Original Article

Near-infrared spectroscopy monitoring during unilateral antegrade cerebral perfusion: Does time matter?

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ABSTRACT

Objectives: Currently, antegrade cerebral perfusion (ACP) for the protection of brain in thoracic aorta surgery has been considered superior to other methods. Adequate perfusion of the opposite hemisphere may sometimes be challenging in the unilateral application of this method. The present study aims to evaluate the opposite hemisphere perfusion via regional oxygen saturation (rSO2) values.

Design: Observational and descriptive

Setting: Department of Cardiovascular Surgery and Department of Anesthesiology and Reanimation, Turkey Yuksek Ihtisas Training and Research Hospital, Ankara, Turkey

Subjects: Adult patients undergoing elective ascending and aortic arch surgery with ACP performed by the same team

Intervention: Two groups according to the unilateral ACP duration, Group 1 (n = 22) was composed of 15 minutes or less unilateral ACP duration, Group 2 (n = 17) was more than 15 minutes.

Main outcome measure(s): Effects of unilateral ACP duration in aortic surgery and aortic arch surgery on bilateral cerebral rSO2 as measured by near-infrared spectroscopy (NIRS) were prospectively investigated. Bihemispheric regional rSO2 values were measured at nine time points during surgery. Any p-value less than 0.05 was considered statistically significant.

Results: While no difference was observed between the right and left hemisphere rSO2 values in Group 1, the difference between the right and left hemisphere values in Group 2 statistically increased towards the end of the ACP period (p <0.05).

Conclusions: We concluded that 15 minutes or less unilateral ACP may be performed at moderate hypothermia without any asymmetry between hemispheres with NIRS monitoring.

KEYWORDS: cardiac surgery, cerebral blood flow, thoracic aortic aneurysm

INTRODUCTION

Anesthesia management in aortic surgery is closely related with maintaining the brain perfusion pressure at appropriate levels, decreasing the metabolic needs of the brain by anesthetic drugs and hypothermia, and close monitoring of this demand/supply balance. Thanks to the novel surgical strategies, and cerebral perfusion and intraoperative monitoring techniques developed in recent years, maximal cerebral protection is attained and neurologic events occurring post-aortic surgery are reduced[1].

In thoracic aortic surgery, to reduce the neurologic events, following the deep hypothermic circulatory arrest (DHCA) technique, which is used to protect the brain, other techniques, such as antegrade cerebral perfusion (ACP) and retrograde cerebral perfusion (RCP), have gained popularity. Issues accompanying prolonged DHCA application[2], the association of RCP with cerebral edema, and the concerns about its possible inadequacy in maintaining sufficient perfusion[3,4] resulted in wider use of the ACP technique[5]. The dilemma of unilateral or bilateral application of ACP has been a topic of discussion in the literature[6,7]. The most important drawback of unilateral use of ACP is

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the uncertainty associated with providing sufficient perfusion to the opposite hemisphere\[1].

With the use of modern perfusion techniques, aortic surgery is performed at higher body temperatures, sufficiency of perfusion is accurately monitored by real-time monitoring techniques, and thereby malperfusion can be detected at early periods, so sufficient perfusion is provided immediately before the occurrence of an irreversible brain damage\[8\]. For example, near-infrared spectroscopy (NIRS) is a real-time, useful, easy-to-use, and non-invasive method for cerebral oxygen monitoring.

In the present study, effects of unilateral ACP duration in aortic surgery and aortic arch surgery on bilateral cerebral regional oxygen saturation (rSO\textsubscript{2}) as measured by NIRS were prospectively investigated. Our aim was to evaluate the contralateral hemisphere perfusion via regional rSO\textsubscript{2} values in terms of asymmetry.

**SUBJECTS AND METHODS**

**Patient population**

The study included patients undergoing elective ascending and aortic arch surgery by the same team after obtaining the ethics committee permission and written consents of the patients. Reporting guideline STROBE has been implemented for this paper. Patients undergoing emergency surgery, those with a history of cerebrovascular event, those with a cerebral vascular disease (any degree of carotid stenosis and any known pathological vascular disease of the brain), and those who were not performed by the unilateral ACP technique were not included in the study. The study was completed after recruiting 39 patients between January and December 2014. Demographic data, intraoperative surgery data and intensive care-hospital stay durations were recorded.

