# *Impact of haemodynamic alterations on arterial blood gases during off-pump coronary revascularization*

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## ABSTRACT

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Cardiac stabilization during "off-pump" coronary revascularization (OPCAB) has been implicated in causing intraoperative hemodynamic disturbances. Stroke volume and cardiac output reductions may alter the ventilation/perfusion ratio in the lungs and compromise the gas exchange. This study was conducted to determine the impact of heart's stabilization on arterial blood-gas profile in patients undergoing OPCAB surgery. After institutional approval and informed consent, 57 patients undergoing OPCAB procedures were studied. LIMA was anastomosed to LAD in all patients. In 20 patients a second coronary vessel received a graft, while in 5 patients a third vessel was also anastomosed under propofol-remifentanil (TIVA) anesthetic technique. $FiO_2$ was equal to 1. Compression fork-type stabilizer was used. Full hemodynamic profile, mixed venous oxygen saturation, acid base status, end-tidal partial pressure of carbon dioxide and ST-segment changes were monitored before heart's stabilization (T1 values-baseline), 5 minutes after stabilization (T2 values), before stabilizer's removal (T3 values) and 10 minutes after stabilizer's removal (T4 values). Oxygen delivery and consumption, VD/VT and Qs/Qt were calculated. Ventilation was kept unchanged during data collection. Statistical analysis for pairwise comparisons with baseline values (T1) was performed with Dunnett's two-sided multiple-comparison procedure. Statistical analysis was performed using the t-paired test. A value of $p<0.05$ was considered statistically significant. During LIMA→LAD grafting (n=57) cardiac stabilization and anastomotic maneuvering caused significant hemodynamic changes. Cardiac output, stroke volume and mixed venous oxygen saturation decreased significantly (4.44 ± 1.0 → 3.43 ± 0.8 L/min, 70.6 ± 15.5 → 52.6 ± 14.2 ml, 83.5 ± 4.7 → 76.5 ± 8.0 % respectively; $p<0.001$ for all) while systolic, diastolic and mean

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pulmonary pressure, central venous pressure and capillary wedge pressure increased significantly during stabilizer's application (T2, T3 values). Calculated $O_2$ delivery and consumption were decreased. PH, bicarbonate and base excess decreased significantly at all times compared to baseline (7.45 ± 0.03 → 7.43 ± 0.03, 23.9 ± 1.44 → 22.9 ± 1.98 mEq/L, 0.06 ± 1.6 → -0.98 ± 1.9 respectively; $p<0.001$ for all) while arterial partial pressure and end-tidal partial pressure of carbon dioxide decreased at T2, T3 interval and increased at T4. Arterial partial pressure of oxygen increased significantly after stabilizer's placement (T2, T3 interval) and decreased in stage T4. Qs/Qt was decreased during anastomotic maneuvering. IN OPCAB SURGERY, THE HEMODYNAMIC CHANGES DUE TO the heart's stabilization caused significant changes in the arterial blood gas profile. The reduction of systemic flow and tissue perfusion led to increased plasma hydrogen ion concentration. Restoration of flow was followed by "wash-out" phenomena. Arterial tension and exhalation of $CO_2$ were primarily influenced by the decreased $O_2$ consumption, the increased VD/VT and the buffering of protons after the stabilizer's removal. In this study population, the deterioration in gas exchange was minor. Although these changes are not persistent, they may have implications in the intraoperative management of patients with compromised alveolar gas-exchange.

