Original Article

Short-term outcomes of mild (≥30 ℃) *vs*. moderate hypothermic circulatory arrest in aortic arch surgery

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Background: Hypothermia and antegrade cerebral perfusion (ACP) strategies in open aortic arch surgery (AAS) have improved significantly. The significance of the gradual temperature rise to mild hypothermia is quite apparent, however, its safety remains a challenge. Therefore, our objective was to explore the safety and efficacy of mild hypothermic circulatory arrest (Mi-HCA, ≥30 ℃).

Methods: This retrospective cohort study enrolled in a total of 372 patients, and was performed at the Beijing Anzhen Hospital between January 2017 and November 2022. Among the 372 patients, 81 received AAS at ≥30 ℃, and the remaining 291 received the same at 22–29.9 ℃. Most acute type A aortic dissection (ATAAD) patients received total arch replacement (TAR) and frozen elephant trunk (FET) operation.

Results: Mi-HCA patients exhibited strongly augmented systemic temperature (26.19±1.63 *vs*. 31.40±0.79 ℃, P<0.01). The surgical, cardiopulmonary bypass (CPB), cross-clamp, circulatory arrest, and ACP durations were drastically diminished among Mi-HCA patients (all P<0.01). Moreover, the major adverse events (MAEs) incidence of Mi-HCA patients was significantly decreased (25.43% *vs*. 14.81%, P<0.05). Simultaneously, the Mi-HCA strategy also exhibited enhanced protection of blood cells, as well as myocardial and hepatic function. Nevertheless, multivariate logistic regression analysis revealed that Mi-HCA strategy (≥30 ℃) was not a stand-alone risk factor for MAEs following AAS.

Conclusions: The short-term outcomes and safety of Mi-HCA, in combination with ACP, in AAS are satisfactory. Additionally, relative to the traditional moderate hypothermic circulatory arrest (MHCA) approach, it can substantially decrease operation duration while improving patient clinical outcomes.

Keywords: Mild hypothermic circulatory arrest (Mi-HCA); moderate hypothermic circulatory arrest (MHCA); type A aortic dissection (TAAD); major adverse events (MAEs)

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Introduction

Aortic arch surgeries (AASs), particularly, acute type A aortic dissection (ATAAD) or complex arch pathologies, come with complex challenges that require attention. Cerebral and visceral organ protection is absolutely critical during open arch repair, and it necessitates systemic hypothermic management and brain perfusion during the circulatory arrest period. The past two decades have seen

considerable advancements in brain protection strategies from isolated deep hypothermic circulatory arrest (DHCA) (1) application in initial early experience to retrograde cerebral perfusion (RCP) or antegrade cerebral perfusion (ACP, selective unilateral *vs.* bilateral) (2-4).

Multiple investigations have revealed the superior performance of ACP over DHCA alone, particularly at times when extended arch reconstruction is prolonged (5-7). In terms of the degree of hypothermia (8), warmer temperature (moderate-to-mild hypothermia) is considered safe, and comparable to colder temperature (deep hypothermia), when ACP is involved (5,6,9-11). At present, however, there is still much concern about the safety of mild hypothermic circulatory arrest (Mi-HCA) in clinical practice.

Here, we retrospectively evaluated the safety and efficacy of Mi-HCA (≥30 ℃) versus conventional moderate hypothermic circulatory arrest (MHCA) in a patient population consisting primarily of ATAAD patients who received total arch replacement (TAR) and frozen elephant trunk (FET) operation. We present this article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-796/rc).

Highlight box

Key findings

- The short-term outcomes and safety of mild hypothermic circulatory arrest (Mi-HCA), in combination with antegrade cerebral perfusion (ACP), in aortic arch surgery (AAS) are satisfactory.

What is known and what is new?

- Multiple investigations have revealed the superior performance of ACP, along with moderate-to-mild systemic hypothermia, over deep hypothermic circulatory arrest alone during AAS. At present, however, there is still much concern about the safety of Mi-HCA in clinical practice.
- Mi-HCA, in combination with ACP, provided adequate neurologic and visceral organ protection for acute type A aortic dissection (ATAAD) patients who underwent AAS. Relative to the conventional moderate hypothermic circulatory arrest strategy, Mi-HCA substantially reduced operation duration and enhanced patient clinical outcome.

