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Clinical Research

Safety of Hypothermic Circulatory Arrest During Unilateral Antegrade Cerebral Perfusion for Aortic Arch Surgery

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ABSTRACT

Background: Hypothermic circulatory arrest (HCA) with adjunctive unilateral antegrade cerebral perfusion (UACP) is widely used as a cerebral protection strategy during aortic arch surgery. However, the ideal temperature for HCA during UACP remains unknown. The study compared clinical outcomes of patients in different temperature groups for HCA during UACP.

Methods: From January 2009 to January 2016, 1691 patients who underwent aortic arch surgery for HCA during UACP in Beijing Anzhen Hospital were categorized into 2 groups according to nasopharyngeal temperature before initiating systemic circulatory arrest: the low temperature group (≤ 24°C, 22.9°C; 22.0°C-23.5°C; n = 1207) and the high temperature group (24.1°C-28.0°C, 24.6°C; 24.3°C-24.9°C; n = 484). After balancing the differences of

RÉSUMÉ

Contexte : L'arrêt circulatoire en hypothermie profonde (ACHP) avec perfusion cérébrale antérograde unilatérale (PCAU) est une technique couramment employée pour protéger le cerveau durant une intervention chirurgicale touchant la crosse aortique. La température idéale de l'hypothermie à maintenir durant la PCAU n'a toutefois pas encore été déterminée. Les auteurs ont comparé les résultats cliniques observés chez des patients ayant subi une intervention sous ACHP avec PCAU à différentes températures.

Méthodologie : De janvier 2009 à janvier 2016, 1 691 patients ayant subi une chirurgie de la crosse aortique sous ACHP avec PCAU à l'hôpital Anzhen de Beijing ont été divisés en deux groupes, en fonction de la température nasopharyngée mesurée avant l'arrêt de la circulation générale : le groupe à faible température (≤ 24 °C, 22,9 °C;

Cerebral protection strategies such as deep hypothermic circulatory arrest (HCA) with adjunctive antegrade cerebral perfusion can improve the clinical outcomes of aortic arch surgery.[1,2] However, these procedures are associated with a high mortality rate and permanent neurologic dysfunction.[3,4] Over the past decade, antegrade cerebral perfusion has been used in conjunction with a steady increase in temperature to avoid the complications caused by deep hypothermia.[3,5-7] The combination of moderate HCA and antegrade cerebral perfusion is increasingly being used as a standard neuroprotection protocol in many high-volume centers.[6,8] Although many studies have focused on the optimum temperature for HCA during different antegrade cerebral perfusion patterns, it still remains controversial in different surgery procedures.

The purpose of this study was to compare the clinical outcomes of patients who underwent aortic arch surgery with unilateral antegrade cerebral perfusion (UACP) and HCA at different hypothermia levels during the past 7 years at our center to determine the most appropriate temperature management strategy during circulatory arrest.

Methods

This study was approved by the Institutional Review Board of Beijing Anzhen Hospital, Capital Medical University (No. 2017016X).

Study population and data collection

From January 2009 to January 2016, 1691 aortic arch surgeries were performed at Beijing Anzhen Hospital. Patients were retrospectively screened against the inclusion criteria. All data pertaining to preoperative and intraoperative conditions

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baseline conditions by propensity score matching, 473 pairs of patients were matched, and the prognosis was compared with matched patients.

Results: The multivariable Cox regression analysis shows the high temperature group was an independent predictor for 30-day mortality (hazard ratio [HR], 0.55; 95% confidence interval [CI], 0.33-0.93; $P = 0.03$). After matching, the high temperature group was still an independent predictor of 30-day mortality (HR, 0.55; 95% CI, 0.32-0.98; $P = 0.04$). In subgroup analyses, there was an interaction between the high temperature group and UACP $>$ 40 minutes for 30-day mortality ($P_{\text{for interaction}} < 0.05$). The high temperature group had a significant protective effect in the UACP $\leq$ 40 minutes subgroup (HR, 0.30; 95% CI, 0.12-0.74; $P = 0.01$) but not in the UACP $>$ 40 minutes subgroup (HR, 1.00; 95% CI, 0.46-2.20; $P = 0.99$).

Conclusions: This study shows that the high temperature (24.1°C-28.0°C) management strategy for HCA during UACP is safer for UACP $\leq$ 40 minutes. High temperature benefits were not found in patients for UACP $>$ 40 minutes.

