DeBakey reported the first series of 138 aortic arch replacements using selective cerebral perfusion in 1962 (1). Primarily two methods for cerebral perfusion were utilized: the first, a constructed passive shunt from the ascending to descending aorta with limbs for carotid artery perfusion and the second, use of cardiopulmonary bypass (CPB) and bilateral normothermic carotid artery perfusion. Although encouraged by some success, the overall mortality was 22% with the stroke rate not reported. The first description of antegrade cerebral perfusion from the axillary artery was reported by Panday et al. (2), whereby a pre-emptive right subclavian to left carotid bypass allowed right axillary perfusion to circulate to the brain and femoral artery cannulation to the corpus during aortic arch replacement - a clever technique that avoids cannulation of the brachiocephalic vessels. Frist and associates (3) published a series by the Stanford group of ten patients operated on using a combination of low-flow CPB and moderate (25-28 °C) hypothermic selective antegrade cerebral perfusion (SACP); mortality was 30%, but no patients suffered a stroke. Other early champions of hypothermic selective antegrade cerebral perfusion included Matsuda, Kazui and Bachet. Matsuda et al. (4) used deep hypothermia (16-20 °C) and SACP in 34 patients with 3 deaths and one stroke. Kazui et al. demonstrated a technique for arch replacement with branched grafts using hypothermic SACP at 25 °C with 9.1% early mortality and no strokes in 11 patients (5). This remains to be one of the most widely practiced techniques today. Bachet et al. reported a series of 54 aortic arch reconstructions using deep hypothermic SACP (6-12 °C) and moderate systemic hypothermia with outstanding results; a temporary neurological dysfunction (TND) rate of 3.7%, stroke rate of 1.8%, and mortality of 13% (6). This method originally described by Guilmet (7) was termed “cold cerebroplegia”. Finally, Dr. Kouchoukos published a series of extensive thoracic aortic aneurysm resections utilizing the “arch first” technique with limit circulatory arrest to the brain, right axillary artery perfusion and excellent neurological outcomes (8).

As clinical use of SACP increased, refinement of the formulation was increasingly necessary. Examination of experimental work in perfusion pressure, flow, temperature,
pH management, and hematocrit helped define safe parameters for delivery of SACP. In terms of unilateral versus bilateral cerebral perfusion, the right brachial or axillary artery, the common carotid artery, or the direct cannulation of the brachiocephalic vessel all demonstrate efficacy when delivered within safe parameters. Lastly, whilst the brain is being perfused, one must not forget about the lower body, particularly the ischemic tolerance of the spinal cord.

The optimal pressure for the delivery of hypothermic SACP in the porcine model was described by Halstead et al. (9) and Haldenwang et al. (10). Dividing experimental animals into three groups with SACP delivered at 50, 70 and 90 mmHg at 20 °C, a pattern of increasing cerebral blood flow with increasing pressure led initially to similar cerebral metabolic suppression, but an elevated metabolic rate in the post-CPB period in the 90 mmHg group. An accompanying rise in intracranial pressure (ICP) throughout the SACP interval led to inferior neurobehavioral recovery in the chronic model. As a note of caution when applying these findings clinically, many older patients have chronic hypertension and atherosclerotic cerebrovascular disease, which may affect autoregulation and possibly the uncoupling during hypothermic perfusion. For this reason some investigators focus on cerebral blood flow, preferring to search for the ideal upper and lower limits. For Haldenwang et al. (10), using two groups of animals separated into 8 and 18 mL/kg/min hypothermic SACP, a similar pattern emerged showing equivalent cerebral metabolic suppression. However, the high perfusion pressure group demonstrated increased “luxury” regional blood flow with elevated ICP and sagittal sinus pressure (SSP), markers for poorer cerebral preservation. Two studies defined the lower limit of hypothermic SACP; Tanaka et al. (11), in a canine model, decreased 25 °C SACP from 100% baseline cerebral blood flow (CBF) towards zero, while concurrently evaluating cerebral function with continuous somatosensory evoked potentials (SSEP) monitoring and ultimately histological outcomes. Maintaining CBF at 100% of baseline and decreasing it to 50% revealed no signs of cerebral compromise. However, a decrease in flow to 25% of baseline (mean arterial pressure of 25 mmHg) demonstrated loss of SSEP and mild cellular injury. A recent study by Jonsson et al. (12) using hypothermic (20 °C) SACP, beginning at 8 mL/kg/min and a controlled stepwise reduction to 6, 4 and 2 mL/kg/min, exhibited rising cerebral lactate in magnetic resonance spectroscopy and decreased venous saturations below the 6 mL/kg/min threshold. Clinically, Shimizu et al. (13) directly monitored the flow distribution through three cannulas in the brachiocephalic, left carotid, and left subclavian arteries during hypothermic (<25 °C) SCP. The target pressure at the tip of the cannulas ranged between 30 and 50 mmHg, with flow adjusted accordingly. Total flow rates and flow ratios in the supraaortic vessels were 5.8, 3.3, 3.4 mL/kg/min and 46.5%, 26.5%, and 27.0%, respectively. Total flow in these vessels was significantly lower in patients with adverse neurologic events (732 vs. 806 mL/min). The authors suggest that flow rates >10 mL/kg/min may be necessary when SCP at moderate hypothermia is used.