**Anesthetic management**

Orally 0.15 mg kg\textsuperscript{-1} diazepam was administered as night-time premedication and 0.1 mg kg\textsuperscript{-1} morphine was administered i.m. 30 minutes before the surgery. Cannulation of the two peripheral veins and the left radial artery was made in the OR. Pulse oximetry, electrocardiography, and invasive arterial blood pressure were monitored. Before anesthesia induction of the patient, NIRS optodes (Equanox, Nonin Medical Inc, Minnesota, USA) were placed on the bilateral left and right forehead regions 1 cm above the brow curve line. Following preoxygenation, patients were induced with 10 \mu g kg\textsuperscript{-1} fentanyl, 0.1 mg kg\textsuperscript{-1} midazolam, 0.6 mg kg\textsuperscript{-1} rocuronium, and 1 mg kg\textsuperscript{-1} lidocaine. Maintenance was attained by the total intravenous anesthesia technique using fentanyl, rocuronium, and midazolam. After intubation, the patient was ventilated with FiO\textsubscript{2} 50\%, tidal volume 6 mL kg\textsuperscript{-1} and PaCO\textsubscript{2} 35-45 mmHg was targeted. Central venous cannulation was attained via the left internal jugular vein. Nasopharyngeal temperature monitoring was performed. Blood gas management during cardiopulmonary bypass was performed with the alpha-stat strategy.

**Surgical technique and cerebral protection**

Following the right axillary artery and right atrial two-stage venous cannulation, cardiopulmonary bypass was started as described previously\[9\]. Cardiopulmonary bypass was initiated via roller-pump, open reservoir, and Nipro\textsuperscript{®} oxygenator. Target flow rate was 2.4 L min\textsuperscript{-1} m\textsuperscript{-2} at 36 °C. Composition of the prime volume was Ringer Lactate and adjunctives. The patient was cooled down to nasopharyngeal 28 °C. Cardiac arrest was initiated by crystalloid antegrade and selective coronary ostial cardioplegia (Plegisol\textsuperscript{®}), and thereafter maintained by 1:4 mixed blood retrograde cardioplegia at 20-minute intervals. Surgical field CO\textsubscript{2} flood was not used routinely. Antegrade cerebral perfusion was initiated with flow through the RCA (8-10 mL kg\textsuperscript{-1} min\textsuperscript{-1}), via axillary artery. All arch vessels were clamped during the ACP period. The primary method that has been used to lower cerebral oxygen and metabolic demand and reduce ischemic injury is the establishment of cerebral hypothermia. Additional pharmacologic adjuncts (barbiturates or propofol) that decrease neuronal activity may play a role, so five minutes before low flow, 5 mg kg\textsuperscript{-1} propofol was administered\[10,11\]. During ACP, all distal anastomoses were performed as an open distal anastomosis in all patients, including the patients undergoing isolated ascending aortic surgery.

**Neuromonitoring**

NIRS data were monitored throughout the operation, and recorded at the following time points: baseline values before anesthesia induction (Phase 1), at the beginning of cardiopulmonary bypass (Phase 2), during cooling down (32 °C) (Phase 3), at the beginning of ACP application (Phase 4), at the beginning of distal anastomosis with graft during ACP (at about the 5th min of ACP)(Phase 5), at the end of ACP (Phase 6), during warming up (32 °C) (Phase 7), after the end of cardiopulmonary bypass (Phase 8), and end of operation (Phase 9). The control of the perfusion and taking preventive measures, such as checking the oximeter-equipment-cannula position, optimizing the hematocrit, arterial oxygen and carbon dioxide pressure, and increasing the anesthetic depth were planned for cases where there is more than 30% change compared to baseline values, more than 30% difference between two hemispheres, or any value lower than 40%\[12\].
Statistical analysis

Continuous variables with normal distribution were expressed as mean ± standard deviation, and categorical variables were expressed as number and percentage. Demographic features and perioperative variables were compared by Mann-Whitney U test and chi-square test. Right and left rSO₂ values recorded at nine time points during the operation were compared by Mann-Whitney U test for both all patients and individually for each group. rSO₂ change compared with the baseline was calculated in terms of percentage and analyzed. The standard deviation values of the NIRS group were found to be varying in the range of 10 - 12%. In this case, considering that 1 standard deviation between groups is significant, and that 5% type 1 error and 0.80 type 2 error are assumed to occur, power of the study was calculated as 82%. Any p-value less than 0.05 was considered statistically significant. All statistical analyses were carried out using SPSS for Windows 15.0 (SPSS Inc., Chicago, IL, USA).

