# Comparison of short-term outcomes of mild and moderate hypothermic circulatory arrest in aortic arch surgery: a single center retrospective cohort study

**Kai Zhu^, Songbo Dong, Xudong Pan, Jun Zheng, Sihong Zheng, Yongmin Liu, Lizhong Sun**

Department of Cardiovascular Surgery, Beijing Anzhen Hospital, Capital Medical University, Beijing, China

*Contributions:* (I) Conception and design: K Zhu, X Pan; (II) Administrative support: J Zheng, S Zheng, Y Liu, L Sun; (III) Provision of study materials or patients: K Zhu, S Dong, X Pan; (IV) Collection and assembly of data: K Zhu; (V) Data analysis and interpretation: K Zhu, S Dong; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

*Correspondence to:* Lizhong Sun, MD. Department of Cardiovascular Surgery, Beijing Anzhen Hospital, Capital Medical University, 2 Anzhen Rd., Beijing 100029, China. Email: Lizhongsun@foxmail.com.

**Background:** Aortic arch surgery is one of the major challenges in modern aortic surgery, special cerebral and visceral organ protective strategies are still under progress. Whether mild hypothermic circulatory arrest (Mi-HCA) can be safely used in aortic arch surgery (AAS) is the focus of attention.

**Methods:** From January 2017 to June 2021, a retrospective cohort study of 138 consecutive patients was conducted at Beijing Anzhen Hospital. The study comprised patients who underwent AAS performed by a single surgeon during moderate-to-mild HCA. According to the core temperature at the beginning of circulatory arrest, the patients were divided into three groups: $T_1$ group (n=45; 25.76±0.75 ℃), $T_2$ group (n=43; 28.79±0.81 ℃), $T_3$ group (n=50; 31.46±0.79 ℃). Perioperative clinical data were analyzed to assess the differences between groups.

**Results:** In this cohort, the average durations of the operation, cardiopulmonary bypass (CPB), cross-clamp, circulatory arrest, and selective antegrade cerebral perfusion (SACP) were 6.53±1.48 h, 184.07±56.69 min, 101.04±37.92 min, 23.01±9.86 min, and 27.18±11.52 min, respectively. We observed new postoperative permanent neurological dysfunction (PND) in 12 patients (8.7%) and transient neurological dysfunction in 18 patients (13.04%). The in-hospital mortality rate was 6.52% (n=9). The durations of the operation, CPB, cross-clamp, circulatory arrest, and SACP were significantly reduced in the Mi-HCA group (i.e., $T_3$ group, P<0.001; P<0.001; P<0.001; P=0.002; P<0.001, respectively). The incidence of PND and major adverse events (MAEs) were significantly reduced among the three groups (P=0.025; P=0.035). Multivariate logistic regression analysis models showed that Mi-HCA was an independent protective factor in reducing postoperative MAEs [relative risk (RR) =0.12; 95% confidence interval (CI): 0.02–0.90; P=0.0385].

**Conclusions:** The short-term outcomes of Mi-HCA combined with SACP in AAS were acceptable. Similarly, the protection of distal organs and the spinal cord was observed compared to the MHCA strategy, and a lower incidence of MAEs was obtained. Current data suggest that the mild hypothermia strategy can be safely applied for AAS.

**Keywords:** Mild hypothermic circulatory arrest (Mi-HCA); aortic arch surgery (AAS); neurological complications; major adverse events (MAEs)

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^ ORCID: 0000-0002-6329-7628.

## Introduction

Aortic arch surgery (AAS) remains one of the hurdles that modern aortic surgery has yet to overcome. For cerebral and visceral organ protection, systemic temperature management and brain perfusion techniques are required during periods of circulatory arrest. To improve surgical safety, a variety of cerebral protective strategies have been developed. Griepp *et al.* (1) first introduced deep hypothermic circulatory arrest (DHCA) technology in the 1970s, and the open aortic procedure was conducted within that limited time. Serious flaws in this method were gradually discovered. To overcome these restrictions and extend the permissible time of open aortic surgeries, the use of retrograde cerebral perfusion (RCP) and antegrade cerebral perfusion (ACP) with varying levels of systemic hypothermia has been devised (2-4). Because RCP taking place via the superior vena cava failed to provide adequate cerebral blood flow, ACP with varying degrees of hypothermia has become more popular during the last 2 decades (5).

Bachet and Kazui (2,3) popularized selective ACP (SACP), which provides a near physiological method of cerebral perfusion and appears to be the most promising strategy for lowering mortality and morbidity in AAS. Multiple studies have shown that ACP is superior to DHCA alone in terms of survival and neurological outcomes, particularly when extended arch rebuilding with longer periods of circulatory arrest is expected (6-8). However, several technical details of ACP are still debatable. During a period of circulatory arrest, there is no unanimity on the optimal systemic hypothermia and brain perfusion techniques. In recent years, more and more data recommended that using a warmer temperature with ACP is safe and identical to using a cooler temperature, moderate HCA (MHCA) combined with SACP had been greatly affirmed and promoted in many cardiac surgery centers. On the other hand, when the temperature increases to mild hypothermia (>28 ℃), the safety of cerebrum and visceral organ is still under concerned.

Hence, we conducted a retrospective study to investigate the safety and efficacy of mild HCA (Mi-HCA) in a group of patients with acute type A aortic dissection (aTAAD) who underwent total arch replacement (TAR) and the frozen elephant trunk (FET) operation. We present the following article in accordance with the STROBE reporting checklist (available at https://atm.amegroups.com/article/view/10.21037/atm-22-952/rc).

## Methods

### *Study design*

This study is a retrospective observational cohort study. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013), with no additional risk to the patients. The Ethics Committee of Beijing Anzhen Hospital, Capital Medical University (No. 2019030X) approved this study, and all patients gave written informed consent.

