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Invited Review / *Davetli Derleme*

Antegrade cerebral perfusion: A review of its current application

Antegrad beyin perfüzyonu: Güncel uygulama hakkında derleme

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ABSTRACT

The technique of antegrade cerebral perfusion has been adopted by many aortic surgery centers as the routine method of brain protection with some variations in its implementation. These variations stem from the issues with regard to the perfusion pressure, flow, temperature, pH management, hematocrit value, cannulation sites, and unilateral versus bilateral application. In this review, the prespecified issues were discussed and some recommendations about the implementation of antegrade cerebral perfusion were given.

Keywords: Aortic surgery, antegrade cerebral perfusion, cerebral protection.

ÖZ

Antegrad beyin perfüzyon tekniği pek çok aort cerrahisi merkezi tarafından rutin beyin korunma yöntemi olarak kabul görmüş olup, uygulanmasında bazı farklılıklar vardır. Bu farklılıklar perfüzyon basıncı, akım, sıcaklık, pH idaresi, hematokrit değeri, kanülasyon yerleri, tek veya çift taraflı uygulama gibi değişkenlerden kaynaklanmaktadır. Bu derlemede, belirtilen bu değişkenler hakkında bilgiler verildi ve antegrad beyin perfüzyonunun uygulanmasına ilişkin bazı öneriler sunuldu.

Anahtar sözcükler: Aort cerrahisi, antegrad beyin perfüzyonu, beyin korunması.

Since its first introduction in relatively large series of arch replacement procedures by Kazui et al.,[1] and Bachet et al.,[2] the technique of antegrade cerebral perfusion (ACP) has been adopted by many aortic centers as the routine method of brain protection with some variations in its implementation stemming from perfusion pressure, flow, temperature, pH management, hematocrit value, cannulation sites, and unilateral versus bilateral application. In this review, these issues were discussed and some recommendations about the implementation of ACP were given.

Basic Science

Human brain weighs about 1,500 g and uses 15% of the total metabolic energy. This demand can be supplied by an average blood flow of 50 mL (3 mLO^2) per 100 g of brain tissue per min. The mechanism of blood flow changes (with the adjustment of cerebral vascular resistance) according to the metabolic need is called autoregulation, and this safety feature can maintain adequate blood flow in a wide range of perfusion pressures (mean: 50 to 130 mmHg).[3] Autoregulation may be lost in deep hypothermia, resulting in a 'luxury' perfusion of the brain with a risk of increased intracerebral pressures and cerebral edema.[4]

Animal studies

The porcine model was mostly used to address the issues related to the aforementioned variables. Halstead et al.[5] reported that alpha-stat management for ACP provided more effective metabolic suppression and better preservation of cerebral autoregulation than pH-stat. In another study, these authors also suggested that selective cerebral perfusion (20°C) at 50 mmHg provided neuroprotection superior to those at higher pressures.[6] In a study comparing hypothermic ACP

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Table 1. Some of the clinical applications of antegrade cerebral perfusion at moderate hypothermia

Authors	Year	Flow (mL/kg/min) * L/min	Pressure (mmHg)	Temperature (°C)	Perfusate (°C)
Zierer et al.[8]	2012	1.6±0.4 *	75-85†	28-32	28
Misfeld et al.[9]	2013	8-12	40-60	23-28	#
Kazui[10]	2013	10	40	25	#
Preventza et al.[12]	2015	10-15	60-70	22-24	22-24
Urbanski et al.[11]	2020	1.4±0.3*	90	31	28
Angleitner et al.[13]	2020	10-15	50-60	20-28	#
Norton et al.[14]	2020	10	50-70	24-28	18-22

† Arterial cannula pressure; # Not specified, but the temperature of the cerebral perfusate was reported to be similar to the core temperature in the majority of studies.

with low (20%) and high (30%) hematocrit groups, both groups had equivalent cerebral metabolic suppression, while the low hematocrit group had higher cerebral blood flow which may be injurious possibly due to an embolic load.[7]

Clinical studies

Pressure, flow, temperature

Clinical applications of ACP at moderate hypothermia with different variations in flow, pressure, and temperature have been reported. Some of them are summarized in Table 1.[8-14] Accordingly, in series with warmer temperatures, the flow and pressure were kept higher.

In most of the studies, the flow rates of ACP are the same for unilateral or bilateral applications. One should consider these flow rates as the total blood supply to the brain delivered either one or more sources.

Unilateral versus bilateral ACP

There are numerous clinical studies and meta-analyses comparing the outcomes of unilateral and bilateral ACP.[12-16] They found similar mortality and neurological event rates. However, the outcome measures such as mortality and stroke are multifactorial, particularly in the setting of emergent operations for acute dissections and cannot be attributed to the type of ACP implementation. In general, the preference of bilateral application has been based upon factors, such as predicted long periods of ACP (>40 to 50 min), decrease in near infrared spectroscopy (NIRS) values, and incomplete circle of Willis.[13,16]

Cannulation sites

The right subclavian, innominate, carotid and brachial arteries have been used for cannulation either directly or through a side graft.[8-14,17-19] The advantages and risks are briefly shown in Table 2. Arch grafts, either straight or multibranched, can be cannulated either directly or through a side arm for ACP.