22,0 °C-23,5 °C; n = 1 207) et le groupe à température élevée (24,1 °C-28,0 °C, 24,6 °C; 24,3 °C-24,9 °C; n = 484). Après équilibrage des différences par appariement par scores de propension pour tenir compte des caractéristiques initiales, les patients ont été jumelés en 473 paires, et le pronostic des patients formant ces paires a été comparé.

Résultats : Les résultats de l'analyse multivariée par régression de Cox montrent que l'appartenance au groupe à température élevée était un facteur de prédiction indépendant de la mortalité à 30 jours (rapport des risques instantanés [RRI] de 0,55; intervalle de confiance [IC] à 95 % 0,33-0,93; $p = 0,03$). Après appariement, l'appartenance au groupe à température élevée constituait toujours un facteur de prédiction indépendant de la mortalité à 30 jours (RRI de 0,55; IC à 95 %, 0,32-0,98; $p = 0,04$). Les analyses de sous-groupes ont révélé une interaction entre l'appartenance au groupe à température élevée et une PCAU $>$ 40 minutes à l'égard de la mortalité à 30 jours ($p_{\text{pour l'interaction}} < 0,05$). L'appartenance au groupe à température élevée avait un effet protecteur significatif chez les patients ayant subi une PCAU $\leq$ 40 minutes (RRI de 0,30; IC à 95 %, 0,12-0,74; $p = 0,01$), mais pas chez ceux ayant subi une PCAU $>$ 40 minutes (RRI de 1,00; IC à 95 %, 0,46-2,20; $p = 0,99$).

Conclusions : L'étude montre que la stratégie de prise en charge à température élevée (24,1 °C-28,0 °C) durant l'ACHP avec PCAU est plus sûre si la PCAU dure 40 minutes ou moins. Aucun bienfait supplémentaire n'a été observé chez les patients du groupe à température élevée qui ont subi une PCAU de plus de 40 minutes.

were collected from patients' electronic medical records at the Capital Medical University affiliated with Beijing Anzhen Hospital. The study design is illustrated in Figure 1.

Surgical techniques

The surgical procedures (hemiarch replacement, total arch replacement, frozen elephant trunk with total arch replacement) were selected on the basis of the extent of dissection or aneurysm as described in the Supplemental Material. These procedures were detailed in previous studies.[9] For total aortic arch replacement with frozen elephant trunk, our surgical protocol involves a 4-branched graft and implantation of a stent-graft into the descending aorta. Aortic reconstruction was performed in the following order: proximal descending aorta (to restore lower-body perfusion), left carotid artery (to restore bilateral cerebral perfusion), ascending aorta (to resume myocardial perfusion), left subclavian artery, and innominate artery.

Arterial inflow during cardiopulmonary bypass (CPB) was established via the right axillary artery, innominate artery, femoral artery, or ascending aorta. Venous drainage was performed using a single 2-stage cannula in the right atrium. Pressure monitoring was established via the left radial and femoral arteries. The alpha-stat strategy was used during CPB. Hypothermia (18.1°C-28.0°C) was the standard temperature management strategy used during circulatory arrest and UACP. The temperature chosen depends on factors such as age, preoperative condition, aortic pathology, and the complexity of the planned aortic arch reconstruction.

UACP was instituted without placement of an additional catheter when the right axillary artery or innominate artery was chosen as the site for arterial inflow during CPB to ensure continuous cerebral perfusion. When the ascending aorta was chosen as the site for arterial inflow, UACP was achieved via innominate artery cannulation. The flow rate of UACP was maintained between 5 and 10 mL/kg/min. The mean perfusion pressure was maintained between 50 and 80 mm Hg.

Definitions

Thirty-day mortality is defined as all-causes and intraoperative and postoperative death within 30 days after surgery. Permanent neurologic dysfunctions include stroke and paraplegia. The neurologic dysfunction assessment is detailed in the Supplemental Material. Stroke is defined as the presence of neurologic deficits such as coma, abnormal movements of limbs (hemiplegia), numbness or sensory loss affecting one side of the body, and epilepsy up to hospital discharge,[2,10] with confirmation of diagnosis by a neurologist or correlation of clinical diagnosis with morphological changes shown on neuroimaging examination.[11] If the patient had a history of stroke, stroke was defined as any newly acquired sensorimotor deficit that persisted at the time of hospital discharge, confirmed by neurologic consultation and neuroimaging examination.[11] Paraplegia includes weakness, numbness, or bilateral sensory loss affecting the limbs that did not resolve until hospital discharge.