### *Patients*

From January 2017 to June 2021, a total of 140 patients were enrolled in the investigation, with a single surgeon (XD Pan, performing AAS independently since early 2015) performing AAS, uniformly applying SACP [unilateral: n=67 (48.55%); bilateral: n=71 (51.45%)] during moderate-to-mild systemic hypothermia (28.77±2.50 ℃). Due to a preoperative cerebral infarction with sequelae, 2 individuals were ruled out (final cohort: 138 patients). Patients were split into 3 groups based on their core temperature at the start of HCA: $T_1$ group (n=45; 25.76±0.75 ℃), $T_2$ group (n=43; 28.79±0.81 ℃), and $T_3$ group (n=50; 31.46±0.79 ℃).

Preoperative aortic computed tomography angiography (CTA) was routinely performed to verify the diagnosis and to ascertain the involvement of each organ: cerebral malperfusion refers to the involvement of unilateral or bilateral carotid artery by dissection, and the true lumen is compressed; spinal cord malperfusion refers to the intercostal arteries originating from the false lumen of the descending thoracic aorta, and the false lumen is thrombotic; renal malperfusion refers to unilateral or bilateral renal arteries originating from the false lumen, and the cortex is poorly developed.

Clinical information from the initial hospitalization was entered into our institutional database prospectively, and all data collection and verification were conducted by two experienced cardiovascular surgery graduate students. Patients who were discharged were followed up with clinic visits after 3 months, 6 months, and yearly thereafter, or were interviewed by telephone. Survival, reintervention, and adverse events were all recorded by the outpatient physician. Annual echocardiogram and CTA were recommended.

### *Follow-up*

All survivors in the cohort had preliminary follow-up by

 

September 2021, with an average of 28.5±16.4 (range, 3 to 56) months. There were no serious cardiac or cerebral adverse events during the follow-up period. In the third year after surgery, one of the Marfan syndrome patients had a second procedure due to dilatation of the distal aorta, whereas the other patients received no additional treatment.

### *Definitions*

According to the international consensus guidelines (9), deep hypothermia is defined as between 14.1–20 ℃, moderate hypothermia is defined as between 20.1–28 ℃, and mild hypothermia is defined as between 28.1–34 ℃. The primary endpoint of the current investigation was the appearance of major adverse events (MAEs), and MAEs were defined as the presence of any of the 4 following conditions: permanent neurological dysfunction (PND), paraplegia, new postoperative chronic kidney insufficiency, and in-hospital mortality. The presence of a localized neurological deficit was characterized as PND, which was validated as a new deficiency using CT scanning or magnetic resonance imaging of the brain. The occurrence of reversible postoperative delayed wakefulness, agitation, confusion, or transitory delirium was characterized as temporary neurological dysfunction (TND). The CT scanning was required to be normal, with resolution of all symptoms before discharge (10,11). In-hospital mortality was defined as death occurring in the hospital during the perioperative period.

### *Surgical techniques*

All procedures were conducted via a median sternotomy with cardiopulmonary bypass (CPB) and SACP by cannulation of the right axillary artery and right atrium. Before the procedure, temperature probes were implanted to monitor the esophagopharyngeal and bladder temperatures. The ascending aorta was clamped and transected just distal to the sinotubular junction, and antegrade perfusion of cardioplegia was started after the ascending aorta was clamped and transected. During the cooling time, proximal surgeries such as aortic valve and aortic root reconstruction were conducted. Cooling was limited to a bladder temperature of 28–32 ℃, based on the estimated period of open arch reconstruction as determined by the preoperative CTA scan findings. When the core temperature reached the target after the aortic arch was opened, systemic circulation was arrested and SCP began. The TAR with FET surgical technique (also known as the Sun operation) has been reported previously (12-15). A FET (MicroPort Medical Company Limited, Shanghai, China) was implanted in the descending aorta, followed by TAR with a four-branched prosthetic graft (Maquet Cardiovascular, Wayne, NJ, USA). After the descending aortic anastomosis was complete, distal reperfusion was started. The left carotid artery was initially reconstructed to achieve bilateral perfusion, the ascending aorta was subsequently anastomosed, and the innominate and subclavian arteries were eventually treated.

In recent years, the hypothermic and SACP strategies have evolved. Between 2017 and 2018, the primary method of choice was unilateral SACP (uSACP) with MHCA. Warmer hypothermia (i.e., Mi-HCA) became more popular after 2019, and we initially chose bilateral SACP (bSACP) for better cerebral and visceral organ perfusion. Once the required temperature was reached in bSACP and Mi-HCA cases, the three supra-arch branches were clamped. The right axillary and left common carotid arteries were used to initiate SACP. Following that, FET was implanted and a distal arch anastomosis was performed. Subsequently, distal reperfusion was resumed. The ascending aorta was reconstructed first for reducing cardiac ischemia, followed by the left subclavian artery, the left carotid artery, and finally, the innominate artery.

### *Statistical analysis*

The Kolmogorov-Smirnov test was employed for the determination of the normality of continuous data. The Student's *t*-test was used to compare data with a normal distribution, which was expressed as mean ± standard deviation (SD). To describe non-normally distributed data, the median and interquartile range were used, and the Mann-Whitney U-test was employed for their comparison. For categorical variables, Chi-squared or Fisher's exact tests were used. Univariate logistic regression analysis was performed to investigate the relationship between neurological complications and MAEs. The connection between core temperature and PND and MAEs was explored using multivariate logistic regression. The preoperative clinical characteristics and intraoperative data were added to constructed the model respectively, according to our previous study (15). Three models were constructed as follows: (I) not adjusted; (II) adjusted for sex/age/body mass index (BMI)/emergency surgery/Marfan syndrome/

hypertension/coronary artery disease/diabetes mellitus/preoperative cerebrovascular history/smoking history; (III) adjusted for operation duration/CPB duration/cross-clamp duration/perfusion pressure during SACP/SACP flow/SACP duration. The three models were compared side by side.

