Does poor oxygenation during one-lung ventilation impair aerobic myocardial metabolism in patients with symptomatic coronary artery disease?

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Abstract

One-lung ventilation is used during a variety of surgical procedures, even in patients with pre-existing coronary artery disease. The study purpose was to elucidate if myocardial metabolism crosses the anaerobic threshold under hypoxemia during one-lung ventilation. Therefore, we determined myocardial metabolism as a marker for anaerobic myocardial metabolism in patients with significant multi-vessel coronary artery disease undergoing one-lung ventilation during minimally-invasive coronary artery bypass grafting. Twenty patients with multi-vessel coronary artery disease underwent minimally-invasive revascularisation on cardiopulmonary bypass. One-lung ventilation was used for at least 45 min prior to cardiopulmonary bypass. Blood samples were drawn from arterial and coronary sinus blood at various times throughout the procedure to determine myocardial metabolism. After institution of one-lung ventilation arterial partial pressure of oxygen decreased significantly, down to levels between 50 and 70 mmHg. During one-lung ventilation, pH and lactate levels in both arterial and coronary sinus blood remained constant. Significant changes of pH and lactate levels were observed only after cardiopulmonary bypass. No clinically significant signs of myocardial ischemia occurred in any patient. Aerobic myocardial metabolism was unaffected during one-lung ventilation in all patients. Therefore, one-lung ventilation can be applied to patients with multi-vessel coronary artery disease with an acceptable risk of turning myocardial metabolism to an anaerobic state.

Keywords: One-lung ventilation; Minimally-invasive surgery; Myocardial ischemia

1. Introduction

One-lung ventilation (OLV) is widely used to allow for adequate surgical exposure during a variety of surgical procedures, e.g. thoracic spine surgery, oesophageal surgery, and procedures on the heart and lungs. Despite physiological mechanisms to compensate the mismatch of ventilation and perfusion in the non-ventilated lung, a significant decrease of both, arterial oxygen tension (PaO\textsubscript{2}) and oxygen saturation (SaO\textsubscript{2}) is almost ever observed during OLV. Neither the extent of decrease, nor the particular patient in whom PaO\textsubscript{2} and SaO\textsubscript{2} will drop to potentially harmful levels can be predicted. Patients with clinically significant or previously unknown coronary artery disease may be exposed to the risk of impaired myocardial oxygen supply during prolonged periods of hypoxemia. This study sought to determine whether critically low levels of oxygenation during OLV will affect aerobic myocardial metabolism in patients with severe multi-vessel coronary artery disease.

2. Material and methods

After approval by the institutional review board and obtaining informed written consent, a total of 20 adults with symptomatic two-vessel coronary artery disease and stable angina pectoris (Canadian Cardiovascular Society Class II), who underwent coronary artery bypass grafting through a small lateral thoracotomy, were studied.

2.1. Cannulation and monitoring

In any patient, the Port Access system (Heartport, Redwood, CA), that is described elsewhere in detail [1] was used for cardiopulmonary bypass. Continuous invasive arterial blood pressure monitoring was performed via both right and left radial arteries. After induction of anaesthesia, both, a 9 F triple-lumen coronary sinus catheter (Endosinus Catheter, Heartport), advanced into the coronary sinus for
application of retrograde cardioplegia, and an 8.3 F single lumen pulmonary vent catheter (Endopulmonary Vent, Heartport) advanced into the pulmonary trunk for decongestion of the pulmonary arteries during cardiopulmonary bypass, were introduced into the internal jugular vein.

Cardiopulmonary bypass was achieved by cannulation of the femoral vessels with a venous drainage cannula advanced into the superior vena cava, and an intraaortic occlusion catheter with a separate lumen to administer antegrade cardioplegia (Endoaortic Clamp, Heartport). The intraaortic occlusion clamp catheter was positioned 2–3 cm distal from the aortic valve. Both placement and positioning of all catheters was accomplished by transoesophageal echocardiography (TEE).

