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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 ($\dot{Q}_S/\dot{Q}_T$), ventilation–perfusion ($\dot{V}_A/\dot{Q}$) mismatch, and low mixed venous oxygen tension on arterial oxygenation during cardiac surgery.**

Methods: **$\dot{V}_A/\dot{Q}$ distribution was studied in nine patients undergoing coronary artery revascularization surgery. The obtained data related to $\dot{V}_A/\dot{Q}$ distribution were perfusion of lung regions with $\dot{V}_A/\dot{Q} < 0.005$ ($\dot{Q}_S/\dot{Q}_T$), perfusion of lung regions with $0.005 < \dot{V}_A/\dot{Q} < 0.1$ ("low"-$\dot{V}_A/\dot{Q}$ regions), ventilation of lung regions with $10 < \dot{V}_A/\dot{Q} < 100$ ("high"-$\dot{V}_A/\dot{Q}$ regions), and ventilation of lung regions with $\dot{V}_A/\dot{Q} > 100$ (dead space [$\dot{V}_D/\dot{V}_T$]). 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, 4 h postoperatively during mechanical ventilation, and on the 1st postoperative day during spontaneous breathing.**

Results: **In the awake state, $\dot{Q}_S/\dot{Q}_T$ was 4 ± 4%, and perfusion of low-$\dot{V}_A/\dot{Q}$ regions was 3 ± 5%. The sum of $\dot{Q}_S/\dot{Q}_T$ and low-$\dot{V}_A/\dot{Q}$ units correlated with the alveolar–arterial oxygen tension gradient ($P_A-a_{O_2}$) ($r = 0.63$, $P < 0.05$). After induction of anesthesia, $\dot{Q}_S/\dot{Q}_T$ increased to 10 ± 9% ($P = 0.069$). Sternotomy had little effect on shunt, but $\dot{Q}_S/\dot{Q}_T$ increased to 22 ± 8% ($P < 0.01$) after separation from extracorporeal circulation, which was correlated with a significantly higher $P_A-a_{O_2}$ ($r = 0.77$, $P < 0.05$). Postoperatively, gas exchange improved rapidly, as assessed by a decrease of $P_A-a_{O_2}$ from 341 ± 77 to 97 ± 36 mmHg ($P < 0.01$) and a reduced $\dot{Q}_S/\dot{Q}_T$ (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, $P < 0.05$). $\dot{Q}_S/\dot{Q}_T$ had increased to 11 ± 6% ($P < 0.05$), but little perfusion of low-$\dot{V}_A/\dot{Q}$ units was observed. A correlation was found between $P_A-a_{O_2}$ and $\dot{Q}_S/\dot{Q}_T$ ($r = 0.82$, $P < 0.03$).**

Conclusions: **$\dot{Q}_S/\dot{Q}_T$ is a major component of impaired gas exchange before, during, and after cardiac surgery. $\dot{Q}_S/\dot{Q}_T$ 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 $\dot{Q}_S/\dot{Q}_T$. 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-$\dot{V}_A/\dot{Q}$ 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 elimination. Surgery, cardiac: cardiopulmonary bypass.)**

IMPAIRED lung function is still a major complication after cardiac surgery and presents frequently with a reduced arterial oxygen tension (Pa_{O_2}) 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, Pa_{O_2}, mixed venous oxygen tension ($P\bar{v}_{O_2}$), and arterial carbon dioxide tension (Pa_{CO_2}) 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 ($P_A-a_{O_2}$), venous admixture, and dead space. Arterial blood gases are also influenced by nonpulmonary factors such as $P\bar{v}_{O_2}$ or cardiac output.

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Furthermore, alterations of inspired oxygen fraction have been shown to affect ventilation–perfusion ($\dot{V}_A/\dot{Q}$) 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 ($\dot{Q}_S/\dot{Q}_T$) may develop as a consequence of anesthesia; (2) that surgery and ECC have additional impact on $\dot{Q}_S/\dot{Q}_T$; and (3) that low cardiac output and $P\bar{v}_{O_2}$ due to ischemic cardiac disease contribute to decreased Pa_{O_2}. Finally, we hypothesized that perfusion of relatively hypoventilated alveoli ("low"-$\dot{V}_A/\dot{Q}$ regions) is a mechanism of impaired oxygenation, particularly during air-breathing. The multiple inert gas elimination technique (MIGET) allows an evaluation of $\dot{V}_A/\dot{Q}$ 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 $\dot{V}_A/\dot{Q}$ 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 flunitrazepam 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 β-adrenoceptor blocking drugs or nitrates was maintained on the day of surgery. Anesthesia (257 ± 59 min) was induced with intravenous fentanyl (5–10 $\mu g \cdot kg^{-1}$), thiopental (1.5–2.5 $mg \cdot kg^{-1}$), and pancuronium (0.1 $mg \cdot kg^{-1}$) 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 $ml \cdot kg^{-1}$) and ventilatory frequency were adjusted to maintain normal Pa_{CO_2} (Pa_{CO_2} = 36–44 mmHg). The membrane oxygenator (Maxima®, Medtronic, Anaheim, CA) was primed with 2,000 ml acetated 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 cardioplegic cardiac arrest (42 ± 17 min), which was achieved by infusion of 1,180 ± 350 ml cardioplegic 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 $\mu g \cdot kg^{-1} \cdot min^{-1}$) in each case during and after separation from ECC. In addition, one patient required positive inotropic support (dobutamine 5 $\mu g \cdot kg^{-1} \cdot min^{-1}$).