The R package and Empower Stats (https://www.empowerstats.net/cn/; X&Y Solutions, Inc., Boston, MA, USA) were used to analyze the data. All of the evaluations were two-sided. P values <0.05 were considered statistically significant.

## Results

### *Demographic characteristics*

*Table 1* summarizes the preoperative clinical features of the patients, including 114 (82.61%) males and 24 (17.39%) females. The average age was 48.60±10.96. AAS was performed in 112 patients with TAAD, 24 patients with type B aortic dissection with ascending aortic or aortic arch aneurysm, and 2 patients with a degenerative aortic arch aneurysm. The majority of them had to undergo emergency surgery (79.71%). Hypertension was the most common comorbidity, which was present in 120 patients (86.96%); however, only 22 (18.33%) of them were aware of it and maintained adequate medication management. In the cohort, 10 patients (7.25%) had Marfan syndrome and 73 patients had a smoking habit (52.9%).

There were no significant differences among the three groups in terms of age, sex, BMI, emergency surgery, Marfan syndrome, hypertension, coronary artery disease, diabetes mellitus, preoperative cerebrovascular history, smoking history, the incidence of malperfusion, and preoperative laboratory data. In terms of the distribution of aortic disease among the three groups, the proportion of TAAD was higher in the $T_1$ group (P=0.038).

### *Operative data*

*Table 2* lists the operative data and surgical procedures. The average durations of the operation, CPB, cross-clamp, circulatory arrest, and SACP in the whole cohort were 6.53±1.48 h, 184.07±56.69 min, 101.04±37.92 min, 23.01±9.86 min, and 27.18±11.52 min, respectively. The durations of the operation, CPB, cross-clamp, circulatory arrest, and SACP were significantly shortened in the three groups (all P<0.05), and the SACP flow was increased (6.70±2.82 *vs.* 8.14±2.35 *vs.* 8.49±1.59; P<0.001).

### *Perioperative mortality and morbidity*

The postoperative outcomes are detailed in *Table 3*. The mean consciousness recovery time was 7.17±6.15 h. The mean ventilation time was 25.19±27.48 h, the mean ICU stay time was 49.57±52.83 h, and the mean hospital stay time was 14.65±6.63 days. The mean chest tube drainage within the first 24 h was 752.32±520.89 mL. Re-exploration for bleeding was performed in 11 patients (7.97%). New postoperative renal failure requiring continuous renal replacement therapy (CRRT) took place in 14 patients (10.14%), with acute kidney injury (AKI) in 12 patients (8.70%) and chronic kidney insufficiency in 2 patients (1.45%). TND was observed in 18 patients (13.04%), and PND occurred in 12 patients (8.7%). Ten patients (7.25%) developed various degrees of postoperative paraplegia, and 3 patients (2.17%) suffered monoplegia of the lower limbs. In-hospital mortality from all causes in the cohort was 6.52% (9 patients).

Among the groups, there were no significant differences in the proportions of re-exploration for bleeding, renal failure with CRRT, TND, paraplegia, and in-hospital mortality. The incidences of PND and MAEs were significantly reduced among the 3 groups (P=0.025; P=0.035). Meanwhile, chest tube drainage within the first 24 h, postoperative PRBC transfusion, and total PRBC transfusion all showed a clear downward trend (P=0.015, P=0.043, and P=0.011, respectively).

### *Univariate analysis*

Univariate analysis was used to analyze the relationship between core temperature, sex, age, BMI, emergency surgery, Marfan syndrome, hypertension, coronary artery disease, diabetes mellitus, preoperative cerebrovascular history, smoking history, operation duration, CPB duration, cross-clamp duration, perfusion pressure during SACP, SACP flow, SACP duration between TND, PND, paraplegia, MAEs, and in-hospital mortality. Sex, age, BMI, emergency surgery, Marfan syndrome, hypertension, coronary artery disease, diabetes mellitus, preoperative cerebrovascular history, smoking history, perfusion pressure during SACP, SACP flow, and SACP duration were not associated with TND, PND, paraplegia, MAEs, or in-hospital mortality. Core temperature, operation duration, CPB duration, and cross-clamp duration were significantly associated with PND and MAEs (all P<0.05). Moreover, operation duration was significantly associated with TND

 

**Table 1** Preoperative clinical profiles

| Variables | $T_1$ (n=45) | $T_2$ (n=43) | $T_3$ (n =50) | P value |
|---|---|---|---|---|
| Age, years | 47.29±10.48 | 47.67±11.22 | 50.58±11.09 | 0.277 |
| Male | 39 (86.67) | 35 (81.40) | 40 (80.00) | 0.671 |
| Emergency | 36 (80.00) | 32 (74.42) | 42 (84.00) | 0.518 |
| BMI, kg/$m^2$ | 26.30±4.09 | 26.99±4.63 | 27.27±4.98 | 0.579 |
| Classification | | | | 0.038* |
| TAAD | 43 (95.56) | 30 (69.77) | 39 (78.00) | |
| Type B aortic dissection with proximal aneurysm | 2 (4.44) | 12 (27.91) | 10 (20.00) | |
| Aortic arch aneurysm | 0 (0.00) | 1 (2.33) | 1 (2.00) | |
| Marfan syndrome | 4 (8.89) | 5 (11.63) | 1 (2.00) | 0.178 |
| Hypertension | | | | 0.449 |
| No | 6 (13.33) | 7 (16.28) | 5 (10.00) | |
| Good drug control | 4 (8.89) | 7 (16.28) | 11 (22.00) | |
| Poor control | 35 (77.78) | 29 (67.44) | 34 (68.00) | |
| Coronary artery disease | 2 (4.44) | 3 (6.98) | 3 (6.00) | 0.876 |
| Diabetes mellitus | 1 (2.22) | 5 (11.63) | 1 (2.00) | 0.062 |
| Preoperative cerebrovascular history | 4 (8.89) | 3 (6.98) | 3 (6.00) | 0.860 |
| Smoking history | | | | 0.924 |
| No | 19 (42.22) | 16 (37.21) | 21 (42.00) | |
| Yes | 23 (51.11) | 25 (58.14) | 25 (50.00) | |
| Quit smoking more than 3 months | 3 (6.67) | 2 (4.65) | 4 (8.00) | |
| Malperfusion | | | | |
| Cerebrum | 10 (25.64) | 5 (12.50) | 11 (22.00) | 0.318 |
| Spinal cord | 8 (20.00) | 2 (5.41) | 6 (12.50) | 0.159 |
| Renal | 13 (30.23) | 14 (33.33) | 7 (14.00) | 0.068 |
| Alanine aminotransferase, U/L | 23.00 (17.00–47.00) | 21.00 (15.00–28.75) | 24.00 (14.00–43.00) | 0.166 |
| Aspartate aminotransferase, U/L | 24.00 (18.00–31.00) | 20.00 (16.00–24.00) | 24.50 (18.00–35.00) | 0.064 |
| Creatinine, μmol/L | 94.70±49.15 | 88.00±37.05 | 103.15±45.86 | 0.270 |
| Troponin I, pg/mL | 12.00 (10.00–47.50) | 10.00 (0.00–30.00) | 10.00 (5.20–40.60) | 0.071 |
| Blood glucose value, mg/dL | 130.31±33.18 | 128.96±28.56 | 134.27±32.70 | 0.698 |
| Lactic acid, mmol/L | 1.62±0.84 | 1.49±0.79 | 1.90±1.23 | 0.123 |

