**Ventilation-Perfusion Inequality in Patients Undergoing Cardiac Surgery**

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**Background:** Impaired gas exchange is a major complication after cardiac surgery with the use of extracorporeal circulation. Blood gas analysis gives little information on underlying mechanisms, in particular if the impairment is multifactorial. In the current study we used the multiple inert gas technique with recordings of hemodynamics to analyze the separate effects of intrapulmonary shunt (Qs/Qt), ventilation-perfusion (V̅a/Q̅) mismatch, and low mixed venous oxygen tension on arterial oxygenation during cardiac surgery.

**Methods:** V̅a/Q̅ distribution was studied in nine patients undergoing coronary artery revascularization surgery. The obtained data related to V̅a/Q̅ distribution were perfusion of lung regions with V̅a/Q̅ < 0.005 (Qs/Qt), perfusion of lung regions with 0.005 < V̅a/Q̅ < 0.1 ("low" V̅a/Q̅ regions), ventilation of lung regions with 10 < V̅a/Q̅ < 100 ("high" V̅a/Q̅ regions), and ventilation of lung regions with V̅a/Q̅ > 100 (dead space [V̅d/V̅t]). In addition, arterial and mixed venous oxygen and carbon dioxide tensions and systemic and pulmonary hemodynamics were analyzed. Recordings were made before and after induction of anesthesia, after sternotomy, 45 min after separation from extracorporeal circulation, and postoperatively during mechanical ventilation, and on the 1st postoperative day during spontaneous breathing.

**Results:** In the awake state, Qs/Qt was 4 ± 4%, and perfusion of low-V̅a/Q̅ regions was 3 ± 5%. The sum of Qs/Qt and low-V̅a/Q̅ units correlated with the alveolar-arterial oxygen tension gradient (Pa-aO₂) (r = 0.63, P < 0.05). After induction of anesthesia, Qs/Qt increased to 10 ± 9% (P = 0.009). Sternotomy had little effect on shunt, but Qs/Qt increased to 22 ± 8% (P < 0.01) after separation from extracorporeal circulation, which was correlated with a significantly higher Pa-aO₂ (r = 0.77, P < 0.05). Postoperatively, gas exchange improved rapidly, as assessed by a decrease of Pa-aO₂ from 341 ± 77 to 97 ± 36 mmHg (P < 0.01) and a reduced Qs/Qt (5 ± 4%, P < 0.05). On the 1st postoperative day, arterial oxygen tension was significantly lower than preanesthesia values (58 ± 6 vs. 68 ± 8 mmHg, P < 0.05). Qs/Qt had increased to 11 ± 6% (P < 0.05), but little perfusion of low-V̅a/Q̅ units was observed. A correlation was found between Pa-aO₂ and Qs/Qt (r = 0.82, P < 0.03).

**Conclusions:** Qs/Qt is a major component of impaired gas exchange before, during, and after cardiac surgery. Qs/Qt increases after induction of general anesthesia, probably because of development of atelectasis. After separation from extracorporeal circulation, accumulation of extravascular lung water or further collapse of lung tissue may aggravate Qs/Qt. Postoperatively, oxygenation improves, possibly because of recruitment of previously nonventilated alveoli or resolution of extravascular lung water. During spontaneous breathing, additional mechanisms such as altered mechanics of the chest, perfusion of low-V̅a/Q̅ regions, and decreased mixed venous oxygen tension may contribute to impaired gas exchange. (Key words: Lung(s); gas exchange; ventilation-perfusion; Measurement techniques: multiple inert gas exchange. Surgery, cardiac; cardiopulmonary bypass.)

**IMPAIRED** lung function is still a major complication after cardiac surgery and presents frequently with a reduced arterial oxygen tension (PaO₂) and hemoglobin oxygen saturation during air breathing.1-3 The underlying causes seem to be multifactorial, including effects of anesthesia and muscle paralysis,4,5 sternotomy,6 pleurotomy,7 extracorporeal circulation (ECC),8,9 accumulation of extravascular lung water due to alterations of the alveolar-capillary membrane,10,11 lung collapse during ECC,12 phrenic nerve paralysis secondary to topical cooling of the heart,13 altered mechanics of the rib cage,6,14 retention of airway secretions, and postoperative hypoventilation or insufficient cough due to pain.15 Traditionally, PaO₂, mixed venous oxygen tension (PvO₂), and arterial carbon dioxide tension (PaCO₂) as well as expired carbon dioxide tension are used to assess pulmonary gas exchange.16 These indices may allow calculation of alveolar-arterial oxygen tension difference (Pa-aO₂), venous admixture, and dead space. Arterial blood gases are also influenced by nonpulmonary factors such as PvO₂ or cardiac output.
Furthermore, alterations of inspired oxygen fraction have been shown to affect ventilation–perfusion (\(V_{A}/Q\)) distribution, for example, \(via\) released hypoxic pulmonary vasoconstriction or the development of resorption atelectasis.\(^{17,18}\)

Our hypotheses were (1) that intrapulmonary right-to-left shunt (\(Q_{s}/Q_{t}\)) may develop as a consequence of anesthesia; (2) that surgery and ECC have additional impact on \(Q_{s}/Q_{t}\); and (3) that low cardiac output and \(P_{\text{a}}O_{2}\) due to ischemic cardiac disease contribute to decreased \(P_{\text{a}}O_{2}\). Finally, we hypothesized that perfusion of relatively hypoventilated alveoli ("low-\(V_{A}/Q\) regions) is a mechanism of impaired oxygenation, particularly during air-breathing. The multiple inert gas elimination technique (MIGET) allows an evaluation of \(V_{A}/Q\) relationships in more detail without interference with physiologic gases.\(^{19,20}\) Thus, a clinical study was done in cardiac surgical patients using the MIGET for analysis of \(V_{A}/Q\) distribution in the awake state, after induction of anesthesia, before and after cardiopulmonary bypass, and after surgery.