The UACP time interval is defined as the period from the onset of circulatory arrest to the reperfusion of left carotid artery, which is equivalent to bilateral antegrade cerebral perfusion. The lower-body circulatory arrest (LBCA) time interval is defined as the period from the onset of circulatory arrest and UACP to the reperfusion of proximal descending aorta, which is equivalent to distal aortic perfusion.

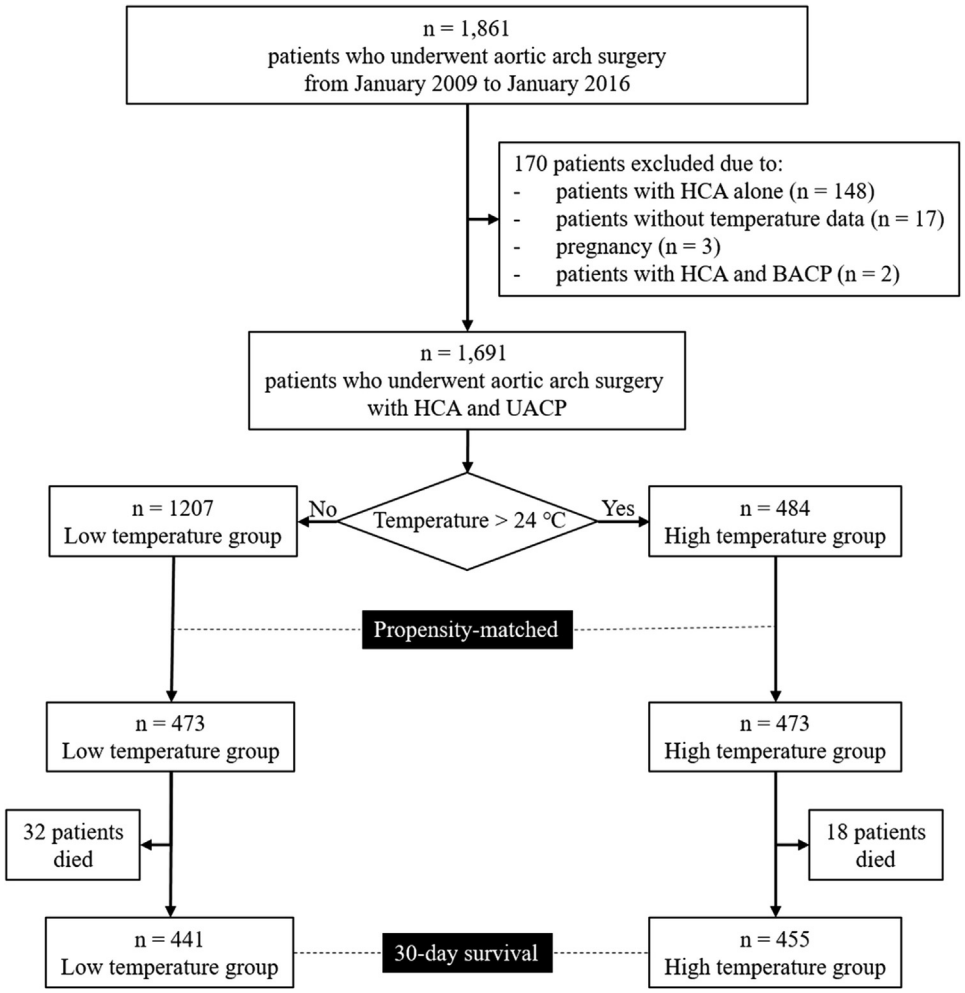

Figure 1. Study population. BACP, bilateral antegrade cerebral perfusion; HCA, hypothermic circulatory arrest; UACP, unilateral antegrade cerebral perfusion.