Continuous data are presented as the mean ± SD or median (interquartile range), and categorical data as number (%). *, P<0.05. BMI, body mass index; TAAD, type A aortic dissection; SD, standard deviation.

and in-hospital mortality (P=0.0483; P=0.0027), and CPB duration and cross-clamp duration were significantly related to in-hospital mortality (P=0.0034; P=0.0108). Analysis results are summarized in *Table 4*.

### *Multivariate analysis*

Multivariate logistic regression analysis models for PND/MAEs are shown in *Table 5*. With model I and model

**Table 2** Operative data and surgical procedures

| Variables | $T_1$ (n=45) | $T_2$ (n=43) | $T_3$ (n=50) | P value |
|---|---|---|---|---|
| Core temperature, ℃ | 25.76±0.75 | 28.79±0.81 | 31.46±0.79 | <0.001* |
| Operating methods | | | | 0.449 |
| Ascending aorta replacement with TAR | 23 (51.11) | 17 (39.53) | 25 (50.00) | |
| Bentall procedure with TAR | 13 (28.89) | 10 (23.26) | 13 (26.00) | |
| Hemiarch replacement | 9 (20.00) | 16 (37.21) | 12 (24.00) | |
| Operation duration, h | 7.13±1.22 | 6.75±1.59 | 5.80±1.31 | <0.001* |
| CPB duration, min | 221.82±56.80 | 182.00±57.09 | 151.86±30.37 | <0.001* |
| Cross-clamp duration, min | 128.76±28.07 | 99.56±39.74 | 77.38±26.09 | <0.001* |
| Perfusion pressure during SACP, mmHg | 66.40±16.49 | 68.12±24.53 | 69.10±14.48 | 0.787 |
| SACP flow, mL/(kg·min) | 6.70±2.82 | 8.14±2.35 | 8.49±1.59 | <0.001* |
| Circulatory arrest duration, min | 25.69±10.68 | 24.74±10.31 | 19.12±7.34 | 0.002* |
| SACP duration, min | 36.38±8.26 | 26.93±11.43 | 19.12±7.34 | <0.001* |
| Intraoperative transfusion of PRBCs, u | 0 [0, 4] | 0 [0, 4] | 0 [0, 0] | 0.059 |

Data are presented as mean ± SD, median [interquartile range], or number (%) as appropriate. *, P<0.05. TAR, total arch replacement; CPB, cardiopulmonary bypass; SACP, selective antegrade cerebral perfusion; PRBCs, packed red blood cells; SD, standard deviation.

**Table 3** Operative outcomes

| Variables | $T_1$ (n=45) | $T_2$ (n=43) | $T_3$ (n=50) | P value |
|---|---|---|---|---|
| Hospital stay time, days | 13.73±7.15 | 16.43±7.47 | 13.98±5.17 | 0.124 |
| Consciousness recovery time, h | 7.32±6.38 | 6.20±4.43 | 7.84±7.13 | 0.446 |
| Ventilation time, h | 24.36±28.32 | 18.99±20.20 | 31.07±31.11 | 0.112 |
| ICU stay time, h | 49.38±59.58 | 37.13±32.87 | 60.17±58.78 | 0.114 |
| Chest tube drainage, mL/24 h | 934.89±553.28 | 668.60±498.36 | 660.00±474.74 | 0.015* |
| Postoperative transfusion of PRBCs, u | 2 [0, 4] | 0 [0, 4] | 0 [0, 3.75] | 0.043* |
| Total transfusion of PRBCs, u | 4 [0, 8] | 4 [0, 6] | 0 [0, 4] | 0.011* |
| Re-exploration for bleeding | 7 (15.56) | 1 (2.33) | 3 (6.00) | 0.059 |
| Renal failure with CRRT | 8 (17.78) | 4 (9.30) | 2 (4.00) | 0.083 |
| TND | 7 (15.91) | 8 (19.05) | 3 (6.00) | 0.150 |
| PND | 8 (18.60) | 2 (4.76) | 2 (4.00) | 0.025* |
| Paraplegia | 4 (9.30) | 4 (9.52) | 2 (4.00) | 0.510 |
| Monoplegia of lower limbs | 0 (0.00) | 1 (2.38) | 2 (4.00) | 0.425 |
| MAEs | 15 (33.33) | 8 (18.60) | 6 (12.00) | 0.035* |
| In-hospital mortality | 3 (6.67) | 3 (6.98) | 3 (6.00) | 0.981 |

Data are presented as mean ± SD, median [interquartile range], or number (%) as appropriate. *, P<0.05. ICU, intensive care unit; PRBCs, packed red blood cells; CRRT, continuous renal replacement therapy; TND, temporary neurological dysfunction; PND, permanent neurological dysfunction; MAEs, major adverse event; SD, standard deviation.