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 cetobemidon (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-

eter 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. Pa_{O_2}, $P\bar{v}_{O_2}$, and Pa_{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. $P_A–a_{O_2}$ 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.[19,22,23] A mixture of inert gases (sulphur hexafluoride, ethane, cyclopropane, enflurane, diethylether, and acetone) dissolved in isotonic saline was infused at a constant rate (3 $ml \cdot min^{-1}$) 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 $\dot{V}_A/Q < 0.005$ ($\dot{Q}_S/\dot{Q}_T$), perfusion of lung regions with $0.005 < \dot{V}_A/\dot{Q} < 0.1$ (low-$\dot{V}_A/\dot{Q}$ regions), ventilation of lung regions with $10 < \dot{V}_A/\dot{Q} < 100$ (high-$\dot{V}_A/\dot{Q}$ regions), ventilation of lung regions with $\dot{V}_A/\dot{Q} > 100$ (dead space [$\dot{V}_D/\dot{V}_T$]), the mean $\dot{V}_A/\dot{Q}$ ratio of the ventilation and perfusion distribution ($\dot{V}_{mean}$ of $\dot{V}_A/\dot{Q}$ and $\dot{Q}_{mean}$ 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.[24] Knowing the $\dot{V}_A/\dot{Q}$ distribution, blood flow, $P\bar{v}_{O_2}$, hemoglobin concentration, and slope of the oxygen dissociation curve, Pa_{O_2} can be determined by means of an iterative procedure.[25,26] Thus, expected (calculated) and measured Pa_{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.[27] After separation from ECC, the infusion of the inert gases was started (3 $ml \cdot min^{-1}$), 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

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 multiple analysis of variance.[28] Correlations between different 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 hemodynamic abnormalities were observed before, during, or after surgery. Mean systemic arterial pressure decreased 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 postoperative course. Cardiac index was higher after admission 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, Pa_{O_2} (83 ± 10 mmHg) and Pa_{CO_2} (40 ± 2 mmHg) while the patients were breathing air were normal. Pa_{O_2} was lower after premedication before induction of anesthesia (68 ± 8 mmHg, $P < 0.05$), and Pa_{CO_2} was slightly increased (44 ± 3 mmHg, $P < 0.05$). After induction of anesthesia, P_A–a_{O_2} increased 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, P_A–a_{O_2} had decreased to 97 ± 36 mmHg and was not statistically different from the values obtained after induction of anesthesia. On the 1st postoperative day, Pa_{O_2} while the patients were breathing air was lower when compared with the preanesthesia state (Pa_{O_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 ventilation and perfusion distributions to the raw data of retention and excretion was good throughout the investigation, and the remaining sum of squared differences remained < 6 in 50 of 54 individual measurements. The averaged difference between expected (calculated) and measured Pa_{O_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)

	Awake	After Induction of Anesthesia	After Sternotomy	After Extracorporeal Circulation	4 h Postoperatively	20 h Postoperatively
HR (beats/min)	55 ± 8	56 ± 10	62 ± 17	70 ± 15*	84 ± 10†	85 ± 10†
$P_{SA_{mean}}$ (mmHg)	98 ± 15	83 ± 11*	85 ± 5*	75 ± 5†	79 ± 6*	82 ± 11*
$P_{PA_{mean}}$ (mmHg)	21 ± 4	18 ± 4	18 ± 4	18 ± 4	19 ± 3	19 ± 4
P_{RA} (mmHg)	9 ± 5	8 ± 4	8 ± 4	9 ± 5	8 ± 3	7 ± 3
P_{PAO} (mmHg)	12 ± 4	11 ± 4	14 ± 5	14 ± 3	12 ± 3	10 ± 5
CI ($l \cdot min^{-1} \cdot m^2$)	2.11 ± 0.45	1.90 ± 0.57	1.85 ± 0.39	2.40 ± 0.63	2.78 ± 0.87*	2.58 ± 0.50*
Pa_{O_2} (mmHg)	68 ± 8	172 ± 56†	150 ± 48†	303 ± 76†	125 ± 33*	58 ± 6*
Pa_{CO_2} (mmHg)	44 ± 3	39 ± 4*	38 ± 12*	36 ± 4*	36 ± 5*	40 ± 3*
P_A-a_{O_2} (mmHg)	25 ± 10	126 ± 46†	148 ± 44†	341 ± 77†	97 ± 36*	40 ± 9*
Sa_{O_2} (%)	93.3 ± 2.7	97.9 ± 1.9†	98.2 ± 1.6†	99.4 ± 1.6†	97.8 ± 1.8†	91.5 ± 3.7*
$P\bar{v}_{O_2}$ (mmHg)	33 ± 3	41 ± 5†	39 ± 6†	42 ± 6†	39 ± 5*	29 ± 3*
$S\bar{v}_{O_2}$ (%)	65.7 ± 6.1	78.1 ± 4.4†	73.9 ± 5.7†	74.9 ± 6.8†	72.3 ± 10.4*	62.1 ± 12.6*
$\dot{V}_{O_2}I$ ($ml \cdot min^{-1} \cdot m^2$)	110 ± 25	74 ± 19†	71 ± 24†	116 ± 85	132 ± 32	122 ± 42
$\dot{D}_{O_2}I$ ($ml \cdot min^{-1} \cdot m^2$)	359 ± 112	338 ± 121	281 ± 121	487 ± 564*	368 ± 87	350 ± 123

HR = heart rate; $P_{SA_{mean}}$ = mean systemic arterial pressure; $P_{PA_{mean}}$ = mean pulmonary arterial pressure; P_{RA} = right atrial pressure; P_{PAO} = pulmonary artery occlusion pressure; CI = cardiac index; Pa_{O_2} = arterial oxygen tension; Pa_{CO_2} = arterial carbon dioxide tension, P_A-a_{O_2} = alveolar arterial P_{O_2} – gradient; Sa_{O_2} = arterial oxygen saturation; Pv_{O_2} = mixed venous oxygen tension; Sv_{O_2} = mixed venous oxygen saturation; $\dot{V}_{O_2}I$ = oxygen consumption index; $\dot{D}_{O_2}I$ = oxygen delivery index.