Intraoperative monitoring consisted of direct arterial blood pressure monitoring in both radial arteries, central venous pressure, pulse oximetry, and 5-lead ECG with continuous, automated ST-segment analysis in leads I, II, and V5. TEE was primarily used for positioning of the Port Access cannulas and to continuously monitor the endoaortic balloon. However, at any time during SLV when significant ST-segment alterations were observed, both ventricles were examined for eventual regional wall motion abnormalities. A transgastric mid-short axis view at the level of the midpapillary muscles was chosen.

2.2. Anaesthesia and patient positioning

All patients received intramuscular premedication with 0.06 mg Fentanyl and 3 mg Droperidol one hour prior to the induction of anaesthesia. After induction of anaesthesia with sufentanil (25 μg), etomidate (0.2 mg/kg) and succinylcholine (1 mg/kg), the patients had their tracheas intubated with a left endobronchial 37–41 F double-lumen tube (Kendall, Neustadt, Germany). Correct position of the tube was verified by both, auscultation and fiberoptic bronchoscopy. Intraoperatively, patients were in supine position with the left chest slightly elevated.

Anaesthesia was maintained with an endtidal concentration of 1.1–1.4 vol.% enflurane with oxygen 50% in air. Five patients who complained about unstable angina were initially ventilated with 100% oxygen. The respiratory rate was set to 10 breaths per minute, and tidal volume was set to 8–10 ml/kg and adjusted by means of repeated arterial blood gas analyses to maintain arterial partial pressure of carbon dioxide and pH within the normal ranges of 32–45 mmHg and 7.34–7.47, respectively. During the entire procedure, 25 μg of sufentanil were administrated for analgesia whenever deemed necessary.

Immediately before skin incision, the endobronchial lumen of the double-lumen tube was occluded to allow selective ventilation of the right lung. Respiratory rate, tidal volume and inspired oxygen concentration were maintained unless the arterial oxygen saturation as measured by pulse oximetry dropped below 92%, or if arterial blood gas analysis demonstrated an arterial partial pressure of oxygen <100 mmHg. Similar to double-lung ventilation, respiratory rates and tidal volumes were adjusted to maintain pH as described and arterial carbon dioxide tension at approximately 40 mmHg. One-lung ventilation was terminated when 100% CPB was achieved.

Preparation of the left internal thoracic artery and its subsequent grafting onto the left anterior descending artery, as well as additional saphenous vein bypass grafts, were performed through a 7–8 cm left anterolateral thoracotomy in the 3rd or 4th intercostal spaces.

2.3. Measurements

To evaluate oxygenation, pH and serum lactate levels, arterial blood gas analyses were performed immediately before incision under double-lung ventilation as a baseline value (Baseline), and 15, 30 and 45 min after institution of OLV (OLV + 15 min, OLV + 30 min, OLV + 45 min). A further analysis was performed after weaning from CPB and return to double-lung ventilation (End). At the same time points, blood samples were obtained from the coronary sinus and analysed for pH and lactate content. Automated ST-segment analysis at J+60 ms for leads I, II and V5 were recorded continuously (Hellige Marquette Solar 8000 Patient Monitor, Marquette Medical Systems, Milwaukee, WI). An ST-segment alteration of ≥1 mm (0.1 mV) from baseline that persisted for more than 60 s was considered significant. In every instance, the samples were immediately analysed in a point of care laboratory (ABL3, Acid Base Laboratory/Hemoxymeter, Radiometer, Copenhagen, Denmark).

2.4. Statistical analysis

All data are presented as mean ± S.D. or median and range when appropriate. Calculation and data analysis were performed using a statistical package (GraphPad InStat 3.0, GraphPad Software, San Diego, CA). Statistical significance was determined with either Wilcoxon matched pairs test or Friedman analysis with Dunn’s α-adjustment. Differences were considered to be statistically significant if P < 0.05.

3. Results

Twenty patients (14 males, 6 females, mean age: 63.3 ± 9.6 years) with symptomatic coronary artery disease underwent myocardial revascularisation with the Port Access system. On the median, patients received three grafts. Preoperative left ventricular ejection fraction was 68.0 ± 4.6%. In all but one patient the preoperative pulmonary function testing was not suggestive of coexisting pulmonary disease, nor was the preoperative chest X-ray examination. Preoperative FVC was 4.1 l ± 0.8, preoperative FEV1 was 2.8 l ± 0.7.