**Table 4** Univariate analysis

| Exposure | Statistics | TND | PND | Paraplegia | MAEs | In-hospital mortality |
|---|---|---|---|---|---|---|
| Core temperature, ℃ | 28.77±2.50 | 0.90 (0.74, 1.10), 0.2999 | 0.72 (0.55, 0.95), 0.0197* | 0.90 (0.70, 1.17), 0.4401 | 0.83 (0.70, 0.98), 0.0281* | 1.04 (0.79, 1.37), 0.7818 |
| Grouping | | | | | | |
| $T_1$ | 45 (32.61%) | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| $T_2$ | 43 (31.16%) | 1.24 (0.41, 3.80), 0.7017 | 0.22 (0.04, 1.10), 0.0650 | 1.03 (0.24, 4.40), 0.9721 | 0.46 (0.17, 1.23), 0.1201 | 1.05 (0.20, 5.51), 0.9540 |
| $T_3$ | 50 (36.23%) | 0.34 (0.08, 1.40), 0.1335 | 0.18 (0.04, 0.91), 0.0382* | 0.41 (0.07, 2.34), 0.3127 | 0.27 (0.10, 0.78), 0.0157* | 0.89 (0.17, 4.67), 0.8939 |
| Operation duration, h | 6.53±1.48 | 1.43 (1.00, 2.03), 0.0483* | 1.84 (1.20, 2.81), 0.0052* | 1.31 (0.84, 2.04), 0.2270 | 1.74 (1.29, 2.36), 0.0003* | 1.87 (1.24, 2.81), 0.0027* |
| CPB duration, min | 184.07±56.69 | 1.01 (1.00, 1.02), 0.0855 | 1.01 (1.00, 1.02), 0.0368* | 1.01 (1.00, 1.02), 0.2200 | 1.01 (1.00, 1.02), 0.0024* | 1.01 (1.00, 1.02), 0.0034* |
| Cross-clamp duration, min | 101.04±37.92 | 1.01 (1.00, 1.02), 0.0941 | 1.02 (1.00, 1.04), 0.0112* | 1.00 (0.99, 1.02), 0.7213 | 1.02 (1.01, 1.03), 0.0030* | 1.02 (1.01, 1.04), 0.0108* |

Data are presented as β (95% CI), P value/OR (95% CI), P value. *, P<0.05. TND, temporary neurological dysfunction; PND, permanent neurological dysfunction; MAEs, major adverse event; CPB, cardiopulmonary bypass; CI, confidence interval; OR, odds ratio.

**Table 5** Multivariate analysis

| Outcome variables | Model I | Model II | Model III |
|---|---|---|---|
| Y = PND | | | |
| Core temperature, ℃ | 0.72 (0.55, 0.95), 0.0197* | 0.61 (0.42, 0.88), 0.0088* | 0.69 (0.45, 1.06), 0.0934 |
| Grouping | | | |
| $T_1$ | 1.0 | 1.0 | 1.0 |
| $T_2$ | 0.22 (0.04, 1.10), 0.0650 | 0.04 (0.00, 0.83), 0.0377* | 0.11 (0.01, 0.96), 0.0463* |
| $T_3$ | 0.18 (0.04, 0.91), 0.0382* | 0.09 (0.01, 0.64), 0.0157* | 0.13 (0.01, 1.67), 0.1164 |
| Y = MAEs | | | |
| Core temperature, ℃ | 0.83 (0.70, 0.98), 0.0281* | 0.79 (0.64, 0.96), 0.0204* | 0.75 (0.53, 1.04), 0.0827 |
| Grouping | | | |
| $T_1$ | 1.0 | 1.0 | 1.0 |
| $T_2$ | 0.46 (0.17, 1.23), 0.1201 | 0.32 (0.10, 1.04), 0.0585 | 0.18 (0.03, 0.93), 0.0411* |
| $T_3$ | 0.27 (0.10, 0.78), 0.0157* | 0.25 (0.08, 0.80), 0.0193* | 0.12 (0.02, 0.90), 0.0385* |

Data are presented as OR (95% CI), P value/RR (95% CI), P value. *, P<0.05. Model I: not adjusted; model II: adjusted for sex, age, BMI, emergency surgery, Marfan syndrome, hypertension, coronary artery disease, diabetes mellitus, preoperative cerebrovascular history, smoking history; model III: adjusted for operation duration, CPB duration, cross-clamp duration, perfusion pressure during SACP, SACP flow, SACP duration. PND, permanent neurological dysfunction; MAEs, major adverse event; OR, odds ratio; CI, confidence interval; RR, relative risk; BMI, body mass index; CPB, cardiopulmonary bypass; SACP, selective antegrade cerebral perfusion.

II, there was a significant association between the core temperature and PND/MAEs (all P<0.05). In model III, adding surgery-related covariates, the correlation between core temperature and PND/MAEs was no longer obvious. However, the $T_3$ group still had significantly reduced MAEs [relative risk (RR) =0.12; 95% confidence interval (CI): 0.02–0.90; P=0.0385]. The incidence of postoperative MAEs in the $T_3$ group was 88% lower compared to that in the $T_1$ group.

## Discussion

The most controversial issues of aortic surgery, particularly in aTAAD or complex aortic arch pathologies involving the distal arch and descending aorta, are the different protective techniques in open arch surgery and the associated neurological and visceral prognosis. To enhance outcomes following AAS, several techniques for the protection of the brain and visceral organs during open distal anastomosis have been used and compared during the last two decades. In AAS, there is no universally accepted consensus on the optimal temperature of HCA. Acceptance of ACP, especially in combination with moderate-to-mild systemic hypothermia, has certainly increased in recent years. The ACP method of cerebral perfusion is more physiological, and it extends the safe duration for open arch distal anastomosis. Furthermore, during moderate-to-mild hypothermia, distal body circulatory arrest means faster cooling and rewarming durations, which may result in better surgical outcomes (6,16).

