Original Article

Mild hypothermic circulatory arrest with selective cerebral perfusion in open arch surgery

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Background: This study aimed to evaluate whether the use of mild hypothermic circulatory arrest (HCA) with selective cerebral perfusion (SCP) in open arch procedure provides comparable perioperative results to moderate HCA for patients with dissected or degenerative arch pathologies.

Methods: Between January 2017 and September 2020, a total of 88 consecutive patients (mean age 47±11 years, 71 males) underwent open arch repair under a single surgeon at our institution with mild or moderate systemic hypothermia assisted by unilateral or bilateral SCP. Patients were divided into groups according to the nasopharyngeal temperature at the beginning of HCA: a moderate HCA group (n=47, 53.4%) and a mild HCA group (n=41, 46.6%). The postoperative mortality, morbidity, and visceral organ functions between these groups were analyzed retrospectively.

Results: Compared to the moderate HCA group, the mild HCA group had a significantly higher core temperature (nasopharynx: 24.4±0.8 *vs.* 28.5±2, P<0.001; bladder 25.9±0.9 *vs.* 30±1.2, P<0.001), and the incidence of major adverse events (MAE) in this group was markedly lower (21.3% *vs.* 4.9%, P=0.031). No differences were identified between the two groups refer to in-hospital mortality, permanent neurological deficit (PND), temporary neurological deficit (TND), and paraplegia (8.5% *vs.* 2.4%, P=0.366; 8.5% *vs.* 0, P=0.120; 6.4% *vs.* 7.3%, P=1.0; 4.3% *vs.* 2.4%, P=1.0, respectively). In the moderate HCA group, 6 patients (12.8%) developed acute renal failure needing replacement therapy, which did not occur in the mild HCA group (P=0.028). The duration of ventilator support and intensive care unit stay was shorter in the mild HCA group, as well as a decreased volume of drainage during the first 24 h and reduced platelet transfusion.

Conclusions: The preliminary results of the mild HCA group with SCP applied in open arch repair, mainly in total arch replacement (TAR) and stented elephant trunk (SET) implantation for aortic dissection, were satisfactory. Furthermore, comparable inferior outcomes were obtained with mild HCA compared with that of the conventional moderate HCA strategy. These encouraging surgical and postoperative results favor this more aggressive hypothermia strategy in open arch repair.

Keywords: Mild hypothermic circulatory arrest (mild HCA); moderate hypothermic circulatory arrest (moderate HCA); type A aortic dissection (TAAD); open arch repair

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Introduction

Arch surgery is one of the major challenges in modern aortic surgery, especially for complex arch pathologies or acute type A aortic dissection (TAAD). Special cerebral and visceral organ protection is mandatory in open arch repair to improve clinical safety. Deep hypothermic circulatory arrest (HCA), introduced by Griepp *et al.* in the mid-1970s (1), allowed for a short period of circulatory arrest and was considered an essential component of open arch surgery. The application of selective cerebral perfusion (SCP), which was first introduced by Bachet and Kazui (2-4), is an important adjunct to deep HCA. It provided a near physiological method of cerebral perfusion, allowed for a relative higher core temperature during distal anastomosis, and offered a key advantage in reducing mortality and morbidity in the aortic arch field.

Numerous studies have established the superiority of SCP over deep HCA alone, specifically due to its better survival and neurological results, especially in complex cases that involve time-consuming arch repair (5-7). However, there is currently no consensus regarding the optimal level of hypothermia that cardiopulmonary bypass (CPB) can be discontinued in arch repair. The safe limits of distal HCA at higher temperatures have not yet been clearly defined and are not well recognized in clinical practice.

Herein, we performed a retrospective comparative study to explore the safety and efficacy of mild HCA applied in a cohort consisting mainly of TAAD patients treated with total arch replacement (TAR) and stented elephant trunk (SET) implantation. We present the following article in accordance with the STROBE reporting checklist (available at http://dx.doi.org/10.21037/jtd-20-3550).

Methods

All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Ethics Committee of Beijing Anzhen Hospital, Capital Medical University. Written informed consent was obtained for each participant.