The success of SACP in total aortic replacement has led to a generalized trend for warmer temperatures by many experienced centers. A study by Khaladj et al. (14) used a porcine model of SACP for 90 minutes at 10, 20 and 30 °C, and compared outcomes to HCA alone. Consistently higher ICP occurred in the 30 °C group during SACP and with reperfusion when compared to baseline and the 20 °C animals. The moderate hypothermia (20 °C) animals showed sufficient cerebral metabolic suppression, and earlier recovery of EEG with significantly less expression of HSP-72 (heat shock protein 72 kDa). A recent study by Numata et al., suggests that as compared to colder temperatures, SCP at ≥28 °C results in low mortality and incidence of permanent neurologic injury (6.1%) without compromising end-organ function (15).

Controversy persists over the pH management of hypothermic SACP. Some studies in children suggest a benefit of pH-stat over alpha-stat, but this is unsubstantiated in adults. Halstead et al. (16), comparing strategies in a porcine model, found that alpha-stat animals exhibited better suppression of cerebral metabolic rate of oxygen (CMRO2), with lower cerebral blood flow and improved early neurobehavioral recovery. Dr. Kazui’s group examined the effect of old cerebral infarct during hypothermic SACP (17). A rise of serum lactate, VADL, and glutamate all indicate additional ischemia of the chronic penumbra of the old cerebral injury. This area relies on collateral circulation with disturbed autoregulation and possible pressure/flow dependency. Elevated serum glutamate is associated with early neurologic deterioration after acute ischemic stroke (18). Ohkura et al. (19), using the same cerebral infarction model, demonstrated the attenuation of chronic ischemia of the infarct penumbra using pH-stat management during hypothermic SACP. pH-stat management may provide better protection against cerebral
ischemia after previous stroke when compared to alpha-stat. These results should be interpreted with caution as patients with old CVAs from atherosclerotic cerebrovascular disease may not have normal CO₂ reactivity.

Experimental animal studies comparing low hematocrit (20%) and high hematocrit (30%) hypothermic SACP suggest a benefit to the higher group (20). The 20% group produces higher cerebral blood flow during SACP with equivalent levels of cerebral metabolic suppression, once again demonstrating “luxury” perfusion and the possible attendant increased embolic load. Intracranial pressure showed a trend towards lower values in the high hematocrit animals with better and earlier neurobehavorial recovery.

The delivery of SACP can be unilateral or bilateral. The dependence of unilateral perfusion on the integrity of the Circle of Willis (CoW) is debatable. Merkkola and associated (21) performing anatomic autopsies on 98 brains using a 0.5 mm threshold for sufficient arterial diameter determined that 14% of specimens were unsuited for unilateral perfusion due to deficient anterior communicating artery or left posterior communicating artery. CT angiography was recommended for identification of high risk patients needing bilateral SACP. An additional study from Papantchev et al. (22) suggested that up to 42.4% of eastern Europeans have some incomplete anatomic variation of the Circle of Willis affecting the use of unilateral SACP. Besides pre-operative CT angiography, the authors suggest the use of near infrared spectroscopy (NIRS), transcranial Doppler (TCD), and EEG to assess cerebral perfusion.