* $P < 0.05$.

† $P < 0.01$.

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)

	Awake	After Induction of Anesthesia	After Sternotomy	After Extracorporeal Circulation	4 h Postoperatively	20 h Postoperatively
RSSD	1.63 ± 1.4	1.96 ± 1.44	1.46 ± 0.87	3.11 ± 3.05	1.09 ± 0.58	1.44 ± 1.30
Q_{mean} of $\dot{V}_A/\dot{Q}$	0.66 ± 0.27	1.44 ± 1.49*	0.91 ± 0.32	1.17 ± 0.67	0.97 ± 0.58	0.83 ± 0.16
log SD_Q	0.86 ± 0.33	1.35 ± 0.44*	1.05 ± 0.43	1.16 ± 0.52	1.04 ± 0.44	0.68 ± 0.26
V_{mean} of $\dot{V}_A/\dot{Q}$	1.02 ± 0.49	2.75 ± 2.17*	1.71 ± 0.81	1.93 ± 0.97	1.64 ± 0.67	1.08 ± 0.31
log SD_V	0.57 ± 0.18	0.58 ± 0.1	0.72 ± 0.29	0.46 ± 0.10	0.63 ± 0.13	0.48 ± 0.10
F Q low $\dot{V}_A/\dot{Q}$ units	0.03 ± 0.05	0.09 ± 0.08	0.05 ± 0.05	0.05 ± 0.03	0.04 ± 0.05	0.01 ± 0.02
$\dot{Q}_S/\dot{Q}_T$	0.04 ± 0.04	0.10 ± 0.09	0.12 ± 0.08*	0.22 ± 0.08†	0.05 ± 0.04	0.11 ± 0.06*
F V high $\dot{V}_A/\dot{Q}$ units	0.02 ± 0.01	0.06 ± 0.01*	0.07 ± 0.01*	0.06 ± 0.01†	0.05 ± 0.02†	0.03 ± 0.01
$\dot{V}_D/\dot{V}_T$	0.43 ± 0.11	0.26 ± 0.10†	0.35 ± 0.04*	0.27 ± 0.09†	0.27 ± 0.08†	0.41 ± 0.10*
$\dot{Q}_T$ (l/min)	4.0 ± 1.1	3.7 ± 1.4	3.4 ± 0.9	4.6 ± 1.5	5.0 ± 1.2*	5.0 ± 0.9*
$\dot{V}_E$ (l/min)	5.7 ± 1.0	7.3 ± 1.1†	7.3 ± 1.1†	7.2 ± 1.1†	8.1 ± 1.8†	8.7 ± 1.5†
$F_{I_{O_2}}$	0.21	0.48 ± 0.04†	0.48 ± 0.04†	0.96 ± 0.01†	0.37 ± 0.04†	0.21

RSSD = remaining sum of squared differences; Q_{mean} of $\dot{V}_A/\dot{Q}$ = mean ventilation – perfusion ($\dot{V}_A/\dot{Q}$) ratio of perfusion distribution; log SD_Q = log standard deviation of perfusion; V_{mean} of $\dot{V}_A/\dot{Q}$ = mean ventilation – perfusion ratio of ventilation distribution; log SD_V = log standard deviation of ventilation; F Q of low $\dot{V}_A/\dot{Q}$ units = fraction of blood flow to low $\dot{V}_A/\dot{Q}$ units ($\dot{V}_A/\dot{Q}$ ratio of 0.005 – 0.1); $\dot{Q}_S\dot{Q}_T$ = inert gas shunt; F V high $\dot{V}_A/\dot{Q}$ units = fraction of ventilation to high $\dot{V}_A/\dot{Q}$ units ($\dot{V}_A/\dot{Q}$ ratio of 10 – 100); $\dot{V}_D/\dot{V}_T$ = inert gas dead space; $\dot{Q}_T$ = total blood flow (cardiac output); $\dot{V}_E$ = expired minute ventilation; $F_{I_{O_2}}$ = 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 $\dot{Q}_S/\dot{Q}_T$ (4 ± 4% of cardiac output) was observed. In addition, perfusion of low-$\dot{V}_A/\dot{Q}$ regions (3 ± 5% of cardiac output) was observed in four patients (patients 2, 6, 7, and 8). P_A–a_{O_2} was correlated with $\dot{Q}_S/\dot{Q}_T$ plus perfusion of low-$\dot{V}_A/\dot{Q}$ regions ($r = 0.63$, $P < 0.05$). Dead space ventilation averaged 43% with an expired minute volume of 5.7 ± 1.0 $l \cdot min^{-1}$. For an example, see figure 1.

After induction of anesthesia, $\dot{Q}_S/\dot{Q}_T$ 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-$\dot{V}_A/\dot{Q}$ regions (28% of cardiac output). Development of shunt was correlated with increased P_A–a_{O_2} ($r = 0.71$, $P < 0.05$). A broader perfusion distribution was observed in all patients as assessed by a higher log SD_Q ($P < 0.05$).