Patients

From January 2017 to September 2020, a total of 88 patients underwent open arch repair under a single surgeon (XD Pan) at Beijing Anzhen Hospital. According to the nasopharyngeal temperature at the beginning of HCA, patients were categorized as mild and moderate HCA groups according to the international consensus guidelines (8): (I) the moderate HCA group: 24.4 ℃ (n=47, 53.4%); (II) the mild HCA group: 28.5 ℃ (n=41, 46.6%). In almost all cases, the bladder temperature was approximately 1–2 ℃ higher than the nasopharyngeal temperature. The mean bladder temperature during open arch repair in the moderate HCA group was 25.9 ℃, and was 30 ℃ in the mild HCA group. SCP was applied for cerebral protection in all cases.

The relevant clinical characteristics of the patients are summarized in *Table 1*. The patient cohort consisted of 71 males and 17 females, with a mean age of 47 years (range, 19–71 years). Indications for arch repair were TAAD in 84 patients, type B dissection with root aneurysm in three patients, and degenerative aortic aneurysm in one patient. The most prevalent comorbidity was arterial hypertension, which was diagnosed in 72 patients (81.8%), followed by smoking in 47 (53.4%) and pericardial effusion in 42 (47.7%). Severe or moderate aortic regurgitation was found in 25 patients (28.4%), malperfusion in 12 cases (13.6%), chronic kidney disease in 10 cases (11.4%), and cardiac tamponade in 8 cases (9.1%).

Transthoracic echocardiography and computed tomography angiography (CTA) were routinely conducted preoperatively for confirmation of diagnosis, to identify involved aortic valves and pericardial effusion, and to evaluate cardiac function. Survivors were followed by clinic visits mainly. The referring physician recorded survival, re-intervention, and adverse events. Follow-up echocardiography and CTA were suggested annually.

Definitions

Death occurring in the hospital during the perioperative period was defined as in-hospital mortality. Permanent neurological deficit (PND) was identified as a newly developing neurological deficit verified by cranial CT scan. Temporary neurological deficit (TND) referred to the occurrence of reversible delirium, agitation, confusion, or motor deficit, which was resolved before discharge (verified by a normal CT scan). The definition of postoperative acute kidney injury (AKI) was cited from the Kidney Disease Improving Global Outcomes criteria (9), and was diagnosed when the value of postoperative creatinine was 1.5-fold higher than the baseline level or an increase in creatinine of 0.3 mg/dL occurred within 48 h postoperatively. Major adverse events (MAE) referred to any of the following

Table 1 Preoperative clinical profiles

Variables	Moderate HCA group (n=47)	Mild HCA group (n=41)	P value
Age, years	47±9.9	46.9±12.2	0.952
Male	40 (85.1%)	31 (75.6%)	0.26
Acute TAAD	36 (76.6%)	36 (87.8%)	0.174
Chronic TAAD	10 (21.3%)	2 (4.9%)	0.031
Degenerative aortic aneurysm	0	1 (2.4%)	0.466
Type B aortic dissection with root aneurysm	1 (2.1%)	2 (4.9%)	0.596
Hypertension	39 (83%)	33 (80.5%)	0.762
Smoking	26 (55.3%)	21 (51.2%)	0.701
Malperfusion	6 (12.8%)	6 (14.6%)	0.799
Pericardial effusion	24 (51%)	18 (44%)	0.502
Cardiac tamponade	3 (6.4%)	5 (12.2%)	0.465
Diabetes mellitus	1 (2.1%)	4 (9.8%)	0.18
Marfan syndrome	2 (4.3%)	4 (9.8%)	0.411
Chronic kidney disease	6 (12.8%)	4 (9.8%)	0.745
Dialysis	0	1 (2.4%)	0.466
Previous cerebrovascular history	4 (8.5%)	1 (2.4%)	0.366
Aortic regurgitation (moderate or severe)	18 (38.3%)	7 (17.1%)	0.028
Ejection fraction	61.1±5	62±5.7	0.462
Admission laboratory data			
Creatinine (μmol/L)	95.3±48	105.4±87	0.494
Aspartate aminotransferase (IU/L)	24 [18, 33]	21 [16, 30]	0.424
Total bilirubin (μmol/L)	20.5±10.1	22.2±8.7	0.411

Continuous data are presented as mean ± SD or median [interquartile range (IQR)], and categorical data are presented as the n (%). HCA, hypothermic circulatory arrest; TAAD, type A aortic dissection.

conditions: paraplegia, PND, continuous renal replacement therapy (CRRT) for acute renal failure, and in-hospital mortality.

