Myocardial oxygen tension during surgical revascularization. 
A clinical comparison between blood cardioplegia and 
crystalloid cardioplegia

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Abstract

Objective: The aim of this study was to assess the effect of cardioplegic solutions on myocardial oxygenation during surgical revascularization.

Methods: In 30 patients, randomized to receive crystalloid (CC) or blood (BC) cardioplegia, myocardial oxygen tension was measured continuously by polarography.

Results: The two groups were comparable in terms of patients’ age, sex, pre-operative ejection fraction, coronary disease, perfusion time, and aorta cross-clamping time. However, the BC group required 22% more of cardioplegic solution to stop electrical activity of the heart. Throughout the pre- and post-cardiac arrest periods, oxygen tension between the two groups was similar. At the end of the observation (4th day), myocardial oxygenation increased over 200% in relation to the values before revascularization. During the first infusion of cardioplegia, oxygen tension in the CC group was lower compared to the BC group (0.1 mmHg vs 1.3 mmHg; \( P < 0.05 \)) being the only significant difference between the two groups during cardiac arrest. Throughout the cardiac arrest, myocardial oxygen tension was close to zero regardless of the type of cardioplegia used. Post-operatively, addition of oxygen to the respiratory air increased myocardial oxygenation by over 17% resulting in a positive correlation \( (r = 0.94; P < 0.05) \) between myocardial oxygen tension and peripheral saturation.

Conclusions: In conclusion, the differences in myocardial oxygen tension between the CC and BC groups are trivial. Thus, any potential beneficial effect of blood cardioplegia compared to crystalloid cardioplegia must be due to other circumstances than its oxygen carrying capacity. An important observation is a significant increase in myocardial oxygenation during oxygen supplement to the respiratory air.

Keywords: CABG surgery; Cardioplegia; Oxygen; Myocardial protection

1. Introduction

Myocardial protection during cardiac surgery can be accomplished by the use of crystalloid potassium cardioplegia as described by Gay and Ebert [1] in 1973 or by blood potassium cardioplegia as described by Follette et al. [2] in 1977. In recent years, the latter has gained increased interest due to several studies indicating superiority of blood cardioplegia, both experimentally [3–6] and clinically [7–11]. In several of these studies, it has been suggested that addition of blood to cardioplegic solutions increases oxygen supply to the myocardium. On the other hand, a number of studies [12–16] show similar myocardial protective value of both cardioplegic methods. In all these studies, the cardioprotective value of the cardioplegic solutions was evaluated by hemodynamic or biochemical parameters such as systolic and diastolic function, myocardial oxygen consumption, creatine kinase myocardial band (CKMB), lactate, ATP, etc., and the myocardial oxygenation has been described only qualitatively by extrapolation of clinical data. However, myocardial oxygenation during cardioplegia can be determined directly by measurement of oxyhemoglobin or free oxygen in the tissue. Recently, myocardial oxygen saturation during cardiac surgery has been assessed in a study using near-infrared spectroscopy [17]. Another technique, which allows continuous quantitative determination of the partial pressure of oxygen physically dissolved in tissue \( (p_{\text{O}_2}) \), is polarography.

In the present study, we applied polarography to assess the effect of crystalloid and blood cardioplegia on myocardial oxygen tension during surgical revascularization of the heart. Furthermore, our purpose was to detect any differences in post-operative clinical, hemodynamic, and biochemical data in relation to pre- and post-operative oxygenation of the heart.

2. Materials and methods

Thirty patients subjected to elective coronary artery bypass surgery were randomized to receive either crystalloid...
(CC group) or blood cardioplegia (BC group). They participated in the study in conformance with the principles outlined in the Declaration of Helsinki II and with the approval of the Ethics Committee for Medical Research in Copenhagen (KF 11-104/01). Informed written consent was obtained from each patient.

The LICOX CMP (Mielkendorf, Germany) is a polarographic device, which determines the \( p_{\text{tO}_2} \) by the Clark principle: oxygen diffuses from tissue (e.g., myocardium) through the semi-permeable membrane of the catheter tube (microprobe) into the inner electrolyte chamber. Here, the \( p_{\text{tO}_2} \) is transformed to OH\(^-\) ions at a negatively polarized metal electrode (the polarographic cathode). The current from \( p_{\text{tO}_2} \) reduction induces a signal detectable by the LICOX’s sensor. With this method it is possible to measure the interstitial myocardial oxygen tension, however, the measurements do not relate to oxygen consumption in the myocardium.