Statistical analyses

Continuous variables are summarized as median and interquartile range, and categoric variables are summarized by frequency with percentage. Continuous variables were compared using the Mann−Whitney *U* test. The Fisher exact and chi-square tests were used to compare differences in proportions among the categoric data. Survival rates were estimated using the Kaplan−Meier survival curves. The log-rank test was used to compare unadjusted survival curves. For multivariable Cox regression analyses and logistic regression analyses, all factors related to the dependent variable in univariate analysis with a $P < 0.10$ were included (Supplemental Tables S1-S4). $P < 0.05$ is defined as statically significant.

To minimize the effects of bias during temperature selection and the potential confounding factors in this observational study, the differences in baseline preoperative and intraoperative conditions were adjusted by using propensity score matching.[12] All preoperative and intraoperative baseline covariates listed in Table 1 and Supplemental Table S5 were used to build the initial logistic regression model, predicting the selection of the temperature management strategy. Rectal temperature, CPB time, and rewarming time were dependent on the temperature of LBCA initiation, and were not included in the final matching model.

After calculating each patient's propensity score to select the temperature management strategy, patients who underwent low temperature HCA were matched with patients who underwent high temperature HCA for 1:1 analysis without replacement, based on the log odds of the propensity score ("logit"). By using the estimated logits, a randomly selected patient in the low temperature group was matched to the patient in the high temperature group with the closest estimated logit value, with a maximum 30% difference between the 2 logits. Investigators were blinded to data pertaining to other patients during the matching process. Supplemental Figures S1 and S2 show a love plot for the absolute differences in the baseline covariates before and after matching, and a jitter plot for propensity-score distribution, respectively. Paired Wilcoxon and McNemar tests were used for the matched cohort. The 30-day survival rates after surgery of matched samples were shown using the Kaplan−Meier survival curves, and the effects of low temperature group and high temperature group were presented as a hazard ratio (HR) with associated 95% confidence intervals (CIs) from the Cox regression analysis.

Table 1. Preoperative and Intraoperative Conditions of the Matched Patients in Different Temperature Management Groups

	LT	HT		SD
	N = 473	N = 473	*P*	(%)
Nasopharyngeal temperature (°C)*	22.9 (22.0-23.5)	24.6 (24.3-24.9)	-	-
Rectal temperature (°C)*	25.2 (24.1-26.7)	26.2 (25.5-27.4)	-	-
Year of operation	2014 (2012-2015)	2013 (2012-2015)	0.9	1.7
Gender (male)	359 (75.9)	356 (75.3)	0.8	1.5
Age (y)	47 (40-56)	48 (41-56)	0.3	7.2
BMI	25.1 (22.7-27.7)	25.3 (23.4-27.0)	0.8	4.3
Pathological type			0.3	3.4
Acute aortic dissection	249 (52.6)	242 (51.2)		
Subacute aortic dissection	69 (14.6)	63 (13.3)		
Chronic aortic dissection	109 (23.0)	121 (25.6)		
Aortic aneurysm	38 (8.0)	42 (8.9)		
Pseudoaneurysm	8 (1.7)	5 (1.1)		
NYHA	III (II-III)	III (II-III)	0.9	0.2
LVEF	63 (58-68)	63 (58-68)	0.3	6.8
Coronary artery disease	38 (8.0)	44 (9.3)	0.6	4.5
Hypertension	340 (71.9)	354 (74.8)	0.3	6.7
Diabetes mellitus	22 (4.7)	18 (3.8)	0.6	4.2
Chronic kidney disease	14 (3.0)	13 (2.7)	1.0	1.3
Marfan syndrome	18 (3.8)	18 (3.8)	1.0	0.1
Pericardial tamponade	6 (1.3)	6 (1.3)	1.0	0.1
Acute heart failure	2 (0.4)	1 (0.2)	1.0	3.8
Coma	1 (0.2)	1 (0.2)	1.0	0.1
Lower-limb malperfusion	41 (8.7)	37 (7.8)	0.7	3.1
Tracheotomy	0 (0.0)	1 (0.2)	-	6.5
CRRT	3 (0.6)	4 (0.8)	1.0	2.5
Previous stroke	12 (2.5)	18 (3.8)	0.4	7.2
Redo-sternotomy	30 (6.3)	28 (5.9)	0.9	1.8
Cannulation site of UACP			0.4	5.7
Right axillary artery	401 (84.8)	391 (82.7)		
Innominate artery	72 (15.2)	82 (17.3)		
Main surgical procedure			0.4	5.5
Hemiarch replacement	87 (18.4)	100 (21.1)		
TAR	15 (3.2)	10 (2.1)		
TAR and FET	371 (78.4)	363 (76.7)		
Concomitant procedures				
Ascending aorta replacement	239 (50.5)	247 (52.2)	0.7	3.4
Bentall	180 (38.1)	174 (36.8)	0.7	2.6
CABG	27 (5.7)	31 (6.6)	0.7	3.5
Valve surgery	23 (4.9)	24 (5.1)	1.0	1.0
Extra-anatomic bypass	39 (8.2)	40 (8.5)	1.0	0.8
Flow (mL/kg/min)	5 (5-5)	5 (5-5)	1.0	0.1
Times (min)				
UACP time	36 (29-45)	35 (27-44)	0.2	9.4
Crossclamp time	95 (78-118)	93 (75-121)	0.1	3.4
LBCA time	23 (19-32)	23 (18-29)	0.9	9.4
CPB time*	181 (153-209)	173 (147-207)	0.1	11.5
Rewarming time*	81 (68-100)	77 (65-94)	< 0.05	21.7