Surgical techniques

The hypothermic and SCP strategy has been evolving in recent years. Unilateral selective cerebral perfusion (uSCP) with moderate HCA was the primary method of choice between 2017 and 2019. After 2019, there was a trend toward bilateral selective cerebral perfusion (bSCP) and mild HCA. Sun's procedure has been applied widely in open arch repair for treating extensive arch pathology in indicated patients at our institution, and the technique involving TAR with SET implantation has been reported in our previous study (10,11). Indications for TAR in this study referred to either of the following conditions: atherosclerotic aneurysm in the arch and descending aorta, aortic root aneurysm complicated by type B aortic dissection with involved arch, as well as TAAD with involved arch vessels, a primary arch tear, intimal intussusception in the arch, and Marfan syndrome. In patients with uSCP and moderate HCA, the right axillary artery was cannulated for CPB and SCP. The procedure involved implantation of a SET (Cronus, MicroPort, China) in the descending aorta, followed by TAR with a four-branched graft (Vascutek, Terumo, Japan). After completing the distal arch anastomosis, lower body reperfusion was performed. To minimize the cerebral and coronary ischemia, the sequence of aortic reconstruction was special (i.e., proximal descending aorta, then left carotid artery, then ascending aorta, then left subclavian artery, and finally, innominate artery).

In cases with bSCP and mild HCA, the supra-aortic vessels were clamped once the target temperature was reached. Bilateral hemispheres were perfused via the right axillary and left common carotid artery. Next, we implanted the SET and performed distal arch anastomosis. Lower body reperfusion was subsequently resumed. We anastomosed the ascending aorta firstly, and then the left subclavian artery, the left carotid artery, and the innominate artery finally.

Statistical analysis

All perioperative data were collected prospectively. Statistical analysis was performed using SPSS 22.0 (SPSS, Inc., Chicago, IL, USA). The normality of continuous data was evaluated by Kolmogorov-Smirnov test. Data with normal distribution were expressed as mean ± standard deviation (SD) and were assessed by the Student's *t*-test. Median and interquartile range were applied to describe non-normally distributed data, and the Mann-Whitney U-test was performed for comparing. Chi-squared or Fisher's exact tests were applied for categorical variables. The mixed effect analysis of variance model was used to evaluate the differences in the variations of postoperative levels of aspartate aminotransferase, creatinine, and total bilirubin over time.

Results

Demographic characteristics

The significant differences between the mild and moderate HCA groups were not identified in term of age, sex, incidence of malperfusion, acute TAAD, cardiac tamponade, Marfan syndrome, and cardiac function. The incidence of chronic TAAD and moderate or severe aortic regurgitation were higher in the moderate HCA group (21.3% *vs.* 4.9%, P=0.031; 38.3% *vs.* 17.1%, P=0.028, respectively).

Operative data

The operative data and surgical procedures are listed in *Table 2*. Compared with the moderate HCA group, the mild HCA group had a significantly higher core temperature (nasopharynx: 24.4±0.8 *vs.* 28.5±2, P<0.001; bladder 25.9±0.9 *vs.* 30±1.2, P<0.001). The distribution of the intimal tear in TAAD patients was comparable between the two groups. No differences existed between the groups in the incidence of hemiarch replacement, TAR with SET implantation, and concurrent procedures, such as ascending aorta replacement, aortic sinus repair, bypass, the Bentall procedure, and coronary artery bypass grafting (CABG). Unilateral SCP was applied in 44 (93.6%) patients in the moderate HCA group, while bSCP was performed in 35 cases (85.4%) in the mild HCA group. Compared to the mild HCA group, patients in the moderate HCA group were characterized by a markedly longer duration for all of the following: CPB time (221.8±54.3 *vs.* 186.7±55.3, P=0.004), cross-clamp time (130±24.9 *vs.* 106.8±33, P<0.001), HCA time (25.8±10.4 *vs.* 19.8±9.5, P=0.006), and SCP time (36.8±8.3 *vs.* 21.1±10.7, P<0.001).