What is the implication, and what should change now?

- These positive intraoperative and postoperative outcomes suggest that the mild hypothermia strategy can be safely applied for AAS.

Methods

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study received ethical approval from the Beijing Anzhen Hospital, Capital Medical University (approval No. 2019030X). Due to the retrospective nature of this study, informed consent was waived.

Patients

Since 2019, our surgical team gradually raised the temperature during AAS to ≥30 ℃ (range, 30 to 32.9 ℃), and bilateral ACP (bACP) was preferred for enhanced cerebral and visceral organ perfusion. Herin, we integrated all aortic dissection patient databases from 2017 to provide a detailed summary of this practice.

We recruited 421 AAS patients between January 2017 and November 2022 from the Department of Cardiovascular Surgery of Beijing Anzhen Hospital. Our selection criteria included only type A aortic dissection (TAAD) or aortic arch aneurysm patients, who received AAS with ACP. Subsequently, we eliminated patients with prior neurological injury and remaining serious complications from analysis. Post surgery, we also eliminated patients who expired within 48 hours of surgery, as the neurological outcomes cannot be accurately verified. Ultimately, we included only 372 patients in the analysis, who primarily suffered from ATAAD (*Figure 1*). We assigned patients to two groups based on their bladder temperature at hypothermic circulatory arrest (HCA) onset: (I) control group (i.e., CTL group or CG): 26.19±1.63 ℃ (n=291), ranging from 22.0 to 29.9 ℃; (II) Mi-HCA group: 31.40±0.79 ℃ (n=81), ranging from 30.0 to 32.9 ℃. Moreover, the nasopharyngeal temperature was 24.68±1.52 ℃ among CG patients, and 30.39±1.48 ℃ among Mi-HCA patients.

Table 1 presents the preoperative clinical profiles of both cohorts, which included 287 (77.15%) males and 85 (22.85%) females, with a mean age of 49.01±11.16 years. AAS was conducted in 348 (93.55%) ATAAD patients, and in 24 patients with ascending aortic and arch aneurysm or chronic TAAD. Emergency surgery was performed in most participants (94.62%). Among comorbidities, hypertension was the most prevalent, with incidences in 313 patients (84.14%). Lastly, 29 patients (7.80%) had Marfan syndrome.

Preoperative aortic computed tomography angiography

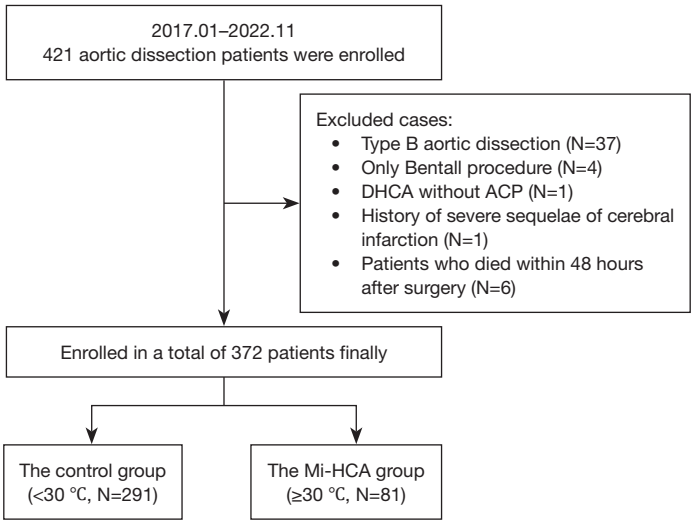

Figure 1 Study inclusion and exclusion criteria technical roadmap. DHCA, deep hypothermic circulatory arrest; ACP, antegrade cerebral perfusion; Mi-HCA, mild hypothermic circulatory arrest.