Table 1: Preoperative patient characteristics

<table>
<thead>
<tr>
<th>Features</th>
<th>Group 1 ACP ≤ 15 min (n = 22)</th>
<th>Group 2 ACP &gt; 15 min (n = 17)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender</td>
<td>13 (59.1%)</td>
<td>8 (47.1%)</td>
<td>0.435</td>
</tr>
<tr>
<td>Age (years)</td>
<td>60.18 ± 10.03</td>
<td>56.47 ± 13.83</td>
<td>0.510</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>0.94 ± 0.23</td>
<td>0.92 ± 0.21</td>
<td>0.812</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>40.72 ± 4.34</td>
<td>43.05 ± 4.57</td>
<td>0.138</td>
</tr>
</tbody>
</table>

Values are means ± SD or number (%) where shown.

RESULTS

Patient data

Mean ACP duration for the entire study population was found to be 16.4 ± 5.9 minutes. The patient population was divided into 2 groups, namely Group 1 (22 patients with ACP duration 15 minutes and less) and Group 2 (17 patients with ACP duration more than 15 minutes). No difference was observed between groups in terms of individual differences, such as age, gender, and creatinine and hematocrit values (Table 1). Cross-clamping and total perfusion durations, the lowest intraoperative hematocrit value, blood transfusions performed, neurological event (permanent stroke or transient ischemic attack), and ICU-hospital stay were similar in both groups (Table 2).

Table 2: Intraoperative and postoperative variables

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group 1 ACP ≤ 15 min (n = 22)</th>
<th>Group 2 ACP &gt; 15 min (n = 17)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPB time (min)</td>
<td>124.95 ± 42.25</td>
<td>123.00 ± 31.10</td>
<td>0.967</td>
</tr>
<tr>
<td>Cross-clamp time (min)</td>
<td>79.77 ± 37.53</td>
<td>71.65 ± 26.69</td>
<td>0.812</td>
</tr>
<tr>
<td>ACP time (min)</td>
<td>13.77 ± 1.48</td>
<td>19.71 ± 7.46</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Intraoperative transfusion (units)</td>
<td>1.45 ± 1.14</td>
<td>1.06 ± 1.09</td>
<td>0.305</td>
</tr>
<tr>
<td>Lowest hematocrit (%)</td>
<td>21.60 ± 3.12</td>
<td>23.91 ± 3.68</td>
<td>0.081</td>
</tr>
<tr>
<td>Neurological dysfunction</td>
<td>1 (4.5%)</td>
<td>1 (6.3%)</td>
<td>1.000</td>
</tr>
<tr>
<td>ICU stay (days)</td>
<td>2.45 ± 0.616</td>
<td>2.00 ± 0.71</td>
<td>0.942</td>
</tr>
<tr>
<td>Hospital stay (days)</td>
<td>9.05 ± 5.92</td>
<td>8.69 ± 7.58</td>
<td>0.529</td>
</tr>
</tbody>
</table>

Values are means ± SD or number (%) where shown.
ACP: Antegrade cerebral perfusion; CPB: Cardiopulmonary bypass; ICU: Intensive care unit

NIRS measurements

In terms of the nine rSO₂ values recorded, right and left rSO₂ values for Group 1 (ACP duration ≤ 15 minutes) were similar at all measurement phases; however, a statistically significant difference was observed in Group 2 (ACP duration > 15 minutes) between the right and left rSO₂ values at Phases 5 and 6 (p = 0.024 and 0.023, respectively)(Figure 1). The left rSO₂ value in Group 2 was lower than the right rSO₂ value at Phase 5 (at the beginning of distal arch anastomosis with graft) and Phase 6 (at the end of ACP). In this group, the right and left rSO₂ values were recorded as 58.6 ± 11.9% (95% CI: 52.5 - 64.7) and 49.5 ± 10.2% (95% CI: 44.2 - 54.7), respectively, at Phase 5. At Phase 6, the right and left rSO₂ values were observed as 58.8 ± 11.1% (95% CI: 53.1 - 64.5) and 49.8 ± 8.8% (95% CI: 45.2 - 54.3), respectively (Table 3). When the two groups were compared, no statistically