During cardiac operation, the REVOXODE (\( p_{\text{tO}_2} \) catheter microprobe) was placed in the anterior wall of the left ventricle myocardium between the left anterior descending coronary artery and the left circumflex coronary artery using the implantation needle. The tip of the microprobe was fixed with a single thin suture (7/0 Prolene). The \( p_{\text{tO}_2} \) was continuously measured during surgery and through the first 16 post-operative hours (Fig. 1). The measurements were continued until day 4 to allow control of changes in myocardial oxygenation in relation to oxygen supply: subsequent measurements were made once a day with and without the addition of nasal oxygen (8 L of \( p_{\text{tO}_2} \) to the respiratory air. Mean arterial blood pressure (MAP), heart rate (HR), and peripheral saturation (SAT) were measured as well.

The only difference between the two cardioplegic solutions was the addition of blood in proportion 1:4 (e.g., 200 mL of cardioplegia and 800 mL of blood, Table 1) and 60 mmol of potassium to the blood cardioplegic solution. Initially, approximately 800 mL of cold (4—5\(^\circ\)C) non-oxygenated crystalloid cardioplegic or cold (4—5\(^\circ\)C) blood cardioplegic solution was administered antegrade through the aortic root immediately after aorta cross-clamping. For the sake of standardization, other forms of cardioplegia like retrograde infusion or infusion through vein grafts were not used. Subsequent infusions of 200—300 mL were used if there was clinical or electrical evidence of myocardial activity or if the period of aorta cross-clamping exceeded 20 min. The blood cardioplegic solution was infused using the Cardiovascular Systems CAPIOX\textsuperscript{TM} CDIT\textsuperscript{TM} Sarns\textsuperscript{TM} (TERUMO EUROPE N.V., Leuven, Belgium).

Crystalloid cardioplegic solution was not oxygenated and topical ice was not used. Control of myocardial temperature during surgery was completed in only half of the patients and then abandoned due to technical difficulties.

During the operation, saturation (SAT) (\( S_a\text{O}_2 \), Hewlett-Packard 86S, Andover, MA, USA) was recorded (Fig. 1). Blood samples for arterial oxygen tension (\( p_{\text{aO}_2} \) and hematocrit (hct) (Fig. 2) were obtained anaerobically and analyzed on an ABL-615 apparatus (Radiometer, Copenhagen, Denmark). CKMB was chosen as a marker of post-operative ischemia as its response to ischemia is more rapid compared to troponin T (Fig. 3).

A sufficient number of subjects for the study were estimated by the power analysis, relating minimal relevant difference to type 2 errors. The results are expressed as mean \( \pm SE \). Wilcoxon signed rank test was used to compare the related samples (comparisons within the group) and the Mann—Whitney test for comparing independent samples (comparisons between the groups). The Spearman test was used for correlation analyses.

### 3. Results

There were no differences between the CC and BC groups in terms of patients’ age, sex, pre-operative ejection fraction, perfusion time, and aorta cross-clamping time (Table 2). However, owing to electrical evidence of myocardial activity, the BC group required 1442 mL of cardioplegic solution on average compared to 1186 mL in the CC group (Table 2), a difference of 22%.

### Table 1: Composition of the cardioplegic solutions

<table>
<thead>
<tr>
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<th>Crystalloid</th>
<th>Blood</th>
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<tbody>
<tr>
<td>Na(^+) (mmol/L)</td>
<td>147</td>
<td>147</td>
</tr>
<tr>
<td>K(^+) (mmol/L)</td>
<td>20</td>
<td>80</td>
</tr>
<tr>
<td>Mg(^2+) (mmol/L)</td>
<td>16</td>
<td>16</td>
</tr>
<tr>
<td>Ca(^2+) (mmol/L)</td>
<td>2.3</td>
<td>2.3</td>
</tr>
<tr>
<td>Cl(^-) (mmol/L)</td>
<td>205</td>
<td>205</td>
</tr>
<tr>
<td>Procaine (mmol/L)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Blood (mL/L)</td>
<td>0</td>
<td>800</td>
</tr>
</tbody>
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Fig. 1. Cardioplegia 2, 3: \( p_{\text{tO}_2} \) during subsequent infusions of cardioplegia; Obs 1, 2, 3: the lowest \( p_{\text{tO}_2} \) values after the first, second, and third cardioplegic administration; 1—16 h: hours after the end of perfusion; 2—4: post-operative days; \( p_{\text{tO}_2} \): addition of 7 L of \( p_{\text{tO}_2} \) to the respiratory air. Statistical significant difference with the previous value; (\( * \)) statistical significant difference between the two groups; values are given as mean \( \pm SE \).
All operations in both groups were uneventful and none of the patients developed signs of myocardial ischemia during the peri- and post-operative period.