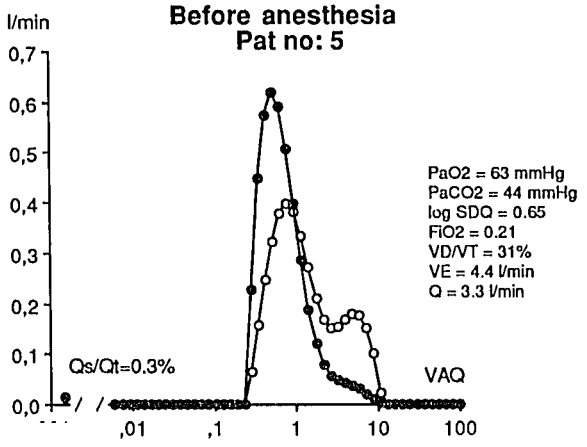
Sternotomy induced only small alterations of $\dot{Q}_S/\dot{Q}_T$, but after separation from ECC there was a marked increase of $\dot{Q}_S/\dot{Q}_T$, to 22 ± 8% ($P < 0.01$). Only a small fraction of cardiac output was distributed to low-$\dot{V}_A/\dot{Q}$ areas, and P_A–a_{O_2} was correlated with $\dot{Q}_S/\dot{Q}_T$ ($r = 0.77$, $P < 0.05$).

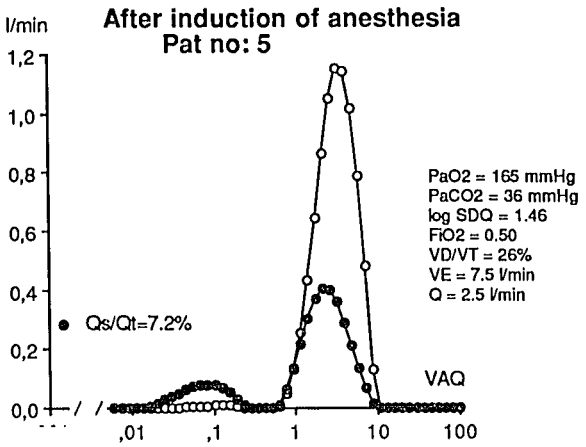
Four hours postoperatively, $\dot{Q}_S/\dot{Q}_T$ had decreased to less than presternotomy values, a state that in turn was associated with an improvement of P_A–a_{O_2}. On the 1st postoperative day, all patients revealed considerable amounts of shunt (11 ± 6%, $P < 0.05$) but almost no perfusion of low-$\dot{V}_A/\dot{Q}$ areas. A correlation was found between P_A–a_{O_2} and $\dot{Q}_S/\dot{Q}_T$ ($r = 0.82$, $P < 0.03$). Duration of anesthesia, cardiac surgery, or ECC were not correlated with P_A–a_{O_2} or $\dot{Q}_S/\dot{Q}_T$. Because $P\bar{v}_{O_2}$ was low the 1st postoperative day, its influence on arterial oxygenation was analyzed. This was done by recalculating the expected Pa_{O_2}, using the same $\dot{V}_A/\dot{Q}$ distribution, cardiac output, hemoglobin concentration, and oxygen dissociation curve as in the initial analysis but replacing the measured $P\bar{v}_{O_2}$ (29 mmHg on average; table 1) with a fixed value of 40 mmHg. This was done in all nine patients, and expected Pa_{O_2} increased from 59 ± 8 mmHg (the same as the measured value; table 1) to 69 ± 9 mmHg.

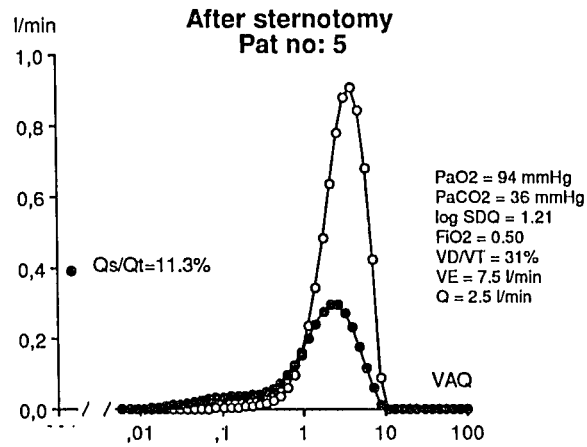
Discussion

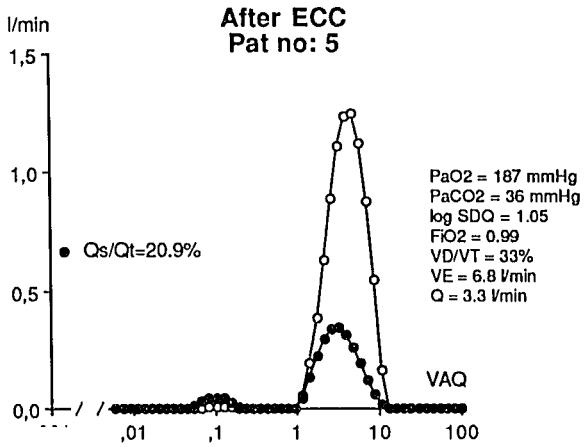
Ventilation–Perfusion Relationship in the Awake State and after Induction of Anesthesia