Table 3: Right and left rSO₂ values of each group

<table>
<thead>
<tr>
<th>NIRS Phases</th>
<th>Group 1 - ACP ≤ 15 min</th>
<th>p-value</th>
<th>Group 2 - ACP &gt; 15 min</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase 1</td>
<td>62.3 ± 7.3</td>
<td>0.805</td>
<td>66.9 ± 12.9</td>
<td>9.986</td>
</tr>
<tr>
<td>Phase 2</td>
<td>55.0 ± 6.9</td>
<td>0.733</td>
<td>61.4 ± 11.1</td>
<td>0.334</td>
</tr>
<tr>
<td>Phase 3</td>
<td>54.6 ± 9.2</td>
<td>0.760</td>
<td>55.1 ± 8.3</td>
<td>0.407</td>
</tr>
<tr>
<td>Phase 4</td>
<td>52.3 ± 6.8</td>
<td>0.733</td>
<td>56.5 ± 13.1</td>
<td>0.163</td>
</tr>
<tr>
<td>Phase 5</td>
<td>52.9 ± 5.9</td>
<td>0.323</td>
<td>58.6 ± 11.9</td>
<td>0.024</td>
</tr>
<tr>
<td>Phase 6</td>
<td>53.2 ± 6.9</td>
<td>0.869</td>
<td>58.8 ± 11</td>
<td>0.023</td>
</tr>
<tr>
<td>Phase 7</td>
<td>54.9 ± 9.5</td>
<td>0.638</td>
<td>57.8 ± 11.2</td>
<td>0.301</td>
</tr>
<tr>
<td>Phase 8</td>
<td>60.9 ± 10.1</td>
<td>0.753</td>
<td>59.9 ± 9.6</td>
<td>0.448</td>
</tr>
<tr>
<td>Phase 9</td>
<td>59.5 ± 10.3</td>
<td>1.000</td>
<td>63.5 ± 9.9</td>
<td>0.361</td>
</tr>
</tbody>
</table>
significant difference was observed in both right and left hemisphere in terms of rSO$_2$ values recorded at Phases 5 and 6.

No statistically significant difference was observed between the groups in terms of right and left rSO$_2$ value percentage differences between baseline and each time interval (p > 0.05).

Follow-up

No statistically significant difference was observed between the groups in terms of postoperative ventilation duration, low cardiac output syndrome, duration of intensive care and hospital stay, neurologic complications, nor in the need for inotropes. In one patient in each group, temporary postoperative neurological dysfunction (p = 1.000) was observed. Mean ICU stay, and mean hospital stay for Groups 1 and 2 were found to be 2.45 ± 6.16 and 2.00 ± 2.71 days, and 9.05 ± 5.92 and 8.69 ± 7.58 days, respectively (Table 2).

DISCUSSION

In the present study, in patients with 15 minutes or less ACP duration, no statistically significant difference was observed between right and left hemisphere rSO$_2$ values, and they were within normal limits. However, as the ACP duration prolonged, a difference between hemispheres in terms of rSO$_2$ values, as measured by NIRS, occurred, and the left rSO$_2$ values started to decrease. While the perfusion of the left hemisphere was similar to that of the right hemisphere following an average ACP of 13.8 minutes (Group 1), it decreased after an average ACP of 19.7 minutes (Group 2).

NIRS is a non-invasive continuous trend monitor used in brain oxygenation observation. Any change over 30% compared to baseline, a difference of over 30% between two hemispheres, and any value falling below 40% is considered as a risk for brain hypoperfusion and an intervention is recommended. The advantage of NIRS monitoring is that it can be used during hypothermia, low flow perfusion, and even circulatory arrest because its application does not depend on pulse, pressure, or temperature[13-15].

