Integrated cerebral perfusion for hypothermic circulatory arrest during transverse aortic arch repairs


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Received 12 October 2009; received in revised form 12 February 2010; accepted 14 February 2010; Available online 20 March 2010

Abstract

Objectives: Antegrade cerebral perfusion (ACP) during hypothermic circulatory arrest (HCA) for ascending/transverse arch repair is used for cerebral protection. This study evaluates ACP in combination with retrograde cerebral perfusion (RCP) during extended HCA and compares it to RCP-only. Methods: Between January 2005 and April 2007, we performed 64 consecutive arch repairs requiring extended HCA (>40 min). RCP-only was used with 34 patients and ACP with brief RCP (‘integrated’) was used with 30 patients. Mean HCA time was 51 ± 13 min. Mean RCP-only time was 47 ± 9.6 min; in the integrated group, mean ACP time was 42 ± 14.4 min with an added RCP time of 10.8 ± 7.6 min. For the entire cohort, 95% (61/64) underwent total arch repair, and 67% (43/64) had elephant trunk reconstruction. Variables predictive of mortality and neurological outcomes were analysed prospectively, but technique selection was non-randomised. Results: Preoperative and operative variables did not differ between the RCP-only and the integrated groups except for aortic valve replacement, which was more frequently performed in the integrated group (33% (10/30) vs 12% (4/34), P = 0.05), and preoperative renal dysfunction, which was more frequent in the RCP group (26% (9/34) vs 7% (2/30), P = 0.04). No significant difference was observed in outcomes between the groups; however, the integrated group had higher mortality, stroke and temporary neurological deficit than RCP-only. Conclusions: The observed trends in actual outcomes were a cause for concern. ACP combined with a short period of RCP did not provide better outcomes than RCP-only. The use of RCP remains warranted in our experience.

Keywords: Aortic surgery; Hypothermic circulatory arrest; Cerebral perfusion

1. Introduction

The debate concerning the optimal strategy for cerebral protection during ascending and transverse aortic arch repair remains unresolved. Since Griepp’s study reporting the initial use of profound hypothermic circulatory arrest (PHCA) for transverse arch repairs [1], differing approaches have been used in combination with profound hypothermic circulatory arrest with the goal of reducing neurologic complications [2,3]. Neurologic complications including stroke and reversible injuries such as temporary neurologic deficit (TND) or encephalopathy have been reported to occur in as many as 5–40% of these repairs [4,5]. Furthermore, it was previously recognized that greater lengths of circulatory arrest were associated with greater risk for neurologic injury [6].

In order to address the concerns of neurologic injury, several techniques have been devised for cerebral protection. Ueda was the first to report retrograde cerebral perfusion (RCP) used in conjunction with PHCA during ascending and transverse arch repairs [2]. Reported advantages of RCP were flushing out of atheromatous debris, uniform cerebral cooling, ease of use and potential nutritive support [2,4,7]. Antegrade cerebral perfusion (ACP) used by many groups claimed improved neurological outcomes during arch repair [3]. It was suggested that providing ACP would allow for longer duration of cerebral protection due to the improved ability to provide direct nutritive flow and oxygen to cerebral tissues [8–12]. The difficulty in assessing the efficacy of these approaches, however, has been related to the varying cannulation strategies, differing monitoring approaches and the use of combinations of techniques.

We adopted the use of RCP as the main method of cerebral protection since 1993 following animal and clinical results [13,14]. Since that time, we have reported satisfactory results regarding neurological outcome during ascending and arch repairs [4]. Despite satisfaction with our results, we...
were willing to compare RCP with other approaches. Acknowledging recent reports touting favourable results with ACP, we decided to evaluate integrating the use of ACP and RCP in order to gain the benefits of both during transverse aortic arch repair with extended cerebral ischaemia.

2. Materials and methods

The Committee for the Protection of Human Subjects at the University of Texas Houston Medical School approved review of the data collected for this study. The study design was a retrospective observational study.