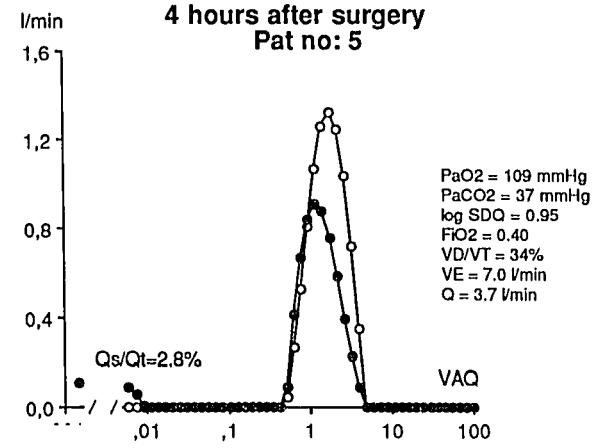
Before induction of anesthesia, Pa_{O_2} was lower than on the day before surgery. Both $\dot{Q}_S/\dot{Q}_T$ (4 ± 4% of cardiac output) and an increased scatter of $\dot{V}_A/\dot{Q}$ ratios (increased log SD_Q) with perfusion of low-$\dot{V}_A/\dot{Q}$ regions (3 ± 5% of cardiac output) contributed to the decreased Pa_{O_2}. The effects of premedication on respi-











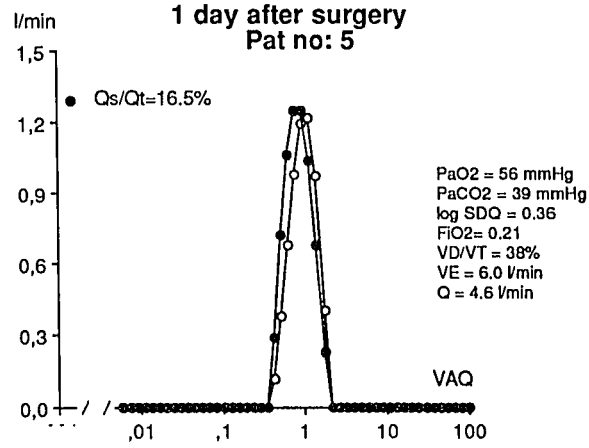


Fig. 1. Distribution of alveolar ventilation ($\dot{V}_A$, open circles) and blood flow ($\dot{Q}$, closed circles) against ventilation–perfusion ($\dot{V}_A/\dot{Q}$) ratio on a logarithmic scale. Each individual data point represents a defined fraction of $\dot{V}_A$ or $\dot{Q}$. Total blood flow 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 $0.005 < \dot{V}_A/Q < 0.1$ ("low"-$\dot{V}_A/\dot{Q}$ regions) after induction of anesthesia as well as the increased logarithmic standard deviation of perfusion (log SD_Q). After sternotomy, $\dot{Q}_S/\dot{Q}_T$ increased slightly, associated with decreased perfusion of low-$\dot{V}_A/\dot{Q}$ 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-$\dot{V}_A/\dot{Q}$ regions and the low log SD_Q, indicating a normal $\dot{V}_A/\dot{Q}$ distribution. $\dot{Q}$ = cardiac output; $\dot{V}_E$ = expired minute ventilation; V_D/V_T = dead space; $F_{I_{O_2}}$ = inspired oxygen fraction; ECC = extracorporeal circulation.

ratory 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. $\dot{V}_D/\dot{V}_T$ also was increased, although Pa_{CO_2} was still in the upper normal range (tables 1 and 2). In addition, $P\bar{v}_{O_2}$ and cardiac output were comparatively low, reflecting not only the effect of premedication but also the pretreatment with β-adrenoceptor blocking drugs in the majority of our patients. A decreased $P\bar{v}_{O_2}$ may substantially contribute to hypoxemia in the presence of impaired lung function, particularly during air-breathing.[20] Thus, the combined effects of $\dot{V}_A/\dot{Q}$ mismatch due to maldistribution of the inspired gas to dependent lung regions increased $\dot{V}_D/\dot{V}_T$ and $\dot{Q}_S/\dot{Q}_T$ and decreased $P\bar{v}_{O_2}$ have caused gas exchange impairment in cardiac surgical patients before induction of anesthesia.[20,29,30]

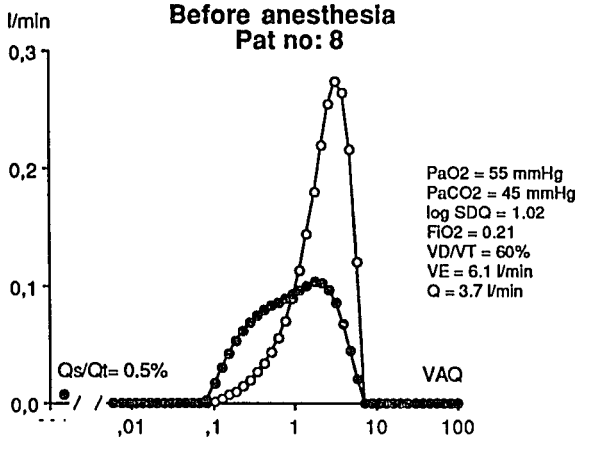
During anesthesia and muscle paralysis, mean $\dot{Q}_S/\dot{Q}_T$ was 10%, which agrees well with published data.[4,5,31] The reconstructed $\dot{V}_A/\dot{Q}$ curves also showed perfusion of low-$\dot{V}_A/\dot{Q}$ regions (figs. 1 and 2). A previous study with non–cardiac surgical patients has found a good correlation between oxygen tension–derived parameters (venous admixture) and perfusion of nonventilated areas plus low-$\dot{V}_A/\dot{Q}$ regions, as measured with MIGET both in the awake state and after induction of anesthesia.‖ Development of bilateral atelectasis as assessed by thoracic computed tomography has been identified as a major cause of shunt in anesthetized patients.[5,31] In our study, the rapid increase of $\dot{Q}_S/\dot{Q}_T$ 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-$\dot{V}_A/\dot{Q}$ areas (fig. 2) could be seen. Gunnarsson *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 $\dot{V}_A/\dot{Q}$ mismatching may occur.[32]