Table 1 Preoperative clinical profiles

Variables	CTL (N=291)	Mi-HCA (N=81)	P
Age, years	48.68±11.17	50.20±11.14	0.28
Male	227 (78.01)	60 (74.07)	0.46
Classification			0.02*
ATAAD	277 (95.19)	71 (87.65)	
AA or chronic TAAD	14 (4.81)	10 (12.35)	
Emergency	277 (95.19)	75 (92.59)	0.52
BMI, kg/m^2	26.55±4.16	27.23±4.52	0.20
Hypertension	245 (84.19)	68 (83.95)	0.96
Diabetes mellitus	18 (6.19)	1 (1.23)	0.13
Coronary artery disease	10 (3.44)	1 (1.23)	0.51
Prior cerebrovascular disease history	14 (4.81)	6 (7.41)	0.52
Chronic kidney failure	2 (0.69)	0	>0.99
Marfan syndrome	24 (8.25)	5 (6.17)	0.54
Prior aortic interventional therapy	5 (1.72)	2 (2.47)	>0.99
Smoking history			0.24
No	150 (51.55)	42 (51.85)	
Yes	134 (46.05)	34 (41.98)	
Quit smoking more than 3 months	7 (2.41)	5 (6.17)	
Diameter of the aortic sinus, mm	41.78±7.06	41.84±8.04	0.95
LVEDD, mm	49.33±6.65	48.89±8.48	0.62

Table 1 *(continued)*

Table 1 *(continued)*

Variables	CTL (N=291)	Mi-HCA (N=81)	P
LVEF, %	62.24±5.27	61.35±6.07	0.19
AI			0.90
No	75 (25.86)	24 (29.63)	
Mild	104 (35.86)	26 (32.10)	
Moderate	68 (23.45)	19 (23.46)	
Severe	43 (14.83)	12 (14.81)	
Malperfusion			
Cerebrum	81 (29.67)	18 (22.78)	0.21
Coronary artery	22 (7.69)	4 (5.00)	0.41
Spinal cord	22 (8.12)	12 (15.79)	<0.05*
Abdominal organ	34 (12.06)	8 (10.26)	0.66
Renal	43 (15.25)	15 (18.99)	0.42
Lower limbs	26 (9.15)	7 (8.75)	0.91
Location of the primary break			0.06
Unobvious	38 (13.33)	4 (5.13)	<0.05*
Ascending	150 (52.63)	47 (60.26)	
Aortic arch	58 (20.35)	11 (14.10)	
Descending	39 (13.68)	16 (20.51)	
Hemopericardium	205 (70.45)	33 (40.74)	<0.01*
Pericardial tamponade	28 (9.62)	10 (12.35)	0.47

Continuous data are presented as mean ± SD, and categorical data as number (%). *, P<0.05. CTL, the control group; Mi-HCA, mild hypothermic circulatory arrest; ATAAD, acute type A aortic dissection; AA, aortic aneurysm; BMI, body mass index; LVEDD, left ventricular end-diastolic dimension; LVEF, left ventricular ejection fraction; AI, aortic valve insufficiency; SD, standard deviation.

(CTA) was routinely conducted to verify the diagnosis and ascertain the involvement of each organ. Individual organ malperfusion was described as impaired circulation to corresponding downstream organs, thereby giving rise to ischemia and organ dysfunction owing to dissection-associated aorta and its branch vessel obstruction.

Patient clinical information was collected and recorded prospectively in the hospital medical records database, with proper verification by two experienced cardiovascular surgery graduate students. Discharged patients underwent three months, six months, and yearly thereafter follow-ups, or were interviewed over telephone. Patient survival, reintervention, and adverse events data were documented by the outpatient physician.

Definitions

We followed the international consensus guidelines (8), yet elevated the systemic temperature criterion to 30 ℃ among Mi-HCA patients to explore the safety of Mi-HCA even up to 30 ℃. The primary endpoint was the occurrence of major adverse events (MAEs), which were described as the emergence of any of the four following conditions: permanent neurological dysfunction (PND), paraplegia, new postoperative acute kidney injury (AKI) necessitating continuous renal replacement therapy (CRRT), and mortality. Postoperative new localized neurological deficits were regarded as PND, and validated via brain computed tomography (CT) scanning or magnetic

resonance imaging (MRI). Reversible postoperative delayed wakefulness, agitation, or transitory delirium was designated as temporary neurological dysfunction (TND). The CT scanning was required to be normal, with resolution of all symptoms before discharge (12,13).