We employed right axillary artery cannulation as the primary CPB and the uSACP method in AAS under MHCA at our institute, with good results in terms of perioperative mortality and neurological prognosis over time (13,14,17). Since 2017, we have been experimenting with Mi-HCA in open arch repair assisted by uSACP or bSACP, primarily in aTAAD patients who underwent TAR and FET procedures (15).

Patients with a higher core temperature had a shorter operation, CPB, cross-clamp, and SCP times, which might be explained by the shorter cooling and rewarming times and aortic reconstruction process. We resumed cardiac perfusion after insertion of a FET and distal arch anastomosis in patients who had an open distal anastomosis assisted by bSACP with Mi-HCA, which was the major cerebral perfusion strategy in the cohort. We had to finish the left carotid artery first to restore bilateral cerebral perfusion following distal anastomosis, in contrast to patients with uSACP under MHCA, and then resume cardiac perfusion. As a result, we believe that the warmer core temperature and improved aortic reconstruction process contributed to the shorter operation, CPB, cross-clamp, and SCP times. Additionally, problems associated with extended CPB were reduced, such as coagulation issues, AKI, visceral dysfunctions, and death, among others (18-20). As shown above, in these groups, there was a significantly lower volume of chest tube drainage during the first 24 h, a decrease in postoperative PRBC transfusion and total PRBC transfusion in hospital, as well as a lowering trend of intraoperative PRBC transfusion. This finding was comparable to that of Keenan *et al.* (18), who found a link between prolonged CPB time and a higher risk of postoperative hemorrhage.

The incidence of postoperative TND was observed to have a reduced trend in patients with a warmer core temperature, while for PND, there was a significant decrease in the $T_2$ and $T_3$ groups compared with the $T_1$ group. The 8 cases who suffered postoperative PND in the $T_3$ group were all aTAAD patients. One suffered a left cerebral hemisphere infarction and remained unconscious after surgery, and finally died of circulatory failure on the third day after the operation. One patient experienced right carotid artery involvement, severe compression of the true lumen, transient loss of consciousness, and left lower limb dysfunction preoperatively. The postoperative CT scanning revealed lateral infarction of the basal ganglia of the right brain parenchyma. Furthermore, in another patient, the perfusion pressure of the right axillary artery cannulation was excessively high throughout the procedure. Thus, we switched to femoral artery cannulation and combined it with the left common carotid artery cannulation procedure. Despite this, the patient suffered left-sided hemiplegia after surgery, and a color Doppler ultrasound of the carotid artery revealed a dissection of the right common carotid artery, as well as several cerebral infarctions on CT. The other 5 patients suffered postoperative regional cerebral infarctions of varying degrees, 2 of them had affected breathing and coughing function and needed long-duration ventilator assistance, and all had a good prognosis at the final follow-up. In this work, the postoperative incidence of PND was comparable to that in the literature (17,21).

Through univariate analysis of various factors, we found that intraoperative core temperature had a significant correlation with the incidence of postoperative PND and MAEs, along with the operation duration, CPB duration, and cross-clamp duration. Subsequently, in the multivariate logistic regression analysis, model I was not adjusted, and model II was adjusted for various preoperative covariates. Warmer core temperature showed a significant positive effect on the incidence of postoperative PND and MAEs. For avoiding a large deviation result on account of a relatively limited sample size, we added some surgery-related covariates to form model III. As suspected, the correlation between core temperature and PND/MAEs was no longer obvious. We simply observed a significant decrease in the incidence of MAEs in the three groups, so we can conclude that an appropriate warmer core temperature (i.e., Mi-HCA) is conducive to lowering the incidence of postoperative MAEs.

There is sufficient data to imply that using a warmer temperature with ACP is safe and identical to using a cooler temperature, as reported in 2021 by The American Association for Thoracic Surgery expert consensus document (5). El-Sayed Ahmad *et al.* (21) conducted 587 successive AAS with SACP under moderate-to-mild systemic hypothermia from 2000 to 2015. Postoperative PND occurred in 6% of patients (n=33), paraplegia in 0.17% of patients (n=1), renal failure with CRRT in 8% of patients (n=49), and 30-day mortality in 6% of patients (n=36). SACP in combination with moderate-to-mild HCA appears to provide adequate neurological and visceral organ protection in AAS, according to their findings.

In terms of AAS's safer SCP techniques, there is no evidence that either unilateral or bilateral brain perfusion is preferable in terms of brain protection and outcomes (22-25). In our clinical experience, bSACP was chosen at the start of Mi-HCA because it was a more physiological and intuitively safer technique of cerebral protection, avoiding the risk of left hemisphere hypoperfusion in patients with an incomplete Willis circle. Concerns about cerebral hyperperfusion, which causes brain tissue edema when perfusing the brain from only one side, occur in addition to concerns about total cerebral perfusion. On the other hand, uSACP is easily placed and does not require any manipulation of the supra-arch vessels. In the $T_3$ group, a 65-year-old male patient with pseudoaneurysm of the aortic arch and extensive calcification and degeneration underwent TAR and FET procedures under Mi-HCA and bSACP, and a large cerebral infarction occurred in the right occipitotemporal lobe after the operation. We speculated that it may be atherosclerotic plaque shedding caused by manipulation in the aortic arch.