2.1. Patient population

Between January 2005 and April 2007, we performed 266 consecutive cases of ascending and transverse arch repairs requiring PHCA. Of this cohort, 64 patients underwent ascending and transverse arch repairs requiring extended hypothermic circulatory arrest (>40 min). All patients in this subgroup had complete transverse arch repair with reattachment of the great vessels. Proximal arch repairs without direct reattachment of the great vessels including hemiarch repairs were excluded since PHCA time was less than 40 min. Of the 64 patients who underwent extended PHCA, 34 patients were treated using RCP and formed the RCP-only group. Thirty patients were treated with a combination of both ACP and RCP and they formed the integrated group. Among all patients, 95% (61/64) underwent total arch repair, with 67% (43/64) having elephant trunk reconstruction. Procedures performed are listed in Table 1.

2.2. Technique

Our approach for transverse arch repairs is briefly described here. Basic features of our current technique for acute dissection or aneurysm of the distal ascending or transverse aortic arch include cardiopulmonary bypass, PHCA and RCP. Cardiopulmonary bypass was established by directly cannulating the ascending aorta after interrogation with trans-oesophageal echocardiography or epiaortic ultrasound for aneurysmal disease. For aortic dissection, peripheral cannulation was preferred via the femoral or axillary artery. The rationale of the approach for cannulation in acute aortic dissection has been described previously [15]. Cerebral monitoring with near-infrared spectroscopy or power-mode transcranial Doppler confirmed adequate cerebral perfusion during perfusion. Systemic cooling is initiated and the patient’s temperature is monitored using both nasopharyngeal and bladder temperature probes. Myocardial protection is achieved using continuous retrograde cold blood cardioplegia through the coronary sinus, supplemented with direct intermittent antegrade coronary ostia infusion once the aorta was opened. A 10-lead electroencephalogram (EEG) monitored cerebral function. Once the EEG is isoelectric, which coincided with a nasopharyngeal temperature of 15–20 °C, cardiopulmonary bypass was discontinued and circulation was arrested. RCP was begun through the superior vena cava cannula. Total caval isolation was obtained. RCP flow rate varied depending on the information obtained from bilateral power-mode transcranial Doppler ultrasound or bilateral near-infrared spectroscopy. Although a higher ‘opening’ pressure is required, the maintenance flow rate is often below 500 ml min⁻¹, maintaining the pressure in the superior vena cava line below 25 mmHg [16]. For the ascending and arch portions of extensive aortic aneurysms, we performed the first stage of the elephant trunk technique. In the case of a severely atheromatous descending thoracic aorta, we modified the elephant trunk procedure by placing a separate Dacron tube graft into the proximal descending thoracic aorta and reconstructing a bevelled transverse arch. In the case of total arch replacement, the great vessels (i.e., innominate, left common carotid and subclavian arteries) were reattached as an island to the graft. If the great vessels were aneurysmal, they were replaced by separate bypass grafts. After completion of the distal arch reconstruction, RCP was discontinued and an aortic cannula was placed into the side arm of the new aortic graft. With the patient in the Trendelenburg position, CPB flow was initiated antegrade through the newly inserted aortic cannula, and all debris and air was evacuated prior to applying the cross-clamp. Proximal reconstruction included supracoronary anastomosis, aortic valve replacement, aortic root replacement with a compo-

<table>
<thead>
<tr>
<th>Procedures</th>
<th>Number</th>
<th>% (integrated group)</th>
<th>% (RCP group)</th>
<th>%</th>
<th>P-value</th>
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<td>9</td>
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<td>7</td>
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</tr>
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<td>6</td>
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<td>5</td>
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<td>Assist device (LVAD)</td>
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<td>1.6</td>
<td>1</td>
<td>3</td>
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<td>2</td>
<td>3</td>
<td>1</td>
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<tr>
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</table>

site valve graft, valve-preserving root replacement or root reconstruction for acute dissection (see Table 1).