Values are n (%) or median (interquartile range).

BMI, body mass index; CABG, coronary artery bypass grafting; CPB, cardiopulmonary bypass; CRRT, continuous renal replacement therapy; FET, frozen elephant trunk; HT, high temperature group; LBCA, lower-body circulatory arrest; LT, low temperature group; LVEF, left ventricular ejection fraction, NYHA, New York Heart Association; SD, standardized difference; TAR, total arch replacement; UACP, unilateral antegrade cerebral perfusion.

*These factors were not included in the propensity score matching model.

To further explore the independent risk associated with temperature management strategy in prespecified patient subgroups after propensity score matching, interaction term analyses were performed by the introduction of a temperature by risk subgroup interaction term to multivariable Cox proportional hazard regression model. The following prespecified subgroups were explored: gender, age > 50 years, acute aortic dissection, New York Heart Association > II, hypertension, cannulation site of UACP, total aortic arch replacement with frozen elephant trunk, concomitant ascending aorta replacement, Bentall, UACP time > 40 minutes, crossclamp time > 100 minutes, CPB time > 200 minutes, LBCA time > 20 minutes, and rewarming time > 90 minutes. Propensity score matching was performed using "MatchIt" packages in R

software 3.5.1 (www.r-project.org). Other data analyses were performed using SPSS v22.0 statistics package (IBM Corp, Armonk, NY).

Results

Demographic characteristics

From January 2009 to January 2016, 1691 aortic arch surgeries with UAPC in the setting of HCA were performed at the Capital Medical University affiliated with Beijing Anzhen Hospital. Of 1691 surgeries, 1207 patients underwent circulatory arrest under low temperature ($\leq$ 24.0°C) and 484 patients underwent circulatory arrest under high temperature (24.1°C-28.0°C, Fig. 1). The percentage of patients who underwent the high temperature management strategy increased from 2.2% to 36.9% over the study period (Supplemental Fig. S1). There were significant differences in the demographics and comorbidities of patients between the low temperature and high temperature groups (Supplemental Table S5). Although the 30-day survival in the high temperature group was higher than in the low temperature group (Supplemental Fig. S2), this result was unconvincing because of patients' baseline data differences in the different groups.

Impact of temperature management strategy on outcomes in multivariable Cox regression model

The high temperature group was still an independent protective factor for 30-day mortality after using a multivariable Cox regression model to minimize the effect of differences in the baseline data (Supplemental Table S1; HR, 0.55; 95% CI, 0.33-0.93; $P = 0.03$). No correlations between outcomes (stroke, paraplegia, and acute renal dysfunction requiring continuous renal replacement therapy) and temperature management strategy were found in multivariable logistic regression analyses (Supplemental Tables S2-S4).

Impact of temperature management strategy on outcomes after propensity score matching

The propensity score matching was used to further minimize the effect of differences and confirm the result of multivariable Cox regression analysis. After matching, a total of 473 pairs of patients were matched. The preoperative and intraoperative conditions for the matched cohort in different groups are shown in Table 1. The 30-day survival rates in the high temperature group were still higher than in the low temperature group (Fig. 2; 96.2% vs. 93.2%; HR, 0.55; 95% CI, 0.32-0.98; $P = 0.04$). The comparison of other postoperative complications between the 2 groups is reported in Supplemental Table S6. Only in-hospital mortality in the high temperature group was lower than in the low temperature group (3.8% vs. 7.2%, $P < 0.01$).