Perioperative mortality and morbidity

Table 3 shows the details of the postoperative outcomes. Compared with the moderate HCA group, the incidence of MAE in the mild HCA group was notably lower [10 (21.3%) *vs.* 2 (4.9%), P=0.031]. No significant differences were identified in the proportions of in-hospital mortality between the groups, with 4 deaths (8.5%) recorded in the moderate HCA group and 1 death (2.4%) in the mild HCA group (P=0.366). The reasons for mortality in the moderate HCA group were as follows: low cardiac output syndrome in two patients treated by TAR and SET implantation, pulmonary embolism in one patient with hemiarch replacement, and disseminated intravascular coagulation in one patient with TAR and SET implantation. In the mild HCA group, one patient developed severe myocardial infarction 1 day after TAR and SET implantation.

New postoperative neurological complications, such as PND, occurred in four patients in the moderate HCA group, while there were no such occurrences in the mild HCA group (8.5% *vs.* 0, P=0.12). Of the four patients with PND, two experienced right cerebral infarction, and bilateral cerebral infarction developed in one, and left cerebral infarction in one. The incidence of TND in the moderated HCA group was 6.4% (3/47), and 7.3% (3/41) in the mild HCA group (P=1.0). Of the six patients that experienced TNDs, all experienced agitation, and temporary delirium occurred in two patients in the mild HCA group. All of these TNDs resolved completely before

Table 2 Operative outcomes

Variables	Moderate HCA group (n=47)	Mild HCA group (n=41)	P value
Lowest bladder temperature	25.9±0.9	30±1.2	<0.001
Lowest nasal temperature	24.4±0.8	28.5±2	<0.001
Location of intimal tear in TAAD			
Ascending aorta	21/46 (45.7%)	22/38 (57.9%)	0.264
Aortic arch	14/46 (30.4%)	13/38 (34.2%)	0.712
Descending aorta	6/46 (13%)	1/38 (2.6%)	0.121
Multiple tears	4/46 (8.7%)	0	0.123
Unidentified	1/46 (2.2%)	2/38 (5.3%)	0.587
Hemiarch replacement	8 (17%)	2 (4.9%)	0.097
TAR with SET implantation	39 (83%)	39 (95.1%)	0.097
uSCP	44 (93.6%)	6 (14.6%)	<0.001
bSCP	3 (6.4%)	35 (85.4%)	<0.001
Operation time, h	7.1±1.2	7.1±1.5	0.916
CPB time, min	221.8±54.3	186.7±55.3	0.004
Cross-clamp time, min	130±24.9	106.8±33	<0.001
Lower body circulatory arrest time, min	25.8±10.4	19.8±9.5	0.006
Selective cerebral perfusion time	36.8±8.3	21.1±10.7	<0.001
Aortic sinus repair	18 (38.3%)	8 (19.5%)	0.054
Ascending aorta replacement	32 (68.1%)	28 (68.3%)	0.983
Bentall	15 (31.9%)	13 (31.7%)	0.983
Extra-anatomic bypass	0	1 (2.4%)	0.466
CABG	1 (2.1%)	3 (7.3%)	0.335

HCA, hypothermic circulatory arrest; uSCP, unilateral selective cerebral perfusion; bSCP, bilateral selective cerebral perfusion; CPB, cardiopulmonary bypass; CABG, coronary artery bypass grafting.

discharge.

No significant differences were identified in the rate of paraplegia, AKI, tracheotomy, and re-exploration for bleeding. The rate of renal failure requiring CRRT was higher in the moderate HCA group (12.8% *vs.* 0, P=0.028). Compared with the moderate HCA group, the duration of ventilator support was shorter in the mild HCA group {15 [12, 19] *vs.* 12 [10, 14], P=0.004}, as was the duration of the intensive care unit (ICU) stay {18.3 [14, 59.8] *vs.* 16.7 [13, 26], P=0.034}. The volume of drainage during the first 24 h was lower in the mild HCA group (748.7±415.8 *vs.* 601.7±223, P=0.042), as was the amount of platelets transfusion [0 (0, 1) *vs.* 0 (0, 0), P=0.009].

