Institutional report - Cardiac general

The effect of using microplegia on perioperative morbidity and mortality in elderly patients undergoing cardiac surgery

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Abstract

Old age is a significant risk factor for perioperative morbidity and mortality following cardiac surgery and optimal myocardial protection strategy should be sought in this group of patients. We, therefore, reviewed the data on 295 consecutive patients older than 75 years who underwent any cardiac surgical procedure. Microplegia was used in 144 patients compared to 151 patients who had the standard 4:1 blood cardioplegia. Logistic regression analysis was used for propensity matching to balance the differences between the two groups. The microplegia group included more females and sicker patients as indicated by higher Parsonnet scores. There were differences in the pump time, aortic cross-clamp time, procedure type and surgeons between the two groups. These differences were balanced using the propensity matching. In-hospital mortality, acute renal injury and confusion were higher in the microplegia group (17%, 34%, 35%, respectively) compared to the standard 4:1 cardioplegia group (9%, 23%, 24%, respectively) (P=0.04, 0.04, 0.04, respectively). These differences were not statistically significant after propensity matching. These results demonstrate that the use of microplegia is safe in patients older than 75 years who are undergoing cardiac surgery and results in similar in-hospital morbidity and mortality to the standard 4:1 blood cardioplegia.

Keywords: Microplegia; Cardioplegia; Myocardial protection; Morbidity; Mortality

1. Introduction

Elderly patients represent an emerging population of patients with increasing prevalence of cardiac surgical problems. Good surgical results could be achieved in a low-risk subgroup of this cohort provided that optimum operative and perioperative management are attained. Minimizing pump time and cross-clamp time is an important aspect of operative optimization. However, long ischemia times are unavoidable sometimes given the combined procedures those elderly patients may need or the advanced pathology they may have as a result of the aging process (i.e. poor targets or heavily calcified valves). Studying the effect of different myocardial protection strategies in this group of patients is extremely important.

Calafiore and his group proposed minimally diluted oxygenated blood with concentrated arresting agents as an alternative technique to the standard 4:1 dilution of blood to crystalloid solution and they claimed that this technique is safe, reliable, and effective for myocardial protection and deserves further assessment [1]. There are multiple potential advantages for this strategy: reduced systemic hemodilution, reduced myocardial edema, improved metabolic and systemic recovery, better O2 delivery and buffer-

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ing capacity, improved K+ and glucose control, reduced transfusion rates. Menasché suggested that undiluted blood cardioplegia or ‘miniplegia’ would retain all the advantages of blood cardioplegia without the potential disadvantages of hemodilution [2, 3].

Despite this growing interest in microplegia, its use is still limited due to the lack of adequate evidence to support its clinical advantages and also due to the reported disadvantages of using all blood cardioplegia. Velez showed in an experimental study that the use of all blood cardioplegia can result in impairment of endothelial function (relaxation with acetylcholine) compared to the 4:1 diluted cardioplegia [4]. Additionally, the use of all blood cardioplegia carries the theoretical risk of increased concentration of inflammatory mediators (i.e. tumor necrosis factor and interleukins) and cells (polymorph nuclear leukocytes), which are stimulated during both cardiopulmonary bypass and myocardial ischemia [5].

The aim of this study was to evaluate the effect of using microplegia on the morbidity and in-hospital mortality in elderly patients undergoing cardiac surgery.