**Materials and Methods**

Nine patients scheduled for coronary artery bypass graft surgery were studied (age 69 ± 3 yr [range 65–75 yr], weight 78 ± 13 kg [range 62–98 kg], and height 172 ± 9 cm [range 156–181 cm]). Inclusion criteria for the investigation were (1) stable angina pectoris due to coronary artery disease, (2) left ventricular ejection fraction > 40%, (3) left ventricular end-diastolic pressure < 15 mmHg, (4) absence of significant preoperative lung malfunction as determined by clinical examination, chest radiography, lung function test, and blood gas analysis,\(^{21}\) and (5) absence of coexisting renal, hepatic, or cerebrovascular diseases or insulin-dependent diabetes mellitus. Spirometry revealed a forced expired volume in 1 s of 80 ± 11% and a forced vital capacity of 80 ± 8% of the predicted value. Three patients presented with a decreased forced expired volume in 1 s (range 65–78% of predicted value) and forced vital capacity (range 69–75% of predicted value), indicating the presence of minor to moderate obstructive pulmonary disease.

The study was approved by the Ethical Committee of Uppsala University Hospital, and informed consent was obtained from each patient.

**Anesthesia and Mechanical Ventilation**

All patients had received 1–2 mg fentanyl orally the evening before surgery and 10–15 mg morphine and 0.4–0.6 mg scopolamine intramuscularly 60 min before the anesthesia. Preoperative treatment with \(\beta\)-adrenoceptor blocking drugs or nitrates was maintained on the day of surgery. Anesthesia (257 ± 50 min) was induced with intravenous fentanyl (5–10 \(\mu\)g \(\text{kg}^{-1}\)), thiopental (1.5–2.5 mg \(\text{kg}^{-1}\)), and pancuronium (0.1 mg \(\text{kg}^{-1}\)) and maintained by fentanyl and a volatile inhalational anesthetic (halothane 0.5–1.0 MAC).

After tracheal intubation, the lungs were ventilated with intermittent positive-pressure ventilation. The inspired oxygen fraction was 0.48 ± 0.04 in nitrogen. Tidal volume (10–12 ml \(\text{kg}^{-1}\)) and ventilatory frequency were adjusted to maintain normal \(P_{\text{a}}\text{CO}_2\) (\(P_{\text{a}}\text{CO}_2 = 36–44\) mmHg). The membrane oxygenator (Maxima\(^{\text{a}}\), Medtronic, Anaheim, CA) was primed with 2,000 ml acetylated Ringer’s solution. During ECC (duration 87 ± 32 min), body core temperature was decreased to 30 ± 0.5°C. The lungs were noninflated during cold cardiopulmonary cardiac arrest (42 ± 17 min), which was achieved by infusion of 1,180 ± 350 ml cardiopulmonary solution. After declamping of the aorta the lungs were ventilated with 100% oxygen with half the minute volume used before ECC, and full ventilation was restored before separation from ECC. Nitroglycerin was given in low doses (0.2–0.5 \(\mu\)g \(\text{kg}^{-1}\) \(\text{min}^{-1}\)) in each case during and after separation from ECC. In addition, one patient required positive inotropic support (dobutamine 5 \(\mu\)g \(\text{kg}^{-1}\) \(\text{min}^{-1}\)).

At the end of surgery (185 ± 47 min), a total balance of +3,960 ± 840 ml for crystalloids and −650 ± 195 ml for blood loss was noted. In the intensive care unit (ICU), mechanical ventilation was maintained in the above-described manner, and the inspired oxygen fraction was adjusted to maintain arterial oxygen saturation greater than 95%. Adequate analgesia and sedation were achieved with repetitive doses of ketobemidon (1–3 mg) and midazolam (2.5–5 mg) according to standard procedures at our institution. Each patient was successfully separated from intermittent positive-pressure ventilation and the trachea extubated 6–11 h postoperatively. Fluid balance on the 1st postoperative day was −2,190 ± 1,150 ml and +570 ± 660 ml for crystalloids and colloids, respectively.

**Cardiopulmonary Monitoring**

Before induction of anesthesia, a 20-G catheter was introduced into the left or right radial artery for pressure measurements and blood sampling. A triple-lumen, thermistor-tipped, 7.5-French pulmonary artery cath-
ceter was transcutaneously introduced via the right internal jugular vein into a pulmonary arterial wedge position. Pulmonary arterial pressure, right atrial pressure, and pulmonary arterial occlusion pressure relative to atmospheric pressure were measured. Mean systemic arterial pressure and mean pulmonary arterial pressure were obtained by electric integration of the pressure signal. The ECG lead V5 was continuously recorded and used for heart rate calculation. $P_{aO_2}$, $P_{a\text{O}_2}$, and $Pa\text{CO}_2$ were determined by standard techniques (ABL 3", Radiometer, Copenhagen, Denmark). Cardiac output was measured by thermodilution. Ten milliliters ice-cold 0.9% saline solution was injected rapidly into the right atrium, with the dilution recorded by a cardiac output computer (Sirecust 942, Siemens-Elema, Stockholm, Sweden). Cardiac output measurements were made during an end-expiratory pause, and the mean of three determinations was calculated. Derived data such as cardiac index and oxygen consumption index and oxygen delivery index were calculated using standard formulas. $Pa-a\text{O}_2$ was calculated from the alveolar gas equation. Arterial and mixed venous oxygen saturations were measured from arterial and mixed venous blood samples by spectrophotometry (OSM 3", Radiometer).

