Role of Moderate Hypothermia and Antegrade Cerebral Perfusion during Repair of Type A Aortic Dissection

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Abstract

The goal of this study was to compare early postoperative outcomes and actuarial survival between patients who underwent repair of acute type A aortic dissection with deep or moderate hypothermia.

A total of 132 consecutive patients from a single academic medical center underwent repair of acute type A aortic dissection between January 2000 and June 2014. Of those, 105 patients were repaired under deep hypothermia (< 24 C°), while 27 patients were repaired under moderate hypothermia (≥24 C°). Median ages were 62 years (range: 27–86) and 59 years (range: 35–83) for patients repaired under deep hypothermia compared with patients repaired under moderate hypothermia, respectively ($p = 0.451$). Major morbidity, operative mortality, and 10-year actuarial survival were compared between groups.

Operative mortality was 17.1 and 7.4% in the deep and moderate hypothermia groups, respectively ($p = 0.208$). Incidence of permanent stroke was 12.4% in the deep hypothermic circulatory arrest group and 0% in the moderate hypothermia group ($p = 0.054$). Actuarial 5- and 10-year survival demonstrated a trend for lower long-term mortality with moderate hypothermia compared with deep hypothermia (69% 5-year and 54% 10-year for deep hypothermia vs. 79% 5-year and 10-year for moderate hypothermia, log-rank $p = 0.161$).

Moderate hypothermia is a safe and efficient alternative to deep hypothermia and may have protective benefits. Stroke rate was lower with moderate hypothermia.

Keywords
- aortic dissection
- hypothermia
- outcomes
- mortality
- morbidity
- renal failure
- cardiac surgery

Acute type A aortic dissection is a severe condition requiring immediate surgical intervention and is associated with high rates of morbidity and mortality. Despite improvements in accurate early diagnosis, cerebral protection methods, and prompt repair, recent studies continue to report postoperative mortality rates reaching 15 to 26%.[1–5] The deep hypothermic arrest technique of distal anastomosis in aortic surgery disrupts blood flow to the brain and other vital organs, leaving them vulnerable to injury. Morbidity and mortality caused by brain-related complications during aortic arch surgery are the most prevalent, with cerebral protection by hypothermic circulatory arrest (HCA) or cerebral perfusion.[6–8] Nevertheless, literature directly addressing temperature selection during acute type A aortic dissection is at a minimum.

Deep HCA (DHCA) has been the foundation of cerebral protection during aortic arch surgery since the reintroduction of HCA by Griepp et al in 1975.[9] Advantages offered by DHCA include bloodless aortic arch replacement and lowered systemic and cerebral cellular metabolism. However,

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achieving such temperatures requires extensive cooling and rewarming times.[10] As a viable alternative to address concerns raised regarding DHCA, the use of moderate hypothermia (MH) with antegrade perfusion of cerebral vessels has become increasingly popular in the past decade. MH has been found to reduce cardiopulmonary bypass (CPB) times, postoperative inflammation, rebleeding, and organ dysfunction.[11] Although there have been extensive studies detailing the safety and efficacy of both approaches, minimal reports specifically comparing temperature selection for repair of acute type A aortic dissection exist. The purpose of this study was to compare the early clinical outcomes of MH versus deep hypothermia (DH).

Methods

Patients

The Society of Thoracic Surgeons Databases at the University of Iowa Hospitals and Clinics were queried to identify all patients who underwent repair of aortic dissection between January 2000 and June 2014. A total of 127 patients underwent repair for acute type A aortic dissections. Of those, 105 were repaired under DH and 27 were repaired under MH. Patients with a type A dissection who did not undergo emergent surgical treatment were excluded.

A preoperative diagnosis of aortic dissection was accomplished using computed tomographic angiography, transesophageal echocardiography (TEE), or magnetic resonance imaging. The diagnosis was later confirmed at the time of operation. A database was created for entry of demographic information, procedural data, and postoperative outcomes. Dedicated data-coordinating personnel retrospectively entered the said information. Study approval from the Institutional Review Board was obtained. Consistent with the Health Insurance Portability and Accountability Act of 1996, patient confidentiality was consistently maintained.