In comparison to cerebral protection provided by hypothermia and SACP, the spinal cord and distal viscera were at risk of ischemia, since hypothermic protection was only provided during circulatory arrest while the open arch distal anastomosis was conducted. The most common measure of distal visceral dysfunction observed in AAS was AKI, which was also a major predictor of morbidity and mortality. We found a decreasing trend in the incidence of new postoperative renal failure needing CRRT in the three groups in this investigation. Cao *et al.* (26) found that the incidence of renal failure requiring CRRT was reduced in MHCA compared to DHCA. Also, Zhou *et al.* (19) reported that CPB duration was identified as the only modifiable predictor of AKI, and patients may benefit from MHCA due to the shorter CPB duration. The incidence of new renal failure requiring CRRT in the current study population under moderate-to-mild HCA (i.e., $T_2$ and $T_3$ groups) was 6.45%, which was equivalent to that reported in the literature. In a Japanese national database of 4,707 patients undergoing thoracic aortic surgery, Motomura *et al.* (27) reported that the morbidity of acute renal failure needing dialysis was 6.7%. In a prior report from our institute, the proportion of patients who required CRRT after AAS under MHCA was 7.9% (17). As a result, we believe that the incidence of kidney injury in Mi-HCA cases was comparable to that in MHCA cases.

There is still no consensus on the safe limit of ischemia tolerance of the spinal cord during HCA under warmer hypothermia. In this study population, the incidence of paraplegia with mild hypothermia was 4%, superior to the $T_1$ or $T_2$ group, which was similar to our earlier reports (13,14,17,28). In a porcine model, Strauch *et al.* (29) compared the safe limit of tolerance of the spinal cord to ischemia. They found that mild hypothermia (32 ℃) substantially raised the spinal cord's tolerance to ischemia up to 50 min. El-Sayed Ahmad *et al.* (30) observed one case of postoperative paraplegia in a cohort of 63 patients who underwent distal body circulatory arrest for more than 1 h under moderate-to-mild systemic hypothermia. They also believed that warmer cerebral perfusion would aid in enhancing collateral flow to the spinal cord from the brain, which would help to protect the spinal cord. In the descending aorta, the substantial backflow of blood necessitates continual suction during open arch repair. Additionally, it was noticed that the blood backflow volume from the distal descending aorta was unexpectedly larger in individuals receiving Mi-HCA in our clinical practice (15).

Above importantly, Mi-HCA combined with SACP in AAS provided comparable distal viscera and spinal cord protection to MHCA. The length of circulatory arrest is a significant influence on distal organ ischemia injury. HCA took an average of 23.01±9.86 min in this trial, while Mi-HCA took an average of 19.12±7.34 min. The special surgical strategy may explain the significantly shorter duration of HCA. The distal body was reperfused upon completion of the open arch anastomosis. In the vast majority of cases, the anastomosis between the 4-branched prosthetic graft and the distal descending aorta bearing the intraluminal stented graft took less than 30 min. To avoid distal viscera and spinal cord ischemia, hemostasis and additionally strengthened sutures were used once the continuous suture was completed. We recommend a balloon-tipped cannula put into the descending aorta for distal body perfusion when extensive arch rebuilding necessitates a longer duration of HCA, even exceeding 60 min.

The use of Mi-HCA combined with SACP in AAS significantly reduced the duration of the operation, CPB, cross-clamp, circulatory arrest, and SACP, as well as related problems. Meanwhile, in comparison to MHCA, the method may provide similar organ and spinal cord protection. Furthermore, maintaining an appropriate warmer core temperature is an independent protective factor in lowering postoperative MAEs.

### *Limitations*

The present study has some limitations, the most significant of which is that it is a retrospective study with small sample size. All aortic arch pathologies and surgical treatments were included in the patient cohort, and the study analyzed the short-term outcomes of several surgical treatments in AAS patients. Because the duration of HCA in this cohort was relatively short, particularly in the $T_3$ group (19.12±7.34 min), it is impossible to offer a clear determination of the safe time limit under mild hypothermia based on existing data. Finally, data on long-term consequences were inadequate, necessitating additional research.

## Conclusions

In this cohort trial, we demonstrated that Mi-HCA with SACP could be safely and consistently applied for AAS in a variety of pathologies. The preliminary results for Mi-HCA were satisfactory. Equal distal organ and spinal cord protection were attained compared to the MHCA method, and a decreased occurrence of MAEs was reported compared to MHCA patients. These positive intraoperative and postoperative results support the use of mild hypothermia in AAS.

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## Footnote

*Reporting Checklist:* The authors have completed the STROBE reporting checklist. Available at https://atm.amegroups.com/article/view/10.21037/atm-22-952/rc

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*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The Ethics Committee of Beijing Anzhen Hospital, Capital Medical University (No. 2019030X) approved this study, and all patients gave written informed consent.



