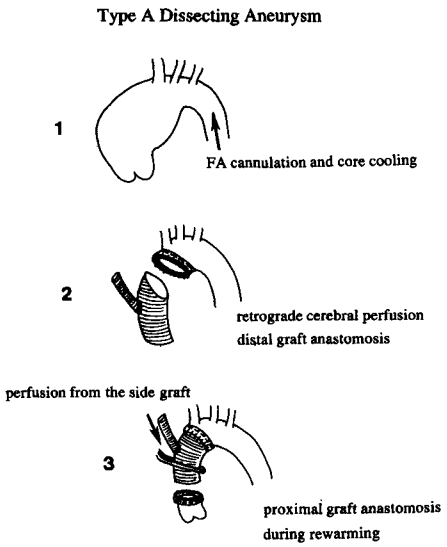


Fig. 2. Reconstruction of proximal arch aneurysm. FA: femoral artery.

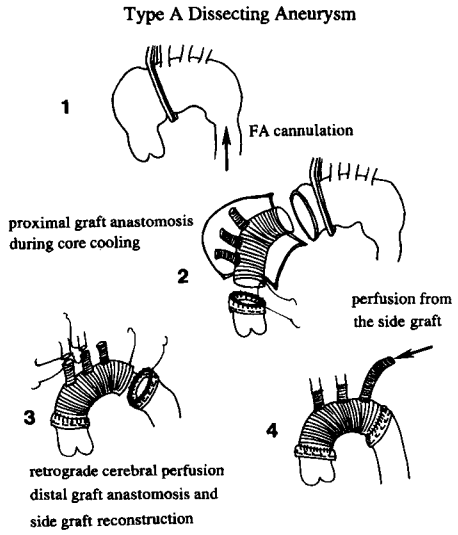


Fig. 3. Reconstruction of transverse arch aneurysm. FA: femoral artery.

2) Replacement of the transverse arch: Arterial perfusion and core cooling were carried out via the femoral artery. During core cooling, the ascending aorta was cross clamped and proximal anastomosis of the graft was performed. When the rectal temperature reached 20℃, circulatory arrest and RCP were initiated. The brachiocephalic and carotid arteries and the distal side of the graft were anastomosed and the RCP was stopped. A clamp was placed between the left carotid graft and the branch grafts. Air and small debris were evacuated

completely through branch grafts by femoral perfusion. Arterial perfusion from the side graft was started to prevent residual atheromatous plaque from flowing to the cerebral vessels. After cardiopulmonary bypass ceased, reconstruction of the left subclavian artery was performed (Fig. 3).

3) Replacement of the distal arch: Arterial perfusion and core cooling were carried out via the ascending aorta. When the rectal temperature reached 20℃, circulatory arrest and RCP were initiated. The aortic arch was transected completely and proximal anastomosis was performed. Air and small thrombi in the graft were completely evacuated, and the distal side of the graft was clamped. At this time, RCP was stopped and separate extracorporeal perfusion via the ascending aorta and femoral artery was reinstituted. The distal anastomosis was completed during rewarming. In this procedure, median sternotomy plus anterolateral thoracotomy was necessary. Long-term respiratory support was necessary in three patients due to pulmonary bleeding or phrenic nerve paralysis. Recently, we have changed the surgical procedure. First, distal anastomosis is performed, followed by proximal anastomosis during retrograde cerebral perfusion. This can be accomplished through a median sternotomy, and no aortic cross clamp is necessary. Pulmonary complications are thus significantly decreased (Fig. 4).

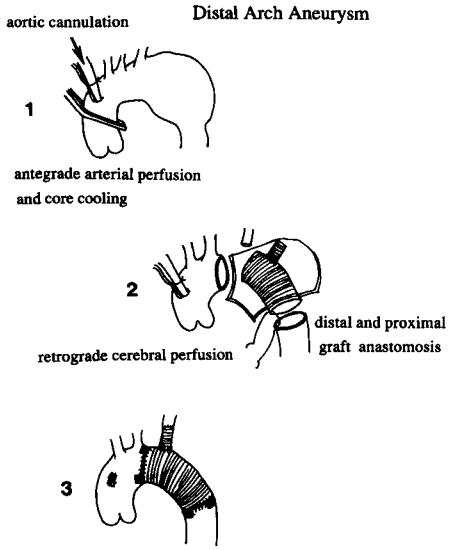


Fig. 4. Reconstruction of distal arch aneurysm.