Association of temperature management strategy and 30-day mortality among different subgroups

The association of temperature management strategy and 30-day mortality was evaluated further among the prespecified subgroups (Fig. 3). The impacts of temperature management strategy in the 2 different subgroups (UACP > 40 and UACP $\leq$ 40 minutes) were significantly different ($P_{\text{for interaction}} < 0.05$). The association of the high temperature group with better mortality was stronger among patients who underwent UACP $\leq$ 40 minutes (HR, 0.30; 95% CI, 0.12-0.74; $P = 0.01$), whereas this association was not found among patients who underwent UACP > 40 minutes (HR, 1.00; 95% CI, 0.46-2.20; $P = 0.99$).

Discussion

This large retrospective study of patients undergoing aortic arch surgery with HCA and UACP showed that a high temperature (24.1°C-28.0°C) is more effective in providing cerebral protection than a low temperature ($\leq$24.0°C) in patients undergoing UACP for less than 40 minutes. However, the benefits of high temperature were not found in patients who underwent UACP for more than 40 minutes.

The patients' demographics and etiology of aortic disease in this study varied significantly from previous studies.[8,13-15] The mean age of patients was lower and the proportion of male patients was higher[16] in this study. Most patients had an aortic dissection, and only 7.8% of them had an aortic aneurysm, which was the main pathology in other studies.[17] These results might be due to the racial backgrounds[18] and low rates of hypertension control[19] in China. The percentage of patients who were diagnosed with Marfan syndrome (3.1%) was lower than previously reported.[18,20,21] The incidence of coronary artery disease, diabetes, and renal failure was also lower, which might be due to the lower mean age.[3,6,22]

The short-term mortality rate and the rate of stroke in the present study were lower than those in other case series reported in the literature (mortality, 8%-15.9%; rate of stroke, 6%-10.5%).[2,3,6,21] As in previous studies,[15,23] it was found that high temperature management strategy is beneficial, and the present study confirmed that a high temperature management strategy not only increased the incidence of stroke but also reduced mortality. This may be related to a reduction

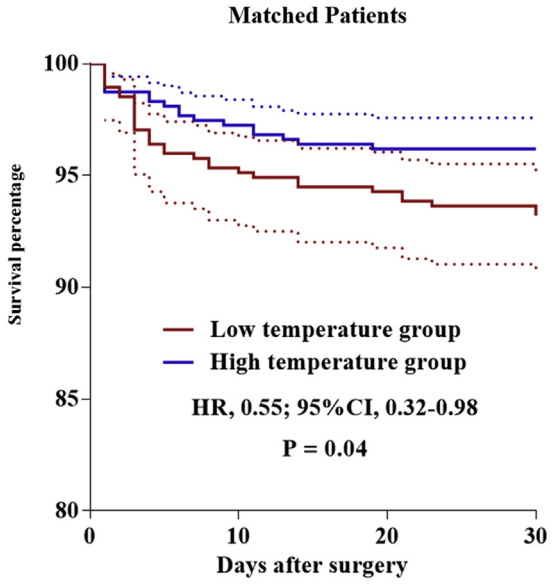

Figure 2. Kaplan–Meier survival curves in low and high temperature groups for matched patients. CI, confidence interval; HR, hazard ratio.

