



# Aortic arch aneurysm surgery: what is the gold standard temperature in the absence of randomized data?

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## Abstract

In the absence randomized data for assessing the best and optimal temperature for managing open aortic arch surgery patients, cerebral protection method is still performed through hypothermic circulatory arrest with or without the use of adjuncts. A recent consensus has emerged setting to define the temperature levels. In an attempt, this was aimed to establish a solid ground for future trials in aortic arch surgery. This article reviews the current literature and the evidences behind using different temperature methods and their outcomes in patients undergoing open aortic arch surgery.

**Keywords** Hypothermia · Aorta · Aneurysm · Aortic arch · Circulatory arrest · Deep hypothermic circulatory arrest · Thoracic aortic surgery

## Introduction

Aortic arch surgery is a complex and technically challenging surgery performed in modern cardiac surgery. It requires a period of hypothermic circulatory arrest to allow neuroprotection, and enable direct visualization of the diseased aortic arch for reconstruction [1]. DeBakey et al. [2], using cardiopulmonary bypass, reported in 1957 their first successful resection and graft replacement of an aneurysm of the aortic arch. In 1975, Griep et al. [3] described a series of four patients who had undergone prosthetic replacement of the aortic arch using a combination of surface cooling and cardiopulmonary bypass to produce total body hypothermia; reporting a mortality of 25%. The surgical outcomes for aortic arch aneurysm repair have evolved significantly over the intervening years, and in most high volume international centres, mortality is less than 10% and stroke risk less than 5% [4].

This has come about through refinements in operative techniques, organ protection strategies, and postoperative care [4].

The advent through coupling hypothermic circulatory arrest with antegrade selective cerebral perfusion (ACP) by Bachet and Kazui in the 1980s [5–7] made this practice robust and safer.

In modern aortic arch surgery, choice of cooling temperature has been supported by multiple observational studies [4]; however, such studies lack high-quality value and are limited with lack of randomized controlled trial data [8–11]. Moreover, DHCA has been challenged with the neuroprotective effects of ACP with core body temperature of up to 35 °C avoiding major complications associated with prolonged cardiopulmonary bypass (CPB) and DHCA [12–14]. Nevertheless, such new concept of mild–moderate hypothermic circulatory arrest (HCA) has been adapted by many aortic surgeons internationally, although it exposes the body organs to prolonged period of ischaemia at higher temperature and potentially causing more harm [15].

## What is the optimal temperature for HCA?

Despite the progress made in the past few decades on the operative fronts to tackle and manage aortic diseases entailing the arch of the aorta, replacement of this portion of the vessel remains a surgical challenge and is associated with

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significant morbidity and mortality due to the circulatory arrest period.

The optimal temperature for DHCA coupled with selective antegrade or retrograde cerebral protection remains debatable and unclear. Deep hypothermia significantly reduces cerebral oxygen requirements; however, the safe duration of DHCA is limited and prolonged periods of DHCA are associated with postoperative neurologic dysfunction and sequelae. In the current evidence, the issue regarding delivery of the neuroprotective perfusate is disengaged from temperature and the focus of neuroprotection depends on multiple factors (1) method of delivery and cannulation, (2) anatomy of the brain circulation, and (3) temperature of hypothermia coupled with adjuncts.

The choice of cooling temperature not only requires insight into delivery or cannulation techniques but also other factors such as complexity of the aortic arch pathology and condition, age, comorbidities, and most importantly surgeon's expertise and preference [16].

Through a wide consensus, the definition of hypothermia level has been identified in aortic arch surgery. This was achieved despite lack of robust evidence. The group classified hypothermia as: profound hypothermia < 14 °C, deep hypothermia 14.1–20.0 °C, moderate hypothermia 20.1–28.0 °C, and mild hypothermia 28.1–34.0 °C. However, it is imperative to invoke that brain oxygen consumption can be reduced to almost 10% at 8 °C [17]; however, complete reduction in brain activities will not be achieved regardless of temperature cooling level [18, 19].

### Deep hypothermic circulatory arrest

The use of deep hypothermic circulatory arrest has been challenged since the introduction of antegrade and retrograde cerebral perfusion (ACP and RCP respectively) as supportive mechanism to extend the degree of neuroprotection with adequate cerebral perfusion [20].