All laboratory findings were also within normal limits. Four patients had a history of myocardial infarction, however, no regional wall motion abnormalities were detected during both routine preoperative transthoracic echocardiography and fluoroscopy.

3.1. Respiratory data

Time required for one-lung ventilation ranged from 49 to 184 min (mean: 77 ± 30 min). After initiation of one-lung ventilation, arterial partial pressure of oxygen decreased significantly and remained virtually constant during the period of one-lung ventilation. Despite administration of
100% of oxygen, a PEEP level of 10 cm H\(_2\)O and CPAP applied to the non-ventilated lung, a PaO\(_2\) < 100 mmHg was noted in 12 patients at least once during the course of one-lung ventilation. Once double-lung ventilation was restarted, any patient’s PaO\(_2\) improved to more than 100 mmHg, and on the average, did not differ significantly from baseline (Fig. 1). Arterial oxygen saturation declined during OLV, but returned to baseline when DLV was reestablished. The hemoglobin content remained stable during OLV; and the decrease observed at the end of the operation was due to hemodilution on CPB (Table 1).

### 3.2. Myocardial metabolism

During the course of the study, arterial pH decreased significantly after 45 min of one-lung ventilation, but remained within the physiologic range. A significantly lower pH was noted after CPB. The serum lactate levels remained constant during one-lung ventilation and increased significantly after weaning from CPB. Both coronary sinus blood pH and lactate concentrations were not affected by one-lung ventilation, but similar to arterial pH and lactate levels, decreased and increased significantly after CPB. With the exception of 45 min after initiation of one-lung ventilation, arterial pH was always significantly higher as compared to coronary sinus pH. This difference was most clearly observed after release of the aortic crossclamp and cardiac reperfusion. Lactate levels were similar in both arterial and coronary sinus blood (Table 1).

No patient required plasma volume expanders or vasopressor or inotropic support because of haemodynamic instability. Episodes of ST-segment alteration of ±1 mV from baseline were observed in leads I (n = 7), II (n = 3) and V5 (n = 16), appeared randomly at least once during OLV, and were not combined with haemodynamic disturbances. ST-segment alterations returned to baseline at the end of surgery. Performing a TEE examination whenever significant ST-segment alteration occurred, no regional wall motion abnormalities of both ventricles were detected using a short axis transgastric view.

### 4. Discussion

Minimally-invasive and endoscopic techniques have added new options to less traumatic treatment of a variety of diseases in many surgical disciplines. However, most of these techniques require one-lung ventilation for sufficient exposure of the thoracic anatomy. Many previous studies have demonstrated that OLV may be associated with a severe decrease in oxygenation or even frank hypoxia [2–6]. To date, there are no studies evaluating the effects of OLV on oxygenation and myocardial metabolism, being a sensitive marker of global mismatch of myocardial oxygen supply and demand, in patients with severe, multi-vessel coronary artery disease.

We could demonstrate that during OLV oxygenation worsens significantly. Maintenance of arterial partial pressure of oxygen above 100 mmHg was no longer possible in the majority of our patients once OLV was started. Despite ventilation with 100% of oxygen and adding PEEP or CPAP to the dependent and non-dependent lungs, respectively, arterial partial pressure of oxygen declined to 70 or less in four patients. In patients with severe coronary artery disease, these low oxygen levels appear as a cause of concern.

Regardless of the fact that oxygenation was not satisfactory, no patient developed haemodynamic instability that required inotropic or vasopressor support. This held true even in four patients whose arterial oxygen saturation was only around 70–90%. No previously unknown myocardial wall motion abnormalities were detected by TEE in any patient. In this context it is important to state that TEE was primarily used for positioning and reassessment of the port-access cannulas [7]. Because the required planes and views are different to those required for systematical assessment of ventricular function according to acknowledged guidelines [8], the transgastric short axis view was used exclusively.

