

Practice variations in the conduct of hypothermic circulatory arrest for adult aortic arch repair: focus on an emerging European paradigm

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ABSTRACT

Introduction: Hypothermic circulatory arrest for adult aortic arch repair is still high-risk. Despite decades of clinical experience, significant practice variations exist around the world. These practice variations in hypothermic circulatory arrest may offer multiple opportunities to improve practice. The hypothesis of this study was that the current conduct of adult hypothermic circulatory arrest in Europe has significant variations that might suggest opportunities for risk reduction.

Methods: An adult hypothermic circulatory arrest questionnaire was developed and then administered at thoracic aortic sessions at international conferences during 2010 in Beijing and Milan. The data was collected, abstracted and analyzed.

Results: The majority of the 105 respondents were anesthesiologists based in Europe and China. The typical adult aortic arch repair in Europe was with hypothermic circulatory arrest at moderate hypothermia utilizing bilateral antegrade cerebral perfusion, typically monitored with radial arterial pressure and cerebral oximetry. Brain temperature was frequently measured at distal locations. The preferred neuroprotective agents were steroids, propofol and thiopental.

Conclusions: The opportunities for outcome improvement in this emerging European paradigm of tepid adult aortic arch repair include nasal/tympanic temperature measurement and adoption of unilateral antegrade cerebral perfusion monitored with radial artery pressure and cerebral oximetry. The publication of an evidence-based consensus would enhance these practice-improvement opportunities.

Keywords: aortic arch repair, hypothermic circulatory arrest, China, Europe, temperature monitoring, retrograde cerebral perfusion, antegrade cerebral perfusion, steroids, propofol, neuroprotection, cerebral oximetry, questionnaire, moderate hypothermia.

INTRODUCTION

Hypothermic circulatory arrest (HCA) for adult aortic arch repair has become a standard technique in thoracic aortic surgery (1, 2). First reported in 1975, the HCA technique for adult aortic arch repair has yet to be further determined to achieve an

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optimal conduct (1-4). Three major neuroprotective techniques in HCA for adult aortic arch repair have been championed in the contemporary era: profound hypothermia alone, retrograde cerebral perfusion (RCP), and antegrade cerebral perfusion (ACP). Although profound HCA alone provides excellent neuroprotection in experienced centers, concomitant RCP as part of an integrated protocol for adult aortic arch repair has also been shown to provide effective neuroprotection, especially when HCA times are below (30-45) minutes (5-10). Furthermore, ACP has also become a mainstream cerebral perfusion adjunct during HCA, especially in the setting of prolonged DHCA times beyond (30-45) minutes (11-13). Recent evidence suggests that both ACP techniques, i.e. unilateral and bilateral, can result in equivalent clinical outcomes (11-13). The excellent neuroprotection provided by ACP has led to the emergence of adult aortic arch repair with moderate hypothermic circulatory arrest at temperatures $\geq 25^{\circ}\text{C}$ (14-16).

Given these developments, it is not surprising that significant variations have evolved in the conduct of HCA for adult aortic arch repair around the world (1-18). The current factual base for this specialized technique suffers from a severe lack of high-quality evidence to guide best practice (19). Although our previous work explored the conduct of HCA in China, the aforementioned considerations suggest considerable global variation in the practice of adult HCA (20). As a result, we designed this study with the purpose of evaluating the current practice of aortic arch repair in Europe and Asia to assess practice variations. The study hypothesis was that the contemporary conduct of HCA for adult aortic arch repair varies significantly between European and Asian centers that might offer future opportunities for outcome improvement.

METHODS

A 10-item questionnaire was developed by a consensus process between the senior investigators to assess the conduct of HCA for adult aortic arch repair (please see online supplement for full copy).

The questionnaire was formulated both in English and Chinese. This questionnaire was administered at two recent international conferences: the 12th International Congress of Cardiothoracic and Vascular Anesthesia convened September 2010 in Beijing, China; and, the 4th International Congress on Aortic Surgery and Anesthesia 'How to do it' convened December 2010 in Milan, Italy. The completed questionnaires were collected, abstracted and analyzed in an electronic database. The data were summarized in tabular and graphic formats. The design and focused administration of the questionnaire precluded complex statistical analysis.

No patient or respondent identifiers were collected: participation in this study was voluntary and anonymous. The study was granted expedited approval by the institutional review board at the University of Pennsylvania in Philadelphia, Pennsylvania, United States of America. In view of the observational nature of the study, study consent was waived as well.