The use of cardiopulmonary bypass (CPB) during coronary artery bypass grafting (CABG) represents a modality with multilevel invasiveness followed by immediate and long-term complications[1,2]. Avoidance of CPB in "off-pump" coronary revascularization (OP-CAB) is considered advantageous as neuro-physiologic disorders, stroke, renal and respiratory failure, nerve injury, whole-body inflammatory response and coagulation disorders are likely to be prevented or less severe [3,4,5,6]. Although criticism for complete revascularization with OPCAB exists, this technique is considered as an alternative that offers better early outcomes. Nevertheless, OPCAB is associated with intraoperative hemodynamic instability due to mobilization and stabilization of the heart or myocardial ischemia occurring during coronary occlusion [7]. Manipulation of the heart and reduced myocardial performance can lead to decreased systemic and pulmonary flow and pulmonary congestion[8]. A trans-esophageal echocardiography study showed that five minute coronary occlusion was associated with a significantly elevated pulmonary arterial pressure during minimally invasive coronary artery bypass surgery[9]. Reduced cardiac output and elevation of left atrial, pulmonary venous and pulmonary arterial pressures in patients receiving constant and unchanged mechanical ventilation is expected to alter the ventilation/perfusion ratio. Presently, the impact of heart's stabilization on the intraoperative arterial blood-gas profile in patients undergoing CABG procedures without CPB has not been rigorously examined.

Tissue oxygen availability is primarily determined by arterial oxygen content and local perfusion. Additionally, arterial carbon dioxide tension impacts on peripheral tissue perfusion and oxygenation by influencing systemic vascular resistance and flow and by shifting the oxyhemoglobin's curve and consequently acting on oxygen unloading[10,11,12]. Although hypercapnia is often associated with hypoventilation and decreased alveolar $O_2$ concentrations, it may cause a complex interaction between altered cardiac output, hypoxic pulmonary vasoconstriction and intrapulmonary shunt resulting an increased $PaO_2$ at a given inspired oxygen concentration[13]. Short periods of hypercapnia improved tissue oxygenation in anesthetized volunteers[14]. In patients scheduled for abdominal or orthopaedic surgery, subcutaneous tissue oxygen

tension and cerebral oxygen saturation were higher when end-tidal $CO_2$ was increased[15]. These reports demonstrate the importance of $PaCO_2$ value in oxygen tissue availability, especially when systemic flow and oxygen delivery are compromised. Furthermore, "tuning" the ventilator in mechanically breathing patients, even with an opened chest, aims not only to proper gas exchange but to improved oxygen delivery as well, as positive pressure respiration may interact with hemodynamics. Consequently, close monitoring of the blood gas profile and fine adjustment of the ventilator parameters are particularly important when a surgical technique affects the haemodynamic state of a patient. We therefore tested the hypothesis that the intraoperative haemodynamic disturbances alter the blood-gas status in patients undergoing "off-pump" CABG.

## PATIENTS AND METHODS

### Patient population

After obtaining institutional approval and informed consent, elective patients undergoing "off-pump" coronary revascularization were studied. Patients undergoing emergency or urgent operations were excluded from the study. Patients with severe restrictive or obstructive pulmonary disease were also excluded. All patients had selective coronary angiography before operation. Decision for surgical treatment of their coronary artery disease was made on the basis of conventional criteria. Ejection fraction was determined from the most recent among left ventriculography and transthoracic echocardiography. Final decision to proceed to OPCAB was made by the surgeon intraoperatively. Haemodynamically unstable patients, receiving inotropic or vasoactive drug infusions at the time of the completion of preparation of the left internal mammary artery (LIMA) graft were excluded, irrespectively of the chosen operative technique. The LIMA graft was directed to the left anterior descending (LAD) coronary branch and this anastomosis was performed first in all patients. In case of hemodynamic instability at any point of the procedure leading to conversion to conventional CABG, the patient was also excluded. The patient was placed to CPB when there was a value of MAP less than 50 mmHg, $S_VO_2$ less than 60%, a change in ST segment greater than 2.5 mV or a haemodynamically significant arrhythmia, and when these changes could not be corrected with pharmacologic treatment. The final study population included 57 patients, of which 32 (56.1%) had single-vessel disease, 20 (35.0%) had double-vessel disease and 5 (8.7%) had triple-vessel disease. Patient characteristics are

**Table 1.** Patient characteristics.

| **Characteristics** | **Patient's Group (n=57)** |
|---|---|
| Age (yr) | 61.9 ± 7.2 |
| Gender (m/f) | 39/18 |
| BW (kg) | 79.2 ± 9.5 |
| BSA ($m^2$) | 1.88 ± 0.15 |
| EF (%) | 52.6 ± 7.5 |
| NYHA (No of patients - I/II/III/IV) | 6/37/14/0 |
| History of myocardial infarction (No of patients - %) | 36 – 63.1% |
| History of hypertension (No of patients - %) | 29 – 50.8% |
| History of diabetes mellitus (No of patients - %) | 15 – 26.3% |
| History of COPD (No of patients - %) | 9 – 15.7% |

Values are expressed as mean ± SD, numbers or percentage.