Measurement of Ventilation–Perfusion Distribution

The technique for measuring $\dot{V}_A/\dot{Q}$ distribution has been described in detail elsewhere. A mixture of inert gases (sulphur hexafluoride, ethane, cyclopropane, enflurane, diethylether, and acetone) dissolved in isotonic saline was infused at a constant rate (3 ml·min⁻¹) into a peripheral vein. After an equilibration period of 40 min, arterial and mixed venous blood samples and mixed expired gas samples were obtained and analyzed by gas chromatography (5880A, Hewlett-Packard, Little Falls, DE). Blood–gas partition coefficients were determined by a two-step procedure. These data and the calculated retentions and excretions were transformed into a multicompartmental (50 compartments) plot of blood flow and ventilation against $\dot{V}_A/\dot{Q}$ by α-numeric analysis with enforced smoothing (scalar factor 40). The data related to the $\dot{V}_A/\dot{Q}$ distribution were limited to perfusion of lung regions with $\dot{V}_A/\dot{Q} < 0.005 \left( \dot{Q}_A/\dot{Q}_T \right)$, perfusion of lung regions with $0.005 < \dot{V}_A/\dot{Q} < 0.1 \left(\text{low-} \dot{V}_A/\dot{Q} \text{ regions}\right)$, ventilation of lung regions with $10 < \dot{V}_A/\dot{Q} < 100 \left(\text{high-} \dot{V}_A/\dot{Q} \text{ regions}\right)$, ventilation of lung regions with $\dot{V}_A/\dot{Q} > 100 \left(\text{dead space } \dot{V}_A/\dot{V}_T \right)$, the mean $\dot{V}_A/\dot{Q}$ ratio of the ventilation and perfusion distribution ($\dot{Q}_{\text{mean}}$ of $\dot{V}_A/\dot{Q}$, respectively), and the dispersion around the means expressed as the logarithmic standard deviation of ventilation and perfusion distribution ($\log SD_v$ and $\log SD_Q$, respectively). Subdivisions of blood flow and ventilation were expressed as fractions of cardiac output and expired minute ventilation, respectively. The remaining sum of squared differences between measured and calculated retentions and excretions was calculated. The remaining sum of squared differences should not exceed 6 in more than 50% of the tests. Knowing the $\dot{V}_A/\dot{Q}$ distribution, blood flow, $P_{a\text{O}_2}$, hemoglobin concentration, and slope of the oxygen dissociation curve, $Pa\text{O}_2$ can be determined by means of an iterative procedure. Thus, expected (calculated) and measured $Pa\text{O}_2$ values were analyzed for possible differences.

Experimental Procedure

$\dot{V}_A/\dot{Q}$ distribution was first determined while the patients were awake, before induction of anesthesia. After 40 min for equilibration of the inert gases, cardiopulmonary measurements were made while the patient was breathing air. Then anesthesia was induced in the above-described manner. Recordings were made after a period of 20 min to achieve stable hemodynamic and respiratory conditions. After sternotomy, but before pericardiotomy, cardiopulmonary data were assessed again. During ECC, the inert gas infusion was stopped. A sufficient rewarming period after completion of the bypass surgery was allowed to avoid postoperative temperature decreases in the pulmonary artery. After separation from ECC, the infusion of the inert gases was started (3 ml·min⁻¹), and another 40 min for equilibration of the inert gases was allowed. Approximately 45 min after cardiopulmonary bypass and 20 min after closure of the sternum, ventilatory and hemodynamic measurements were made during stable cardiopulmonary conditions.

The operation was terminated, and the patient was transferred to the ICU. Four hours after admission to the ICU, cardiopulmonary status was again determined during sedation and mechanical ventilation. Finally, the patients were studied on the 1st postoperative day (approximately 20 h after cardiac surgery) during spontaneous air-breathing.

Statistical Analysis

All data were sampled and analyzed on a Systat statistical program (Systat, Evanston, IL). The results are presented as mean values and standard deviation. The

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significance of a difference between two conditions was
analyzed by Student’s paired t test. The significance of
differences between three or more conditions or the
influence of more than one factor was tested by mul-
tiple analysis of variance. Correlations between dif-
ferent parameters were analyzed with Spearman’s test.
A level of $P < 0.05$ was considered significant.

Results

Hemodynamics
The data are presented in table 1. No gross hemo-
dynamic abnormalities were observed before, during,
or after surgery. Mean systemic arterial pressure de-
creased after induction of anesthesia from 98 ± 15 to
83 ± 11 mmHg ($P < 0.05$) and remained within this
range after sternotomy, after ECC, and during the post-
operative course. Cardiac index was higher after ad-
mission of the patient to the ICU ($P < 0.05$) and on
the 1st postoperative day ($P < 0.05$) as compared with
control.