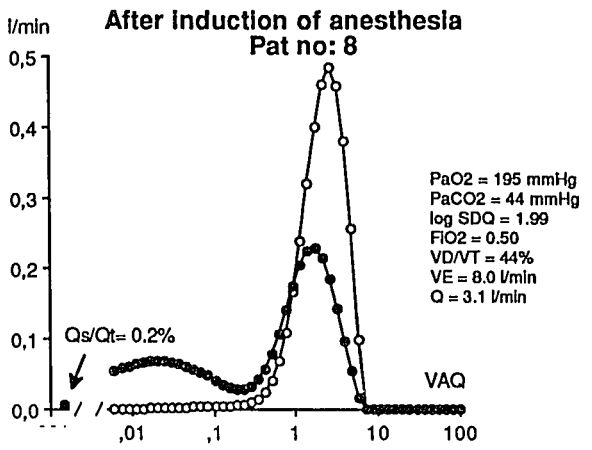
Ventilation–Perfusion Relationship after Sternotomy and Separation from Cardiopulmonary Bypass

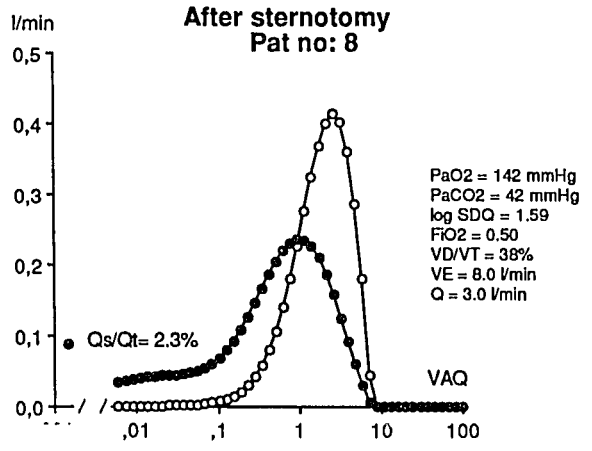
Sternotomy had only minor effects on systemic and pulmonary hemodynamics and on gas exchange. Lung volume may have increased after sternotomy,# and $\dot{V}_A/\dot{Q}$ relationships showed an elevated dead space, increased ventilation of high-$\dot{V}_A/\dot{Q}$ areas, and diminished perfusion of low-$\dot{V}_A/\dot{Q}$ regions (table 2). However, these changes were small and were not associated with marked alteration of P_A–a_{O_2}. After separation from ECC, lung function was significantly impaired, and $\dot{Q}_S/\dot{Q}_T$ had almost doubled. Despite a potentially unstable situation after cardiopulmonary bypass, the retention and excretion data of the inert gases resulted in technically adequate $\dot{V}_A/\dot{Q}$ distributions (table 2), and measured and calculated (from $\dot{V}_A/\dot{Q}$ distribution) Pa_{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, *p*H, 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.[33] 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.[10,11,34] The density and weight of pul-

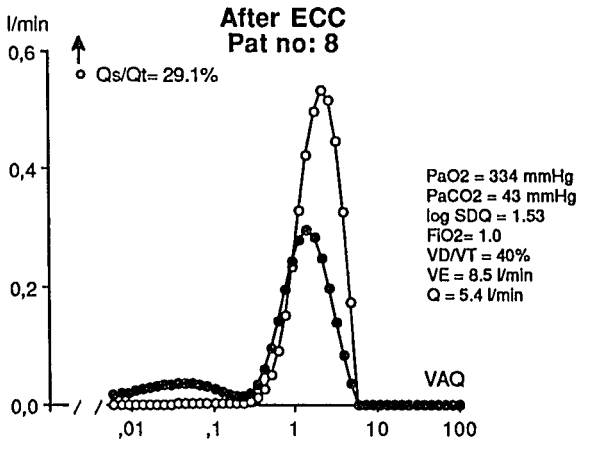
‖ Gunnarsson L: Atelectasis, ventilation distribution and gas exchange during anesthesia and in the postoperative period. Thesis. University of Uppsala, 1991, pp 20–30.

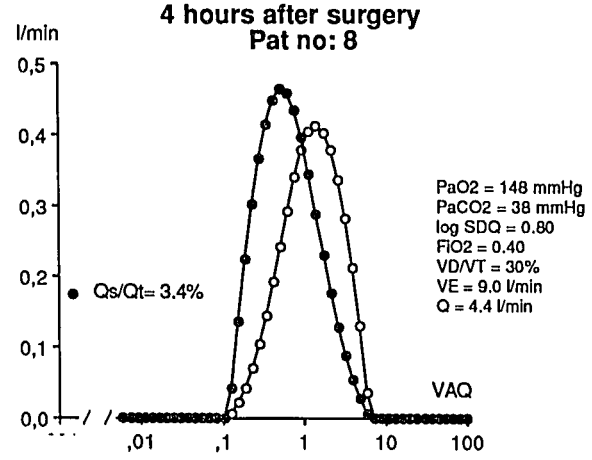
Jonmarker C: Measurement of functional residual capacity by sulfur hexafluroide washout. Thesis. University of Lund, 1985, pp 16–27.