Surgical techniques

All surgical procedures were performed using a median sternotomy with cardiopulmonary bypass (CPB) and ACP under moderate-to-mild hypothermia (25–32 ℃) via cannulation of the right axillary artery and right atrium. First, proximal aortic root operations, including ascending aorta replacement or Bentall procedure, were completed. Subsequently, our TAR with FET surgical protocols (otherwise called the Sun operation) were detailed in our previous studies (14,15). More recently, there have been substantial advancements in hypothermia and ACP strategies (16-18). Since 2019, there has been a rise in warmer hypothermia (i.e., Mi-HCA), and we prefer to employ the right axillary and left common carotid arteries for bACP. After that, other procedures were generally the same.

Statistical analysis

All data analyses employed SPSS 25.0 (IBM Corp., Armonk, NY, USA). Continuous data normality were assessed using the Shapiro-Wilk test. Normally distributed variables were analyzed via the Student's *t*-test, and were presented as mean ± standard deviation (SD). Non-normally distributed variables were analyzed using the Mann-Whitney *U*-test, and were presented as median and interquartile range. To evaluate categorical variables, we utilized the Chi-squared or Fisher's exact tests. P values <0.05 were set as the significance threshold. Lastly, we performed multivariate logistic regression analysis to identify stand-alone risk factors for postoperative MAEs.

Results

Patient demographics

We observed a higher incidence of ATAAD in the CG (95.19% *vs.* 87.65%, P=0.02). Spinal cord malperfusion was more prominent among Mi-HCA patients than CG (8.12% *vs.* 15.79%, P<0.05). Hemopericardium incidences were more prevalent among CG (70.45% *vs.* 40.74%, P<0.01), whereas, pericardial tamponade incidences showed no difference between the two cohorts. Simultaneously, there were no significant differences in patient age, gender, emergency surgery, body mass index (BMI), hypertension, prior cerebrovascular disease, and other preoperative basic status between the two cohorts (*Table 1*). Table S1 presents the preoperative blood test results of both cohorts, with no discernible difference between the two cohorts.

Operative information

As shown in *Table 2*, among the 372 patients, 330 (88.71%) received TAR, the remaining 42 (11.29%) received proximal-right hemiarch replacement. The application of surgical procedures was comparable between the two groups. Most Mi-HCA patients (76, 93.83%) received bACP, conversely, CG patients mostly underwent the uSACP strategy (248, 85.22%; P<0.01). We observed marked reductions of operation, CPB, cross-clamp, circulatory arrest, and ACP durations among the Mi-HCA patients (all P<0.01), with substantial elevations in CPB pump pressure during ACP and ACP flow (all P<0.05). Additionally, the Mi-HCA patients, also required less intraoperative packed red blood cells (PRBCs) transfusion (P=0.04).

Perioperative mortality and morbidity

Table 3 provides a detailed summary of the postoperative patient outcomes. We observed a marked reduction in MAEs incidences among Mi-HCA versus CG patients [74 (25.43%) *vs.* 12 (14.81%), P<0.05]. Postoperative mortality did not change significantly between the cohorts [20 (6.87%) *vs.* 6 (7.41%), P=0.87]. Relative to CG, the TND (22.76% *vs.* 16.05%), PND (11.00% *vs.* 8.64%), AKI with CRRT (13.06% *vs.* 6.17%), re-intubate the ventilator (10.31% *vs.* 4.94%), tracheotomy (5.84% *vs.* 1.23%) incidences were slightly lower, but did not reach significance (all P>0.05). In addition, there were no differences in paraplegia and monoplegia of lower limbs between the two cohorts (all P>0.05), as well as in hospitalization, consciousness recovery, ventilation, or intensive care unit (ICU) stay durations.

Meanwhile, we observed reduction in chest tube drainage volume during the first 24 h among the Mi-HCA patients (P=0.05), along with a significant decrease in total PRBCs transfusion during hospitalization (P=0.01).