Definitions

The Society of Thoracic Surgeons' national cardiac surgery database definitions were used for this study. Acute type A aortic dissection was defined as any dissection that involved the ascending aorta with presentation within 2 weeks of the onset of symptoms. Previous cerebrovascular accident was defined as history of central neurologic deficit persisting for more than 24 hours. Chronic renal insufficiency was defined as a serum creatinine value > 2.0 mg/dL. Diabetes was defined as a history of diabetes mellitus, regardless of duration of disease or need for oral agents or insulin. Recent myocardial infarction was defined as myocardial infarction occurring within 7 days. Depressed ejection fraction was defined as ejection fraction $< 40\%$. Hemodynamic instability was defined as hypotension (systolic blood pressure < 80 mm Hg) or the presence of cardiac tamponade, shock, acute congestive heart failure, and myocardial ischemia and/or infarction. Prolonged CPB time was defined as time more than the 75th percentile, which was equal to 240 minutes. Prolonged ventilatory support was defined as pulmonary insufficiency requiring ventilatory support > 24 hours postoperatively. Postoperative stroke was defined as any new major (type I) neurologic deficit presenting in-hospital and persisting for > 72 hours. Acute renal failure was defined as one or both of the following: (1) an increase in the serum creatinine to > 2.0 mg/dL and/or a $>$ twofold increase in the most recent preoperative creatinine level or (2) a new requirement for dialysis postoperatively. Operative mortality includes both (1) all deaths occurring during the hospitalization in which the operation was performed (even if death occurred after 30 days from the operation), and (2) those deaths occurring after discharge from the hospital, but within 30 days of the procedure.

Operative Technique

Intraoperatively, the diagnosis of type A aortic dissection was confirmed by TEE for all patients. Bilateral radial arterial lines were established. Cerebral oximetry was typically used at our institution. A median sternotomy was created to provide access. Total CPB was provided by arterial cannulation of the femoral artery or right axillary artery and venous cannulation of the right atrium. Cold blood cardioplegia administration through an antegrade approach via the ostia of the coronary arteries and/or retrograde through the coronary sinus was performed to ensure myocardial protection. The right superior pulmonary vein provided access for vent placement into the left ventricle. Restoration of the aortic root was accomplished by resection of the intimal tear followed by repair or resuspension of the aortic valve and replacement of the ascending aorta. After reaching the preferred mean cooling temperature range of 13 to 28°C, the aortic clamp was removed and the aortic arch was examined. Antegrade cerebral perfusion was typically used in MH patients via the right axillary artery. Once circulatory arrest was instituted at the MH group, the innominate artery was clamped and antegrade perfusion was administered via the right axillary artery. Retrograde cerebral perfusion was not typically used at our institution. The distal anastomosis was then completed and antegrade aortic perfusion was established. Either a root replacement with a composite valve graft and coronary button reimplantation or a valve replacement with mechanical or tissue prosthesis was indicated for patients with irreparable damage of the aortic root or valve. Reinforcement of the proximal and distal suture lines was accomplished using Teflon (polytetrafluoroethylene) strips or, for some patients, biological glue (BioGlue surgical adhesive, Cryolife, Kennesaw, Georgia, United States).

Data Analysis

Univariate Analysis

Univariate comparisons of preoperative, operative, and postoperative variables were performed between patients repaired under DH ($n = 105$) and those repaired under MH ($n = 27$). Normal distribution of continuous variables was assessed using the Kolmognov–Smirnov test. Continuous variables were tested using either the Student's t-test or the Mann–Whitney test, while categorical variables were assessed by the chi-square or Fisher's exact test, depending on the distribution of data. All tests were two-sided and a

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p-value of ≤ 0.05 was considered statistically significant. All analyses were conducted using SPSS statistical software Version 21 (IBM Corp, Armonk, New York, United States).