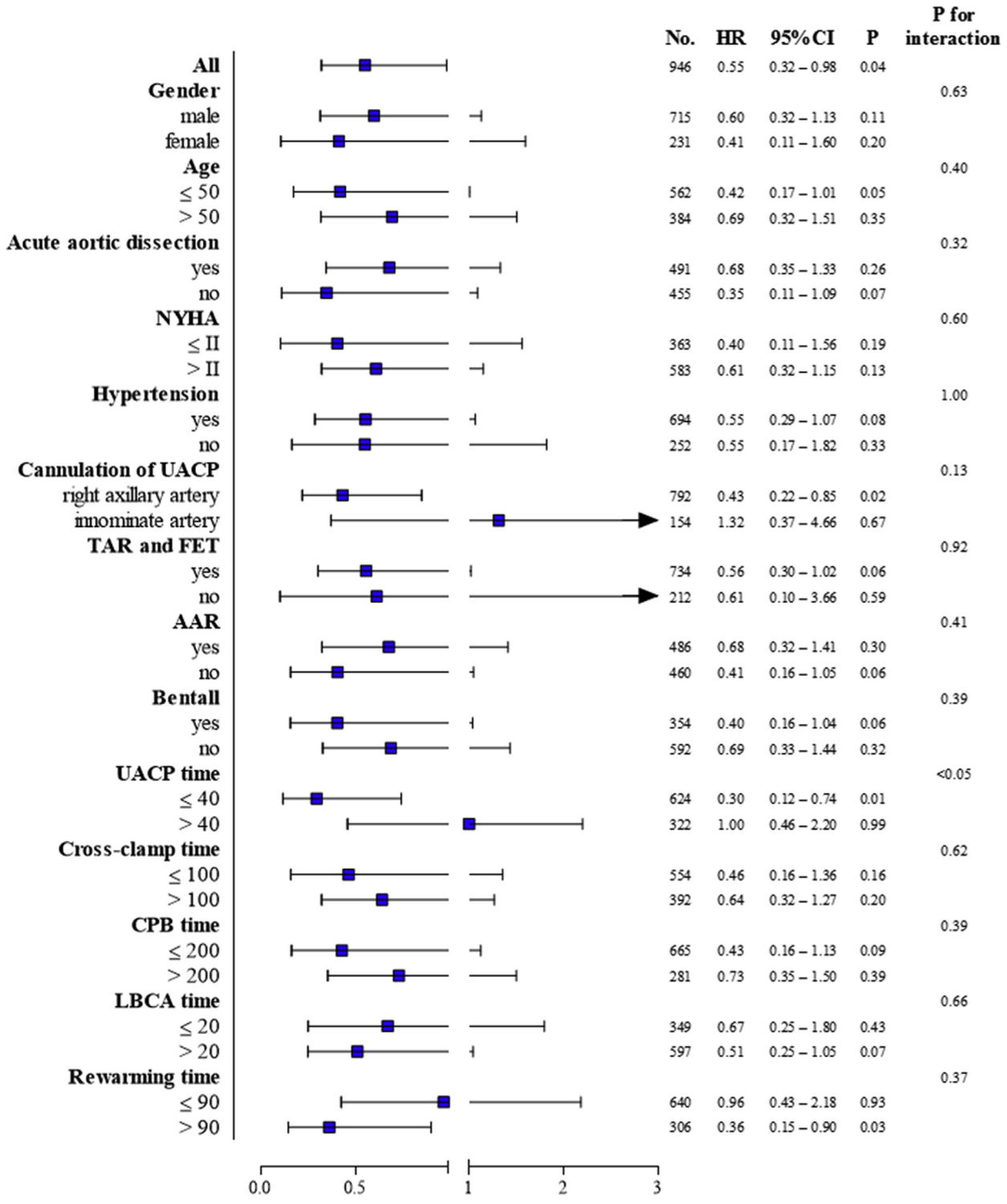

Figure 3. Subgroup analyses of different temperature management strategies with 30-day mortality. Subgroups analyses are shown for 30-day mortality between patients in the low temperature group and the high temperature group during HCA with UACP. The *P* for interaction represents the likelihood of interaction between the variables and the relative treatments. Coronary artery disease (n = 82), diabetes mellitus (n = 40), chronic kidney disease (n = 27), Marfan syndrome (n = 36), pericardial tamponade (n = 12), acute heart failure (n = 3), previous coma (n = 2), previous lower-limb malperfusion (n = 78), previous tracheotomy (n = 1), previous continuous renal replacement therapy (n = 7), stroke history (n = 30), redo-sternotomy (n = 58), concomitant coronary artery bypass grafting (n = 58), valve surgery (n = 47), and concomitant extra-anatomic bypass (n = 79) were not included in the subgroup analyses because the number of patients in these subgroups were too low. AAR, ascending aorta replacement; CI, confidence interval; CPB, cardiopulmonary bypass; FET, frozen elephant trunk; HR, hazard ratio; LBCA, lower-body circulatory arrest; NYHA, New York Heart Association; TAR, total arch replacement; UACP, unilateral antegrade cerebral perfusion.

in CPB time, postoperative bleeding, endothelial dysfunction, neuronal apoptosis, and postoperative pulmonary complications, which are typically associated with deep hypothermia.[3,6,23] However, these benefits were demonstrated only in patients who underwent UACP for periods that did not exceed the safety threshold (40 minutes). When UACP time exceeds the safety threshold, the benefits of high temperature diminishes. Thus, a high temperature management strategy may not be suitable for high-risk patients with longer UACP time.