2. Methods

This is a case control study with a retrospective analysis of the prospectively collected data. The study was approved by McGill University Health Centre Ethics Committee. All data were obtained from McGill University...
cardiac surgery database. Missing data were obtained by reviewing the patient’s chart. The study included all patients older than 75 years who underwent any cardiac surgical procedure between November 2005 and May 2007. The patients were divided into two groups according to the type of cardioplegia solution used based on surgeon’s preference. The surgeons preferred to use microplegia in cases where they expected longer cross-clamp time in which a larger amount of cardioplegia needed to be administered, which may cause more cardiac edema and dysfunction postoperatively. These preferences were based on theoretical assumptions. Group I received the standard cardioplegia solution with 4:1 dilution [Blood: Crystalloids (Pregisol, Hospira, Inc, Lake Forest, IL)]. Group II received whole blood cardioplegia using the Quest myocardial protection system (MPS) (Quest Medical, Allen, TX) with the potassium concentrated solution administered through a separate syringe through the Quest MPS. Cardioplegia solution was administered cold (4–10 °C) and consisted of high-dose (100 mEq/l) or low-dose (40 mEq/l) potassium at the discretion of the cardiac surgeon. A single-clamp technique was used, and cardioplegia was given in an antegrade fashion in all patients. Retrograde cardioplegia was administered selectively in some patients when desired by the cardiac surgeon. A ‘hot shot’ of 1 l of warm cardioplegia is administered before removal of the aortic cross-clamp.

2.1. Statistical analysis

Statistical analysis was performed using NCSS statistical software (2004). Continuous variables were compared using either the two-sample t-test or the Wilcoxon rank sum test as appropriate by the distribution of data. Categorical variables were compared using χ²-test or Fisher’s exact test depending on the number of items in each group. A stepwise logistic regression was done to select variables that were significantly different between the two groups and potentially affecting the outcome. These variables were used on a logistic regression to get propensity scores. These propensity scores were stratified (sub-classification) using quintiles. We used this technique to avoid excluding any patient from the study. The propensity scores where computed and ranked from lowest to highest. Then the subjects were put in five groups according to the similarity of their propensity scores, using the quintiles of the distribution of propensity scores. The idea of sub-classification is that subjects in each quintile are very similar with respect to their values on the covariates. Next, we investigated the balance in the covariates after propensity scores were computed. None of these variables was significantly different. We further investigated interactions between microplegia use and quintiles. None of the covariates presented a significant interaction between microplegia use and quintiles.

3. Results

3.1. Demographic and operative characteristics

A total of 295 patients were included in the study. Standard 4:1 cardioplegia was used in 151 patients (Group I). The rest of the patients (144 patients) received microplegia (Group II). Group II included more females (49% vs. 37%, respectively, P=0.04) and patients with congestive heart failure (65% vs. 46%, respectively, P=0.001) than group I. We used the Parsonnet score [6] to estimate the perioperative mortality in our patients, which was higher in group II than group I (mean=28±12 vs. 24±11, respectively, P=0.002). These differences disappeared after propensity matching. The rest of preoperative characteristics were similar between the two groups as shown in Table 1. More patients in group II underwent complex cardiac procedures compared to group I (15% vs. 4%, respectively, P=0.003). Consequently, pump times and cross-clamp times were