Results

Preoperative Characteristics

Preoperative characteristics are summarized in ►**Table 1**. Patients who underwent DH demonstrated higher preoperative hypertension ($p = 0.004$) and instability ($p = 0.008$). Patients in the MH group had higher rates of arrhythmias ($p = 0.032$) and trends toward higher levels of creatinine ($p = 0.06$). All other preoperative variables evaluated were not significantly different between the groups.

Table 1 Preoperative patient characteristics

Variable[a]	Deep ($n = 105$)	Moderate ($n = 27$)	p-Value
Age, y	62 (27–86)	59 (35–83)	0.451
Surgical era			0.198
2000–2006	37 (35.2%)	6 (22.2%)	...
2007–2014	68 (64.8%)	21 (77.8%)	...
Diabetes	9 (8.6%)	2 (7.4%)	0.845
Hypertension	74 (70.5%)	11 (40.7%)	0.004
Ejection fraction	5 (4.8%)	2 (7.4%)	0.584
COPD	13 (12.4%)	4 (14.8%)	0.736
Creatinine	1.1 (0.4–3.9)	1.05 (0.7–6.7)	0.06
Female gender	33 (31.4%)	5 (18.5%)	0.186
Arrhythmias	6 (5.7%)	5 (18.5%)	0.032
NYHA class			0.354
I	6 (5.7%)	1 (3.7%)	...
II	32 (30.5%)	13 (48.1%)	...
III	41 (39.0%)	9 (33.3%)	...
IV	26 (24.8%)	4 (14.8%)	...
History of cerebrovascular accident	9 (8.6%)	2 (7.4%)	0.845
Hemodynamic instability	29 (27.6%)	1 (3.7%)	0.008
Number of diseased vessels			0.492
Zero	90 (85.7%)	26 (96.3%)	...
One	7 (6.7%)	0 (0%)	...
Two	4 (3.8%)	0 (0%)	...
Three	4 (3.9%)	1 (3.7%)	...
EF $<$ 40	5 (4.8%)	2 (7.4%)	0.584

Abbreviations: COPD, chronic obstructive pulmonary disease; EF, ejection fraction; NYHA, New York Heart Association.
[a]Continuous data are shown as median (range) and categorical data are shown as percentage.

Operative Characteristics

Operative characteristics of patients repaired for acute type A aortic dissection under DH and MH are presented in ►**Table 2**. Patients repaired under DH had higher CPB times ($p < 0.001$), a higher incidence of prolonged CPB of greater than 240 minutes ($p = 0.015$), longer circulatory arrest times ($p \leq 0.001$), and more frequent usage of a hemiarch technique ($p = 0.032$) compared with patients repaired under MH. Conversely, patients repaired under MH had higher systemic temperatures than those repaired under DH ($p < 0.001$). Also, cerebral protection and cannulation methods varied between the groups ($p = 0.01$ and $p = 0.034$, respectively) with more patients who underwent DH having retrograde cerebral perfusion and femoral cannulation compared with the patients who underwent MH.

Postoperative Characteristics

Postoperative characteristics are depicted in ►**Table 3**. Incidence of stroke was higher in the DH group than in

Table 2 Operative patient characteristics

Variable[a]	Deep ($n = 105$)	Moderate ($n = 27$)	p-Value
CPB time $>$ 240 min	37 (35.2%)	3 (11.1%)	0.015
CPB time, min	219 (102–535)	173.5 (89–263)	< 0.001
Circulatory arrest time, min	31.5 (0–146)	18.5 (0–46)	< 0.001
Systemic temperature	18 (13–23)	26.50 (24–28)	< 0.001
Aortic valve procedure			0.749
Nothing	41 (39.0%)	12 (44.4%)	...
Replacement	4 (3.8%)	2 (7.4%)	...
Resuspension	43 (41.0%)	10 (37.0%)	...
Bentall	17 (16.2%)	3 (11.1%)	...
Hemiarch technique	89 (84.8%)	18 (66.7%)	0.032
Total arch replacement	7 (6.7%)	2 (7.4%)	0.892
Cerebral Perfusion			0.01
No cerebral perfusion	39 (37.1%)	13 (48.1%)	...
Retrograde	28 (26.7%)	0 (0%)	...
Antegrade	38 (36.2%)	14 (51.9%)	...
Cannulation method			0.034
Axillary	25 (23.8%)	13 (48.1%)	...
Femoral	74 (70.5%)	12 (44.4%)	...
Both	6 (5.7%)	2 (7.4%)	...
BioGlue/Felt strip			0.028
BioGlue	31 (29.5%)	13 (48.1%)	...
Felt strip	25 (23.8%)	9 (33.3%)	...
Both	49 (46.7%)	5 (18.5%)	...