In aortic aneurysm surgery, compared to unilateral perfusion, bilateral cerebral perfusion allows longer time for circulatory arrest. However, the manipulation of arch vessels by direct cannulation may increase the stroke incidence[15]. The unilateral ACP method involves the unilateral brain perfusion by right axillary, or proximal brachial or subclavian artery, and assumes that the circle of Willis is intact, and thus contra lateral hemisphere is perfused. Previous anatomical and angiographic studies reported that variations of Willis polygon occur in more than 50% of the cases[1,16-18]. Therefore, bilateral monitoring of cerebral oxygenation by NIRS is quite crucial for unilateral ACP. Between patients who experienced a neurological event following aortic surgery with ACP and those who did not, there was a statistically significant difference in terms of operation duration and low rSO$_2$ duration[13,14]. Since metabolic demands are suppressed by mild hypothermia and anesthesia, low-flow and low-pressure perfusion during ACP are considered adequate[19]. However, despite this suppression, when the Willis polygon is incomplete or the ACP duration takes longer, cross-perfusion may not be sufficient and neurologic sequelae secondary to the hypoperfusion may occur[13,14]. This condition warrants the need for the determination of a reliable period for ACP. In the present study, with increasing ACP duration, and in about the middle and towards the end of ACP, the difference between right and left hemisphere rSO$_2$ values increased. NIRS monitoring is a trend analysis method, and it showed no difference was observed in percentage changes.

Fig 1. Figure shows the trend monitoring of rSO$_2$ for each group (A: Group 1 and B: Group 2). At the upper part of the figure (A), it can be seen that the trend was similar along the time period for the Group 1 patients, whereas for Group 2, there is a gap between the trends at the ACP period corresponding to the period of midway to the end of ACP. (ACP: antegrade cerebral perfusion, NIRS: near-infrared spectroscopy, rSO$_2$: regional oxygen saturation)
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compared to baseline values, which shows that, even though a difference was observed in the over 15 minutes group at phases 5 and 6, this difference was not a pathological change. However, when each rSO₂ value is considered individually, rSO₂ values were not found to be lower than the previously set cut-off values in any of the patients. Therefore, no alternative strategies, such as switching to bilateral perfusion or cooling down to lower temperatures, were needed in the present study group. However, even though there was no difference in relative changes in the trend analysis, the differences occurring in Group 2 (ACP duration > 15 minutes) at these phases, albeit within normal limits, may indicate that both surgeons and anesthetists should be alert regarding longer-lasting complex aortic arch interventions. Angeloni et al reported recently in their updated meta-analysis that longer circulatory arrest times during unilateral ACP were significantly associated with increased mortality. They strongly recommended bilateral ACP for prolonged circulatory arrests over 30 minutes. In case of prolonged ACP, deeper hypothermia or bilateral perfusion technique may be more advantageous.

In all patients undergoing ascending aortic replacement in our clinic, the open distal anastomosis technique is used. Even in patients with isolated ascending aortic aneurysm, distal anastomosis is carried out via the open technique during ACP. In cases where only hemiarch replacement is adequate, this anastomosis takes about 10 minutes. The results of the present study showed that the unilateral ACP method can even be used in isolated ascending aortic replacement cases because it allows open distal anastomosis.

Limitations

The present study has three major limitations. First, the number of patients included in the study is relatively low. Second, the duration of ACP is within the normal limits when all the study population is considered. The reason for this is that isolated ascending aortic surgery was performed in most patients and thus distal anastomosis was carried out in shorter terms in these patients. Besides, the number of patients needing a complex aortic arch intervention is low. Third, this is an observational study and the results may be biased by our protocol of surgical technique which forecloses randomization (unilateral vs. bilateral). Through studies involving cases with longer ACP duration, precise time intervals may be set. Nevertheless, the present prospective observational study highlights the effectiveness of a surgical and brain protection technique that is clearly beneficial in patients with a short ACP duration.

CONCLUSION

In aortic surgery, 15 minutes or less unilateral ACP may be performed at moderate hypothermia without any asymmetry between hemispheres with NIRS monitoring. As the ACP duration prolonged, a difference between hemispheres in terms of rSO₂ values occurred, and the left rSO₂ values started to decrease, and they were within normal limits after all.

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