RESULTS

There were 105 study respondents from 3 geographic regions (*Table 1*), with the majority based in Europe (40/105: 38.0%) and Asia (50/105: 47.6%). The majority of respondents from Asia were based in China (43/50: 86.0%). The two dominant professions of the study respondents were anesthesiology (71/105: 67.6%) and cardiac surgery (30/105: 28.6%). The volume of aortic arch repairs (*Figure 1*) and the typical HCA

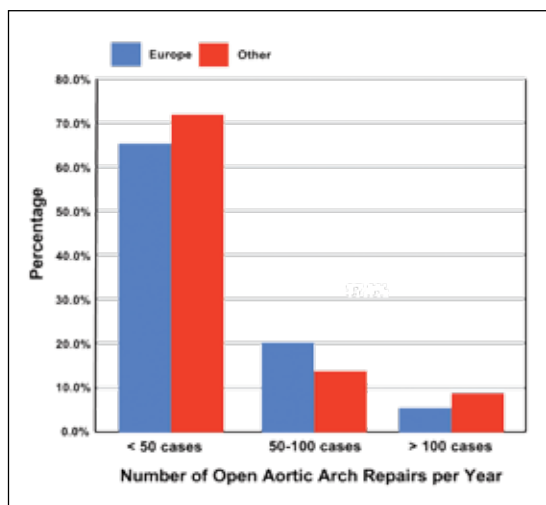
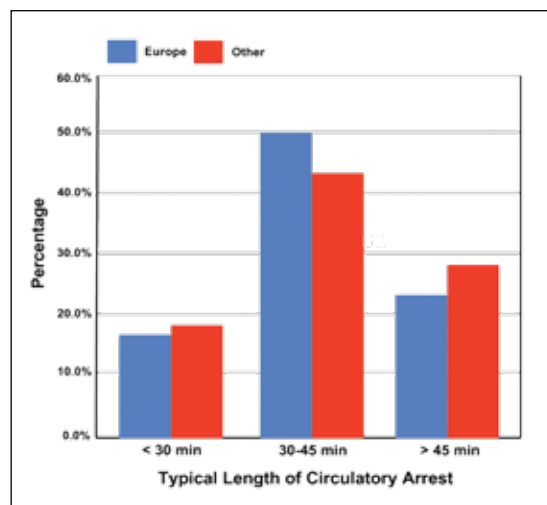
Table 1 - Characteristics of Study Respondents.

Region of Practice	Number of Respondents	Percentage (%)
Europe	40	38.1
Asia (total)	50	47.6
China	43	41.0
Japan	1	0.9
Other Asian nations	6	5.7
North America	15	14.3
United States	7	6.7
Canada	8	7.6
Professions	Number of Respondents	Percentage (%)
Anesthesiologist	71	67.6
Intensivist	2	1.9
Perfusionist	2	1.9
Surgeon	30	28.6

times (*Figure 2*) were similar between European and Non-European centers. A HCA time in excess of 30 minutes was typical for 78.9% of centers in Europe and 76.5% of centers elsewhere. There was a significant difference detected in the level of hypothermia utilized during HCA for adult aortic arch repair (*Figure 3*). Profound hypothermia for arch repair was preferred in the

North American and Asian centers: 85.4% of these centers initiated aortic arch repair at temperatures below 20°C as compared to 35.9% of centers in Europe.

The majority of European centers (64.1%) initiated circulatory arrest at temperatures above 20°C, as compared to elsewhere where moderate hypothermia was uncommon (14.6%).

**Figure 1** - Adult aortic arch repair volume at the surveyed centers.**Figure 2** - Typical circulatory arrest times for adult aortic arch repair.

There was considerable variation in the selection of temperature monitoring sites for assessment of brain hypothermia (*Figure 4*). Nasopharyngeal temperature monitoring was distinctly uncommon for all centers in this study. Although tympanic temperature monitoring was relatively un-

common, there was a trend that this site was preferred in European centers.

There was also considerable variation in the selected end-points for cooling prior to initiation of HCA (*Figure 5*). While greater than 80% of all centers used temperature as a clinical endpoint, cerebral oximetry was utilized in 50% of European centers (compared to 21% of Non-European centers), while electroencephalographic monitoring was used in only 13.2% of European centers but 29% of non-European ones.