Tian et al. [21] concluded in their systematic review and meta-analysis that ACP as adjunct to DHCA provides a greater operative survival in patients undergoing aortic arch surgeries. Svensson et al. [22] in one of the largest series collecting 1352 aortic arch surgery cases utilizing DHCA in adjunct with selective ACP or RCP, reported a postoperative mortality of 6.1%, and stroke rate of 8.3%. Amongst these patients, there were 32% reoperation and 20% were emergency cases with cooling temperature of minimum 18 °C. Gega et al. [23] subsequently reported a satisfactory neuroprotection rate while using DHCA with a cooling temperature to 16–18 °C. They included a series of 394 patients that underwent complex aortic surgeries, with mortality and stroke rates of 6.3 and 4.8%, respectively.

In 2010, Milewski et al. [24] by enrolling 682 patients undergoing elective proximal aortic surgeries utilizing DHCA with CRP with a cooling temperature of 10–12 °C, observed an operative mortality and permanent neurological deficit rate of 2.8 and 2.8% respectively. In that series, 25% of the cases were reoperations, and the minimum DHCA time was 45 min.

Finally, in 2011, Lima et al. [25] reported operative mortality and postoperative stroke rate of 2.9 and 4.1% in a series of 245 hemi-arch replacements. The minimum temperature was 18 °C; the DCHA time of 50 min with the use of selective ACP in 89% and RCP in 11% of the patients.

With current published single-centre observational studies, the outcomes in such high-risk cohort patients using DHCA appear to be satisfactory taking into consideration that the use of adjuncts allowed the operator more flexibility in time and practice. However, it is unclear to date what is the optimal temperature that needs to be attained to be considered as safe.

### Moderate hypothermic circulatory arrest

Since the introduction of selective cerebral perfusion methods, the concept of optimal temperature management and the use of DHCA only have been questioned. The trend have shifted to using moderate hypothermic circulatory arrest (MHCA) [17], despite the fact that there are no randomized multi-centre concrete data to support the superiority of such technique over DHCA alone. The conclusions in using MHCA are purely based on trials from experienced centres demonstrating the clinical efficacy and safety of such MHCA together with the use of ACP [26–29]. The change in the paradigm from DHCA to MHCA was driven in an attempt to avoiding potential complications related to hypothermia and to shorten the duration of cooling and rewarming on CPB [17]. There are multiple single-centre series which reported on such benefits. In a large meta-analysis of 221 patients by Tian et al. [21], the authors demonstrated that DHCA was associated with longer CPB time ( $154 \pm 62$  vs  $140 \pm 46$  min;  $P=0.008$ ), and higher in-hospital mortality (7.7 vs 0.7%;  $P=0.005$ ), and all-cause mortality at 30 days (9.0 vs 2.1%;  $P=0.008$ ) when compared to MHCA. However, use of MHCA was not associated with increased rate of blood transfusion, re-exploration for bleeding or acute renal injuries. Other studies have compared the use of DHCA and MHCA in aortic arch surgery and reported that such procedures can be performed safely under the use of MHCA [30–32]. In a study by Leshnower et al. [33], they have compared the early outcomes of MHCA vs DHCA in a series of 288 patients affected by acute-type A aortic dissection, of which total arch repair was performed in 9 (11.0%) vs 23 (11.2%) patients of the DHCA vs MHCA groups only,

while hemi-arch repair was performed in 88.9% (256/288) of their patients.

On the contrary, other studies concluded that MHCA is associated with poorer neurological and visceral organ outcomes especially in the presence of prolonged CPB times [34–37]. In a separate study conducted by Gong et al. [38], MHCA was adopted for total aortic arch replacement and frozen elephant trunk under unilateral SCP. The authors concluded that such surgical technique was not associated with an increased risk of operative mortality and morbidity, neurological complications, or impaired visceral functions. HCA under 30 min did not significantly affect the incidence of neurological deficits. Zierer et al. [39] showed a marked reduction in chest drain output, CPB time, and intensive care stay in patients being treated with MHCA technique. However, a major issue with the MHCA technique was the protection of the visceral organs, especially kidneys with consequential high rate acute kidney injury encountered during aortic surgery [30, 34]. As such, a study by Legras et al. [40] showed no difference in postoperative neurological outcomes between patients who underwent repair of type A aortic dissection repair using either MHCA or DHCA and this was re-enforced by a further retrospective propensity-matched study by Kamiya et al. [30]. Similar outcomes were reported by Di Eusanio et al. [41] and Pacini et al. [29]. The meta-analysis by Tian et al. [21] concluded that the choice of MHCA in conjunction with ACP in aortic arch surgery patients significantly lowered the risk of stroke (7.3 vs 12.8%;  $P=0.0007$ ) as compared to DHCA.

Regardless of all the reported outcomes from studies, the evidence is strongly suggestive but not conclusive entirely. It is very perceivable that temperature element remains debatable, despite the use of MHCA with ACP as an alternative option in modern aortic arch aneurysm surgery.