Gas Exchange
The data are presented in table 1. One day before
surgery, $\text{PaO}_2$ (83 ± 10 mmHg) and $\text{PaCO}_2$ (40 ± 2
mmHg) while the patients were breathing air were
normal. $\text{PaO}_2$ was lower after premedication before
induction of anesthesia (68 ± 8 mmHg, $P < 0.05$),
and $\text{PaCO}_2$ was slightly increased (44 ± 3 mmHg, $P <
0.05$). After induction of anesthesia, $\text{PaO}_2$ decreased
from 25 ± 10 to 126 ± 46 mmHg ($P < 0.01$) and
increased further after ECC (341 ± 77 mmHg, $P <
0.01$). Four hours after admission to the ICU,
$\text{PaO}_2$ decreased to 97 ± 36 mmHg and was not
statistically different from the values obtained after
induction of anesthesia. On the 1st postoperative day,
$\text{PaO}_2$ while the patients were breathing air was lower
when compared with the preanesthesia state ($\text{PaO}_2$ =
58 ± 6 vs. 68 ± 8 mmHg, $P < 0.05$). All patients had
hemoglobin concentrations > 90 g/l during the
different phases of our study.

Gas Exchange Data Derived from the Multiple
Inert Gas Elimination Technique
The data are presented in table 2. The fit of the ven-
tilation and perfusion distributions to the raw data of
retention and excretion was good throughout the in-
vestigation, and the remaining sum of squared differ-
ences remained < 6 in 50 of 54 individual measure-
ments. The averaged difference between expected
(calculated) and measured $\text{PaO}_2$ was 0.7 mmHg, and

Table 1. Cardiopulmonary Data (Mean ± SD) in the Awake State, after Induction of Anesthesia, after Sternotomy, 45 min
after Separation from Extracorporeal circulation, and 4 h and 20 h Postoperatively (n = 9)

<table>
<thead>
<tr>
<th></th>
<th>Awake</th>
<th>After Induction of Anesthesia</th>
<th>After Sternotomy</th>
<th>After Extracorporeal Circulation</th>
<th>4 h Postoperatively</th>
<th>20 h Postoperatively</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (beats/min)</td>
<td>55 ± 8</td>
<td>56 ± 10</td>
<td>62 ± 17</td>
<td>70 ± 15*</td>
<td>84 ± 10†</td>
<td>85 ± 10†</td>
</tr>
<tr>
<td>$\text{PaO}_2$ (mmHg)</td>
<td>98 ± 15</td>
<td>83 ± 11*</td>
<td>85 ± 5*</td>
<td>75 ± 5†</td>
<td>79 ± 6*</td>
<td>82 ± 11*</td>
</tr>
<tr>
<td>$\text{PaCO}_2$ (mmHg)</td>
<td>21 ± 4</td>
<td>18 ± 4</td>
<td>18 ± 4</td>
<td>18 ± 4</td>
<td>19 ± 3</td>
<td>19 ± 4</td>
</tr>
<tr>
<td>$\text{PaA}$ (mmHg)</td>
<td>9 ± 5</td>
<td>8 ± 4</td>
<td>8 ± 4</td>
<td>9 ± 5</td>
<td>8 ± 3</td>
<td>7 ± 3</td>
</tr>
<tr>
<td>$\text{CI}$ (l·min⁻¹·m⁻²)</td>
<td>12 ± 4</td>
<td>11 ± 4</td>
<td>14 ± 5</td>
<td>13 ± 4</td>
<td>12 ± 3</td>
<td>10 ± 5</td>
</tr>
<tr>
<td>$\text{PaO}_2$ (mmHg)</td>
<td>68 ± 6</td>
<td>172 ± 56†</td>
<td>150 ± 48†</td>
<td>303 ± 76†</td>
<td>125 ± 33*</td>
<td>58 ± 6*</td>
</tr>
<tr>
<td>$\text{PaCO}_2$ (mmHg)</td>
<td>44 ± 5</td>
<td>39 ± 4*</td>
<td>38 ± 12*</td>
<td>36 ± 4*</td>
<td>36 ± 5*</td>
<td>40 ± 9*</td>
</tr>
<tr>
<td>$\text{Sao}_2$ (%)</td>
<td>93.3 ± 2.7</td>
<td>97.9 ± 1.9†</td>
<td>98.2 ± 1.6†</td>
<td>99.4 ± 1.6†</td>
<td>97.8 ± 1.8†</td>
<td>91.5 ± 3.7†</td>
</tr>
<tr>
<td>$\text{PV}_{O_2}$ (mmHg)</td>
<td>33 ± 3</td>
<td>41 ± 5†</td>
<td>39 ± 6†</td>
<td>42 ± 6†</td>
<td>39 ± 5*</td>
<td>29 ± 3*</td>
</tr>
<tr>
<td>$\text{SV}_{O_2}$ (%)</td>
<td>65.7 ± 6.1</td>
<td>78.1 ± 4.4†</td>
<td>73.9 ± 5.7†</td>
<td>74.9 ± 6.8†</td>
<td>72.3 ± 10.4*</td>
<td>62.1 ± 12.6*</td>
</tr>
<tr>
<td>$\text{VO}_{2j}$ (ml·min⁻¹·m⁻²)</td>
<td>110 ± 26</td>
<td>74 ± 19†</td>
<td>71 ± 24†</td>
<td>116 ± 65</td>
<td>122 ± 32</td>
<td>122 ± 42</td>
</tr>
<tr>
<td>$\text{DO}_{2j}$ (ml·min⁻¹·m⁻²)</td>
<td>355 ± 112</td>
<td>338 ± 121</td>
<td>281 ± 121</td>
<td>487 ± 564*</td>
<td>368 ± 67</td>
<td>350 ± 123</td>
</tr>
</tbody>
</table>

HR = heart rate; $\text{PaO}_2$ = mean systemic arterial pressure; $\text{PaCO}_2$ = mean pulmonary arterial pressure; $\text{PaA}$ = right atrial pressure; $\text{CI}$ = pulmonary artery occlusion pressure; $\text{CI}$ = cardiac index; $\text{PaO}_2$ = arterial oxygen tension; $\text{PaCO}_2$ = arterial carbon dioxide tension; $\text{PaA}$ = alveolar arterial $\text{P}_{O_2}$ gradient; $\text{Sao}_2$ = arterial oxygen saturation; $\text{PV}_{O_2}$ = mixed venous oxygen tension; $\text{SV}_{O_2}$ = mixed venous oxygen saturation; $\text{VO}_{2j}$ = oxygen consumption index; $\text{DO}_{2j}$ = oxygen delivery index.