Significant variation was detected in the approach to cerebral perfusion during HCA (*Figure 6*). Cerebral perfusion adjuncts for neuroprotection were more prevalent in European centers (92.0% versus 56.0%) with a preference for bilateral ACP (69.2% of European centers). The breakdown was as follows: RCP 12.8% in Europe versus 17.5% outside Europe; unilateral ACP 28.2% versus 34.9% respectively; and, bilateral ACP 69.2% versus 25.4% respectively. The Non-European centers were

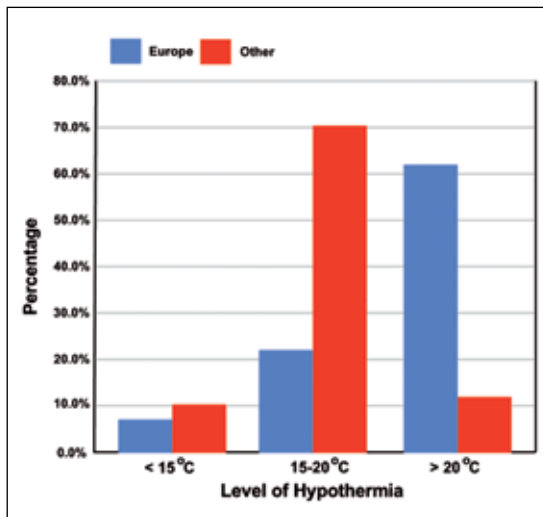


Figure 3 - Typical level of hypothermia during circulatory arrest.

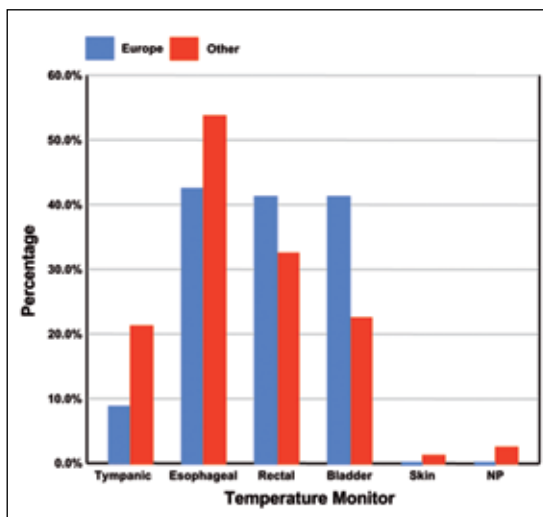


Figure 4 - Location of temperature monitoring during adult aortic arch repair.

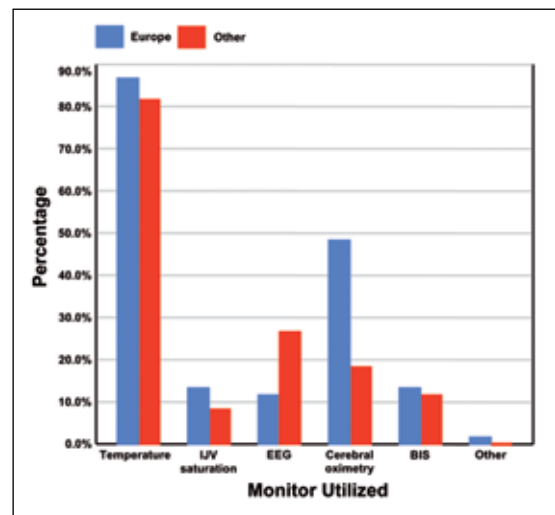


Figure 5 - Clinical endpoints for systemic cooling before initiation of hypothermic circulatory arrest. IJV = Internal Jugular Vein; EEG = Electroencephalography; BIS = Bispectral Index Monitoring.

split more evenly across the 3 modes of cerebral perfusion during HCA: RCP - 17.5%; unilateral ACP - 34.9%; and, and bilateral ACP - 25.4%.

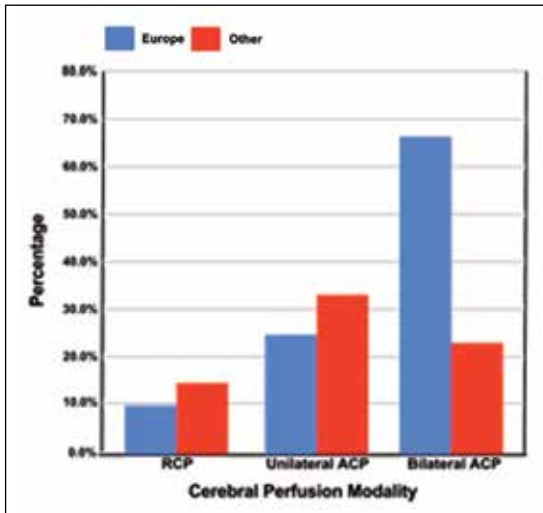


Figure 6 - Selected modalities of cerebral perfusion during adult aortic arch repair.