BW: body weight, BSA: body surface area; EF: ejection fraction; NYHA: New York Heart Association, COPD: chronic obstructive pulmonary disease

summarized in table 1. Six patients (10.5%) were classified as New York Heart Association (NYHA) class I, 37 (64.9%) as class II and 14 (24.5%) as class III. In nine patients (15.7%) ejection fraction was less than 0.45 while no patient had ejection fraction less than 0.25.

**Anesthesia and operation**

Patients continued their medication until the morning of the operation. Preanaesthetic medication consisted of diazepam 10 mg, given orally one hour before admission to the operating room. After arrival, the patients were monitored (*Solar 8000®, Marquette Medical Systems, Milwaukee, USA*) and a bispectral index sensor was placed (*BIS/XP®, Aspect Medical Systems, USA*). A peripheral intravenous and a radial intraarterial catheter were introduced. Intraoperative electrocardioscopy consisted of a 5-leads, ST-segment analysis. The anesthetic induction was achieved with the slow administration of midazolam (1-3 mg) plus fentanyl (100-250 μg) plus etomidate (0.2 mg/kg) and neuromuscular blockade with pancuronium (0.12 mg/kg). After tracheal intubation, patients were mechanically ventilated (*Julian, Draeger, Berlin, Germany*). Mild hypocapnia was maintained ($PaCO_2$ 33-37 mmHg), on the basis of repeated arterial blood sampling. Inspiratory fraction of oxygen in air was between 0.5 and 1.0. For the maintenance of the hypnotic component of anesthesia, the patients received propofol infusion targeting a plasma concentration of 3 μg/ml facilitated by a pump (*Fresenius, Vial, Brezins, France*). Infusion rates were manually calculated to ensure a stable concentration in the next 30 minutes (time necessary for further anesthetic and surgical preparation). A continuous infusion of remifentanil (≈ 20μg/kg/h) was also administered as a means of providing analgesia. After induction and *via* right internal jugular vein, the insertion of a triple-lumen central venous catheter was followed by the placement of a pulmonary artery catheter (*Oximetry TD catheter, Edwards Lifesciences, Berlin, Germany*). Patient's urine temperature was monitored.

Operations were performed by the same surgical and anesthetic team. In all patients, off-pump coronary bypass operation was carried out by using a reusable compression-type stabilizer. After standard median sternotomy, LIMA was routinely dissected with cautery using the intrapleural technique. In all patients it was grafted onto LAD. In case of more than one-vessel disease, the other coronaries were grafted mainly with radial artery from the nondominant forearm or with vein grafts. Grafting was done with the coronary vessel shunted. After mobilization of the LIMA heparin 150 iu/Kg was administrated to the patient, in order to accomplish an activated clotting time greater than 250 seconds. At the end of the procedure, patients received titrated protamine according to the activated clotting time to reverse the anticoagulation effect of the circulating heparin. After the completion of the operation patients were transferred to the intensive care unit, under the same anesthetic regimen titrated to BIS.

**Data collection**

With the pericardium opened and before exposing the heart for stabilization, a full haemodynamic profile was obtained with the thermodilution method. Measurements were performed in triplicate, using cold water. Pulmonary artery occlusion pressure (PAOP) and central venous pressure (CVP) was measured with the patient shortly disconnected from the ventilator. The values of end-tidal $CO_2$, $SvO_2$ and ST-segment displacement (in mV) were also recorded. Next, 20 milliliters of blood were drawn for "washing" the flushing solution from the arterial line and commecially prepared syringes (*Drihep™ Bencton Dickinson Vacutainer Systems, London, U.K.*) were used for blood-gas sampling. Samples were analyzed in an ABL 720 (*Radiometer Copenhagen, Denmark*) analyzer, accepting that $P_{50(st)}$ equals 26.85 mmHg and respiratory quotient (RQ) is 0.86, in 37ºC, after identi-