* $P < 0.05$.
† $P < 0.01$.

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Table 2. Multiple Inert Gas Elimination (MIGET) Data (Mean ± SD) in the Awake State, after Induction of Anesthesia, after Sternotomy, 45 Min after Separation from Extracorporeal Circulation, and 4 h and 20 h Postoperatively (n = 9)

<table>
<thead>
<tr>
<th></th>
<th>Awake</th>
<th>After Induction of Anesthesia</th>
<th>After Sternotomy</th>
<th>After Extracorporeal Circulation</th>
<th>4 h Postoperatively</th>
<th>20 h Postoperatively</th>
</tr>
</thead>
<tbody>
<tr>
<td>RSSD</td>
<td>1.63 ± 1.4</td>
<td>1.96 ± 1.44</td>
<td>1.46 ± 0.87</td>
<td>3.11 ± 3.05</td>
<td>1.09 ± 0.58</td>
<td>1.44 ± 1.30</td>
</tr>
<tr>
<td>Qmean of VA/Q</td>
<td>0.66 ± 0.27</td>
<td>1.44 ± 1.49*</td>
<td>0.91 ± 0.32</td>
<td>1.17 ± 0.67</td>
<td>0.97 ± 0.58</td>
<td>0.83 ± 0.16</td>
</tr>
<tr>
<td>log SDo</td>
<td>0.86 ± 0.33</td>
<td>1.35 ± 0.44*</td>
<td>1.05 ± 0.43</td>
<td>1.16 ± 0.52</td>
<td>1.04 ± 0.44</td>
<td>0.68 ± 0.26</td>
</tr>
<tr>
<td>Vmean of VA/Q</td>
<td>1.02 ± 0.49</td>
<td>2.75 ± 2.17*</td>
<td>1.71 ± 0.81</td>
<td>1.93 ± 0.97</td>
<td>1.64 ± 0.67</td>
<td>1.08 ± 0.31</td>
</tr>
<tr>
<td>log SDv</td>
<td>0.57 ± 0.18</td>
<td>0.58 ± 0.1</td>
<td>0.72 ± 0.29</td>
<td>0.46 ± 0.10</td>
<td>0.63 ± 0.13</td>
<td>0.48 ± 0.10</td>
</tr>
<tr>
<td>F Q low VA/Q units</td>
<td>0.03 ± 0.05</td>
<td>0.09 ± 0.06</td>
<td>0.05 ± 0.05</td>
<td>0.05 ± 0.05</td>
<td>0.04 ± 0.05</td>
<td>0.01 ± 0.02</td>
</tr>
<tr>
<td>Qs/Qt</td>
<td>0.04 ± 0.04</td>
<td>0.10 ± 0.09</td>
<td>0.12 ± 0.08*</td>
<td>0.22 ± 0.08*</td>
<td>0.05 ± 0.04</td>
<td>0.11 ± 0.06*</td>
</tr>
<tr>
<td>F V high VA/Q units</td>
<td>0.02 ± 0.01</td>
<td>0.06 ± 0.01*</td>
<td>0.07 ± 0.01*</td>
<td>0.06 ± 0.01*</td>
<td>0.05 ± 0.02</td>
<td>0.03 ± 0.01</td>
</tr>
<tr>
<td>V0/VT</td>
<td>0.43 ± 0.11</td>
<td>0.26 ± 0.10†</td>
<td>0.35 ± 0.04*</td>
<td>0.27 ± 0.09†</td>
<td>0.27 ± 0.08†</td>
<td>0.41 ± 0.10*</td>
</tr>
<tr>
<td>Qt (l/min)</td>
<td>4.0 ± 1.1</td>
<td>3.7 ± 1.4</td>
<td>3.4 ± 0.9</td>
<td>4.6 ± 1.5</td>
<td>5.0 ± 1.2*</td>
<td>5.0 ± 0.9*</td>
</tr>
<tr>
<td>Ve (l/min)</td>
<td>5.7 ± 1.0</td>
<td>7.3 ± 1.1†</td>
<td>7.3 ± 1.1†</td>
<td>7.2 ± 1.1†</td>
<td>8.1 ± 1.8†</td>
<td>8.7 ± 1.5†</td>
</tr>
<tr>
<td>FiO2</td>
<td>0.21</td>
<td>0.48 ± 0.04†</td>
<td>0.48 ± 0.04†</td>
<td>0.96 ± 0.01†</td>
<td>0.37 ± 0.04†</td>
<td>0.21</td>
</tr>
</tbody>
</table>

RSSID = remaining sum of squared differences; Qmean of VA/Q = mean ventilation — perfusion (VA/Q) ratio of perfusion distribution; log SDo = log standard deviation of perfusion; Vmean of VA/Q = mean ventilation — perfusion ratio of ventilation distribution; log SDv = log standard deviation of ventilation; F Q of low VA/Q units = fraction of blood flow to low VA/Q units (VA/Q ratio of 0.005 – 0.1); Qs/Qt = inert gas shunt; F V high VA/Q units = fraction of ventilation to high VA/Q units (VA/Q ratio of 10 – 100); V0/VT = inert gas dead space; Qt = total blood flow (cardiac output); Ve = expired minute ventilation; FiO2 = inspired oxygen fraction.