For cases of combined ACP and RCP, an initial period of RCP (10 min) to flush out atheromatous debris was performed, followed by ACP. The method for ACP was performed using balloon-tipped catheters as previously described by others [3,8]. The innominate and left common carotid arteries were cannulated with balloon-tipped catheters and cold blood was perfused at a rate of 10 cc kg\(^{-1}\) flow. The right radial arterial line was monitored and maintained between 40 and 60 mmHg. During ACP, the caval isolation was released. No other technique differences existed between the groups. Alpha stat was used for acid/base management.

2.3. Outcome variables

The preoperative factors analysed included age, sex, emergency status, diabetes, hypertension, renal insufficiency, chronic obstructive pulmonary disease (COPD), peripheral arterial disease, cerebrovascular disease and smoking. The operative factors analysed were hypothermic circulatory arrest, RCP and ACP times, aortic cross-clamp time and cardiopulmonary bypass time. Acute dissection referred to dissection occurring within 2 weeks based on initial onset of pain. COPD was defined by a history of chronic bronchitis and emphysema, or less than 60% of predicted forced expired volume in 1 s (FEV1) while on bronchodilators. A serum creatinine level of greater than 2.0 mg dl\(^{-1}\) or the need for dialysis defined renal dysfunction. Glomerular filtration rate (GFR) was estimated using the Cockcroft—Gault equation [17].

Study endpoints included 30-day mortality, stroke and temporary neurological dysfunction (TND). Thirty-day mortality refers to deaths that occurred within 30 days of surgery. Stroke was defined as any gross focal neurological brain injury, either temporary or permanent, as identified on neurologic examination by a neurology consultant and confirmed with computed tomography (CT) or magnetic resonance imaging (MRI). Temporary confusion, delirium, agitation, disorientation or altered mental status denoted TND on all patients who survived operation, as defined by Ergin et al. [5]. We modified this classification by waiting 24 h after complete reversal of anaesthesia prior to the pronouncement of TND. Acute stroke was excluded by CT scan or MRI of the head in all patients suspected of having TND. All patients with TND were followed for the entire hospitalisation for ultimate resolution of dysfunction.

2.4. Statistical analysis

Treatment technique was not randomised but was determined by best medical judgement for each individual case. Analysis was retrospective. Data were collected from chart reviews by a trained nurse abstractor and were entered into a dedicated Microsoft Access database. Data were exported to SAS for analysis, and all computations were performed using SAS version 9.1.3 running under Windows XP. Univariate comparisons of demographic variables were made using unpaired Student’s t-tests and Fisher’s exact tests as appropriate. Comparisons between perfusion techniques with respect to outcomes (e.g., mortality, stroke and TND) were performed by Fisher’s exact test. Multivariable analyses were not conducted due to limitations of sample size. Power calculations were performed for independent proportions using Pass 2005 (Ness, Kayesville, UT, USA). The null hypothesis was rejected at \(P < 0.05\).

3. Results

Preoperative and operative variables did not differ between the RCP-only group and the ACP/RCP group except for aortic valve replacement, which was more frequent in the integrated group with 33% (10/30) versus RCP-only with 12% (4/34; \(P = 0.05\)) and preoperative renal dysfunction, which was more frequent in RCP-only (\(P = 0.04\)) (see Table 2). The mean PHCA time was 51 ± 13 min for the entire cohort of 64 patients. The mean RCP-only time was 47 ± 9.6 min. In the integrated group, the mean ACP time was 42 ± 14.4 min with additional RCP time of 10.8 ± 7.6 min. Differences between the patient groups are listed in Table 3.

Outcomes by cerebral perfusion approach are listed in Table 4. Although there were no significant differences between RCP and integrated groups regarding neurological outcomes or mortality, observed mortality and neurologic morbidity were higher in the integrated group. The use of ACP with RCP was associated with higher observed mortality (20% vs 9%), stroke (13% vs 3%) and TND (21% vs 12%) when compared to RCP-only.