fying arterial blood. This set of haemodynamic and blood-gas values were recorded as baseline values **(T1 values-baseline)**. After exposing the heart, placing the stabilizer to the target site and waiting 5 minutes for haemodynamic stabilization, a new set of data were collected as it is described above **(T2 values)**. These parameters were also obtained at the completion of the anastomosis and before the stabilizer's removal **(T3 values)**, and finally 10 minutes after the placement of the heart in its normal position **(T4 values)**. Ventilation was kept unchanged during data collection.

Inspiratory fraction of oxygen was 1 during this period of time in all patients. Blood samples were drawn before any blood transfusions. BIS and temperature values were recorded during sampling. The administration of cardio-vasoactive drugs was closely registered during any time of the study. Oxygen delivery and consumption, $V_D/V_T$ and $O_s/O_t$ were calculated using standard formulas.

**Statistical analysis**

**Table 2:** Hemodynamic, BIS and temperature values during the 57 anastomoses of the study.

| | T1 (baseline) | T2 | T3 | T4 | p values | | |
|---|---|---|---|---|---|---|---|
| | | | | | T1/T2 | T1/T3 | T1/T4 |
| **HR (beat/min)** | 63.2±10.7 | 66.2±11.0 | 66.0±10.5 | 65.5±10.3 | ns | ns | ns |
| **SAP (mmHg)** | 104.7±10.9 | 95.0±12.2 | 91.2±11.6 | 104.6±11.0 | <0.01 | <0.001 | ns |
| **DAP (mmHg)** | 62.4±8.2 | 61.4±7.1 | 59.8±6.2 | 64.7±7.9 | ns | <0.01 | <0.05 |
| **MAP (mmHg)** | 77.9±8.4 | 73.6±8.4 | 70.8±7.3 | 78.9±8.6 | <0.001 | <0.001 | ns |
| **SPAP (mmHg)** | 28.4±5.0 | 30.8±5.1 | 30.4±5.4 | 28.6±5.4 | <0.001 | <0.001 | ns |
| **DPAP (mmHg)** | 18.3±3.2 | 20.9±3.3 | 20.8±3.5 | 18.7±3.4 | <0.001 | <0.001 | ns |
| **MPAP(mmHg)** | 22.4±3.6 | 25.2±3.4 | 24.8±3.9 | 22.6±3.8 | <0.001 | <0.001 | ns |
| **PAWP(mmHg)** | 15.4±2.7 | 18.3±3.1 | 18.5±3.5 | 15.5±3.0 | <0.001 | <0.001 | ns |
| **CVP (mmHg)** | 13.0±2.4 | 15.4±2.4 | 15.4±2.4 | 13.3±2.5 | <0.001 | <0.001 | ns |
| **CO (L/min)** | 4.44±1.00 | 3.62±0.76 | 3.43±0.79 | 4.22±0.78 | <0.001 | <0.001 | ns |
| **SV (ml)** | 70.5±15.5 | 55.6±14.9 | 52.6±14.2 | 65.2±14.0 | <0.001 | <0.001 | <0.01 |
| **$SVO_2$ (%)** | 83.5±4.7 | 78.0±8.4 | 76.5±8.0 | 81.8±5.2 | <0.001 | <0.001 | <0.05 |
| **SVR** (dynes.sec.cm$^{-5}$) | 1227±255 | 1383±319 | 1399±278 | 1296±295 | <0.001 | <0.001 | <0.05 |
| **PVR** (dynes.sec.cm$^{-5}$) | 131.1±38.7 | 167.3±66.8 | 160.1±72.1 | 139.9±40.1 | <0.001 | <0.001 | ns |
| **ST-segment (mV)** | 0.00±0.4 | 0.14±0.6 | 0.22±0.5 | 0.14±0.4 | ns | <0.001 | <0.05 |
| **BIS value** | 34.91±4.65 | 34.28±4.40 | 33.82±3.68 | 33.95±4.13 | <0.05 | <0.01 | <0.05 |
| **Temperature (ºC)** | 34.53±0.48 | 34.51±0.49 | 34.47±0.47 | 34.43±0.47 | <0.05 | <0.001 | <0.001 |

Values are expressed as mean ± SD.