Perioperative visceral organ functions

As shown in *Figures 1-3*, a significant postoperative escalation in the levels of aspartate aminotransferase, total bilirubin, and creatinine was noticed in both groups (P<0.05). Aspartate aminotransferase and total bilirubin reached their peak concentrations on postoperative day 2 and day 1, respectively, in both groups. Creatinine reached its peak concentration on postoperative day 1 in the moderate HCA group and on day 2 in the mild HCA group. The perioperative trends in the levels of aspartate aminotransferase, total bilirubin, and creatinine did not differ between the groups, as revealed by mixed effect

Table 3 Postoperative results

Variables	Moderate HCA group (n=47)	Mild HCA group (n=41)	P value
MAE	10 (21.3%)	2 (4.9%)	0.031
In-hospital mortality	4 (8.5%)	1 (2.4%)	0.366
PND	4 (8.5%)	0	0.120
TND	3 (6.4%)	3 (7.3%)	1.0
Paraplegia	2 (4.3%)	1 (2.4%)	1.0
AKI	29 (61.7%)	20 (48.8%)	0.224
Renal failure with CRRT	6 (12.8%)	0	0.028
Ventilation time, h	15 [12, 19]	12 [10, 14]	0.004
Tracheotomy	2 (4.3%)	0	0.497
Re-exploration for bleeding	2 (4.3%)	1 (2.4%)	1.0
Chest tube drainage, mL/24 h	748.7±415.8	601.7±223	0.042
ICU stay time, h	18.3 [14, 59.8]	16.7 [13, 26]	0.034
Perioperative blood product use	36 (76.6%)	26 (63.4%)	0.176
RBC transfusion, units	4 (0, 10)	4 (0, 6)	0.113
FFP transfusion, mL	0 (0, 400)	0 (0, 400)	0.246
PLT transfusion, units	0 (0, 1)	0 (0, 0)	0.009

Data presented as mean ± SD, interquartile ranges, or percentages as appropriate. HCA, hypothermic circulatory arrest; MAE, major adverse events; PND, permanent neurologic deficit; TND, temporary neurological deficit; AKI, acute kidney injury; CRRT, continuous renal replacement therapy; ICU, intensive care unit; RBC, red blood cell; FFP, fresh frozen plasma; PLT, platelets.

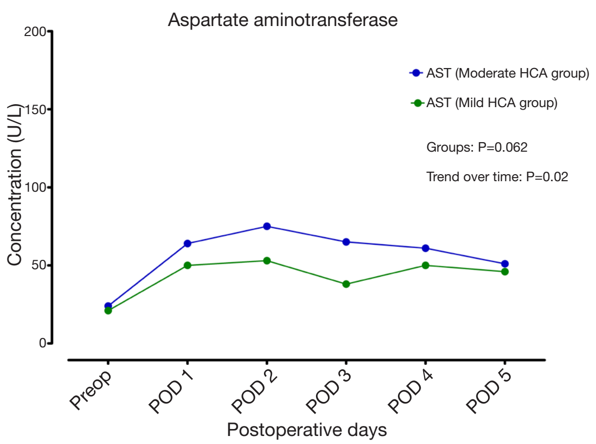

Figure 1 Changes of serum AST concentration with time in the moderate and mild HCA groups. AST, aspartate aminotransferase; HCA, hypothermic circulatory arrest.

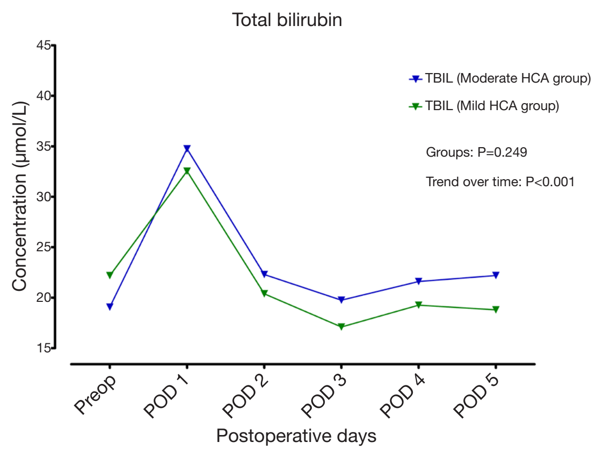

Figure 2 Changes of serum total bilirubin (TBIL) concentration with time in the moderate and mild HCA groups. HCA, hypothermic circulatory arrest.