Left subclavian artery perfusion/occlusion-when?

The left subclavian artery can be kept cross-clamped during ACP to prevent back-bleeding or to monitor left radial artery pressure as an indirect indicator of sufficient cerebral cross-perfusion.[11] In cases of an occluded right vertebral artery, dominant left vertebral artery or lack of adequate intracranial communication, additional left subclavian artery perfusion can be used, as described by Kazui[10]

Table 2. Cannulation sites for antegrade cerebral perfusion

Arterial site	Ease of exposure	Cannula insertion	Risks/limitations
Right brachial	+++	Direct	High line pressure, limited flow in high BMI?
Right subclavian	+	Direct, via graft	Brachial plexus injury
Innominate, right/left carotid	++	Direct, via graft, balloon-tipped catheter	Cerebral embolization

BMI: Body mass index.

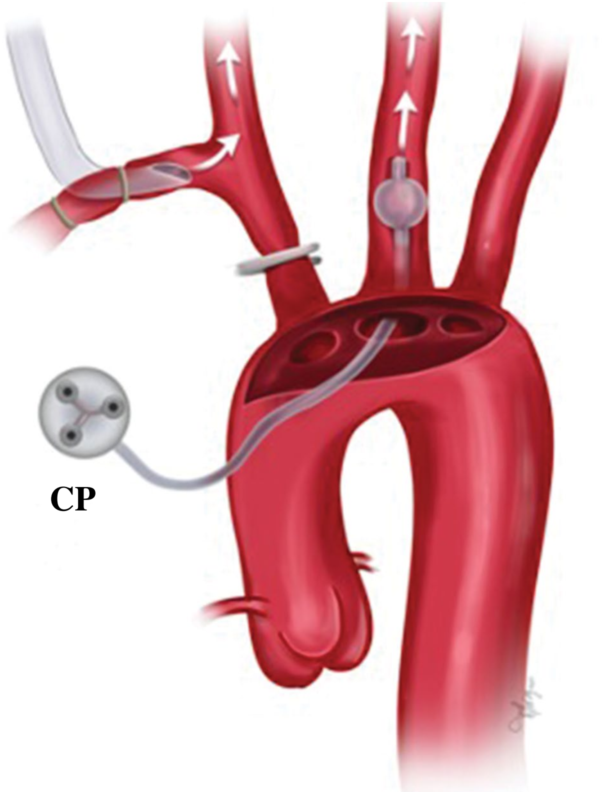

Figure 1. Illustration of the method of antegrade cerebral perfusion. Main pump flow is delivered to the brain for unilateral perfusion through a cannula in the right subclavian artery while the base of the innominate artery is clamped. If bilateral cerebral perfusion is required, the left carotid artery can be perfused through a balloon-tipped catheter connected to the cardioplegia pump head.
CP: Cardioplegia pump.

Lower body ischemia

In a comparison of two groups of 92 patients with ACP and lower body ischemia of more than 60 min, the rate of paraplegia was 18% at a body temperature of 25 to 28°C, while it was 0% at 20 to 24°C.[20] Although the difference was not statistically significant, it raises concern about spinal cord ischemia at higher temperatures. Distal perfusion during aortic arch surgery has been shown to reduce the incidence of end-organ complications, particularly in more extensive and time-consuming procedures.[21] Etz et al.[22] reported that ACP without distal aortic perfusion longer than 90 min at 28°C was associated with an increased risk of paraplegia in a pig model. Therefore, it is reasonable to perfuse the distal aorta by constructing the descending aortic anastomosis at an earlier stage of a prolonged ACP.

Our current ACP application

We use the right subclavian artery for unilateral ACP with a flow of 10 mL/kg/min at 24°C to maintain a pressure of 50 mmHg. If bilateral ACP is required, we perfuse the left carotid artery using the cardioplegia pump head and a balloon-tipped catheter (Figure 1).

Conclusion

The use of ACP is on the rise as in a report from the International Registry of Acute Aortic Dissections (IRAD) database.[23] In a study from the Society of Thoracic Surgeons (STS) database including more than 7,000 acute type A aortic dissection repairs, Ghoreishi et al.[24] reported that circulatory arrest was performed without cerebral perfusion in 29% of the patients. Among those patients in whom cerebral perfusion was used (71%), two-thirds received ACP. Of note, comparison of the outcomes after hypothermic circulatory arrest-alone versus ACP is beyond the scope of this report.

In conclusion, there are limited number of animal studies and numerous relatively large retrospective

Table 3. Suggested ACP variables at different temperatures based on current clinical applications

	Temperature (°C)		
	20-24	24-28	28-32
Flow (mL/kg/min)	8-10	10-12	12-15
Pressure (mmHg)	40-50	50-70	70-80
pH management		Alpha stat	
Hematocrit (%)		20-30	
Prolonged ACP			
- Lower body		Consider early reperfusion	
- Uni/bilateral	Consider	Bilateral	Perfusion

ACP: Antegrade cerebral perfusion.

case series and a few meta-analyses investigating the safe limits of ACP. Some of these studies are covered in this article to give recommendations for safe implementation of ACP (Table 3). Since the results with the current applications are quite satisfactory, there may be no urgent need for a prospective, randomized trial to obtain solid evidence in the near future.

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