### Lesser degree hypothermic circulatory arrest

While DHCA had been challenged with the introduction of MHCA and ACP, hence, providing similar neurological outcomes, this technique has been challenged further using Mild HCA during aortic arch surgery. Despite the fact that prolonged duration of DHCA holds the risk of neurological complications, especially spinal cord injuries, some authors have proposed the use of higher body temperature aimed at shortening total operation time. In the very first series, Urbanski et al. [12] reported a series of 347 patients undergoing aortic arch surgery (hemi-arch  $n=270$ , total arch  $n=77$ ) with a circulatory arrest time of 18 and 29 min, respectively during moderate–mild HCA. They reported 30-day mortality of 0.9%, permanent neurological complications of 2.3, and 1% of the patients' required postoperative dialysis. Zierer et al. [39] analysed 1002 patients from two major centres in Germany, examining the clinical outcomes

in patients undergoing aortic arch surgery using Mild HCA with ACP. In this study, hemi-arch aortic replacement was performed in 68%. Their ACP time was  $36 \pm 16$  min, and the reported mortality was 5.0%, permanent neurological deficits 3.0%, and dialysis rate 4.0%. Finally, the same group [42] conducted a study of Mild HCA that involved 1097 patients between the years of 2000–2012. They examined the use of unilateral and bilateral ACP in patients undergoing aortic arch surgery with mild HCA and routine ACP. The propensity matched analysis showed no difference between unilateral or bilateral use of ACP for mortality (4.0% in both cases;  $P=0.8$ ) as well as no difference in temporary neurologic deficits (5.0 vs 4.0%;  $P=0.8$ ). Such reports of satisfactory outcomes from the high volume and experienced centres in Germany could potentially set the ground for the future studies to identify the ideal temperature for operation on aortic arch in adult patients in conjunction with the use of ACP. Further future studies should potentially explore these questions [11], possibly contributing to adjourn the current guidelines for use of ACP [43, 44].

### What the future holds for optimal temperature in aortic arch surgery?

In current era with multiple diverse and mostly single-centre experiences of using various temperature methods from mild to deep HCA, there is a lack of high-quality evidence in the literature to support use of any degrees HCA except the DHCA. The majority of the MHCA and mild HCA studies are not considered as high clinical evidences, as there are dramatic technical variabilities among aortic arch surgeons and as such they do not provide a solid base for building a standard protocol for practice [5]. There are many factors that contribute to the analyses of such techniques including systemic temperature, cerebral temperature, method of temperature assessment, cerebral perfusion method (ACP, RCP, selective ACP, unilateral or bilateral ACP), perfusion pressure, circulatory arrest time, complexity of the aortic arch repair, in addition to the routine perioperative patient characteristics that contribute to study limitations. Furthermore, the definitions of postoperative neurologic deficits and perioperative mortality remain widespread; therefore, a more detailed and sensitive measures of neurocognition postoperatively should be in place to assist in measuring outcome for using each temperature method [45].

Only recently, a new technique has evolved in aortic arch surgery through fully avoiding circulatory arrest and its complications. Such technique has been pioneered in Australia and it involves the use of branched aortic arch graft within a branch-first continuous perfusion technique that allows the least perfusion interruption of the critical organs [46–49]. Such technique if proved to be an alternative to DHCA with randomized trials and solid data, it will supersede of what is

described by the Germans for the use of Mild HCA in open aortic arch surgery. However, the technique of no HCA has been extended to use hybrid total aortic arch replacement utilizing endovascular aortic stenting for aneurysm and dissection cases, although this technique is in its early stages; however, it could also provide another arm for managing patients with complex aortic arch diseases in near future [50–54].

## Conclusion

The choice of optimal degree of hypothermia for circulatory arrest in aortic arch surgery remains elusive and non-conclusive. Despite the new surgical techniques and methods for such complex surgery, perioperative mortality and neurological deficits still remain high. Therefore, in the absence of controlled comparative data combined with highly variable surgical techniques with the use of novel methods such as mild HCA or total absence of HCA in aortic arch surgery, the results remain controversial, and hence, a large randomized controlled trial is required to verify such outcomes.

Therefore, based on all the literature findings and until solid data are released from reliable controlled studies, deep hypothermic circulatory arrest remains a proved excellent method for cerebral and critical organ protection during complex aortic arch surgery technique, providing acceptable mortality and postoperative neurological consequences.

## Compliance with ethical standards

**Conflict of interest** There are no conflicts of interest or sources of support.

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