Abbreviation: CPB, cardiopulmonary bypass.
[a]Continuous data are shown as median (range) and categorical data are shown as percentage.

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Table 3 Postoperative complications

Variable[a]	Deep ($n = 105$)	Moderate ($n = 27$)	p-Value
Deep sternal wound infection	7 (6.7%)	1 (3.7%)	0.565
Prolonged ventilation	49 (46.7%)	11 (40.7%)	0.581
Acute renal failure	19 (18.1%)	8 (29.6%)	0.185
Hemodialysis	4 (3.8%)	3 (11.1%)	0.131
Hemorrhage-related reexploration	11 (10.5%)	2 (7.4%)	0.633
Cardiac arrest	10 (9.5%)	3 (11.1%)	0.805
Stroke	13 (12.4%)	0 (0%)	0.054
Atrial fibrillation	21 (20.0%)	6 (22.2%)	0.798
Hospital length of stay (d)	9 (0–86)	8 (2–24)	0.25
Operative mortality	18 (17.1%)	2 (7.4%)	0.208

[a]Continuous data are shown as median (range) and categorical data are shown as percentage.

the MH group, but this did not reach statistical significance ($p = 0.054$).

Trends over Time

The use of MH increased over time from one surgical era to the next. However, this did not reach statistical significance when comparing levels of DH and MH use in the two surgical eras ($p = 0.198$).

Discussion

Our study is among the first to directly compare DH versus MH for cerebral protection during circulatory arrest for repair of type A aortic dissection. A previous study analyzing the German Registry for Acute Aortic Dissection Type A reported no significant differences among temperature groups in operative mortality or permanent neurological deficit when they directly compared systemic temperatures in patients with HCA as the only protective method.[12] In contrast, a recent study published by Algarni et al comparing DH to MH found DH to be a predictor of postoperative stroke, low cardiac output syndrome, and operative mortality.[4] Their findings, however, were independent of the cannulation method, cerebral protection method, and circulatory arrest time. The conflicting evidence brought from these two studies prompted our investigation with particular interest paid to cannulation, cerebral protection, and circulatory arrest time.

Principal Findings

In our study, the overall operative mortality was 15.1%, which compares with the bottom end of recent studies.[1–5] Operative mortality in our DH cohort (17.1%) demonstrated greater than twofold increase over that of our MH cohort (7.4%). Likewise, the prevalence of stroke was much higher using DH over using MH (12.4% vs. 0%).

DH without a cerebral perfusion adjunct during aortic surgery has been a proven method of protection with operative mortality rates as low as 6.3% and stroke rates from 3.1 to 8%, but these findings are limited to circulatory arrest times below 40 minutes.[13,14] Potential drawbacks with DH in comparison to MH may be the cause of the increased risks for morbidity and mortality that our study and others have demonstrated. Autoregulation of cerebral blood flow markedly diminishes with decreasing temperature and nearly absolves at 12°C.[10] This effect uncouples cerebral blood flow, for example, from metabolism starting at roughly 22°C and creates an overprovision of blood.[15] Afterwards, extended rewarming periods associated with DH create a secondary vasodilation leading to edema, and the prolonged acidosis in the brain tissue causes reperfusion injury.[16,17] Further, a study by Strauch et al demonstrated that effective reduction in oxygen consumption within brain cells takes place at 28°C and does not improve with increasingly lower temperatures, which calls into question the metabolic benefits of DHCA.[18]