HR for heart rate, AP for arterial pressure, PAP for pulmonary artery pressure (S, D, M for systolic, diastolic and mean respectively), CO for cardiac output, SV for stroke volume, PAWP for pulmonary artery wedge pressure, $SvO_2$ for mixed venous oxygen saturation, SVR for systemic vascular resistance, PVR for pulmonary vascular resistance.

Continuous data were expressed as mean ± standard deviation and categorical data as absolute and relative frequencies. Normality of continuous data was tested with the Kolmogorof–Smirnof test. Analysis for planed pair wise comparisons with baseline values (T1) employed Dunnett's two-sided multiple-comparison procedure. Differences observed for cardiac output, mean arterial pressure and pH were considered for sample size with repeated measures ANOVA achieving more than 80% power with a significance level of 0.05. Power and statistical analyses were performed with the NCSS 2004 (*Number Cruncher Statistical Systems, Kaysville, Utah, USA*). A value of $p<0.05$ was considered statistically significant.

cally unimportant, there was a statistically significant decrease of BIS values from 34.9± 4.7 to 34.0±4.1 during sampling (**T1-baseline** compared to **T4**; $p<0.05$). At the same time, temperature also decreased from 34.5±0.5 to 34.4±0.5 (**T1-baseline** compared to **T4**; $p<0.001$). In all 57 patients, LIMA was anastomosed to LAD in 31.4 ± 9.2 min, time from heart's new position, exposure and stabilization to securing the anastomosed graft on the epicardium. Hemodynamic data obtained during the observation period are shown in table 2. Systolic, diastolic and mean pulmonary pressure, central venous pressure, capillary wedge pressure and systemic and pulmonary vascular resistance were significantly increased (**T1 values-baseline** compared to the most abnormal among **T2** & **T3 values**; $p<0.001$). Systolic, diastolic and mean arterial pressure, cardiac output, stroke volume, mixed venous oxygen saturation and left and right stroke work index decreased signi-

**Table 3:** Findings from blood-gas analysis, $PetCO_2$ and secondary variables during the 57 anastomoses of the study.

| | T1 (baseline) | T2 | T3 | T4 | p values | | |
|---|---|---|---|---|---|---|---|
| | | | | | T1/T2 | T1/T3 | T1/T4 |
| **$PaO_2$** | 397.3±108.3 | 423.5±106.7 | 435.2±100.3 | 382.7±120.3 | <0.001 | <0.001 | ns |
| **$PaCO_2$** | 34.35±3.48 | 33.47±3.47 | 32.96±3.38 | 34.96±3.55 | <0.001 | <0.001 | <0.01 |
| **pH** | 7.452±0.036 | 7.444±0.032 | 7.440±0.033 | 7.433±0.035 | <0.001 | <0.001 | <0.001 |
| **$HCO_3$** | 23.90±1.44 | 23.17±1.66 | 23.05±1.68 | 22.90±1.98 | <0.001 | <0.001 | <0.001 |
| **BE** | 0.06±1.61 | -0.57±1.68 | -0.73±1.69 | -0.98±1.97 | <0.001 | <0.001 | <0.001 |
| **Hb** | 11.58±1.09 | 11.37±1.05 | 11.18±1.14 | 10.90±1.26 | <0.001 | <0.001 | <0.001 |
| **$PetCO_2$** | 25.77±3.18 | 24.68±3.04 | 24.23±2.93 | 25.35±3.04 | <0.001 | <0.001 | ns |
| **VD/VT** | 0.248±0.07 | 0.259±0.8 | 0.261±0.8 | 0.272±0.7 | ns | ns | <0.01 |
| **$VO_2$** | 170.0±50.7 | 168.5±43.9 | 166.8±42.9 | 164.5±41.5 | ns | ns | ns |
| **Qs/Qt** | 0.176±0.07 | 0.138±0.06 | 0.126±0.06 | 0.180±0.07 | <0.001 | <0.001 | ns |