* P < 0.05.
† P < 0.01.

no statistical differences were observed during different points of time for data recordings.

Before induction of anesthesia, a moderate Qs/Qt (4 ± 4% of cardiac output) was observed. In addition, perfusion of low-Va/Q regions (3 ± 5% of cardiac output) was observed in four patients (patients 2, 6, 7, and 8). Pa–aO2 was correlated with Qs/Qt plus perfusion of low-Va/Q regions (r = 0.63, P < 0.05). Dead space ventilation averaged 43% with an expired minute volume of 5.7 ± 1.0 l·min⁻¹. For an example, see figure 1.

After induction of anesthesia, Qs/Qt was 10 ± 9% (P = 0.069), but in one patient (patient 8) almost no shunt was observed (fig. 2). However, this patient revealed a marked perfusion of low-Va/Q regions (28% of cardiac output). Development of shunt was correlated with increased Pa–aO2 (r = 0.71, P < 0.05). A broader perfusion distribution was observed in all patients as assessed by a higher log SDo (P < 0.05).

Sternotomy induced only small alterations of Qs/Qt, but after separation from ECC there was a marked increase of Qs/Qt, to 22 ± 8% (P < 0.01). Only a small fraction of cardiac output was distributed to low-Va/Q areas, and Pa–aO2 was correlated with Qs/Qt (r = 0.77, P < 0.05).

Four hours postoperatively, Qs/Qt had decreased to less than presternotomy values, a state that in turn was associated with an improvement of Pa–aO2. On the 1st postoperative day, all patients revealed considerable amounts of shunt (11 ± 6%, P < 0.05) but almost no perfusion of low-Va/Q areas. A correlation was found between Pa–aO2 and Qs/Qt (r = 0.82, P < 0.03). Duration of anesthesia, cardiac surgery, or ECC were not correlated with Pa–aO2 or Qs/Qt. Because PVi, was low the 1st postoperative day, its influence on arterial oxygenation was analyzed. This was done by recalculation of the expected PaO2, using the same Va/Q distribution, cardiac output, hemoglobin concentration, and oxygen dissociation curve as in the initial analysis but replacing the measured PVi, (29 mmHg on average; table 1) with a fixed value of 40 mmHg. This was done in all nine patients, and expected PaO2 increased from 59 ± 8 mmHg (the same as the measured value; table 1) to 69 ± 9 mmHg.

Discussion

Ventilation–Perfusion Relationship in the Awake State and after Induction of Anesthesia

Before induction of anesthesia, PaO2 was lower than on the day before surgery. Both Qs/Qt (4 ± 4% of cardiac output) and an increased scatter of Va/Q ratios (increased log SDv) with perfusion of low-Va/Q regions (3 ± 5% of cardiac output) contributed to the decreased PaO2. The effects of premedication on respi-

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Before anesthesia
Pat no: 5

PaO2 = 63 mmHg
PaCO2 = 44 mmHg
log SDO = 0.65
FIO2 = 0.21
VD/VT = 31%
VE = 4.4 l/min
Q = 3.3 l/min

Qs/Qt=0.3%

After induction of anesthesia
Pat no: 5

PaO2 = 165 mmHg
PaCO2 = 35 mmHg
log SDO = 1.46
FIO2 = 0.50
VD/VT = 26%
VE = 7.5 l/min
Q = 2.5 l/min

Qs/Qt=7.2%

After sternotomy
Pat no: 5

PaO2 = 94 mmHg
PaCO2 = 36 mmHg
log SDO = 1.21
FIO2 = 0.50
VD/VT = 31%
VE = 7.5 l/min
Q = 2.5 l/min

Qs/Qt=11.3%

After ECC
Pat no: 5

PaO2 = 187 mmHg
PaCO2 = 36 mmHg
log SDO = 1.05
FIO2 = 0.99
VD/VT = 33%
VE = 6.8 l/min
Q = 3.3 l/min

Qs/Qt=20.9%

4 hours after surgery
Pat no: 5

PaO2 = 109 mmHg
PaCO2 = 37 mmHg
log SDO = 0.95
FIO2 = 0.40
VD/VT = 34%
VE = 7.0 l/min
Q = 3.7 l/min

Qs/Qt=2.8%

1 day after surgery
Pat no: 5

PaO2 = 66 mmHg
PaCO2 = 39 mmHg
log SDO = 0.36
FIO2= 0.21
VD/VT = 38%
VE = 6.0 l/min
Q = 4.6 l/min