The choice for monitoring cerebral perfusion during ACP was most commonly direct pressure monitoring in both European and Non-European centers (74.4% versus 73.1%), but European centers also preferred adding cerebral oximetry as well (69.2% versus 44.2%). Pharmacologic neuroprotective adjuncts were frequently used in all study centers, with thiopental as the dominant choice in Europe (61.5% versus 17.7%) and propofol predominating outside of Europe (66.1% versus 28.4%). Steroids were also commonly often administered for neuroprotection across the study centers (Figure 7).

DISCUSSION

This study provides an overview of the current conduct of HCA for adult aortic arch repair in the northern hemisphere, principally as a comparison between Euro-

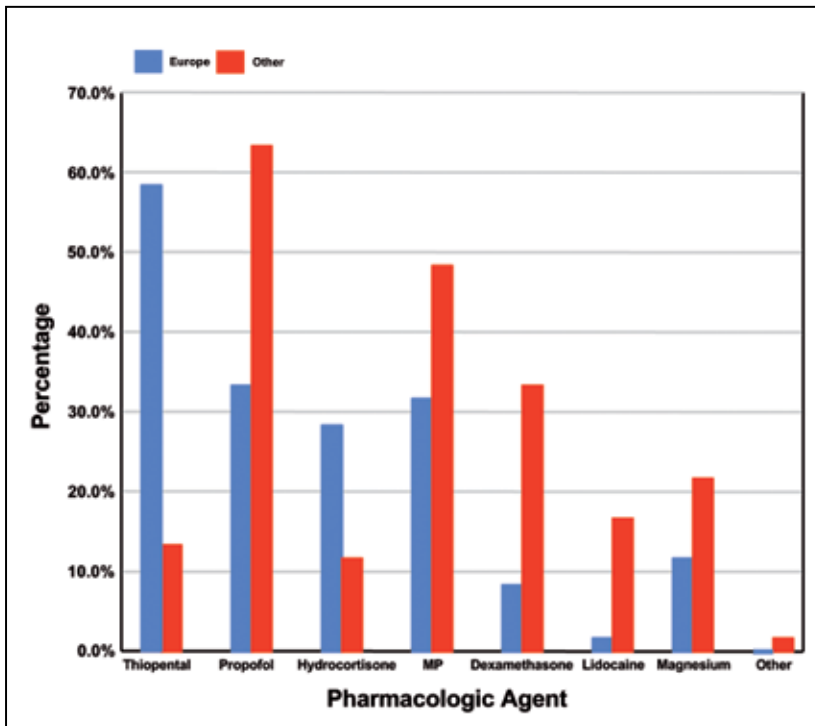


Figure 7 - Frequency of various agents administered for neuroprotection during adult aortic arch repair.

pean and Non-European centers. The predominant country in the Non-European centers was China, given (to the fact) that the study was partly conducted at an international conference in Beijing, China.

The conduct of HCA for adult aortic arch repair in Europe appears to be predominantly at moderate degrees of hypothermia at temperatures above 20°C. This represents a paradigm shift from the classic approach to adult aortic arch repair which was typically conducted with profound hypothermia at temperatures below 20°C (21, 22). The emergence of adult aortic arch repair with moderate-to-mild degrees of hypothermia has recently been experimented in Europe (23, 24). The advantages of this approach include shorter periods of HCA and cardiopulmonary bypass, both of which significantly decrease the risks of bleeding and transfusion after adult aortic arch repair (25, 26).

The practice preference in Europe for moderate HCA maintains excellent neuroprotection with the routine application of ACP despite the absence of profound hypothermia (27, 28). The overwhelming majority of surveyed European centers in this study utilized ACP, with a strong preference for bilateral ACP. Although bilateral ACP guarantees bilateral cerebral perfusion regardless of the circle of Willis, multiple European studies, including a meta-analysis of over 5000 patients, have recently demonstrated that unilateral ACP with adequate monitoring is clinically equivalent (12, 29-31).

