Myocardial protection in operations requiring more than 2 h of aortic cross-clamping

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Abstract

Objective: Long periods of aortic cross-clamping time during cardiac surgery are associated with high rates of morbidity and mortality because of damage to the myocardium. Recently, we have used a method of myocardial protection based on the principles of hyperkalemic cardioplegic arrest. We use antegrade administration of warm, undiluted blood followed by continuous retrograde infusion of tepid, undiluted blood supplemented with potassium and magnesium. In this study, we have retrospectively reviewed our experience with this method of cardioprotection in operations requiring more than 2 h of cross-clamp time. Methods: We retrospectively reviewed the medical records of 1280 patients who underwent myocardial revascularization, valve repair or replacement, or a combination of both operations between January 1, 1994 and December 31, 1997. Patients were divided into two groups: the short cross-clamp group (SXC) (n = 1144) had cross-clamp times <120 min (mean, 78 ± 20 min; range, 35–119 min) and the long cross-clamp group (LXC) (n = 136) had cross-clamp times >120 min (mean, 154 ± 31 min; range, 120–277 min). We compared preoperative, operative, and postoperative variables between the two groups. Results: Significantly more patients in the long cross-clamp group (43.4%) underwent the combined operation than in the short cross-clamp group (2.3%), and the rate of reoperation was significantly higher in the long cross-clamp group (12%) than in the short cross-clamp group (5%). Despite these differences in operative complexity, we found no difference in hospital mortality rates between the two groups. The only significant postoperative differences were that the long cross-clamp group had a greater need for inotropic agents (43 vs. 29%), higher serum levels of creatine kinase (880–583 vs. 613–418) and CK-MB (10.9–6.4 vs. 5.9–5.2), and a longer hospital stay (9.6 vs. 6.1 days). Conclusion: Long, complex operations requiring more than 2 h of cross-clamping can be performed safely with our method of cardioprotection based on continuous retrograde infusion of tepid, hyperkalemic, undiluted blood. © 1999 Elsevier Science B.V. All rights reserved.

Keywords: Cardioplegia; Cardiac surgery; Myocardial protection; Creatine phosphokinase isoenzyme MB

1. Introduction

Complex cardiac operations requiring long periods of aortic cross-clamping are associated with high rates of morbidity and mortality because of damage to the myocardium [1,2]. Our recent approach to myocardial protection has been successful and has allowed us to increase the duration of the cross-clamp period without deleterious effects. We induce cardioplegic arrest by antegrade infusion of warm, undiluted, hyperkalemic, oxygenated blood followed by continuous retrograde infusion of tepid, undiluted blood supplemented with variable amounts of potassium and magnesium.

In the present study, we have retrospectively reviewed our experience with this technique of myocardial protection in surgical procedures requiring cross-clamp times of 2 hours and longer.

2. Materials and methods

2.1. Patients

We retrospectively reviewed the medical charts of 1280 adult patients who underwent myocardial revascularization,
infusion of retrograde blood cardioplegia was initiated by systemic cooling (28 to 32 °C) was begun. A continuous infusion of potassium and magnesium to the infused blood. We gradually reduced the infusion of drugs to a minimum of about 10 cc/h for the duration of cardioplegic arrest. If fibrillation or rhythmic movements were noted, we temporarily increased the infusion rate of the drugs or we added 50 mg of Lidocaine. Myocardial perfusion was visually assessed by noting the engorged red veins and blue arteries and the sight of dark blood from arteriotomies or coronary orifices. When we were unable to see the operating field, the continuous retrograde infusion was briefly interrupted for 2–3 min. Blood was cleared from anastomotic sites with a jet of CO2 gas. Rewarming began and the retrograde infusion was switched to non-cardioplegic blood (potassium and magnesium were discontinued) about 3–5 min before removing the aortic cross-clamp. This procedure washes out the cardioplegic agents and allows the heart to beat spontaneously immediately after removal of the aortic clamp.

2.2. Data collection

We compared preoperative, operative, and postoperative data between the two groups. We collected information on the type of operation, the patient’s age, previous cardiac operations, the preoperative ejection fraction, time on cardiopulmonary bypass, and time of aortic cross-clamping. In addition, we monitored the postoperative use of inotropic agents and intraaortic balloon counterpulsation. Q waves on 12-lead electrocardiograms, serum levels of creatine kinase and its MB isoenzyme (CK-MB) taken 12 h after surgery. Finally, we noted the length of hospital stay and hospital mortality.