There was no statistical difference in the $p_{tiO_2}$ level between the groups during the initial point of observation (pre-perfusion, Fig. 1). After aorta cross-clamping and infusion of the cardioplegic solution, the $p_{tiO_2}$ dropped rapidly from $15.1 \pm 8.5 \text{ mmHg}$ to $1.3 \pm 1.6 \text{ mmHg}$ ($P < 0.0001$) in the BC group, and from $14.7 \pm 7.1 \text{ mmHg}$ to $0.1 \pm 0.4 \text{ mmHg}$ ($P < 0.0001$) in the CC group. The lowest $p_{tiO_2}$ value in the BC group was significantly higher than in the CC group: $1.3 \pm 1.6 \text{ mmHg}$ versus $0.1 \pm 0.4 \text{ mmHg}$ ($P < 0.05$). However, we found no difference in the duration of the low level of $p_{tiO_2}$ between the two groups.

Through the subsequent infusions of cardioplegia, there were transient increases in the $p_{tiO_2}$ in both BC and CC groups from $1.3 \pm 1.6 \text{ mmHg}$ to $3.3 \pm 2.6 \text{ mmHg}$ ($P < 0.05$) and from $0.1 \pm 0.4 \text{ mmHg}$ to $1.7 \pm 1.5 \text{ mmHg}$ ($P < 0.05$), respectively, and during the third infusion from $0.8 \pm 1.4 \text{ mmHg}$ to $3.3 \pm 3.5 \text{ mmHg}$ ($P < 0.05$) and from $0.2 \pm 0.7 \text{ mmHg}$ to $0.8 \pm 0.5 \text{ mmHg}$ (NS), respectively. Comparing the two groups with regard to these increases, the differences observed were not significant, even though the maximum $p_{tiO_2}$ increase during the second and third infusion were 2 and 2.5 mmHg, respectively, in the BC group and only 1.6 and 0.6 mmHg, respectively, in the CC group. Furthermore, we found no significant differences in the time span of the transient increases in the $p_{tiO_2}$ between the two groups.

After aorta declamping, $p_{tiO_2}$ increased comparably in both groups towards a stable level at the end of the operation: BC group to $31.9 \pm 10.2 \text{ mmHg}$ and CC group to $32.6 \pm 12.3 \text{ mmHg}$ (NS).

During the subsequent daily measurements, the $p_{tiO_2}$ increased in both groups: from $36.7 \pm 7.9 \text{ mmHg}$ to $41.0 \pm 7.5 \text{ mmHg}$ (NS), respectively, and from $37.2 \pm 7.3 \text{ mmHg}$ to $41.7 \pm 9.2 \text{ mmHg}$ (NS), respectively.

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Clinical and operative details</th>
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<tr>
<td></td>
<td>CC$^a$ ($n = 15$)</td>
</tr>
<tr>
<td>Mean</td>
<td>Range</td>
</tr>
<tr>
<td>Age (years)</td>
<td>66.2 ± 9.5</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>12/3</td>
</tr>
<tr>
<td>Pre-operative ejection fraction (%)</td>
<td>53 ± 10</td>
</tr>
<tr>
<td>Perfusion time (min)</td>
<td>77 ± 16</td>
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<tr>
<td>Aortic cross-clamp time (min)</td>
<td>43.4 ± 16.1</td>
</tr>
<tr>
<td>Cardioplegia volume (mL)</td>
<td>1186 ± 238</td>
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$^a$ CC: crystalloid cardioplegia.
$^b$ BC: blood cardioplegia.
$^c$ NS: non-significant.
44.9 ± 11.6 mmHg (P < 0.05) in the BC group and from 31.9 ± 11.7 mmHg to 43.8 ± 8.9 mmHg (P < 0.05) in the CC group. From the first to the last point of observation, the pTiO2 increased over 200% in both groups (Fig. 1). Addition of 7 L of nasal oxygen to the respiratory air increased the pTiO2 on average 17.5% in both groups.

During the post-operative period, changes in pTiO2 and SAT followed closely: r = 0.94 (P < 0.05) (Fig. 1), while a negative correlation was found between pTiO2 and pO2: r = −0.94 (P < 0.05). Correlations between pTiO2 and hemodynamic parameters were not significant. Hematocrit remained stable throughout the study (Fig. 2). Creatine kinase washout was similar in both groups (Fig. 3).