## References

1. Griepp RB, Stinson EB, Hollingsworth JF, et al. Prosthetic replacement of the aortic arch. J Thorac Cardiovasc Surg

1975;70:1051-63.
2. Bachet J, Guilmet D, Goudot B, et al. Cold cerebroplegia. A new technique of cerebral protection during operations on the transverse aortic arch. J Thorac Cardiovasc Surg 1991;102:85-93; discussion 93-4.
3. Kazui T, Kimura N, Yamada O, et al. Surgical outcome of aortic arch aneurysms using selective cerebral perfusion. Ann Thorac Surg 1994;57:904-11.
4. Ueda Y, Miki S, Kusuhara K, et al. Surgical treatment of aneurysm or dissection involving the ascending aorta and aortic arch, utilizing circulatory arrest and retrograde cerebral perfusion. J Cardiovasc Surg (Torino) 1990;31:553-8.
5. Malaisrie SC, Szeto WY, Halas M, et al. 2021 The American Association for Thoracic Surgery expert consensus document: Surgical treatment of acute type A aortic dissection. J Thorac Cardiovasc Surg 2021;162:735-58.e2.
6. Zierer A, El-Sayed Ahmad A, Papadopoulos N, et al. Selective antegrade cerebral perfusion and mild (28°C-30°C) systemic hypothermic circulatory arrest for aortic arch replacement: results from 1002 patients. J Thorac Cardiovasc Surg 2012;144:1042-49.
7. Tian DH, Wan B, Bannon PG, et al. A meta-analysis of deep hypothermic circulatory arrest versus moderate hypothermic circulatory arrest with selective antegrade cerebral perfusion. Ann Cardiothorac Surg 2013;2:148-58.
8. O'Hara D, McLarty A, Sun E, et al. Type-A Aortic Dissection and Cerebral Perfusion: The Society of Thoracic Surgeons Database Analysis. Ann Thorac Surg 2020;110:1461-7.
9. Yan TD, Bannon PG, Bavaria J, et al. Consensus on hypothermia in aortic arch surgery. Ann Cardiothorac Surg 2013;2:163-8.
10. Ergin MA, Uysal S, Reich DL, et al. Temporary neurological dysfunction after deep hypothermic circulatory arrest: a clinical marker of long-term functional deficit. Ann Thorac Surg 1999;67:1887-90; discussion 1891-4.
11. Centofanti P, Barbero C, D'Agata F, et al. Neurologic and cognitive outcomes after aortic arch operation with hypothermic circulatory arrest. Surgery 2016;160:796-804.
12. Ma WG, Zhu JM, Zheng J, et al. Sun's procedure for complex aortic arch repair: total arch replacement using a tetrafurcate graft with stented elephant trunk implantation. Ann Cardiothorac Surg 2013;2:642-8.
13. Sun LZ, Qi RD, Chang Q, et al. Surgery for acute type A dissection using total arch replacement combined with stented elephant trunk implantation: experience with 107 patients. J Thorac Cardiovasc Surg 2009;138:1358-62.
14. Sun L, Qi R, Zhu J, et al. Total arch replacement combined with stented elephant trunk implantation: a new "standard" therapy for type a dissection involving repair of the aortic arch? Circulation 2011;123:971-8.
15. Dong SB, Zhang K, Zhu K, et al. Mild hypothermic circulatory arrest with selective cerebral perfusion in open arch surgery. J Thorac Dis 2021;13:1151-61.
16. Urbanski PP, Lenos A, Bougioukakis P, et al. Mild-to-moderate hypothermia in aortic arch surgery using circulatory arrest: a change of paradigm? Eur J Cardiothorac Surg 2012;41:185-91.
17. Wang X, Yang F, Zhu J, et al. Aortic arch surgery with hypothermic circulatory arrest and unilateral antegrade cerebral perfusion: Perioperative outcomes. J Thorac Cardiovasc Surg 2020;159:374-87.e4.
18. Keenan JE, Wang H, Gulack BC, et al. Does moderate hypothermia really carry less bleeding risk than deep hypothermia for circulatory arrest? A propensity-matched comparison in hemiarch replacement. J Thorac Cardiovasc Surg 2016;152:1559-69.e2.
19. Zhou H, Wang G, Yang L, et al. Acute Kidney Injury After Total Arch Replacement Combined With Frozen Elephant Trunk Implantation: Incidence, Risk Factors, and Outcome. J Cardiothorac Vasc Anesth 2018;32:2210-7.
20. Zhang K, Pan XD, Dong SB, et al. Cardiopulmonary bypass duration is an independent predictor of adverse outcome in surgical repair for acute type A aortic dissection. J Int Med Res 2020;48:300060520968450.
21. El-Sayed Ahmad A, Papadopoulos N, Risteski P, et al. The Standardized Concept of Moderate-to-Mild (≥28°C) Systemic Hypothermia During Selective Antegrade Cerebral Perfusion for All-Comers in Aortic Arch Surgery: Single-Center Experience in 587 Consecutive Patients Over a 15-Year Period. Ann Thorac Surg 2017;104:49-55.
22. Krüger T, Weigang E, Hoffmann I, et al. Cerebral protection during surgery for acute aortic dissection type A: results of the German Registry for Acute Aortic Dissection Type A (GERAADA). Circulation 2011;124:434-43.
23. Zierer A, Risteski P, El-Sayed Ahmad A, et al. The impact of unilateral versus bilateral antegrade cerebral perfusion on surgical outcomes after aortic arch replacement: a propensity-matched analysis. J Thorac Cardiovasc Surg 2014;147:1212-7; discussion 1217-8.
24. Tong G, Zhang B, Zhou X, et al. Bilateral versus unilateral antegrade cerebral perfusion in total arch replacement for type A aortic dissection. J Thorac Cardiovasc Surg

 

2017;154:767-75.
25. Norton EL, Wu X, Kim KM, et al. Unilateral is comparable to bilateral antegrade cerebral perfusion in acute type A aortic dissection repair. J Thorac Cardiovasc Surg 2020;160:617-25.e5.
26. Cao L, Guo X, Jia Y, et al. Effect of Deep Hypothermic Circulatory Arrest Versus Moderate Hypothermic Circulatory Arrest in Aortic Arch Surgery on Postoperative Renal Function: A Systematic Review and Meta-Analysis. J Am Heart Assoc 2020;9:e017939.
27. Motomura N, Miyata H, Tsukihara H, et al. Risk model of thoracic aortic surgery in 4707 cases from a nationwide single-race population through a web-based data entry system: the first report of 30-day and 30-day operative outcome risk models for thoracic aortic surgery. Circulation 2008;118:S153-9.
28. Ma WG, Zheng J, Zhang W, et al. Frozen elephant trunk with total arch replacement for type A aortic dissections: Does acuity affect operative mortality? J Thorac Cardiovasc Surg 2014;148:963-70; discussion 970-2.
29. Strauch JT, Lauten A, Spielvogel D, et al. Mild hypothermia protects the spinal cord from ischemic injury in a chronic porcine model. Eur J Cardiothorac Surg 2004;25:708-15.
30. El-Sayed Ahmad A, Papadopoulos N, Risteski P, et al. Is More than One Hour of Selective Antegrade Cerebral Perfusion in Moderate-to-Mild Systemic Hypothermic Circulatory Arrest for Surgery of Acute Type A Aortic Dissection Safe? Thorac Cardiovasc Surg 2018;66:215-21.

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