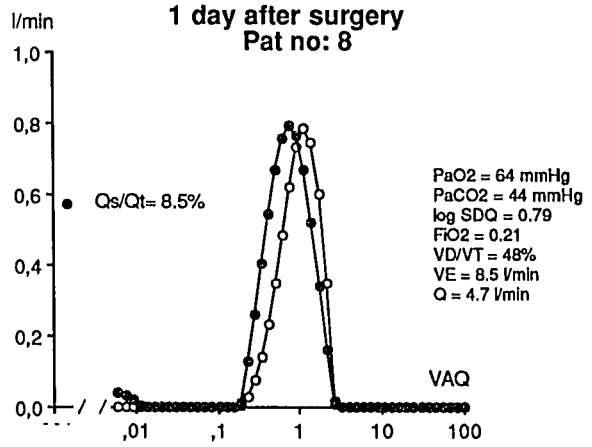


Fig. 2. Ventilation–perfusion ($\dot{V}_A/\dot{Q}$) distribution determined during the same points of time in a patient with moderate obstructive pulmonary disease. Note the absence of shunt ($\dot{Q}_S/\dot{Q}_T$) before and after induction of anesthesia, but a high fraction of blood flow to regions with "low" $\dot{V}_A/\dot{Q}$ ratio. Sternotomy had only minor effects on gas exchange, but significant $\dot{Q}_S/\dot{Q}_T$ was observed after separation from ECC. However, his arterial oxygen tension was higher than that of patient 5 (fig. 1), despite an increased $\dot{Q}_S/\dot{Q}_T$, which can be explained by the higher cardiac output and mixed venous oxygen tension (data not shown). Postoperatively, the same alterations were observed as in patient 5. $\dot{Q}$ = cardiac output; $\dot{V}_E$ = expired minute ventilation; V_D/V_T = dead space; log SD_Q = logarithmic standard deviation of perfusion; $F_{I_{O_2}}$ = inspired oxygen fraction; ECC = extracorporeal circulation.

monary parenchyma increase in the presence of edema, which could also aggravate formation of atelectasis in dependent lung areas.[35,36] 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.[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 $\dot{Q}_S/\dot{Q}_T$ 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.[33] Thus, rapid recovery of lung function after uncomplicated coronary artery bypass graft surgery is unlikely to be a consequence of resorption of lung edema.[11]

Our postoperative data during mechanical ventilation partly agree with earlier studies using MIGET after cardiac surgery. Anjou-Lindskog *et al.* studied patients during mechanical ventilation on the 1st postoperative day after myocardial revascularization and observed an average $\dot{Q}_S/\dot{Q}_T$ of 6.4–7.5%.[17,37] After aortic valve replacement, Gillespie *et al.* found a mean $\dot{Q}_S/\dot{Q}_T$ of 6.1% and an increased log SD_Q, indicating significant $\dot{V}_A/\dot{Q}$ heterogeneity.[38] In contrast, Dantzker *et al.* reported a $\dot{Q}_S/\dot{Q}_T$ of 17.9% 12–18 h after coronary artery bypass surgery.[39] In their study, shunt was defined as perfusion of lung units with $\dot{V}_A/\dot{Q} < 0.01$, and preoperative lung function test revealed a higher incidence of airway obstruction as well as restrictive pulmonary disease.

On the 1st postoperative day, $\dot{Q}_S/\dot{Q}_T$ had increased to 11 ± 6%, but little perfusion of low-$\dot{V}_A/\dot{Q}$ regions was observed (figs. 1 and 2). Oxygenation was significantly more impaired than in the preanesthesia state. In addition to the more pronounced $\dot{V}_A/\dot{Q}$ mismatch, decreased $P\bar{v}_{O_2}$ may have contributed significantly to decreased Pa_{O_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 *et al.*, who found an increase of $\dot{Q}_S/\dot{Q}_T$ and $\dot{V}_A/\dot{Q}$ mismatch when conditions were switched from mechanical ventilation to spontaneous breathing.[39] The close relationship between $\dot{Q}_S/\dot{Q}_T$ and $P_A-a_{O_2}$ 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.[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.[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.[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.[42,43] Second, a high inspiratory oxygen fraction increases $P_A-a_{O_2}$ and $\dot{Q}_S/\dot{Q}_T$, probably by release of hypoxic pulmonary vasoconstriction,[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.[44] Finally, ventilation with 100% oxygen may induce development of absorption atelectasis, particularly in the presence of low-$\dot{V}_A/\dot{Q}$ regions.[22] A simple test of the influence on arterial oxygenation of $P\bar{v}_{O_2}$ was made by replacing measured

$P\bar{v}_{O_2}$ by a fixed value of 40 mmHg. This resulted in a considerable increase in the calculated Pa_{O_2} with given $\dot{V}_A/\dot{Q}$ distributions. It can thus be concluded that $P\bar{v}_{O_2}$ has an important effect on Pa_{O_2} during the postoperative period. However, it should be made clear that many factors will influence $P\bar{v}_{O_2}$, such as cardiac output, oxygen uptake, oxygen dissociation curve, hemoglobin concentration, $\dot{V}_A/\dot{Q}$ distribution, and $\dot{Q}_S/\dot{Q}_T$. "Normalization" of $P\bar{v}_{O_2}$ 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 $\dot{Q}_S/\dot{Q}_T$. In addition, a decreased $P\bar{v}_{O_2}$ 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 $\dot{Q}_S/\dot{Q}_T$. Postoperatively, additional mechanisms such as altered mechanics of the chest, perfusion of low-$\dot{V}_A/\dot{Q}$ regions, and decreased $P\bar{v}_{O_2}$ may contribute to impaired gas exchange.