Qs/Qt=16.5%

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Fig. 1. Distribution of alveolar ventilation (\( \dot{V}_A \), open circles) and blood flow (\( \dot{Q} \), closed circles) against ventilation-perfusion (\( V_A/\dot{Q} \)) ratio on a logarithmic scale. Each individual data point represents a defined fraction of \( V_A \) or \( \dot{Q} \). Total blood flow and total alveolar ventilation correspond to the sum of all blood flow points and ventilation points, respectively. Note the appearance of shunt (\( \dot{Q}_S/\dot{Q}_T \)) and perfusion of lung regions with \( 0.005 < V_A/\dot{Q} < 0.1 \) ("low-\( V_A/\dot{Q} \) regions) after induction of anesthesia as well as the increased logarithmic standard deviation of perfusion (log \SD{\dot{Q}}). After sternotomy, \( \dot{Q}_S/\dot{Q}_T \) increased slightly, associated with decreased perfusion of low-\( V_A/\dot{Q} \) regions. The main effect of ECC on lung function was a marked increase of \( \dot{Q}_S/\dot{Q}_T \), but gas exchange improved within 4 h after cardiac surgery. On the 1st postoperative day \( \dot{Q}_S/\dot{Q}_T \) was elevated again. Note the absence of low-\( V_A/\dot{Q} \) regions and the low log \SD{\dot{Q}}, indicating a normal \( V_A/\dot{Q} \) distribution. \( \dot{Q} \) = cardiac output; \( V_E \) = expired minute ventilation; \( V_B/\dot{V}_T \) = dead space; \( \text{P}O_2 \) = inspired oxygen fraction; ECC = extracorporeal circulation.

respiratory muscle tone, supine body position, and presence of obstructive pulmonary disease in some patients possibly altered the relationship between functional residual capacity and closing capacity. \( V_B/\dot{V}_T \) also was increased, although \( \text{P}aCO_2 \) was still in the upper normal range (tables 1 and 2). In addition, \( P\text{O}_2 \) and cardiac output were comparatively low, reflecting not only the effect of premedication but also the pretreatment with \( \beta \)-adrenoceptor blocking drugs in the majority of our patients. A decreased \( P\text{O}_2 \) may substantially contribute to hypoxemia in the presence of impaired lung function, particularly during air-breathing.\textsuperscript{20} Thus, the combined effects of \( V_A/\dot{Q} \) mismatch due to maldistribution of the inspired gas to dependent lung regions increased \( V_B/\dot{V}_T \) and \( Q_S/\dot{Q}_T \) and decreased \( P\text{O}_2 \) have caused gas exchange impairment in cardiac surgical patients before induction of anesthesia.\textsuperscript{20,20,40}

During anesthesia and muscle paralysis, mean \( Q_S/\dot{Q}_T \) was 10%, which agrees well with published data.\textsuperscript{3,5,51} The reconstructed \( V_A/\dot{Q} \) curves also showed perfusion of low-\( V_A/\dot{Q} \) regions (figs. 1 and 2). A previous study with non–cardiac surgical patients has found a good correlation between oxygen tension–derived parameters (venous admixture) and perfusion of nonventilated areas plus low-\( V_A/\dot{Q} \) regions, as measured with MIGET both in the awake state and after induction of anesthesia.\textsuperscript{5} Development of bilateral atelectasis as assessed by thoracic computed tomography has been identified as a major cause of shunt in anesthetized patients.\textsuperscript{5,51} In our study, the rapid increase of \( Q_S/\dot{Q}_T \) after induction of anesthesia suggests a similar mechanism, although we can provide no radiologic evidence for collapse of basal lung regions. It is noteworthy that in one patient with moderate airway obstruction, almost no shunt could be demonstrated before and after induction of anesthesia, but a high fraction of cardiac output perfusion of low-\( V_A/\dot{Q} \) areas (fig. 2) could be seen. Gunnarsson \textit{et al.} have shown that in patients with chronic obstructive lung disease, shunt during anesthesia rarely develops (and no basal atelectasis develops, as assessed with computed tomographic scanning), but considerable \( V_A/\dot{Q} \) mismatching may occur.\textsuperscript{42}

\textbf{Ventilation–Perfusion Relationship after Sternotomy and Separation from Cardiopulmonary Bypass}

Sternotomy had only minor effects on systemic and pulmonary hemodynamics and on gas exchange. Lung volume may have increased after sternotomy,\textsuperscript{4} and \( V_A/\dot{Q} \) relationships showed an elevated dead space, increased ventilation of high-\( V_A/\dot{Q} \) areas, and diminished perfusion of low-\( V_A/\dot{Q} \) regions (table 2). However, these changes were small and were not associated with marked alteration of \( \text{P}a-\text{a}O_2 \). After separation from ECC, lung function was significantly impaired, and \( Q_S/\dot{Q}_T \) had almost doubled. Despite a potentially unstable situation after cardiopulmonary bypass, the retention and excretion data of the inert gases resulted in technically adequate \( V_A/\dot{Q} \) distributions (table 2), and measured and calculated (from \( V_A/\dot{Q} \) distribution) \( P\text{a}_O_2 \) values were similar, with a mean difference of less than 1 mmHg. At the time of measurement of hemodynamic and respiratory variables and collection of MIGET data (approximately 20 min after closure of the sternum), no rapid alterations of blood temperature, \( pH \), cardiac output, or fluid losses were seen. In a previous study, we found a significant increase of extravascular lung water and pulmonary blood volume after ECC.\textsuperscript{5,4} Possibly, a decrease of colloid osmotic pressure due to priming of the oxygenator, fluid load after ECC, and, to a lesser extent, alterations of the alveolar–capillary membrane enhance fluid filtration into the interstitial or alveolar space.\textsuperscript{10,11,34} The density and weight of pul-


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monary parenchyma increase in the presence of edema, which could also aggravate formation of atelectasis in dependent lung areas.\textsuperscript{35,56} Ventilatory measures such as positive end-expiratory pressure during ECC have not been shown to improve lung function, possibly because transpulmonary pressure was insufficient to open collapsed alveoli.\textsuperscript{12}