Table 2 Surgical data and operational procedures

Variables	CTL (N=291)	Mi-HCA (N=81)	P
Operating methods			0.59
Ascending aorta replacement with TAR and FET	166 (57.04)	48 (59.26)	
Bentall procedure with TAR and FET	94 (32.30)	22 (27.16)	
Hemiarch replacement	31 (10.65)	11 (13.58)	
Cannulation strategy			<0.01*
uSACP	160 (54.98)	2 (2.47)	<0.05*
bACP	22 (7.56)	67 (82.72)	<0.05*
uSACP + femoral artery cannulation	88 (30.24)	3 (3.70)	<0.05*
bACP + femoral artery cannulation	21 (7.22)	9 (11.11)	
Nasopharyngeal temperature, ℃	24.68±1.52	30.39±1.48	<0.01*
Bladder temperature, ℃	26.19±1.63	31.40±0.79	<0.01*
Operation duration, h	7.23±1.23	6.14±1.29	<0.01*
CPB duration, min	202.89±40.09	161.38±31.53	<0.01*
Cross-clamp duration, min	116.55±27.78	84.81±17.75	<0.01*
CPB pump pressure during ACP, mmHg	60.00 (60.00, 70.00)	70.00 (60.00, 79.00)	0.02*
ACP flow, mL/(kg·min)	6.16 (5.30, 7.93)	8.33 (7.50, 9.87)	<0.01*
Radial artery pressure, mmHg	25.00 (19.00, 32.00)	25.50 (20.00, 34.25)	0.54
Circulatory arrest duration, min	25.51±10.72	17.17±6.61	<0.01*
ACP duration, min	33.84±10.34	17.78±6.43	<0.01*
Intraoperative transfusion of PRBCs, U	0 (0, 4.00)	0 (0, 2.00)	0.04*

Data are presented as mean ± SD, median (interquartile range) or number (%) as appropriate. *, P<0.05. CTL, the control group; Mi-HCA, mild hypothermic circulatory arrest; TAR, total arch replacement; FET, frozen elephant trunk; uSACP, unilateral selective antegrade cerebral perfusion; bACP, bilateral antegrade cerebral perfusion; ACP, antegrade cerebral perfusion; CPB, cardiopulmonary bypass; PRBCs, packed red blood cells; SD, standard deviation.

Postoperative visceral organ functions

Table 4 summarizes the patient postoperative blood test results. Relative to CG, Mi-HCA patients exhibited substantially reduced blood glucose value four hours post-surgery [214.00 (184.00, 302.00) *vs.* 206.00 (179.50, 228.00), P=0.01]. Likewise, the 4-hour post-surgical lactic acid (Lac) value was also diminished [3.10 (2.10, 6.60) *vs.* 2.70 (1.70, 3.70), P=0.01]. There was no change in arterial blood gas analysis between the two cohorts beyond 4-hour post-surgery (listed in Table S2).

Relative to CG, the aspartate aminotransferase (AST) content among Mi-HCA patients was considerably reduced on days 1–4 post surgery [54.00 (41.00, 81.00) *vs.* 49.00 (34.00, 69.00); 60.00 (37.00, 102.00) *vs.* 35.00 (24.25, 61.75); 52.00 (29.00, 99.00) *vs.* 31.50 (20.25, 54.00); 50.00 (26.00, 93.00) *vs.* 33.00 (20.00, 66.00), all P<0.05]. Meanwhile, the alanine aminotransferase (ALT) values exhibited a synergistic alteration on days 2–4 post surgery. The troponin I (TNI) values among Mi-HCA patients were significantly decreased, compared to CG on two- or three-day post-surgery [3,050.00 (1,544.95, 6,260.00) *vs.* 1,902.80 (877.33, 3,620.40); 1,810.00 (912.50, 4,297.50) *vs.* 927.35 (388.58, 1,610.30), all P<0.01]. Additionally, the platelet count among Mi-HCA patients were significantly elevated on days 1–3 post-surgery [79.00 (59.00, 110.40) *vs.* 100.00 (68.50, 147.00); 90.00 (59.00, 125.00) *vs.* 110.00 (80.00, 155.00); 97.00 (70.70, 137.50) *vs.* 117.50 (81.50, 159.00), all P<0.05]. The hemoglobin content was strongly enhanced among Mi-HCA patients versus CG on one day