| Table 1 |
| Preoperative characteristics |

<table>
<thead>
<tr>
<th>Variable</th>
<th>Standard 4:1 cardioplegia</th>
<th>Microplegia</th>
<th>Before propensity P-value</th>
<th>After propensity P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>79 ± 4*</td>
<td>79 ± 4*</td>
<td>0.65</td>
<td>0.75</td>
</tr>
<tr>
<td>Sex</td>
<td>54 (37)</td>
<td>70 (49)</td>
<td>0.04</td>
<td>0.92</td>
</tr>
<tr>
<td>Hypertension</td>
<td>121 (83)</td>
<td>113 (79)</td>
<td>0.42</td>
<td>0.25</td>
</tr>
<tr>
<td>Diabetes</td>
<td>42 (29)</td>
<td>33 (23)</td>
<td>0.26</td>
<td>0.30</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>47 (36)</td>
<td>93 (65)</td>
<td>0.001</td>
<td>0.85</td>
</tr>
<tr>
<td>Asthma</td>
<td>3 (2)</td>
<td>3 (2)</td>
<td>0.99</td>
<td>0.65</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>18 (12)</td>
<td>23 (16)</td>
<td>0.38</td>
<td>0.49</td>
</tr>
<tr>
<td>Renal failure</td>
<td>23 (16)</td>
<td>25 (17)</td>
<td>0.83</td>
<td>0.45</td>
</tr>
<tr>
<td>Dialysis dependence</td>
<td>2 (1)</td>
<td>2 (1)</td>
<td>0.99</td>
<td>0.96</td>
</tr>
<tr>
<td>Severe neurologic disorder</td>
<td>4 (3)</td>
<td>6 (4)</td>
<td>0.51</td>
<td>0.58</td>
</tr>
<tr>
<td>Severe peripheral vascular disease</td>
<td>13 (9)</td>
<td>6 (4)</td>
<td>0.1</td>
<td>0.12</td>
</tr>
<tr>
<td>Urgent surgery</td>
<td>77 (53)</td>
<td>65 (45)</td>
<td>0.2</td>
<td>0.70</td>
</tr>
<tr>
<td>Cardiogenic shock</td>
<td>4 (3)</td>
<td>4 (3)</td>
<td>0.98</td>
<td>0.39</td>
</tr>
<tr>
<td>Preoperative IABP</td>
<td>4 (3)</td>
<td>9 (6)</td>
<td>0.38</td>
<td>0.12</td>
</tr>
<tr>
<td>Pulmonary hypertension</td>
<td>22 (15)</td>
<td>32 (22)</td>
<td>0.12</td>
<td>0.44</td>
</tr>
<tr>
<td>PTCA catheterization failure</td>
<td>3 (2)</td>
<td>3 (2)</td>
<td>0.99</td>
<td>0.31</td>
</tr>
<tr>
<td>Recent myocardial infarction</td>
<td>3 (2)</td>
<td>3 (2)</td>
<td>0.99</td>
<td>0.36</td>
</tr>
<tr>
<td>Reoperation</td>
<td>7 (5)</td>
<td>4 (3)</td>
<td>0.58</td>
<td>0.33</td>
</tr>
<tr>
<td>Parsonnet score</td>
<td>24±11*</td>
<td>28±12*</td>
<td>0.002</td>
<td>0.44</td>
</tr>
</tbody>
</table>

*Mean ± S.E.M.
The median total amount of cardioplegia administered in the standard 4:1 cardioplegia group was 3950 (95% CL = 3700–4250) while the median total amount of cardioplegia administered in the microplegia group was 5070 (95% CL = 4602–5544), P < 0.01.

3.2. Perioperative mortality

The crude perioperative mortality was higher in the microplegia group (17%) in comparison to the standard 4:1 cardioplegia group (9%), P = 0.04. When the preoperative and operative differences were controlled for using the propensity matching, this difference became statistically non-significant (P = 0.17), (Fig. 1).

3.3. Postoperative troponin I level and inotropic support

Postoperative peak troponin I levels were used as indicators of myocardial injury. These levels were similar between the two groups [4.67 in 4:1 cardioplegia (95% CL = 3.94–6.46) vs. 4.76 in microplegia (95% CL = 3.7–6.06), P = 0.77]. The duration of inotropic support was longer in the microplegia group compared to the standard 4:1 cardioplegia group (22 h vs. 15 h, respectively, P = 0.005). These differences became non-significant after propensity matching (P = 0.17). The amount of inotropic support is shown in Fig. 2.

3.4. Blood transfusion and hematocrit level

The median quantity of crystalloids administered to patients in the standard 4:1 cardioplegia was larger than the one in the microplegia group [740 cc (95% CL = 690–794) vs. 65 cc (95% CL = 62–67), respectively, P < 0.01]. The mean hematocrit levels both on-pump and postoperatively were similar between the two groups (25 ± 3 and 27 ± 3, respectively, P = 0.93). Packed red blood cells (PRBC) transfusion was indicated in patients with hematocrit level below 24 or in patients with mixed venous oxygen saturation below 65% if hematocrit level is below 27. The total amount of transfused PRBC was not statistically significant between the two groups (4:1 cardioplegia = 454 ± 62, microplegia = 561 ± 56, P = 0.2).