Perhaps the strongest negative effect of DH originates from increased CPB times and subsequent length of operation in comparison with MH.[7,19] Extended CPB times during cardiac surgery are implicated in increased risk of acute renal insufficiency, stroke, and mortality.[20–22] These effects can be compounded based on the condition of the patient. Diminished hematocrit and glycemic levels can increase perioperative risk during the use of CPB.[23,24] In our study, the median CPB time was 219 minutes for the DH group and 173.5 minutes for the MH group ($p < 0.001$). Also, the number of patients reaching the extended CPB time of 240 minutes in the DH group tripled than that of the MH group ($p < 0.015$). An increased prevalence of postoperative risk found using DH might actually arise secondary to increased CPB times.

Trends in DH versus MH Selection over Time

At our institution, MH has only recently become heavily used. A trend for its use is demonstrated by the 21 cases in the 2007 to 2014 surgical era in comparison to the 6 completed in the 2000 to 2006 surgical era ($p = 0.198$). This is further established by the fact that 17 of the 21 MH cases were completed within the past 3 years.

This trend seems to have emerged due to the use of antegrade cerebral perfusion and growing evidence advocating for increased safety and efficacy with MH. DH was no longer necessary with the increased use of antegrade cerebral perfusion. A recent study by Comas et al reported that the use of MH and selective antegrade cerebral perfusion in acute type A aortic dissection cases significantly decreased CPB times, operative mortality, incidence of renal failure, incidence of tracheostomy, and length of hospital stay compared with patients undergoing non-MH with the same selective antegrade cerebral perfusion.[25] Leshnower et al continued one step further and stratified temperatures in the traditional MH range for elective hemiarch replacement.

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They found mild hypothermia (> 28°C) to significantly reduce the incidence of permanent neurological deficits over MH (24–28°C) suggesting improved cerebral protection with warmer temperatures (2.5% vs. 7.2%, $p = 0.01$).[26] Our study demonstrated similar decreases in stroke prevalence for MH over DH, although our study did not reach statistical significance (0% vs. 12.4%, $p = 0.054$).[27]

Clinical Implications

We conducted an observational study to assess the impact of HCA temperature selection on short- and long-term outcomes following repair of acute type A aortic dissection. In this study, we examined an unselected cohort of patients from a single academic institution. This study is among only a few to directly compare use of DH and MH in surgery of acute type A aortic dissections. Temperature selection affected early clinical outcomes following acute type A aortic dissection repair in our analysis. With MH, operative mortality and stroke decreased, and late survival improved. Also, CPB times were dramatically and expectedly reduced in our MH group. Based on the results of our study, the use of MH is recommended, especially with evidence that shorter CPB times are associated with better outcomes. However, further studies are needed to identify patient characteristics that might merit the use of one cerebral protection strategy over the other.

Study Limitations

The lack of power in our study due to the relatively small sample size in the MH group limited the confidence in our findings and precluded multivariable analysis. To this end, potential preoperative confounding factors such as hemodynamic instability and hypertension could not be fully explored. Further study of reoperations on the remaining dissected aorta, the causes of late mortality, and the fate of the false lumen were outside the scope of our analysis. In future, these should be foci for evaluating long-term outcomes of acute type A aortic dissection repair. Our report represents a single institution experience with a limited amount of repairs of type A dissection per year (~10/year). Our institution is a tertiary referral center that accepts patients referred by our institution without the expertise to treat this complex disease. Furthermore, in our study axillary and femoral cannulation varied significantly between the MH and DH groups and thus the higher risk of stroke in the DH group may be related to the higher rate of femoral cannulation in that group. However, we previously reported no differences in stroke risk between the two approaches.[28]

Conclusions

Moderate hypothermia is an effective alternative to for surgical repair of acute type A aortic dissection and appears to have protective benefits.

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