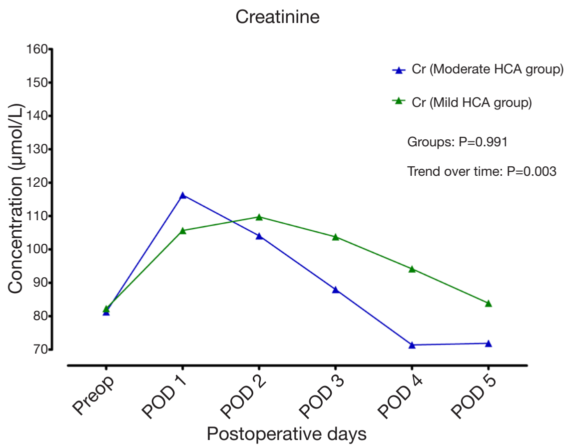

Figure 3 Changes of serum creatinine concentration with time in the moderate and mild HCA groups. HCA, hypothermic circulatory arrest.

analysis of variance modeling (all P>0.05).

Follow-up

By December 2020, follow-up was completed for all survivors, including forty patients in the mild HCA group and 43 cases in the moderate HCA group, with an average of 27±14 months (range, 3 to 47 months). During follow-up, no patients received further intervention in either of the groups, and no major cardiac or cerebral adverse events occurred.

Discussion

Presently, there is disagreement regarding the optimal temperature of deep HCA in complicated arch surgery. Deep hypothermia limits systemic metabolism and provides a bloodless operative field in open arch repair. However, the benefits of deep HCA could be attenuated by the prolonged CPB time contributing to cooling and rewarming. Recently, some benefits of deep HCA have been disputed due to prolonged CPB time, limited safe time of distal arch anastomosis, a higher incidence of neurological dysfunction, and clotting disturbances (12). Harel *et al.* found that more than 180 min of CPB could not only cause a 3- to 4-fold increase in the risk of AKI, but could also elevate in-hospital mortality significantly (13). In a comparative study performed by Fang *et al.* (14), patients with deeper hypothermia showed an increased requirement for platelet transfusion.

To relieve the severe complications of deep HCA and enhance the safe duration of arch procedure, various SCP and HCA strategies have been attempted, and have shown acceptable results (6,15,16). In our institute, we used direct right axillary artery cannulation as our primary CPB and unilateral cerebral protection strategy in open arch procedures under moderate HCA, with satisfactory results in perioperative mortality and neurological morbidity over a long period of time (11,17,18). To reduce the aforementioned side effects of deep HCA, we attempted mild HCA in open arch repair assisted by uSCP or bSCP, mainly in TAAD patients treated with TAR and SET implantation.

In the mild HCA group, one acute TAAD patient with cardiac tamponade developed lasting ventricular fibrillation after removing the cross-clamp during a TAR and SET implantation procedure. Considering the prominent plaque in the anterior descending branch (revealed by aortic CTA), coronary stenosis was suspected, and a concomitant grafting to the anterior descending branch was performed. Despite subsequent extracorporeal membrane oxygenation being applied after grafting, the patient eventually died of circulatory failure 2 days after surgery.

PND did not develop in the mild HCA group, while four cerebral infarctions (8.5%) occurred in the moderate HCA group. Three TNDs were noticed in each group. In this study, the perioperative mortality and morbidity from neurological disorders was comparable to that in the literature. We believe that several factors contribute to this. Firstly, this cohort of patients was relatively young. The atherosclerotic changes in the aortic wall were not severe, and the preoperative comorbidities were low. Secondly, according to our institutional policy as an aortic referral center, many acute TAAD patients with poor conditions, such as cardiac tamponade with unstable circulation, myocardial infarction, or severe malperfusion, may die on the way to hospital. Thirdly, the antegrade SCP was a more physiological and effective method of cerebral protection. During proximal root manipulations, the blood flow was retrograde from the cannulation site to the arch, which may contribute to reduced embolic events in the right hemisphere.