Values are expressed as mean ± SD

$PaO_2$: arterial partial pressure of oxygen (mmHg), $PaCO_2$: arterial partial pressure of carbon dioxide (mmHg), $HCO_3$: bicarbonate concentration (mEq/L), BE: base excess (mEq/L), Hb: hemoglobin concentration (g/dL), $PetCO_2$: end-tidal partial pressure of carbon dioxide (mmHg), $VO_2$: oxygen consumption (ml/min), Qs / Qt as in the text.

## RESULTS

Anesthesia and operation time were 276±54 and 230±53 min respectively. Although clini-

ficantly ($p<0.001$; **T1 values-baseline** compared to the "worst" among **T2 & T3 values**). These changes tended to return to baseline after the stabilizer was removed, showing no statistical difference, except from diastolic arterial pressure, systemic vascular resistance, stroke volume and $SvO_2$ that continued different compared to baseline values (**T1 values-baseline** compared to **T4 values**). During observation, ST- segment was raised from 0.0 to 0.2 (**T1 values-baseline** compared to **T3 values**; $p<0.001$) and returned towards baseline. Practically, only heart rate remained unchanged during anastomotic maneuvering.

Table 3 shows the acid-base and blood gas values during control and observation period for the 57 LIMA→LAD anastomoses of the study. The concentration of bicarbonates, base excess and pH were statistically decreased during the time of heart's positioning and stabilizing and continued towards lower values after the completion of anastomosis, reminding "wash-out" phenomena as this was related to improved haemodynamics (**T1 values-baseline** compared to **T4 values,** which, for these parameters, was the most abnormal; $p<0.001$). Arterial partial pressure of $CO_2$ was decreased during performance of the anastomosis (**T1 values-baseline** to **T3 values**; $p<0.001$) and increased when haemodynamics improved (**T3 values** to **T4 values**; $p<0.001$) even to higher values than baseline (**T1 values-baseline** to **T4 values**; $p<0.01$). This observation is consistent with the previously mentioned "wash-out" phenomena. Exhaled $CO_2$ was also statistically decreased during anastomotic maneuvering and returned to baseline when heart was let to pump freely. Among sampling, the ratio $PetCO_2/PaCO_2$ reached the lowest value in the **T4 values**. Although arterial partial pressure of $O_2$ was increased during anastomotic maneu-vering, oxygen delivery was statistically de-creased (**T1 values-baseline** to **T3 values**; $p<0.001$) due to decreased cardiac output and the progressively lowered haemoglobin's con-centration. Completion of anastomosis and improved haemodynamics were followed by a better oxygen delivery which was still statistically less than baseline (**T1 values-baseline** to **T4 values**; $p<0.01$). The haemato-crit and the haemoglobin concentration were progressively decreased during the observation (**T1 values-baseline** to **T4 values**; $p<0.001$), while changes in the serum concentrations of sodium, potassium, calcium, lactate and glucose were insignificant.

A second coronary vessel was grafted in 20 patients while in 5 patients a third vessel was also anastomosed. In these 25 cases, RIMA was used 4 times, radial artery was used 12 times and vein grafts were used in the remaining. Mean surgical time for these procedures was 26.8±7.8 min. These procedures were not included in our study protocol. Nevertheless, we report that haemodynamic changes and ST- segment elevation were more prominent during anastomoses of vessels other than the LAD. Intraoperatively, no patient received transfusion of packed or any other kind of red blood cells. The majority of the patients received one or two units of fresh frozen plasma (FFP). Twenty-four patients (42.1%) did not require any intraoperative cardio-vasoactive drug support. In the rest of the patients and according to their haemodynamic profile, dobutamine, nitroglycerin, phenylephrine and adrenaline were administered. In general, these drugs were given when the heart was positioned for the second or third vessel. Two patients received β-blockers (esmolol) during the anastomosis. Mean infused volume (not including FFP) was 2750±440ml and it consisted mainly of crystalloid solutions. Baseline urinary output was 1.5±0.9ml/min. It was decreased during the first anastomosis (LIMA→LAD) to 0.5±0.5 ml/min and it was further reduced to 0.3±0.5 ml/min when other vessels were anastomosed. Patients were extubated 216±88 min after arrival in the ICU and they were transferred to the intermediate care the next morning.