4. Discussion

The main purpose of this study was to determine whether the addition of blood to a cardioplegic solution has any effect on myocardial pTiO2 during surgical revascularization compared to crystalloid cardioplegia. Using polarography, the study demonstrated that the pre-operative oxygenation was significantly lower than after surgery for both groups, but more importantly that changes in peri-operative oxygen tensions in the two groups followed closely (Fig. 1). During cardiac arrest pTiO2 was close to zero, never exceeded 5 mmHg and only minimal differences in oxygen tensions were observed between the two groups. The initial infusion of cardioplegia was the only observation point with a significant higher oxygen tension value in the BC group. However, this was without any importance to the immediate post-operative oxygen tension values or biochemical or clinical outcomes. This result was obtained despite the fact that patients in the BC group received oxygenated blood in a cardioplegic solution added in proportion 1:4, which intuitively should result in a higher pTiO2 during cardiac arrest compared to those treated with non-oxygenated crystalloid. However, cold blood cardioplegia in the mentioned proportion might be an insufficient dose to increase pTiO2 in the tissue. Furthermore, oxygen demand in the ischemic tissue can be so high that the delivery of oxygen with the blood cardioplegia is insufficient to increase tissue oxygenation (unbounded O2).

The most important result of this study indicates that regardless of the type of cardioplegia, pTiO2 in the myocardium throughout cardiac arrest remains close to zero and that blood in a cardioplegic solution has no practical value with regard to physically dissolved oxygen. This conclusion correlates with the results of Buttner et al. [12] who showed an almost identical paraclinical, clinical, and biochemical outcomes after surgery with blood and crystalloid cardioplegia. Thus, the beneficial effect of blood cardioplegia compared to crystalloid cardioplegia observed by others [3–11] must be due to other features than the oxygen carrying capacity of blood. It can be blood buffering capacity [18], antioxidant activity [19], oncotic pressure [20], capillary flow distribution [21], and its metabolic substrate [22]. But actually, the beneficial effects of blood cardioplegia can be questioned. Myocardial ischemia and reperfusion induced by cardioplegic arrest subjects the heart to free radical-mediated stress [23]. Furthermore, addition of blood to the cardioplegic solution increases its viscosity and creates the potential for sludging of cells and platelet aggregation in the microcirculation [15]. Endogenously released catecholamines present in the solution may increase basal myocardial metabolism and promote calcium entry into the cell, diminishing the beneficial effects of cardioplegia [24]. Uptake of potassium by the red cell can potentially reduce the extracellular potassium below cardioplegic levels and cause premature return of electrochemical activity [22]. The latter was evident in the present study as the BC group required 22% more of cardioplegic solution. Fortunately, all these theoretical circumstances have only limited clinical impact as morbidity and mortality in both groups were comparable. Thus, crystalloid and blood cardioplegia seems to offer identical protection with regard to low-risk patients [16] with normal left ventricular functions and short aortic cross-clamp times. Blood cardioplegia has demonstrated its greatest benefit in patients with depressed left ventricular function and extended cross-clamp times [10,11,14].

Yet another important finding of this study was an increase in average post-operative myocardial pTiO2 by 17.5% after the addition of O2 to the respiratory air (Fig. 1). This indicates the importance of oxygen supplement not only in the post-operative period but also in the pre-operative period in patients with angina resistant to vasodilators and awaiting invasive treatment. In this regard, one can wonder why patients have no symptoms or clinical signs of ischemia even though the pre-operative pTiO2 is less than half of the post-operative value. However, we do not know how low the pTiO2 has to be to induce symptoms or clinical signs of ischemia.

In this study, the LICOX CMP polarographic device has been used to determine the myocardial pTiO2. One of the disadvantages of this technique is its dependence on temperature. The temperature drift of the pO2 sensitivity of the sensor is approximately 4% according to the manufacturer [25], however, the zero signal does not depend on the temperature. As a consequence, the temperature-induced error is minimized during cardioplegic arrest.

A difficulty encountered directly after the implantation of the microprobe was unstable levels of pTiO2 lasting from 5 to 20 min. A possible explanation is local bleeding resulting from implantation of the microprobe into the tissue. Fortunately, at this stage of the operation, coagulation processes are not compromised by heparin, and the bleeding lasted only a few minutes and the pTiO2 subsequently reached a stable level before extracorporeal circulation was initiated.

In summary, the present study shows that during cardiac arrest myocardial pTiO2 is reduced to near zero values, and post-operatively pTiO2 increases correspondingly in both groups. Furthermore, biochemical and clinical outcomes are similar for operations employing blood and crystalloid cardioplegia. Addition of O2 to the respiratory air during the post-operative period increases myocardial oxygenation. Finally, the study demonstrates a minor disadvantage of blood cardioplegia, which had to be administered in a higher volume in order to sustain cardiac arrest.

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References