Cerebral protection during arch surgery is still a controversial issue. Over the past decade, the acceptance of SCP, in combination with moderate-to-mild systemic hypothermia clearly increased. With respect to the more suitable SCP strategies in open arch procedures, the relative benefits of uSCP compared with bSCP remain undetermined. A previous study of the application of unilateral and bilateral SCP in acute TAAD patients concluded that both strategies were equally effective for cerebral protection, and uSCP was recommended for its simplicity and less manipulation of arch branch vessels (19). The meta-analysis performed by Malvindi *et al.* (20), which consisted of 2,949 bSCPs and 599 uSCPs, found that bSCP allowed for longer SCP time, with increasing safety once the SCP time exceeded 40–50 min. In a study focusing on TAAD with TAR performed by Tong *et al.*, the bSCP did not demonstrate a significantly lower 30-day mortality or PND rate compared with uSCP (21). In a study including 1,081 patients from the German Registry for aTAAD, they found that the early postoperative neurologic results with bSACP and uSACP were similar (22).

In our experience, uSCP was more convenient to establish, and no additional cannula was placed in the operating field. Bilateral SCP represented a more physiologic perfusion strategy, and was related to a reduced risk of hypoperfusion in left hemisphere in patients with an incomplete Willis circle. Also, another manipulation in the left common carotid artery was necessary, and we did not encounter embolic events related to cannulating the left carotid artery.

In this study, patients with mild HCA were characterized by reduced CPB, cross-clamp, and SCP time, which may be explained by the difference in the hypothermia level and sequence of aortic reconstruction to a large extent. Compared to the moderate HCA group, the lowest bladder temperature was markedly higher in patients with mild hypothermia, which contributed to a reduced cooling and rewarming time. For patients that underwent TAR with SET implantation assisted by bSCP, which was the major cerebral perfusion strategy in this group, we resumed the cardiac perfusion upon implantation of a SET and distal arch anastomosis. In contrast to cases with uSCP under moderate hypothermia, we completed the left common carotid artery first to resume bilateral cerebral perfusion after distal arch manipulations, and then performed cardiac perfusion. Thus, we speculate that the higher core temperature and modified sequence of aortic reconstruction helped to shorten the duration of CPB, cross-clamp, and SCP time. The clotting disorders related to prolonged CPB were also alleviated, which was evidenced by the notably reduced volume of drainage during the first 24 h and reduced platelet transfusion in the mild HCA group. This finding was similar to the study by Keenan *et al.*, who reported that prolonged CPB time was related to a higher risk of postoperative bleeding, such that more platelets were required (23).

Compared with cerebral protection by hypothermia and SCP, the distal viscera and spinal cord had a significant risk of ischemia due to single hypothermic protection, especially in the context of constantly increasing core temperature in open arch repair. Acute renal failure was the most frequent marker of visceral organ damage identified in aortic surgery. The incidence of AKI after TAR with SET implantation has been reported to be as high as 77.6% (24). AKI could be a crucial factor related to increased mortality and morbidity after arch repair (25). In a retrospective study performed by Fang *et al.*, which focused on the differences in the incidence of AKI between different hypothermic strategies (deep or moderate) in a cohort of 627 patients undergoing TAR (14), it was concluded that moderate and deep HCA had a comparable effect on AKI after TAR in TAAD, and that hypothermic difference was not a predictor of AKI. Also, Zhou *et al.* reported that patients may benefit from moderate HCA rather than deep HCA due to the modifiability of the CPB duration (24). In this study, the incidence of AKI between the moderate and mild HCA groups was not statistically significant (61.7% *vs.* 48.8%, P=0.224), although a lower incidence of AKI was observed in the mild HCA group. Moreover, the perioperative trends of the level of creatinine did not differ between the groups, as revealed by mixed effect analysis of variance modeling (P=0.991).

Motomura *et al.* reported the rate of acute renal failure requiring dialysis was 7% in a cohort of 4,707 patients undergoing thoracic aortic surgery (26). In the present study population, renal failure requiring CRRT did not develop in the mild HCA group, while six patients received CRRT in the moderate HCA group (12.8% *vs.* 0, P=0.028). We believe that the incidence of kidney injury in cases with mild hypothermia was comparable to that in the moderate HCA group.