## RESULTS

Surgical procedure and mortality: Ascending arch replacement (n=3), Cabrol's operation plus brachiocephalic reconstruction (n=1), ascending aorta replacement (n=8), ascending arch patch plasty (n=2 including 1 ruptured case), transverse arch replacement (n=4), distal arch replacement (n=7), and patch plasty of the distal arch (n=1: ruptured case) were performed. In six of nine of the type A dissecting aneurysms, the intimal tear extended into the aortic arch. Five patients (19.2%) died (three from bleeding from the distal anastomosis, one from postoperative DIC, and one from intraoperative dissection). The remaining 21 patients (80.8%) who survived were neurologically intact. Median pump time was 276±108 minutes (range 151-548 minutes). The mean retrograde perfusion time was 48±16 minutes (range 20-80 minutes). Despite the fact that RCP time exceeded 60 minutes in six patients, four recovered completely (Table II).

Table II. Results of aortic arch aneurysm surgery with more than 60 minutes of retrograde cerebral perfusi.

| age | sex | procedure | RCP ( min) | consciousness | results |
|---|---|---|---|---|---|
| 61 | M | distal arch replace | 64 | | dead : intraope dissection |
| 71 | M | distal arch patch | 73 | clear | alive |
| 68 | M | distal arch replace | 80 | | dead : bleeding |
| 78 | F | distal arch replace | 70 | clear | alive |
| 35 | M | asc Ao replace | 64 | clear | alive |
| 76 | F | asc Ao replace | 65 | clear | alive |

RCP: retrograde cerebral perfusion; Ao:aorta.

Table III. Hemodynamics during retrograde cerebral perfusion.

| | Range | mean±SD |
|---|---|---|
| CPB Time(min) | 151-548 | 276±108 |
| RCP Time(min) | 20-80 | 48±16 |
| CP Flow(ml/min) | 150-500 | 288±93 |
| CVP(mmHg) | 15-31 | 21±5 |
| Rect Temp℃ | 18.4-24.2 | 20.5±2.2 |
| Tympanic Temp℃ | 15.4-19.7 | 17.8±2.1 |

CPB, cardiopulmonary bypass. RCP, retrograde cerebral perfusion.
CP, cerebral perfusion. CVP, central venous pressure.
Rect, rectal.

The remaining two patient died of intraoperative bleeding. In twenty patients excluding the 5 surgical deaths and one accompanying carotid artery dissection, the duration of recovery of consciousness and intubation was a mean 10.4±5.3 hours (range 4-20 hours), and mean 42.2±21.3 hours (range 12-72 hours), respectively. Recovery of consciousness was defined as the time when the patient could answer questions completely using facial expression and hand gestures. The mean RCP flow from the superior vena cava cannula was 288±93 mL/min (range 150-500 mL/min). The maximal central venous pressure (CVP) during RCP was 21±5 mmHg (range 15-31 mmHg). The mean rectal temperature during RCP was 20.5 ±2.2℃ (range 18.4-24.2℃), and mean tympanic temperature was 17.8 ±2.1℃ (range 15.4-19.7℃) (Table III).

## DISCUSSION

Profound hypothermia associated with circulatory arrest is a frequently used method of cerebral protection during surgery on the aortic arch. It necessitates no special equipment, and no cannulation of arteriosclerotic brachiocephalic and carotid arteries. With this technique, open bloodless replacement of the aortic arch without cross clamping is possible. However, this technique allows only a limited time to perform the aortic repair. O'Connor and associates have reported that one hour of circulatory arrest under profound hypothermia produced no detectable neurological changes or histological evidence of cerebral hypoxia [2]. However, this is not completely safe, and may lead to severe transient or permanent neurologic disorders, especially in elderly patients. Svensson et al. have reported that in deep hypothermia with circulatory arrest, stroke risk was increased after 40 minutes of circulatory arrest. Mortality was increased markedly after 65 minutes of circulatory arrest [3]. Fessatidis and colleagues have reported that microscopic cellular damage was seen in all animals after circulatory arrest of longer than 70 minutes [4]. These changes involved mainly the Purkinje cells, particularly in the inferior half of the cerebellum. They concluded that the cerebellar region is the most sensitve to ischemia, and that the circulatory arrest time should not exceed 70 minutes.