**Ventilation–Perfusion Relationship in the Postoperative Period**

Oxygenation was still impaired 4 h after cardiac surgery, but to a lesser extent than shortly after ECC. In particular, low $Q_S/Q_T$ and perfusion of relatively hypoventilated regions were observed (figs. 1 and 2). Although thoracic intravascular fluid volumes remain increased at least 4 h after cardiac surgery, this condition need not be associated with increased extravascular lung water.\textsuperscript{53} Thus, rapid recovery of lung function after uncomplicated coronary artery bypass graft surgery is unlikely to be a consequence of resorption of lung edema.\textsuperscript{11}

Our postoperative data during mechanical ventilation partly agree with earlier studies using MIGET after cardiac surgery. Anjou-Lindskog \textit{et al.} studied patients during mechanical ventilation on the 1st postoperative day after myocardial revascularization and observed an average $Q_S/Q_T$ of 6.4–7.5%.\textsuperscript{17,57} After aortic valve replacement, Gillespie \textit{et al.} found a mean $Q_S/Q_T$ of 6.1% and an increased log $SD_O$, indicating significant $V_A/Q$ heterogeneity.\textsuperscript{58} In contrast, Dantzker \textit{et al.} reported a $Q_S/Q_T$ of 17.9% 12–18 h after coronary artery bypass surgery.\textsuperscript{59} In their study, shunt was defined as perfusion of lung units with $V_A/Q < 0.01$, and preoperative lung function test revealed a higher incidence of airway obstruction as well as restrictive pulmonary disease.

On the 1st postoperative day, $Q_S/Q_T$ had increased to 11 ± 6%, but little perfusion of low-$V_A/Q$ regions was observed (figs. 1 and 2). Oxygenation was significantly more impaired than in the preanesthesia state. In addition to the more pronounced $V_A/Q$ mismatch, decreased $P_{aO_2}$ may have contributed significantly to decreased $P_{aO_2}$ (table 1). Because the data were obtained during spontaneous air-breathing, a comparison with results obtained during different conditions is difficult. However, our MIGET data are in accordance with results from Dantzker \textit{et al.}, who found an increase of $Q_S/Q_T$ and $V_A/Q$ mismatch when conditions were switched from mechanical ventilation to spontaneous breathing.\textsuperscript{49} The close relationship between $Q_S/Q_T$ and $P_{aO_2}$ suggests that blood flow to nonventilated lung regions was the major component of oxygenation deficiency. In patients with acute respiratory failure after cardiac surgery, bilateral collapse of dependent lung regions was diagnosed by computed tomography, and the amount of atelectasis correlated well with calculated venous admixture.\textsuperscript{40} Thus, atelectasis induced during anesthesia or cardiopulmonary bypass probably persists in the postoperative period and may significantly contribute to lung function impairment.

The normal reaction of the lung to regional pathologic states such as atelectasis or edema is a shift of perfusion toward aerated alveoli to minimize oxygenation impairment.\textsuperscript{41} However, several factors may interfere with this mechanism before, during, and after cardiac surgery. First, vasodilators are frequently used in patients with ischemic heart disease. Nitroglycerin causes pooling of blood in the capacitance vessels and a reduction of pulmonary artery pressure.\textsuperscript{37} The latter mechanism would favor distribution of blood flow to dependent lung regions as long as alveolar pressures remain unchanged. Nitroglycerin has also been shown to interfere with hypoxic pulmonary vasoconstriction and may aggravate gas exchange impairment in edematous as well as in atelectatic lungs.\textsuperscript{42,43} Second, a high inspiratory oxygen fraction increases $P_{a-aO_2}$ and $Q_S/Q_T$, probably by release of hypoxic pulmonary vasoconstriction,\textsuperscript{17,18} and the inhalational anesthetic (halothane) used in our patients has also been shown to suppress hypoxic pulmonary vasoconstriction in a dose-dependent manner.\textsuperscript{44} Finally, ventilation with 100% oxygen may induce development of absorption atelectasis, particularly in the presence of low-$V_A/Q$ regions.\textsuperscript{22} A simple test of the influence on arterial oxygenation of $P_{aO_2}$ was made by replacing measured
$P_{O_2}$ by a fixed value of 40 mmHg. This resulted in a considerable increase in the calculated $P_{O_2}$ with given $V_a/Q$ distributions. It can thus be concluded that $P_{O_2}$ has an important effect on $P_{O_2}$ during the postoperative period. However, it should be made clear that many factors will influence $P_{O_2}$ such as cardiac output, oxygen uptake, oxygen dissociation curve, hemoglobin concentration, $V_a/Q$ distribution, and $Q_s/Q_T$.

“Normalization” of $P_{O_2}$ in a theoretical analysis, as done here, does not allow a quantitative analysis of the separate impact of each of the listed variables.

In conclusion, we have shown that gas exchange impairment in cardiac surgical patients is mainly caused by $Q_s/Q_T$. In addition, a decreased $P_{O_2}$ secondary to impaired cardiac performance may contribute to perioperative hypoxemia. Induction of anesthesia seems to be a major underlying factor of gas exchange impairment, and ECC significantly aggravates $Q_s/Q_T$. Postoperatively, additional mechanisms such as altered mechanics of the chest, perfusion of low-$V_a/Q$ regions, and decreased $P_{O_2}$ may contribute to impaired gas exchange.

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References


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