### Table 1

<table>
<thead>
<tr>
<th>Metabolic variables in arterial and coronary sinus blood</th>
<th>Baseline</th>
<th>OLV + 15 min</th>
<th>OLV + 30 min</th>
<th>OLV + 45 min</th>
<th>End</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin content (g/dl)</td>
<td>12.7 ± 1.3</td>
<td>12.4 ± 1.3</td>
<td>12.3 ± 1.4</td>
<td>12.2 ± 1.4*</td>
<td>9.3 ± 0.7*</td>
</tr>
<tr>
<td>SaO(_2) (%)</td>
<td>98.9 ± 0.4</td>
<td>93.6 ± 6.7*</td>
<td>94.1 ± 6.8*</td>
<td>94.1 ± 6.7*</td>
<td>98.6 ± 1.0</td>
</tr>
<tr>
<td>Arterial lactate (mg/dl)</td>
<td>7.2 ± 1.1</td>
<td>7.4 ± 1.3</td>
<td>7.3 ± 1.2</td>
<td>7.7 ± 1.4</td>
<td>24.1 ± 2.4*</td>
</tr>
<tr>
<td>Coronary sinus lactate (mg/dl)</td>
<td>7.6 ± 1.2</td>
<td>7.9 ± 1.3</td>
<td>7.7 ± 1.3</td>
<td>8.0 ± 1.1</td>
<td>24.8 ± 2.6*</td>
</tr>
<tr>
<td>Arterial pH</td>
<td>7.401 ± 0.003*</td>
<td>7.401 ± 0.052*</td>
<td>7.384 ± 0.050*</td>
<td>7.352 ± 0.059*</td>
<td>7.348 ± 0.049*</td>
</tr>
<tr>
<td>Coronary sinus pH</td>
<td>7.343 ± 0.048</td>
<td>7.355 ± 0.020</td>
<td>7.348 ± 0.038</td>
<td>7.354 ± 0.023</td>
<td>7.257 ± 0.034*</td>
</tr>
</tbody>
</table>

*: P < 0.05 vs. Baseline; #: P < 0.05 vs. coronary sinus pH.
Intermittent ST-segment alterations occurred irregularly and independent of OLV time or surgical manipulation. They normalised completely at the end of the operation. As shown elsewhere, similar to haemodynamic changes, these ST segment changes rarely correlate with intraoperative segmental wall motion abnormalities detected with TEE [9,10] and, thus, do not reflect myocardial ischemia. Arterial lactate levels remained stable, and the drop of arterial pH after 45 min of OLV was not of clinical relevance. In coronary sinus blood, pH was constant during OLV, as were the lactate levels.

Under aerobic conditions, free fatty acids (50–60%), glucose (30%), and lactate (20%) are the substrates that are predominantly metabolised by cardiomyocytes. If myocardial oxygen demand exceeds oxygen supply – which in some patients with poor arterial partial pressure of oxygen may seem likely – anaerobic metabolism is used to provide energy equivalents, i.e. ATP. As a result, glucose is increasingly metabolised via the pathway of anaerobic glycolysis. Lactate levels, therefore, increase, and since lactate cannot be metabolised under anaerobic conditions, it is released with coronary sinus blood. H⁺-ions generated during lactate production, cause intracellular acidosis and a drop of coronary sinus pH [11]. Interestingly, no such changes occurred in our patient group. After weaning from CPB we noted significantly increased lactate levels in both arterial and coronary sinus blood, but the extent of increase was similar. In contrast, the coronary sinus pH drop to 7.26 ± 0.03 was statistically significant when compared to the extent of arterial pH decrease after CPB (7.35 ± 0.05). These findings in coronary sinus blood suggest insufficient supply of oxygen and energy substrates for aerobic myocardial metabolism during cardiac arrest. In contrast to other investigators, who demonstrated that warm continuous blood cardioplegia provides sufficient oxygen and substrates to maintain aerobic metabolism [12,13], we used cold intermittent blood cardioplegia, which may explain these results to some extent. The increased lactate levels in both, arterial and coronary sinus blood, result most likely from generalised capillary hyperfusion during CPB.

Several study limitations have to be discussed. First of all, the patient number is rather limited and it cannot be excluded that other statistical significant results would have been reported by investigating a larger population. On the other hand, only small patient numbers have been operated worldwide using this technique. For this reason it is nearly impossible to design a prospective randomised study including a larger patient population. For the same reason, we are not able to provide a safety margin of tolerable minimal PaO₂-values above the anaerobic threshold of the myocardial metabolism. A control group operated via conventional sternotomy and not undergoing OLV would have been desirable. However, as there is no medical reason to insert a transjugular coronary sinus catheter as a routine in coronary patients without aortic valve insufficiency and normal biventricular function, such intervention would rise serious ethical concerns.

