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 Griep et al in 1975.9 Advantages offered by DHCA include bloodless aortic arch replacement and lowered systemic and cerebral cellular metabolism. However,
achieving such temperatures requires extensive cooling and rewarming times. 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. 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, transeosophageal 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 Kolmogrov–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
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.

### 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 \( (p < 0.001) \), 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

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### Table 1 Preoperative patient characteristics

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

Abbreviations: COPD, chronic obstructive pulmonary disease; EF, ejection fraction; NYHA, New York Heart Association.

*Continuous data are shown as median (range) and categorical data are shown as percentage.

### Table 2 Operative patient characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Deep ( (n = 105) )</th>
<th>Moderate ( (n = 27) )</th>
<th>( p )-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPB time &gt; 240 min</td>
<td>37 (35.2%)</td>
<td>3 (11.1%)</td>
<td>0.015</td>
</tr>
<tr>
<td>CPB, min</td>
<td>219 (102–353)</td>
<td>173.5 (89–263)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Circulatory arrest time, min</td>
<td>31.5 (0–146)</td>
<td>18.5 (0–46)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Systemic temperature</td>
<td>18 (13–23)</td>
<td>26.50 (24–28)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Aortic valve procedure</td>
<td></td>
<td></td>
<td>0.749</td>
</tr>
<tr>
<td>Nothing</td>
<td>41 (39.0%)</td>
<td>12 (44.4%)</td>
<td>...</td>
</tr>
<tr>
<td>Replacement</td>
<td>4 (3.8%)</td>
<td>2 (7.4%)</td>
<td>...</td>
</tr>
<tr>
<td>Resuspension</td>
<td>43 (41.0%)</td>
<td>10 (37.0%)</td>
<td>...</td>
</tr>
<tr>
<td>Bentall</td>
<td>17 (16.2%)</td>
<td>3 (11.1%)</td>
<td>...</td>
</tr>
<tr>
<td>Hemiarch technique</td>
<td>89 (84.8%)</td>
<td>18 (66.7%)</td>
<td>0.032</td>
</tr>
<tr>
<td>Total arch replacement</td>
<td>7 (6.7%)</td>
<td>2 (7.4%)</td>
<td>0.892</td>
</tr>
<tr>
<td>Cerebral Perfusion</td>
<td></td>
<td></td>
<td>0.01</td>
</tr>
<tr>
<td>No cerebral perfusion</td>
<td>39 (37.1%)</td>
<td>13 (48.1%)</td>
<td>...</td>
</tr>
<tr>
<td>Retrograde</td>
<td>28 (26.7%)</td>
<td>0 (0%)</td>
<td>...</td>
</tr>
<tr>
<td>Antegrade</td>
<td>38 (36.2%)</td>
<td>14 (51.9%)</td>
<td>...</td>
</tr>
<tr>
<td>Cannulation method</td>
<td></td>
<td></td>
<td>0.034</td>
</tr>
<tr>
<td>Axillary</td>
<td>25 (23.8%)</td>
<td>13 (48.1%)</td>
<td>...</td>
</tr>
<tr>
<td>Femoral</td>
<td>74 (70.5%)</td>
<td>12 (44.4%)</td>
<td>...</td>
</tr>
<tr>
<td>Both</td>
<td>6 (5.7%)</td>
<td>2 (7.4%)</td>
<td>...</td>
</tr>
<tr>
<td>BioGlue/Felt strip</td>
<td></td>
<td></td>
<td>0.028</td>
</tr>
<tr>
<td>BioGlue</td>
<td>31 (29.5%)</td>
<td>13 (48.1%)</td>
<td>...</td>
</tr>
<tr>
<td>Felt strip</td>
<td>25 (23.8%)</td>
<td>9 (33.3%)</td>
<td>...</td>
</tr>
<tr>
<td>Both</td>
<td>49 (46.7%)</td>
<td>5 (18.5%)</td>
<td>...</td>
</tr>
</tbody>
</table>

Abbreviation: CPB, cardiopulmonary bypass.

*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.\(^4\) 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 cannula-
tion method, cerebral protection method, and circulatory
arrest time. The conflicting evidence brought from these two
studies prompted our investigation with particular interest
to 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 mark-
edly diminishes with decreasing temperature and nearly
absolves at 12°C.\(^{15}\) 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 pro-
longed 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 increas-
ingly 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
selective 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 cere-
bral 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 com-
pared 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.

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

*Continuous data are shown as median (range) and categorical data are shown as percentage.*
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%, \( p = 0.01 \)).\(^2\) Our study demonstrated similar decreases in stroke prevalence for MH over DH, although our study did not reach statistical significance (0% vs. 12.4%, \( p = 0.054 \)).\(^2\)

**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.\(^2\)

**Conclusions**

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

**Funding**

None.

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**References**

18. Strauch JT, Spielvogel D, Haldenwang PL, et al. Impact of hypothermic selective cerebral perfusion compared with hypothermic...