Retrograde cerebral perfusion was originally used for evacuation of cerebral air emboli in extracorporeal circulation [5]. In 1987, Ueda and associates first

applied this technique to aortic arch surgery [6]. As RCP (deep hypothermia plus venoarterial cerebral perfusion) needs no arterial cannulation and aortic cross clamp, the operative field is simplified, and the risk of air and debris emboli to the brain is minimized. Another advantage of this method is that only the typical cardiopulmonary circuit is required in any circumstances, with no need for dissection, cannulation, or clamping of the cerebral vessels. Imamaki has reported that 90-minute circulatory arrest was possible using RCP at a rate of 250-300 mL/min of perfusion flow at 20℃ rectal temperature [7]. In our series, recovery of consciousness was complete in the 21 surviving patients. In two patients who had RCP times longer than 70 minutes, recovery of consciousness was also complete. During RCP about 20% of the superior vena cava perfusate was returned through the aorta. The rest drained from the inferior vena cava. Vascular resistance between the superior vena cava and inferior vena cava is lower than that between the superior vena cava and the aorta. This suggests that there are veno-venous shunts between the superior vena cava system and the inferior vena cava system [8]. However, the temperature of the brain was maintained at 20℃, and metabolic products were eliminated by RCP. During circulatory arrest, the blood cells form microaggregates, which may be the genesis of cerebral injury. RCP reduces blood cell microaggregation and may reduce cerebral injury, it may also reduce ischemic damage to the brain during circulatory arrest and extended circulatory arrest time, although there are time limitations.

*Pharmacological cerebral protection*

Liversay and co-workers have reported that vasoconstriction was induced during rapid cooling [9]. Tanaka et al. have reported that after core cooling at a constant perfusion flow rate, cerebral blood flow was significantly reduced because of an increase in the cerebral vascular resistance [10]. Prostaglandin E1 has several effects that result in improvement in the microcirculation. Prevention of blood cell sludging, dilatation of microvessels, prevention of spasms, inhibition of platelet agglutination, and membrane stabilization are provided by prostaglandin E1. We also used a barbiturate, D-mannitol and deferoxamine mesylate (a radical scavenger) to prevent brain edema caused by reperfusion injury. Reperfusion damage may be followed by massive tissue

swelling and secondary compromise of circulation. Such damage may be due to the resupply of water and osmotic equivalents (which exacerbates edema) or of oxygen (which triggers production of injurious free radicals) [11]. Barbiturates (Isozol: thiamylal sodium) have many proven effects for cerebral protection: decreased metabolic demand, decreased vasoconstriction, stabilization of lysosomal membranes, and supression of free radical reactions [12]. Abiko et al. have reported that phenytoin has protective effects against cerebral ischemia which are most remarkable when it is administered together with radical scavengers such as D-mannitol and vitamin E [13]. Yoshimura et al. have reported that prominent brain edema occurred just after resumption of cardiopulmonary bypass followed by 120 minutes of RCP at 20℃ in dogs. However, administration of mannitol before reperfusion significantly prevented brain edema [14]. Brain injury after circulatory arrest for more than 60 minutes is thus caused not only by ischemic changes but also by reperfusion injury [15]. Radical scavengers such as D-mannitol and deferoxamine mesylate are effective for pharmacological cerebral protection. In our series, there was no control group for comparison, so that we could not prove the effectiveness of these medications. However, 21 of 26 patients who survived were neurologically intact, and moreover, four patients in whom RCP exceeded 60 minutes of RCP also recovered completely.

In conclusion, RCP with pharmacological cerebral protection was very useful in preventing cerebral injury during repair of aortic arch aneurysms.

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