Table 3 Postoperative outcomes

Variables	CTL (N=291)	Mi-HCA (N=81)	P
Hospital stay time, days	13.00 (10.00, 17.00)	13.00 (10.00, 17.00)	0.62
Consciousness recovery time, h	5.42 (3.32, 10.00)	5.25 (3.75, 8.17)	0.85
Ventilation time, h	16.08 (12.50, 43.63)	17.33 (11.25, 43.13)	0.46
ICU stay time, h	41.00 (19.08, 107.00)	44.33 (19.88, 88.17)	0.84
Chest tube drainage, mL/24 h	680.00 (450.00, 1,000.00)	600.00 (400.00, 780.00)	0.05
Total transfusion of PRBCs, U	4.00 (0, 8.00)	2.00 (0, 6.00)	0.01*
Total transfusion of fresh frozen plasma, mL	0 (0, 400.00)	0 (0, 400.00)	0.68
Total transfusion of platelet, U	0 (0, 1.00)	0 (0, 0)	0.12
TND	66 (22.76)	13 (16.05)	0.19
PND	32 (11.00)	7 (8.64)	0.54
AKI with CRRT	38 (13.06)	5 (6.17)	0.09
Re-intubate the ventilator	30 (10.31)	4 (4.94)	0.14
Tracheotomy	17 (5.84)	1 (1.23)	0.16
Paraplegia	13 (4.50)	4 (4.94)	>0.99
Monoplegia of lower limbs	4 (1.38)	4 (4.94)	0.13
Mortality	20 (6.87)	6 (7.41)	0.87
MAEs	74 (25.43)	12 (14.81)	<0.05*

Data are presented as median (interquartile range), or number (%) as appropriate. *, P<0.05. CTL, the control group; Mi-HCA, mild hypothermic circulatory arrest; ICU, intensive care unit; PRBCs, packed red blood cells; TND, temporary neurological dysfunction; PND, permanent neurological dysfunction; AKI, acute kidney injury; CRRT, continuous renal replacement therapy; MAEs, major adverse events.

post-surgery [94.00 (83.00, 107.00) *vs.* 99.00 (91.00, 110.00), P=0.04]; On the other hand, creatinine levels were elevated among Mi-HCA patients [100.30 (80.30, 131.90) *vs.* 110.60 (81.25, 173.95), P=0.04].

Multivariate analysis

According to the aforementioned results, combined with prior clinical practice consensus, univariate analysis (summarized in Table S3) revealed that the patient age, gender, prior cerebrovascular disease history, Mi-HCA grouping, operation duration, CPB duration, and cross-clamp duration were linked to postoperative MAEs (all P<0.05).

All variables that satisfied the tolerance >0.1 and variance expansion coefficient <10 in univariate analysis were entered into multivariate logistic regression analysis (presented in *Table 5*) for identification of stand-alone risk factors of postoperative MAEs. Eventually, patient age (OR =1.04, 95% CI: 1.01–1.07, P<0.01), male (OR =0.45, 95% CI: 0.24–0.84, P=0.01), prior cerebrovascular disease history (OR =2.82, 95% CI: 1.04–7.62, P=0.04) and operation duration (OR =1.41, 95% CI: 1.07–1.85, P=0.01) were stand-alone risk factors for MAEs following AAS. According to current investigation, the Mi-HCA strategy did not provide better protection against MAEs, relative to CGs.

Discussion

To date, multiple protection strategies used during AAS, as well as their associated neurological and visceral complications, remain a hot topic of research. Emerging evidences from our prior work and others revealed that the ACP, along with moderate-to-mild systemic hypothermia, is a relatively safe and reproducible procedure during AAS (5,6,16-22). However, the safety of Mi-HCA is controversial in clinical practice, particularly, when the systemic hypothermia approaches ≥30 ℃. In published literature,