Creatine kinase was measured by the standard method (NAC-activated, Deutsche Gesellschaft Fur Klinische Chemie). Measurements were performed on a Hitachi 911 Clinical Chemistry Analyzer (Boeringer Mannheim), with reference values 50 to 280 μ/l. We used an immunologic method to determine CK-MB. CK-M subunits are inhibited by specific antibody, and the remaining CK-B activity was determined by the CK-NAC activated method.

2.3. Surgical technique

Cardiopulmonary bypass was established with either a two-stage atrial cannulation or individual cannulation of the venae cavae according to the type of operation and the surgeon’s preference and with cannulation of the ascending aorta. The extracorporeal circuit comprised a roller pump, a membrane oxygenator and an in-line arterial filter. After aortic cannulation, a balloon-ribbed, self inflatable retrograde cardioplegia catheter (Research Medical, Midvale, UT) was blindly inserted into the coronary sinus with the use of a flexible stylet. After cannulation was completed, cardiopulmonary bypass was initiated at a flow rate of 2.2 l/min per m2, and a vent was placed in the pulmonary artery.

The aorta was cross-clamped before systemic cooling. Immediately after cross-clamping, a mixture of normothermic blood and cardioplegic drugs was slowly infused (200–300 cc/min) into the aortic root through an aortic root needle. The first bolus of cardioplegic drugs comprised 20 mEq of potassium, 8 mEq of magnesium, as suggested by Menasche et al. [3] with an addition of 100 mg of Lidocaine. After diastolic arrest, which was almost always achieved, the aortic root needle was switched to the venting mode, and systemic cooling (28 to 32°C) was begun. A continuous infusion of retrograde blood cardioplegia was initiated by

infusing blood (100–200 cc/min) directly from the oxygenator without additional cooling or warming. Coronary sinus pressure was maintained between 30 and 40 mmHg. A volumetric infusion pump continuously added a concentrated mixture of potassium and magnesium to the infused blood. We gradually reduced the infusion of drugs to a minimum of about 10 cc/h for the duration of cardioplegic arrest. If fibrillation or rhythmic movements were noted, we temporarily increased the infusion rate of the drugs or we added 50 mg of Lidocaine. Myocardial perfusion was visually assessed by noting the engorged red veins and blue arteries and the sight of dark blood from arteriotomies or coronary orifices. When we were unable to see the operating field, the continuous retrograde infusion was briefly interrupted for 2–3 min. Blood was cleared from anastomotic sites with a jet of CO2 gas. Rewarming began and the retrograde infusion was switched to non-cardioplegic blood (potassium and magnesium were discontinued) about 3–5 min before removing the aortic cross-clamp. This procedure washes out the cardioplegic agents and allows the heart to beat spontaneously immediately after removal of the aortic clamp.

2.4. Statistical analysis

Categorical data are reported as absolute values, whereas continuous variables are presented as means and standard deviations. Patient demographic data and operative and postoperative variable were compared between groups by the χ² test if categorical, and by the unpaired Student’s t-test or the Mann–Whitney test if continuous. A P-value of less than 0.05 was considered significant.

3. Results

Of the 1280 patients enrolled in the study, 136 underwent aortic cross-clamping for more than 2 h (mean time, 153.5 ± 31 min; range, 120–277 min) and thus formed the LXC group. The SX group comprised 1144 patients, with a mean cross-clamping time of 78 ± 20 min (range, 35–119 min).

Patient demographic data are presented in Table 1. The two groups differed significantly with respect to the type of surgery. Most patients in the SX group underwent coronary artery bypass grafting, whereas more patients in the LXC group underwent valvular surgery or a combination of both procedures. Furthermore, significantly more operations in the LXC group were reoperations. Finally, more patients in the LXC group had congestive heart failure.

However, because patients in the LXC group had longer cross-clamping times, they were also on cardiopulmonary bypass for longer periods than the SX group (Table 2). In addition, the LXC group required more potassium than did the SX group.

We noted some significant differences between the two
The method of myocardial protection used in the present study is a slight modification of the method first introduced by Menasche et al. [3]. Its major principles are as follows.

1. The use of undiluted, whole blood from the oxygenator supplemented with potassium and magnesium.
2. Initial antegrade cardioplegic arrest, when possible.
3. Continuous retrograde administration of cardioplegia during the period of aortic cross-clamping with the use of variable, but minimal amounts of potassium and magnesium.
4. Continuous monitoring of the amount of cardioplegia (optimally maintained at 150–200 mEq/min) and the perfusion pressure (optimally maintained at 30–40 mmHg).
5. We have shown that our cardioprotective method, which involves the continuous retrograde infusion of non-diluted, tepid blood supplemented with potassium and magnesium, provides adequate myocardial protection for complex, lengthy operations that require long cross-clamp periods. Operative and postoperative results are similar to those obtained in operations with much shorter periods of aortic cross-clamping.