3.5. Postoperative complications

The incidence of postoperative complications was similar between the two groups except for the confusion (Fig. 3) and renal complications (Fig. 4). Although the risk of confusion was higher in the microplegia group (P = 0.03), this difference was statistically non-significant after propensity matching (P = 0.07). Renal complications were classified into three groups according to the RIFLE classification [7, 8]: risk of acute renal injury (postoperative creatinine >1.5 times baseline), acute renal injury (postoperative creatinine >2 times baseline) and acute renal failure requiring dialysis. The incidence of acute renal injury was higher in the microplegia group compared to the standard 4:1 cardioplegia (37% vs. 26%, P = 0.04). However, this


4. Discussion

In the early 1980s, Follette and his colleagues suggested that blood provided the best vehicle for delivery of cardioplegia in potentially injured myocardium [9]. The advocates for crystalloid cardioplegia claimed that under hypothermic conditions, the increased blood viscosity can lead to capillary sludging and tissue underperfusion. Diluted blood cardioplegia (4:1) was advocated to avoid this problem [10, 11]. The interest in whole blood cardioplegia was renewed by Calafiore who proposed a minimally diluted oxygenated blood with concentrated arresting agents as an alternative technique to the standard 4:1 dilution of blood to crystalloid solution [1]. We showed in this study that the use of all blood or minimally diluted blood cardioplegia (microplegia) resulted in similar myocardial protective effect to the standard 4:1 blood cardioplegia as indicated by similar levels of postoperative peak troponin I levels.

This was translated into similar inotropic requirement postoperatively. We also showed that the use of this strategy resulted in similar postoperative morbidity and mortality in this group of elderly patients.

There are two important remarks in this study. First, when initially described by Calafiore [1], the minimally diluted blood cardioplegia was administered in warm temperature. However, his study included relatively younger patients who underwent coronary artery bypass grafting (CABG) only and the cross-clamp times were short (45 min). Pöling and his colleagues [12] showed that in elective CABG with short cross-clamp time, intermittent antegrade warm blood cardioplegia using Calafiore’s cardioplegia is a comparable safe method of myocardial protection to the cold 4:1 blood cardioplegia but cold cardioplegia offers superior protection of the heart, in terms of more rapid normalization of myocardial metabolism, when the clamp times are long. For this reason and for other reported advantages of cold cardioplegia, the microplegia used in our patients was administered in cold temperature.

Second, one of the major advantages of the microplegia is the avoidance of hemodilution and the higher hematocrit level which leads to better oxygen delivery and buffering capacity [13]. We failed in our study to achieve this objective and patients in both groups had equivalent hematocrit levels on pump and postoperatively with similar transfusion requirement, which may have been caused by excessive fluid administration by anesthesia. This may explain why we did not observe any difference in myocardial protection and postoperative morbidity and mortality with the use of microplegia. We think that the beneficial effects of using microplegia could be maximized by restricting the amount of unnecessary fluids administered to the patients in the operating room.

4.1. Study limitations

This is a single centre non-randomized study. Renal complications were assessed using creatinine levels, which is simple and clinically applicable. However, no formal functional assessment of the renal functions were obtained pre- or postoperatively. These limitations have to be considered when interpreting the results of this study. Although we did not detect any actual clinical benefit associated with microplegia in the matched groups, we demonstrated that the safety profile of microplegia is not different in comparison with the standard technique. This opens the door for more studies on cost-effectiveness or using microplegia in subgroups of patients in which excessive fluid administration could be detrimental like in renal failure patients or Jehovah’s Witness patients. This is the first clinical study that reports the results of using microplegia in a wide variety of cardiac surgical procedures in comparison to a control cohort and it also addresses an important subgroup of patients, the elderly, given the importance of achieving superior results in this group through optimum myocardial management.

5. Conclusion

The use of microplegia is safe in elderly patients undergoing cardiac surgery and results in similar in-hospital morbidity and mortality to the standard 4:1 blood cardioplegia. Further studies are needed to explore the beneficial effects of using microplegia in cardiac surgery patients.

References