Myocardial ischemia was assessed by five-lead ECG automated ST-segment analysis and continuous TEE using a short axis transgastric cross-section. Automated ST-segment analysis is known to have low sensitivity together with a high specificity and positive predictive value for myocardial ischemia [14]. In contrast, TEE is reported to be twofold more predictive for myocardial ischemia than automated ST-segment analysis [15]. In our population, no significant segmental wall motion abnormalities were seen throughout the procedure. We do not report a detailed wall motion analysis because, however, the study purpose was the evaluation of myocardial metabolism and not the eventual development of wall motion abnormalities during this type of procedure.

In summary, we could demonstrate that OLV in patients with symptomatic multi-vessel coronary artery disease was associated with a significant decrease in oxygenation. Even in patients whose oxygenation was poor, neither myocardial metabolism, nor TEE was significant for global and segmental ischemia. Based on these data, a 45-min period of OLV does expose patients with symptomatic multi-vessel coronary artery disease to a clinically acceptable risk of impaired intraoperative myocardial oxygen supply. However, because of the limited sample size, individual reactions towards an anaerobic myocardial metabolism cannot be excluded.

References


ICVTS on-line discussion A

Title: Further testing is warranted to detect more subtle degrees...  
Author: Narcis Hudorovic, University Hospital Sestre Milosrdnice, Zagreb 10000, Croatia  
doi:10.1510/icvts.2006.129213A  
eComment: The authors stated that they are not able to provide a safety margin of tolerable minimal PaO2-values above the anaerobic threshold of the myocardial metabolism [1]. Not such a long time ago, we conducted a study of controlled cardiac reoxygenation, in a lethal ischemic swine model, utilizing normoxic bypass and normoxic cardioplegia solution which called into question the beneficial effects of controlled cardiac reoxygenation when employing normoxic conditions. In this study, we specifically combined a normoxic protocol for CPB without titration to hyperoxic levels and tested whether there was any value for controlled cardiac reoxygenation and limiting cardiac dysfunction. We were unable to show any significant advantage to controlled cardiac reoxygenation over normoxic cardioplegia resuscitation utilizing substrate-enhanced cardioplegia. Utilizing a resuscitative protocol, the value of controlling for reoxygenation during the cardioplegic resuscitation was compared in two groups of animals. Its effect on cardiac function following a lethal injury and whether it enabled recovery in acutely injured ventricles were measured utilizing the degree of myocite damage and peroxidative injury based on CK, CK-MB, nitric oxide and specifically conjugated diene levels in the coronary sinus blood. It was shown that even normoxic bypass, although attenuating the liberation of oxygen free radicals, does not prevent reperfusion injury in a hypoxic or ischemic setting when the FiO2 tension is further raised, either gradually or abruptly, to hyperoxic levels [2]. It remains to be proven whether or not there can be further benefit to cardiac resuscitation by gradual reoxygenation to hyperoxic levels while utilizing a normoxic CPB circuit. A major value to titrating the oxygen tension both in the CPB circuit and cardioplegia (to limit reoxygenation injury both on CPB and in myocardial resuscitation) is its clinical simplicity and applicability to both congenital surgery as well as adult cardiac surgery.

The subtle but real difference in conjugated dienes in the controlled reoxygenation brings to question whether further testing is warranted to detect more subtle degrees of improved cardiac preservation with a controlled reoxygenation protocol in the face of normoxic bypass under nonlethal surgical patterns. Further investigation could include comparing the effect of normoxic versus hypoxic CPB in a lethal ischemia model with and without controlled cardiac reoxygenation as it relates to reperfusion injury with determination of nitric oxide, conjugated diene analysis, creatinine kinase serum assays with measuring of subsequent formation of adenosine triphosphate in coronary sinus blood samples. I am hoping that the above mentioned statements could improve the determination of myocardial metabolism, and that we will be able to provide a safety margin of tolerable minimal PaO2-values above the anaerobic threshold.

References