Although cardioplegia has been the preferred method of myocardial protection for more than 20 years [4,5], time of cross-clamping is still a major concern for the cardiac surgeon. Several clinical studies have shown that a long aortic cross-clamp time is a significant risk factor for and predictor of postoperative morbidity and mortality [6,7]. By using a myocardial protective strategy that allows a longer aortic cross-clamp time, the surgeon can achieve better results in complex, long operations. In addition, a longer cross-clamp time can ensure more accurate and meticulous work in shorter ordinary procedures by reducing the time stress.

### Table 1

<table>
<thead>
<tr>
<th>Patient demographics</th>
<th>Patient groups (%)</th>
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</thead>
<tbody>
<tr>
<td>LXC (n = 136)</td>
<td>SXC (n = 1144)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (year)</td>
<td>59.8 ± 13.7</td>
<td>57.5 ± 13.1</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>83 (61)</td>
<td>767 (67)</td>
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</tr>
<tr>
<td>Women</td>
<td>53 (39)</td>
<td>377 (33)</td>
<td></td>
</tr>
<tr>
<td>Type of surgery</td>
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<td></td>
<td></td>
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<tr>
<td>Coronary artery bypass</td>
<td>21 (15)</td>
<td>932 (82)**</td>
<td></td>
</tr>
<tr>
<td>Valvular</td>
<td>56 (41)</td>
<td>185 (16)**</td>
<td></td>
</tr>
<tr>
<td>Combined</td>
<td>59 (43)</td>
<td>27 (2)**</td>
<td></td>
</tr>
<tr>
<td>Ejection fraction</td>
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<tr>
<td>&lt;20%</td>
<td>0 (0)</td>
<td>8 (0.7)</td>
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<tr>
<td>20–29%</td>
<td>6 (4.4)</td>
<td>94 (8.2)</td>
<td></td>
</tr>
<tr>
<td>30–39%</td>
<td>11 (8.1)</td>
<td>95 (8.3)</td>
<td></td>
</tr>
<tr>
<td>40–49%</td>
<td>41 (30)</td>
<td>344 (30)</td>
<td></td>
</tr>
<tr>
<td>&gt;50%</td>
<td>78 (57)</td>
<td>603 (53)</td>
<td></td>
</tr>
<tr>
<td>Diabetic mellitus</td>
<td>79 (58)</td>
<td>344 (30)**</td>
<td></td>
</tr>
<tr>
<td>PVD</td>
<td>25 (18)</td>
<td>252 (22)</td>
<td></td>
</tr>
<tr>
<td>Reoperation</td>
<td>24 (18)</td>
<td>80 (7)**</td>
<td></td>
</tr>
<tr>
<td>Emergent operation</td>
<td>16 (12)</td>
<td>57 (5)*</td>
<td></td>
</tr>
</tbody>
</table>

LXC, long cross-clamp time; PVD, peripheral vascular disease; SXC, short cross-clamp time. *P = 0.001, **P < 0.0001.

4. Discussion

We have shown that our cardioprotective method, which involves the continuous retrograde infusion of non-diluted, tepid blood supplemented with potassium and magnesium, provides adequate myocardial protection for complex, lengthy operations that require long cross-clamp periods. Operative and postoperative results are similar to those obtained in operations with much shorter periods of aortic cross-clamping.

Although cardioplegia has been the preferred method of myocardial protection for more than 20 years [4,5], time of cross-clamping is still a major concern for the cardiac surgeon. Several clinical studies have shown that a long aortic cross-clamp time is a significant risk factor for and predictor of postoperative morbidity and mortality [6,7]. By using a myocardial protective strategy that allows a longer aortic cross-clamp time, the surgeon can achieve better results in complex, long operations. In addition, a longer cross-clamp time can ensure more accurate and meticulous work in shorter ordinary procedures by reducing the time stress.
To improve visualization and surgical precision, carbon dioxide gas jet is used or, if necessary, the retrograde cardioplegic flow is interrupted for short (2–3 min) periods.

The major criticism of the retrograde technique for myocardial protection is that it may not adequately protect the right ventricle [9–14]. However because of this possibility, we monitored the epicardial veins of the right ventricle to ensure they were engorged with bright red blood. Although we could not precisely determine the extent of myocardial perfusion and protection [15], we believe that the right ventricle was adequately protected because we did not see any postoperative cases of isolated right ventricular dysfunction, even in patients with long cross-clamp times. This finding is similar to that of a previous study, which suggested that the problem of right ventricular protection was more evident experimentally than clinically [16].