The importance of the secondary collateral vessels, such as the ophthalmic artery, leptomeningeal vessels and external carotid arteries, may be underestimated. Urbanski and associates (23) published a series of 99 patients with unilateral left common carotid SACP at 30 °C, with only one CVA. The average perfusion time was 18 min but pre-operative CT angiography documented complete CoW in only 60% of patients. All the patients received TCD, EEG, SSEP, and bilateral radial arterial lines. The authors discounted the need for pre-operative CT angiography of the CoW and emphasized the role of extracranial collaterals. Leshnower et al. (24) corroborated the clinical findings with a series of 412 patients undergoing a combination of hemiarch and total arch procedures with unilateral hypothermic SACP at 26 °C for up to 45 minutes, with a stroke rate of 3.6%. In a follow-up manuscript, Urbanski et al. (25) documented the outstanding results of 347 patients (77 total arch replacements) using unilateral SACP at 28 °C for an average of 34 minutes via the left or right common carotid arteries or innominate artery; the overall stroke rate was 0.9% and TND rate of 2.3%. For shorter intervals of SCP (<40 min), Lu et al. (26) confirmed the non-inferiority of unilateral hypothermic (16-20 °C) SCP as compared to bilateral SCP. In the largest series to date, of 1,002 patients, Zierer and colleagues (27) compared unilateral vs. bilateral SCP combined with mild hypothermia (28-30 °C) and found no difference in TND, PND or risk to the lower body. This included 318 total arch replacements with SCP performed for 36±19 minutes (range, 9-135 minutes). A trend was seen towards reduced PND rate with unilateral SCP (2%) vs. bilateral SCP (4%). Nonetheless, concern remains when the duration of SACP is longer than 50 minutes as is necessary for some techniques of total aortic arch replacement. Krahenbuhl et al. (28) followed 292 patients after aortic arch surgery with a combination of deep hypothermic circulatory arrest (DHCA), and unilateral or bilateral cerebral perfusion. Using the SF-36 health survey questionnaire, mid-term follow-up indicated better quality of life in patients with SACP times greater than 40 minutes treated with bilateral SACP. Review of 17 manuscripts involving 3,548 patients by Malvindi et al. (29), using a threshold neurological injury rates of <5%, found 599 patients treated with unilateral SACP for less than 50 minutes and 2,949 patients perfused with bilateral SACP for more than 86 minutes. They recommend the use of bilateral hypothermic SACP if the anticipated interval will be >50 minutes.

A consequence of performing aortic arch repair at warmer temperatures is the vulnerability of the viscera, and in particular, the spinal cord. In the past, using deep hypothermia, and with little knowledge of the spinal cord’s tolerance to ischemia, one could be relatively certain that the interval necessary for aortic arch replacement and the “elephant trunk” procedure would produce no significant spinal injury. A study by Kamiya et al. (30) divided aortic arch patients into two groups based on deep versus moderate hypothermic lower body ischemia. The overall paraplegia rate was 2.1% (8/373) patients. A subgroup analysis of 11 patients with lower body circulatory arrest >60 minutes at moderate temperatures (25-28 °C) showed 2 cases of paraplegia (18.2%). An elegant study by Etz et al. (31), using a porcine model for SACP at 28 °C for 90 and 120 minutes with fluorescent microspheres, determined spinal cord blood flow. After the initiation of SACP, blood flow was nearly absent below the T4-T13 region. Recovered animals showed evidence of paraparesis/paraplegia in both time
intervals, but was more severe in the 120-minute group. Histological specimens demonstrated moderate to severe ischemic lumbar spinal cord damage even in the animals that regained normal function. The severity increased distally and in the 120-minute SACP group. As such, the margin of safety may not be as great as has been widely assumed.

After a review of clinical application and experimental strategy, the following recommendations for the use of non-pulsatile SACP are proposed: perfusion pressure should remain between 40 to 60 mmHg, with a detrimental effect at higher pressures; flow rates ranging from 6 to 10 mL/kg/min depending on the selection of temperature, with higher flows unnecessary; core cooling to between 18 to 30 ºC, contingent on the duration of lower body circulatory arrest and the ability to institute lower body perfusion if the duration is prolonged; SACP temperature delivered within the 20 to 28 ºC range; CPB pH management using alpha-stat; hematocrit between 25% and 30%; NIRS monitoring to detect cannula migration or inadequate perfusion of the left hemisphere with unilateral SACP; and with prolonged unilateral SACP, consider a second cannula for direct support of the contralateral side. Finally, the current warming trend in aortic arch surgery places the spinal cord at risk during SACP. This is probably not an all-or-none phenomenon, with prolonged ischemia injuring some motor neurons that are possibly undetectable on routine clinical exam.

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References