## DISCUSSION

Our study demonstrated that, in patients undergoing off-pump CABG, there are significant changes in the acid-base and blood gas status during the construction of the coronary anastomoses. These disturbances appear to be related to the haemodynamic changes which were also observed in our patients.

Haemodynamic disturbances during OPCAB are mainly due to a reduction in stroke volume. Heart's displacement, ventricular compression and stabilization may cause reduced diastolic loading, improper systolic configuration and reduced ejection, disturbed myocardial oxygenation and abnormal ventricular performance. Transient surgical coronary occlusion, inadequate flow in temporarily shunted coronary vessels and increased ventricular diastolic pressures may difficultly be faced by a reduced arterial pressure in the root of aorta, especially in patients suffering from coronary artery disease where the heart's oxygen supply/needs balance is easily compromised. In animal models, reductions of stroke volume and coronary blood flow and ventricular compression were described when an epicardial stabilizer was used to displace the heart**[16,17]**. Segmental wall motion abnormalities have been documented during epicardial stabilization and transient occlusion of a coronary artery in patients with single vessel disease**[18]**. The type of the stabilizer and the anastomotic site seem to affect cardiac performance. Biswas et al, using transesophageal echocardiography in conjunction with continuous cardiac output monitoring, demonstrated reduced myocardial performance during myocardial displacement with the Octopus stabilizer for grafting the circumflex coronary artery**[19]**. They showed that reversible left ventricular wall motion abnormalities were present significantly more during circumflex coronary artery territory grafting, associated with both regional systolic dysfunction and restrictive diastolic filling, which indicates decreased left ventricular compliance. Mathison et al, using direct left atrial and left ventricular catheters and an Octopus stabilizer, demonstrated that the greatest increase in both left and right ventricular end-diastolic pressures occurred during positioning for circumflex coronary artery grafting**[20]**. Simultaneously, mean arterial pressure decreased 22%, stroke volume decreased 28%, and cardiac output fell 37%, while left and right atrial pressures increased by 59% and 168% respectively. Even with minimal myocardial displacement for left descending artery exposure, end-diastolic ventricular pressure was found increased. Decreased ventricular compliance was present in both of the above studies. It appears to be the primary mechanism leading to decreased stroke volume and hemodynamic instability during off-pump surgery. Similar changes were found in our study population.

In our patients, a significant decrease in $O_2$ delivery was observed during anastomotic maneuvering, although this was partially compensated by the increased $O_2$ extraction and the consequent fall in $SvO_2$. Calculated $O_2$ consumption was lowered during sampling, probably due to ongoing loss of heat under deep general anesthesia, alone or in combination to tissue underperfusion. It seems reasonable that $CO_2$ production followed the same declining pattern. When an unchanged mode of controlled ventilation is employed, $PACO_2$ and $PaCO_2$ are determined by intrinsic factors as $CO_2$ production and total dead space **[21, 22]**. In the other hand, the ventilation/perfusion ratio highly influences $PaO_2$. In case of reduced pulmonary flow and increased VA/Q, arterial tension of $O_2$ is elevated. In our patients $PaO_2$ was increased during anastomotic maneuvering, probably due to the lowered cardiac output and the consequently increased VA/Q together with the mechanism already discussed regarding the decreased alveolar $CO_2$. In conclusion, our study population showed alterations in gas-exchange resulting more or less by the disturbed stroke volume and flow. It seems that, in our patients, the observed haemodynamic changes were not severe or prolonged enough to jeopardize lung

gas-exchange. Nevertheless, ventricular deterioration during OPCAB may be associated with significant VA/Q mismatch especially in patients with left ventricular dysfunction**[23]**. In an animal model mimicking multi-vessel off-pump coronary artery bypass revascularization, a significant decrease in $PaO_2$ and $PaO_2/FIO_2$ was observed during repeated coronary occlusion and reperfusion**[24]**. Increased pulmonary arterial pressures during OPCAB maneuvering have been documented in animals and humans**[7,8,9,23,24]**. In this case, pulmonary congestion leads to insufficient gas-exchange.