This study was a snapshot of HCA practice in Europe during 2010. Given these very recent studies supporting adult aortic arch repair with moderate HCA and unilateral monitored ACP, it is highly likely that the 2010 European preference for bilateral ACP detected in this questionnaire study has shifted towards a preference for monitored unilateral ACP. This possibil-

ity would require confirmation in a subsequent survey of European HCA practice for adult aortic arch repair. The plans for this study are currently in progress.

Monitoring the adequacy of ACP during aortic arch repair extends beyond the realm of cerebral oximetry. It is also essential to monitor the pressure of ACP delivery to ensure adequate perfusion (12, 27-31). This necessity explains the high prevalence of pressure monitoring during ACP reported in this study both in Europe and elsewhere.

A European registry trial recently confirmed the importance of adequate pressure monitoring for ACP during aortic arch repair for acute type A dissection: an ACP pressure above 60 mmHg was significantly associated with a lower risk of permanent neurological dysfunction (12).

The significant variation in selected sites for temperature monitoring of the brain during cardiopulmonary bypass and HCA is prevalent both in European centers and elsewhere. The typical selected site for clinical temperature measurement during arch repair is distal to the brain, significantly raising the risk of mismanagement of brain temperature during the cooling and rewarming phases of cardiopulmonary bypass.

This is somewhat surprising, since multiple studies have demonstrated that tympanic and/or nasal temperatures best approximate brain temperature (32-38). The data from this study demonstrate that nasopharyngeal temperature is rarely monitored during adult HCA and that there is slight preference for tympanic temperature monitoring in Europe. These considerations support the more widespread adoption of nasal or tympanic temperature monitoring for adult aortic arch repair procedures to guide the management of brain temperatures more precisely. Although the extent of hypothermia is no longer as critical in the new European paradigm of adult

aortic arch repair with moderate HCA and ACP, accurate measurement of brain temperature remains important to avoid neurotoxic hyperthermia during rewarming on cardiopulmonary bypass (39-43).

Our study identified a diverse group of neuroprotective agents that were frequently administered for adult aortic arch repair with HCA.

These findings are in agreement with a European survey in which 83% of anesthesiologists administered a neuroprotective drug during HCA (17). The lack of high-quality evidence precludes a strong recommendation for or against this practice (17-19). The endorsement of this practice continues to be based on expert consensus and institutional culture.

A promising development in Europe for accelerated practice enhancement in adult aortic arch repair has been the advent of a multicenter German Registry for Acute Aortic Dissection type A (GERAADA).

This on-line registry has enrolled over 60 hospitals throughout Germany, Switzerland and Austria (44).

This registry has an exclusive European focus and has already led to the development of best practices for acute aortic dissection type A, a very frequent indication for emergency adult aortic arch repair with HCA (44-46). This registry will complement the well-known and long-established International Registry of Acute Aortic Dissection (IRAD) which has enrolled multiple medical centers around the world, including Europe, North America and Asia (full details available at www.iradonline.org, last accessed April 22nd 2013) (47). These registries will continue to foster the journey towards optimal conduct of adult aortic arch repair through practice comparisons.

This clinical trial has the multiple limitations of a pilot study. The limited number of respondents precludes definitive conclu-

sions about the conduct of adult HCA for adult aortic arch repair. Multiple respondents from the same institutions may have participated. Many study participants may not have had English or Chinese as their first languages. Furthermore, clinical outcomes as a result of practice variations in adult HCA were not addressed. Despite these limitations, a suggestive picture of HCA practice for adult aortic arch repair in Europe was evident.

CONCLUSION

Variations in the conduct of adult aortic arch repair with HCA persist worldwide. The results from this study point to a paradigm shift in European practice as compared to centers in Asia and North America. The European paradigm is characterized by a departure from classical aortic arch repair with profound hypothermia with or without concomitant cerebral perfusion. The emerging model of adult aortic arch repair across Europe appears to be characterized by the use of HCA with moderate hypothermia and routine ACP with adequate monitoring of cerebral perfusion. The study results also suggest that brain temperature in this HCA model could be better monitored with more widespread adoption of tympanic or nasopharyngeal temperature monitoring.

The preferred adjunct for cerebral perfusion in Europe appears to be bilateral rather than unilateral ACP. Recent trials from across Europe subsequent to this study suggest a shift towards unilateral ACP due to its equivalent outcomes and ease of application. Further studies are indicated to track the path of this emerging paradigm of tepid adult aortic arch repair with the goal of developing opportunities for best practice, based on outcomes and practice comparisons.

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