Another potential problem with this method of myocardial protection is the use of a large amount of potassium. In our study, the average amount of potassium used was large – 69.8 ± 21.4 mEq per patient, with mean maximal serum concentrations of 5.7 ± 0.8 mmol/l. However, the amount of potassium given to the LXC group per hour of cross-clamping was significantly lower than that in the SXC group (Table 2). Furthermore, most patients required additional procedures (e.g. proximal anastomoses) before removal of the aortic cross-clamp; therefore, we had sufficient time to treat hyperkalemia, and most patients had normal to near normal potassium levels when weaned from cardiopulmonary bypass. We prolonged time on bypass just to lower potassium levels in only a few patients. Moreover, during the time we conducted this study, we were able to reduce the amount of potassium used from 80.9 ± 23.5 mEq in the first 27 months of the study to 64.1 ± 15.5 mEq in the last 21 months (P < 0.0001).

Although more patients in the LXC group had congestive heart failure, left ventricular dysfunction, concurrent disease, and the need for emergent operation, the mortality rate, the use of intraaortic balloon pump, and the incidence of neurologic damage in the LXC group were not significantly different from those in the SXC group or from those cited in the literature [17]. However, we did find that patients in the LXC group had a significantly greater need for inotropic infusion, higher levels of creatine kinase and CK-MB enzymes, and a longer hospital stay than patients in the SXC group. These differences may be attributed to differences in preoperative status and differences in the types of surgeries in each group; however, the differences may also indicate more myocardial damage in the LXC group. An increase in creatine kinase enzyme and its subunit cannot be used reliably as a sole indicator of myocardial damage because of non-specific increases caused by tissue trauma, cardiopulmonary bypass, and transfusion of mediastinal shed blood [18–20]. However, an increase in cardiac isoenzymes combined with an increased need for inotropic agents, both of which were seen in the LXC group in our study, may indicate myocardial damage. Further studies with more sensitive and specific (e.g. troponin and its isoenzymes [21]) biochemical markers can better address this issue.

Several studies have shown that continuous perfusion of the myocardium during the cross-clamp period can avoid myocardial ischemia [22–25], suggesting that cross-clamp time does not necessarily equal time of ischemia. Our findings of equivalent mortality and major morbidity rates between the LXC and SXC groups support this concept. However, our finding of increased levels of cardiac isoenzymes and a greater need for inotropic agents in patients who underwent longer cross-clamp periods may indicate the possibility of myocardial damage.

In conclusion, we have shown in this retrospective study, that myocardial protection involving an initial antegrade followed by retrograde perfusion of the myocardium with non-diluted, tepid blood supplemented with potassium and magnesium affords adequate myocardial protection for complex lengthy operations that require long cross-clamp periods and yields good operative results comparable with those obtained with a much shorter cross-clamp period.

Table 3

<table>
<thead>
<tr>
<th>Patient group (%)</th>
<th>LXC</th>
<th>SXC</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IABP</td>
<td>2 (1.5)</td>
<td>12 (1.0)</td>
<td>0.27</td>
</tr>
<tr>
<td>Inotropic agents*</td>
<td>58 (43)</td>
<td>327 (29)</td>
<td>0.0007</td>
</tr>
<tr>
<td>New Q waves on ECG</td>
<td>5 (3.7)</td>
<td>39 (3.4)</td>
<td>0.19</td>
</tr>
<tr>
<td>Neurologic damage</td>
<td>5 (3.7)</td>
<td>32 (2.8)</td>
<td>0.16</td>
</tr>
<tr>
<td>Creatine kinase (units/l)</td>
<td>880 – 23.5</td>
<td>64.1</td>
<td>0.0001</td>
</tr>
<tr>
<td>Total mortality</td>
<td>6 (4.4)</td>
<td>31 (2.7)</td>
<td>0.26</td>
</tr>
<tr>
<td>Coronary artery bypass</td>
<td>0/21 (0)</td>
<td>17/932 (1.8)</td>
<td>0.7</td>
</tr>
<tr>
<td>Valvular surgery</td>
<td>0/56 (0)</td>
<td>11/185 (5.9)</td>
<td>0.051</td>
</tr>
<tr>
<td>Combined surgery</td>
<td>6/59 (10)</td>
<td>327/11 (1)</td>
<td>0.29</td>
</tr>
</tbody>
</table>

IABP: intra-aortic balloon pump; LXC, long cross-clamp time; LOS, length of stay in hospital; SXC, short cross-clamp time. *Administered for longer than 6 h post-operatively.

References

[5] Conzi VR, Bertranou EG, Blackstone EH, Kirklin J, Digernes SB.