There is still no consensus regarding the safe limit of ischemic tolerance of the spinal cord during HCA at a higher temperature. The Mount Sinai group reported that spinal cord ischemic tolerance was significantly prolonged when cooling to mild hypothermia (32 ℃) prior to aortic cross-clamping. Mild hypothermia substantially increased the spinal cord ischemic tolerance to up to 50 min (27). Zierer *et al.* reported only one case of paraplegia under mild hypothermia with SCP in a cohort of 245 cases undergoing arch surgery (28). A further study by Zierer *et al.* involving 1,002 patients who underwent hemiarch or TAR via SCP (with a mean core temperature of 30 ℃) reported that the rates of early mortality and paraplegia were 5% and 0.3%, respectively (6). They believed that warmer cerebral perfusion might help to improve the collateral flow from the brain to the spinal cord, which was proved by the substantial backflow of blood in the descending aorta necessitating continuous suction during open arch repair. This blood backflow may contribute to the protection of the spinal cord.

In our clinical practice, we also observed that the volume of blood backflow in the descending aorta was considerably higher in patients with mild HCA, and another suction continuously placed in the descending aorta was mandatory. In contrast, intermittent suction was enough to keep a clear operative field during distal arch anastomosis in cases with moderate HCA.

In this study, paraplegia developed in 2 patients (4.3%) from the moderate HCA group, and in 1 patient (2.4%) from mild HCA group, which was consistent with our previous reports (17,18,29). Delayed paraplegia occurred in one male 3 days after a TAR with SET implantation under mild HCA; this patient recovered well 1-week after cerebrospinal fluid drainage. We speculated that rapid thrombus formation in the false lumen, from which the main intercostal artery originated, may have been the major cause in this case, rather than the hypothermic strategy or distal open repair.

A higher incidence of hepatic injury related to the mild hypothermia strategy was not observed in this study, and was verified by the fact that the trends of level of aspartate aminotransferase and total bilirubin did not differ between the groups (all P>0.05). Above all, mild HCA assisted by SCP applied in open arch repair provided a similar inferior visceral and spinal cord protection compared with that of the conventional moderate HCA strategy. We believe that the duration of circulatory arrest was a key factor related to the ischemic injury of lower body end organs. El-Sayed Ahmad *et al.* reported an acceptable organ protection effect in a cohort of elderly patients (mean age 68 years) with open arch repair by moderate-to-mild systemic hypothermia, and the mean circulatory arrest time was 46 min (30). In cases where the duration of arch repair exceeded 60 min, they inserted a balloon-tipped cannula into the descending aorta for lower body perfusion.

In this study, the mean HCA time was 25.8 min in the moderate HCA group, and 19.8 min in the mild HCA group. A markedly shorter duration of HCA was observed, which may be explained by the special surgical strategy. The classic Sun's procedure was applied for most patients in this study, and the lower body was re-perfused upon completion of distal arch anastomosis. In most cases, the anastomosis between the four-branched prosthetic graft and the distal arch containing the intraluminal stented graft required less than 30 min. The pathological distal arch was sandwiched by the unstented part of the SET and the four-branched graft. After a continuous suture, additional reinforced sutures were not usually needed.

The duration of ventilator support and ICU stay was significantly lower in the mild HCA group compared to the moderate HCA group, which may be related to the difference in hypothermia level. Obviously, more evidence is needed to confirm this in the future.

Limitations

This study has some limitations that should be noted. Due to the retrospective nature of the study, we identified associations as opposed to causalities for all of the evaluated relationships. Secondly, this was a single-center study with a relatively small number of patients. Thirdly, the average age of patients was considerably younger compared to Western cohorts. Finally, long-term outcomes were lacking, and therefore, further investigations are required.

Conclusions

In this study, mild HCA with SCP was safely applied for open arch repair in a cohort with various arch pathologies. The preliminary results for mild HCA were acceptable, and a lower incidence of MAEs was observed compared to patients that received moderate HCA. Similar inferior outcomes were also obtained with mild HCA compared to the conventional moderate HCA strategy. These encouraging surgical and postoperative results support this more aggressive hypothermia strategy in open arch repair.

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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. All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Ethics Committee of Beijing Anzhen Hospital, Capital Medical University. Written informed consent was obtained from each patient.

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