Decreased systemic flow and oxygen delivery may cause metabolic acidosis as tissue perfusion and oxygenation may be compromised. An increased plasma concentration of protons was noted in our patients. Even under conditions of aerobic metabolism, the reduced urinary output could play a role for the new equilibrium in acid-base status. Restoration of flow, regionally or systemically, is followed by a transient drop in pH and bicarbonates and an elevation in partial pressure of $CO_2$, as a load of protons is entered in the circulation and buffered**[25,26]**. During exogenous administration of bicarbonates, the produced $CO_2$ may alter the $PetCO_2/PaCO_2$ ratio towards an inconsistent to haemodynamics total dead space. This observation could explain the ongoing decline in VD/VT ratio observed in our patients despite the elevation of pulmonary flow after the removal of the stabilizer. Finally, the method in our study was not sensitive enough to detect any oxygen debt immediately after the completion of the anastomosis as **T4**-samples were drawn 10 minutes later and we cannot comment on an increased $CO_2$ production and exhalation together to a parallel $O_2$ consumption at this period of time.

The Qs/Qt ratio was decreased during anastomotic maneuvering in our patients. In general, Qs/Qt is expected to be increased when cardiac output falls. Under $FiO_2=1$, Qs/Qt represents in part the extrapulmonary shunt which heavily depends on the shunting in coronary circulation. In humans, the venous return of the heart is through multiple routes, including drainage not passing through the orifice of the coronary sinus to the right atrium **[27]**. The presence of vein valves has also been documented in animals and humans**[28]**. Reduction of this part of coronary vein outflow due to application of the stabilizer, temporary coronary shunting and elevation of the heart's intracaviteal pressures could explain the decrease in Qs/Qt observed in our patients.

Myocardial revascularization is accompanied by a significant incidence of serious neurologic injury, persistent cognitive decline and functional impairment**[29,30]**. Embolic phenomena appear to be not the sole etiology**[31]**. Generally, cerebral autoregulation with appropriate bihemispheric carbon dioxide reactivity is considered intact during cardiac operations. Carbon dioxide is a well known factor affecting cerebral vascular resistance and blood volume in the scull**[32]**. Hypocapnia reduces the capacity of brain microcirculation to maintain proper oxygenation during hemodynamic alterations challenging cerebral blood flow. Reduced systemic flow and pressure during OPCAB, as observed by us and others, together with decreased $CO_2$ tension form a dangerous combination for brain integrity. Recently, increased brain regional oximetric values associated with hypercapnia were demonstrated using transcranial near-infrared spectroscopy**[15,33]**. With the same monitoring technique, vasopressor-induced perfusion pressure elevation alone was sometimes inadequate to correct brain regional oximetric values during near-normothermic CPB for myocardial revascularization. Titration towards permissive hypercapnia was often effective in restoring oximetric values to baseline**[34]**. These observations underline the importance of $CO_2$ tension alterations during anastomotic maneuvering in OPCAB which are described in our study.

There are several limitations in our study. It represents the work of a single surgeon, our cases were not urgent, our patients had a more or less good or moderate cardiac function and the grafting of vessels other than the LAD were not included in our protocol as it is incorrect to use more than one data set per patient when the results are evaluated with a paired test. The study is underpowered for $PaCO_2$. The above may limit the applicability of our data in other patient populations. Our findings suggest that stroke volume and cardiac output reduction during OPCAB lead towards metabolic acidosis while restoration of flow is followed by "wash-out" phenomena. Gas exchange in the lungs may not be severely affected. Nevertheless, this operative technique is associated with changes in arterial $O_2$ and $CO_2$ tensions which may further affect tissue oxygenation. These changes, although not persistent and reversible, may have implications in the intraoperative management of patients with severely compromised haemodynamics and/or alveolar gas-exchange.

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