For high temperature management strategy, the key issues identified by researchers are the safety of the spinal cord and visceral organs. Previous studies[8,23,24] concluded that high temperature management strategy may be safe, but only in low-risk patients, because high temperature in high-risk patients (ie, long LBCA) could increase the risk of spinal cord and visceral ischemia in patients. The LBCA time varies in different surgical procedures. The LBCA time at our center was significantly decreased because of early reperfusion of the lower body. Patients with LBCA over the safety threshold (40-60 minutes[6,8]) were rare, accounting for just 10.8% (40 minutes; n = 183) and 1.0% (60 minutes; n = 17). Most of the patients who underwent total arch replacement and frozen elephant trunk procedures are at risk of paraplegia. The incidence rate of paraplegia in our surgical center was lower than in other reported case series focusing on frozen elephant trunk (7.5%-21.7%)[25,26] because of the shorter LBCA time. Thus, the interaction between a high temperature management strategy and a long LBCA time for adverse effect (paraplegia) in this study is difficult to be determined. As the patients' risk level increased, the advantages of a high temperature management strategy decreased or even ceased. Thus, clinicians should apply caution when using the high temperature management strategy to high-risk patients. Nonetheless, larger-scale and multicenter studies are necessary to confirm the safety of a high temperature management strategy in high-risk patients. The underlying mechanism around the risk of mortality and the relationship between UACP/LBCA durations and moderate hypothermia for interaction should be further explored by in-depth studies.

Limitations

There are several limitations to the current study. The assessment of neurologic dysfunction (neurological evaluation and neuroimaging) was not conducted by the neurologist or cardiovascular surgeon when symptoms that suggested postoperative focal/global neurologic deficits or paraplegia were not clearly presented. We recognized the high likelihood of underestimating postoperative permanent neurologic dysfunction.[27] The lack of randomization in this retrospective, observational study can also affect the results. Although we performed propensity score matching to reduce bias of confounding factors, other factors that may affect the selection of temperature cannot be totally considered and included in the matching process. The lower mortality rate in the present study may be partly attributed to the death of some patients in critical condition who did not undergo surgery. Our hospital is the largest referral center for aortic disease in China. Because patients who required aortic arch surgery travel to our center from all over the country, time from the onset of symptoms to operation cannot be controlled. The rate of surgical intervention within 24 hours was lower in the current study than in other studies[2] because of differences in healthcare systems and economic conditions among countries. In some patients with acute type A aortic dissection, timely treatment was not possible because of delayed transportation to the hospital.

As such, the suitable circulatory management strategies (eg, HCA and UACP) can protect organs against ischemic injury during surgical treatment of aortic arch diseases. A high temperature management strategy can effectively provide protection for low-risk patients in whom UACP time does not exceed 40 minutes. However, for high-risk patients who undergo UACP for longer periods of time (>40 minutes), a high temperature management strategy may carry a risk of mortality. The optimal strategy for temperature management should be selected carefully on the basis of patient characteristics and clinical scenario, especially in high-risk patients. Considering the unpredictability and complexity of clinical circumstances and the limitations of retrospective studies, randomized trials are best suited to investigate the effects of temperature management strategy. The present study may serve as a basis for improved experimental design of future randomized trials.

Conclusions

This single-center study demonstrated that the high temperature management strategy (24.1°C-28.0°C) is safe and effective when UACP time did not exceed the safety threshold (≤ 40 minutes). The benefits of the high temperature management strategy were not found in patients who underwent UACP for more than 40 minutes.

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Disclosures

The authors have no conflicts of interest to disclose.

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Supplementary Material

To access the supplementary material accompanying this article, visit the online version of the *Canadian Journal of Cardiology* at www.onlinecjc.ca and at https://doi.org/10.1016/j.cjca.2019.07.007