The only significant difference in postoperative complications occurred with respiratory insufficiency (i.e., prolonged

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Table 2

<table>
<thead>
<tr>
<th>Variable</th>
<th>Integrated group (n = 30)</th>
<th>%</th>
<th>RCP group (n = 34)</th>
<th>%</th>
<th>(P)-value</th>
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<tr>
<td>Age (years)</td>
<td>64 ± 11</td>
<td>56 ± 12</td>
<td></td>
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<td>0.09</td>
</tr>
<tr>
<td>Women</td>
<td>11</td>
<td>37</td>
<td>11</td>
<td>32</td>
<td>0.72</td>
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<td>Emergency</td>
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<td>20</td>
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<td>21</td>
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<tr>
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<td>8</td>
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<td>9</td>
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<td>7</td>
<td>21</td>
<td>0.79</td>
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<td>Re-operation</td>
<td>12</td>
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<td>9</td>
<td>26</td>
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<td>56</td>
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</tr>
<tr>
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<td>33</td>
<td>5</td>
<td>15</td>
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<tr>
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<td>2</td>
<td>7</td>
<td>9</td>
<td>26</td>
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</table>

Abbreviations: HTN: hypertension; COPD: chronic obstructive pulmonary disease.
ventilation, need for tracheostomy and adult respiratory arrest syndrome), which was less frequent in RCP-only (20.6% vs 43.3% in the integrated group; P = 0.05). No difference occurred with postoperative renal insufficiency (RCP-only: 8.8% vs integrated group: 13.3%; P = 0.56) or cardiac complications (RCP-only: 2.9% vs integrated group: 6.7%; P = 0.56). No patient required re-operation for bleeding in either group with no significant differences in perioperative blood product use (Table 3). No significant difference existed in either mean intensive care unit length of stay (RCP-only: 9.4 days vs integrated group: 9.5 days; P = 0.97) or hospital length of stay (RCP-only: 18.4 day vs integrated group: 21.1 days, P = 0.35).

Power analysis of the current cohort revealed a post-hoc power of 0.43. A total cohort of 100 or 200 patients in each group would have been required to achieve a power of 0.79 for the effect size detected. Due to the trend of higher actual mortality and neurologic morbidity, it was decided to suspend for the effect size detected. Due to the trend of higher actual mortality and neurologic morbidity, it was decided to suspend the use of combined antegrade and retrograde cerebral perfusion and return to RCP-only for cerebral perfusion.

4. Discussion

The optimal strategy for cerebral protection during ascending and transverse aortic arch repair remains debatable. Many variables have been associated with neurologic injury following ascending and transverse arch repairs. Preoperative factors included emergency status, presence of aortic dissection, degree of atheromatous disease, diabetic history, history of previous cerebrovascular accidents and presence of renal insufficiency. Operative factors have included cannulation strategy, acid/base management, duration of PHCA [6], temperature management [18] and technique of cerebral perfusion (ACP vs RCP). Considering these variables, it is understandable that no consensus for the optimal approach for cerebral protection during arch repairs has been determined.

It was our interest to analyse our recent experience with ACP and RCP. In determining how to analyse the study cohort, we considered two points. One was to identify the patient cohort at greatest risk for neurologic injury. As previously reported, prolonged circulatory arrest time was an independent risk factor for cerebral injury [6]. For this reason, our analysis only included patients with a circulatory arrest time greater than 40 min, which primarily included first-stage elephant trunk procedures and total arch repairs. This excluded our ascending and partial transverse arch repairs ofentimes involving a PHCA time of less than 25 min. Second, relevant to technique, we wanted to use the technique that would provide not just the best ACP but also potentially the best cerebral protection. For this reason, we adopted a combined approach of ACP with a preceding short period of RCP with the hope of providing the benefits of both RCP (i.e., flushing debris and uniform cerebral cooling) and ACP (i.e., possibly providing superior nutritive flow). Although this was a combined technique, the majority of cerebral perfusion was still provided by ACP (mean ACP time was 42 min). Regarding the technique of ACP, most studies have reported using balloon catheters for direct ostial perfusion via the innominate and left common carotid arteries for ACP [16,19]. However, superiority has not been demonstrated regarding delivery approach for ACP, and the approach we used for ACP remained valid.