Table 4 Postoperative blood test results

Variables	CTL (N=291)	Mi-HCA (N=81)	P
Glu 4 hours, mg/dL	214.00 (184.00, 302.00)	206.00 (179.50, 228.00)	0.01*
Lac 4 hours, mmol/L	3.10 (2.10, 6.60)	2.70 (1.70, 3.70)	0.01*
ALT D1, U/L	20.00 (14.00, 31.00)	20.00 (14.00, 32.00)	0.77
AST D1, U/L	54.00 (41.00, 81.00)	49.00 (34.00, 69.00)	0.02*
Cre D1, μmol/L	100.30 (80.30, 131.90)	110.60 (81.25, 173.95)	0.04*
TNI D1, pg/mL	4,090.00 (2,357.50, 7,159.48)	3,381.60 (1,918.30, 5,493.95)	0.09
Hb D1, g/L	94.00 (83.00, 107.00)	99.00 (91.00, 110.00)	0.04*
PLT D1, $\times10^9$/L	79.00 (59.00, 110.40)	100.00 (68.50, 147.00)	<0.01*
ALT D2, U/L	26.00 (17.00, 48.00)	22.00 (15.25, 34.00)	0.03*
AST D2, U/L	60.00 (37.00, 102.00)	35.00 (24.25, 61.75)	<0.01*
Cre D2, μmol/L	104.10 (73.40, 161.60)	117.95 (77.73, 217.38)	0.13
TNI D2, pg/mL	3,050.00 (1,544.95, 6,260.00)	1,902.80 (877.33, 3,620.40)	<0.01*
Hb D2, g/L	92.00 (82.00, 105.00)	94.00 (86.00, 106.75)	0.14
PLT D2, $\times10^9$/L	90.00 (59.00, 125.00)	110.00 (80.00, 155.00)	<0.01*
ALT D3, U/L	36.00 (21.00, 73.00)	25.50 (18.25, 48.00)	<0.01*
AST D3, U/L	52.00 (29.00, 99.00)	31.50 (20.25, 54.00)	<0.01*
Cre D3, μmol/L	92.40 (66.30, 149.90)	97.20 (70.30, 176.80)	0.34
TNI D3, pg/mL	1,810.00 (912.50, 4,297.50)	927.35 (388.58, 1,610.30)	<0.01*
Hb D3, g/L	88.00 (81.00, 99.00)	91.00 (79.20, 102.00)	0.66
PLT D3, $\times10^9$/L	97.00 (70.70, 137.50)	117.50 (81.50, 159.00)	0.02*
ALT D4, U/L	55.00 (29.00, 109.00)	40.00 (21.00, 78.00)	0.02*
AST D4, U/L	50.00 (26.00, 93.00)	33.00 (20.00, 66.00)	<0.01*

Data are presented as median (interquartile range). *, P<0.05. CTL, the control group; Mi-HCA, mild hypothermic circulatory arrest; Glu, blood glucose value; Lac, lactic acid; ALT, alanine aminotransferase; AST, aspartate aminotransferase; Cre, creatinine; TNI, troponin I; Hb, hemoglobin; PLT, platelets.

Table 5 Multivariate analysis

Exposure = MAEs	OR	95% CI	P
Age, years	1.04	1.01–1.07	<0.01*
Male	0.45	0.24–0.84	0.01*
History of cerebrovascular disease	2.82	1.04–7.62	0.04*
Grouping (Mi-HCA)	0.79	0.37–1.72	0.56
Operation duration, h	1.41	1.07–1.85	0.01*
CPB duration, min	1.01	1.00–1.02	0.09
Cross-clamp duration, min	1.00	0.98–1.01	0.50

*, P<0.05. MAEs, major adverse events; OR, odds ratio; CI, confidence interval; Mi-HCA, mild hypothermic circulatory arrest; CPB, cardiopulmonary bypass.

there are limited reports on the safety and efficacy of Mi-HCA (≥30 ℃) during operation. Herein, we examined the clinical outcomes of ACP combined with Mi-HCA (≥30 ℃), relative to the conventional MHCA, in AAS in patients with ATAAD.

Compared to the conventional MHCA strategy, most Mi-HCA patients (93.83%) utilized bACP, and the ACP pressure and flow were increased. Using Mi-HCA strategy drastically decreased surgical, CPB, cross-clamp, and SCP durations, which may be due to the reduced cooling and rewarming durations and modified aortic reconstruction procedure. Following FET implantation and distal arch anastomosis, we first completed the proximal ascending aorta reconstruction under bACP to resume cardiac

perfusion. Thus, the durations of ACP and cross-clamp were drastically shortened (16-18).