From this analysis, we observed that mortality and neurological outcomes (i.e., stroke and TND) were not
without cerebral monitoring, inadequate flow was observed as guided by cerebral monitoring, and that administering RCP to improve its efficacy. We determined that adopting RCP, we have also modified our technique for renal status (GFR), this group was associated with a lower mortality (20% vs 9%), stroke (13% vs 3%) and TND (21% vs 12%) when compared to RCP alone. Nevertheless, no significant difference was demonstrated in this small, retrospective cohort. Recent reviews have not provided evidence to demonstrate superiority of any specific perfusion technique over another [20]. Moreover, it has recently been suggested that PHCA alone may be adequate protection for these repairs [21].

As a result of this retrospective analysis, we returned to the use of RCP in conjunction with PHCA. Although power calculations would have required another 140 patients to demonstrate a significant difference in endpoints, the observed outcomes led us to suspend the use of ACP with RCP. We acknowledged that a prospective randomised trial of RCP during ascending and transverse arch repairs would be required to determine the true efficacy of RCP and ACP.

Regarding outcomes, it remains unclear why the trends towards worse outcomes were observed with the integrated group. Although more aortic valve replacements were performed in the integrated group, no significant difference could be found regarding the complexity of procedures between the groups. The operative times, circulatory arrest times and aortic cross-clamp times were similar between the groups (Table 2). Previously, we have shown that aortic valve replacement predicted a worse long-term outcome, but not higher early mortality when performed in conjunction with ascending and arch repair [22]. Interestingly, we have recently shown that worse preoperative GFR (as determined by the Cockcroft–Gault equation) predicted higher early mortality, and although RCP-only had a worse preoperative renal status (GFR), this group was associated with a lower observed mortality.

This study should be viewed with certain limitations. Despite minimal differences observed between the groups, inherent biases could not be excluded since the study was not randomised. There was no method for patient selection as surgeon preference determined the specific approach for cerebral perfusion used. All cases were performed by two surgeons (ALE, HJS). Regardless, the two groups were generally similar in preoperative and operative variables lending some validity to the comparisons. Moreover, we also acknowledge that only two approaches for cerebral perfusion were analysed, that is, RCP-only and RCP with ACP. The ACP/RCP group could have been contaminated since a short period of RCP was used. Furthermore, no PHCA-alone group was used as a control. It has been our practice to provide at a minimum RCP during any period of PHCA unless infeasible. Some have suggested that RCP may even be detrimental, with concern for increased cerebral oedema and hyperaemia [23], although others have not [24,25]. On the contrary, our results of the RCP group were comparable to recent results reporting outcomes with either RCP or ACP alone, and we have not observed increased cerebral oedema [15,16]. Since adopting RCP, we have also modified our technique for administering RCP to improve its efficacy. We determined that the adequacy of RCP was dependent on modifying pressure and flow as guided by cerebral monitoring, and that without cerebral monitoring, inadequate flow was observed in over 78% of cases [15,16]. Because cerebral venous capacitance vessels may require a higher pressure to establish retrograde cerebral blood flow, non-guided RCP may not achieve adequate cerebral protection. This may be an explanation for inferior results using non-guided RCP demonstrated in previous studies.

Lastly, the study was not powered to establish significant differences, and this will remain a valid criticism. However, with the difficulties in standardising such procedures from centre to centre, performing a multicentre trial with an adequately powered patient cohort controlling for all variables would be a challenge.

Although no significant differences were established between RCP and integrated groups, the trends in observed outcomes derived from our analysis were a cause for concern. The use of ACP combined with a short period of RCP did not provide better outcomes than RCP alone. Based on our experience, continued use of retrograde cerebral perfusion for extended periods of PHCA remains warranted.

Acknowledgement

We thank Ken Goodrick for his editorial assistance.

References

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