It is natural that complications associated with prolonged CPB duration were reduced, namely, coagulation challenges, inflammatory response, visceral dysfunctions, death, and so on (23-25). As shown above, among Mi-HCA patients, we observed substantially reduced chest tube drainage volume during the first 24 h, as well as decreased PRBCs transfusion. Meanwhile, the warmer hypothermia offered better protection of blood cells, as the Mi-HCA patient platelet counts on post-surgical days 1–3 were substantially elevated, and the hemoglobin were also elevated. Additionally, as proved in our clinical practice, mild hypothermia significantly decreased the hemostasis procedural difficulty and duration.

We observed comparable cerebral and visceral organ protection efficiency between the two groups. Furthermore, the incidences of TND, PND, AKI with CRRT, re-intubate the ventilator, and tracheotomy prevalences were slightly reduced, relative to CG. The detrimental influences of deep hypothermia (25 ℃) on cerebrovascular autoregulation needs particular attention (26,27). In contrast, mild systemic hypothermia (30 ℃) successfully restored cerebral autoregulation and favored equal distribution of flow within the brain (28). Di Eusanio *et al.* (29) revealed that a warmer hypothermia meant a shorter rewarming duration, which consequently reduced microembolism risk while enhancing patient neurological outcome.

Postoperative AKI is the most prominent evaluator of distal visceral dysfunction following AAS, and it is a strong indicator of morbidity and mortality. Zhou *et al.* (24) suggested that the CPB duration was the only modifiable indicator of AKI, and patients may benefit from warmer hypothermia owing to the reduced CPB duration. Similarly, according to the Pacini *et al.* (30) study, temperature >25 ℃ was an independent protective factor for isolated hepatic dysfunction, as shown in our data.

Etz *et al.* reported that the spinal cord is most prone to ischemic injury once the systemic hypothermia reaches >28 ℃ (31). Herein, we revealed that the paraplegic incidence among Mi-HCA patients was 4.94%, which closely corroborated earlier reports (15,32). In a prior investigation, Strauch *et al.* (33) employed a porcine model to evaluate the safety limit of spinal cord ischemic tolerance, and proved that mild hypothermia (32 ℃) significantly enhanced spinal cord tolerance to ischemia up to 50 min. In clinical practice, Fukunaga (21) and El-Sayed Ahmad (22) also demonstrated the safety of prolonged ACP (≥60 min) under moderate-to-mild systemic hypothermia.

Overall, our most significant finding was that Mi-HCA, in combination with ACP, during AAS substantially decreased the surgical, CPB, cross-clamp, circulatory arrest, and ACP durations, and associated challenges, and provided similar or better neurologic and visceral organ protection to MHCA. The circulatory arrest duration strongly impacts organ ischemia injury. In this report, the median circulatory arrest duration among Mi-HCA patients was 16 min, and the longest duration was 56 min (this patient experienced quick post-surgical recovery, without any complications). It is absolutely critical to restore distal perfusion as soon as possible to prevent distal viscera and spinal cord ischemia.

Limitations

As a real word study, this research has certain limitations. Firstly, apart from hypothermia, there are other confounding factors that influence cerebral and visceral perfusion in clinical practice, including unilateral or bilateral ACP, circulatory arrest or ACP duration, and so on. Secondly, we were restricted by the sample size of the Mi-HCA group. As time progresses and the sample size is further expanded, a more comprehensive clinical database will be established for further research.

Conclusions

Herein, we demonstrated that Mi-HCA, in combination with ACP, provided adequate neurologic and visceral organ protection for ATAAD patients who underwent AAS. Relative to the conventional MHCA strategy, Mi-HCA substantially reduced operation duration and enhanced patient clinical outcome.

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Footnote

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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 study was approved by the Beijing Anzhen Hospital, Capital Medical University (approval No. 2019030X). Due to the retrospective nature of this study, informed consent was waived.

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