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References

1. Hammermeister KE, Burchfiel C, Johnson R, Grover FL: Identification of patients at greatest risk for developing major complications at cardiac surgery. Circulation 82(suppl IV):IV-380–IV-389, 1990

2. Singh NP, Vargas FS, Cukier A, Terra-Filho M, Teixeira LR, Light RW: Arterial blood gases after coronary bypass surgery. Chest 102: 1337–1341, 1992

3. Braun SR, Birnbaum ML, Chopra PS: Pre- and postoperative pulmonary function abnormalities in coronary artery revascularization surgery. Chest 3:316–320, 1978

4. Dueck R, Young I, Clausen J, Wagner PD: Altered distribution of pulmonary ventilation and blood flow following induction of inhalation anesthesia. ANESTHESIOLOGY 52:113–125, 1980

5. Hedenstierna G, Tokics L, Strandberg A, Lundquist H, Brismar B: Correlations of gas exchange impairment to development of atelectasis during anaesthesia and muscle paralysis. Acta Anaesthesiol Scand 30:183–191, 1986

6. Kenyon CM, Pedley TJ, Higenbottam TW: Adaptive modelling of the human rib cage in median sternotomy. J Appl Physiol 70: 2287–2302, 1991

7. Jenkins SC, Soutar SA, Forsyth A, Keates JRW, Moxham J: Lung function after coronary artery surgery using the internal mammary artery and the saphenous vein. Thorax 44:209–211, 1989

8. Andersen NB, Ghia J: Pulmonary function, cardiac status, and postoperative course in relation to cardiopulmonary bypass. J Thorac Cardiovasc Surg 59:474–483, 1970

9. Anyanwu E, Dittrich H, Gieseking R, Enders HJ: Ultrastructural changes in the human lung following cardiopulmonary bypass. Basic Res Cardiol 77:309–322, 1982

10. Royston D, Minty BD, Higenbottam TW, Wallwork J, Jones JG: The effect of surgery with cardiopulmonary bypass on alveolar-capillary barrier function in human beings. Ann Thorac Surg 40:139–143, 1982

11. MacNaughton PD, Braude S, Hunter DN, Denison DM, Evans TW: Changes in lung function and pulmonary capillary permeability after cardiopulmonary bypass. Crit Care Med 20:1289–1294, 1992

12. Stanley TH, Liu WS, Gentry S: Effects of ventilatory techniques during cardiopulmonary bypass on postbypass and postoperative pulmonary compliance and shunt. ANESTHESIOLOGY 46:391–395, 1977

13. Benjamin JJ, Cascade PN, Rubenfire M, Wajszcuk W, Kerin NZ: Left lower lobe atelectasis and consolidation following cardiac surgery: The effect of topical cooling on the phrenic nerve. Radiology 142:11–14, 1982

14. Locke TJ, Griffiths, Mould H, Gibson GJ: Rib cage mechanics after median sternotomy. Thorax 45:465–468, 1990

15. Schwieger I, Gamulin Z, Suter PM: Lung function during anaesthesia and respiratory insufficiency in the postoperative period: Physiological and clinical implications. Acta Anaesthesiol Scand 33: 527–534, 1989

16. Riley RL, Cournand A: "Ideal" alveolar air and the analysis of ventilation-perfusion relationships in the lungs. J Appl Physiol 1: 825–847, 1949

17. Anjou-Lindskog E, Broman L, Broman M, Holmgren A: Effects of oxygen on central haemodynamics and $\dot{V}_A/\dot{Q}$ distribution after coronary bypass surgery. Acta Anaesthesiol Scand 27:378–384, 1983

18. Dantzker DR, Wagner PD, West JB: Instability of lung units with low V_A/Q ratios during O_2 breathing. J Appl Physiol 38:886–895, 1975

19. Wagner PD, Saltzman HA, West JB: Measurement of continuous distribution of ventilation-perfusion ratios: Theory. J Appl Physiol 36:588–599, 1974

20. Rodriguez-Rosin R, Wagner PD: Clinical relevance of ventilation-perfusion inequality determined by inert gas elimination. Eur Respir J 3:469–482, 1990

21. Tisi GM. Preoperative evaluation of pulmonary function. Am Rev Respir Dis 119:293–310, 1979

22. Wagner PD, Lavaruso RB, Uhl RR, West JB: Continuous distribution of ventilation-perfusion distribution in normal subjects breathing air and 100% O_2. J Clin Invest 54:54–68, 1974

23. Evans JW, Wagner PD: Limits of $\dot{V}_A/\dot{Q}$ distributions from analysis of experimental inert gas elimination. J Appl Physiol 42:889–989, 1977

24. Wagner PD, West JB: Ventilation-perfusion relationships, Pulmonary Gas Exchange. Edited by West JB. New York, Academic Press, 1980, pp 219–262

25. Kelman GR: Digital computer sub-routine for the conversion of oxygen tension into saturation. J Appl Physiol 21:1375–1376, 1966

26. Kelman GR: Digital computer procedure for the conversion of P_{CO_2} into blood CO_2 content. Respir Physiol 3:111–115, 1967

27. Bazaral MG, Petre J, Novoa R: Errors in thermodilution cardiac output measurements caused by rapid pulmonary artery temperature decreases after cardiopulmonary bypass. ANESTHESIOLOGY 77:31–37, 1992

28. Sachs L: Angewandte Statistik. Berlin, Springer-Verlag 1992, pp 664–673

29. Dueck R, Prutow RJ, Davies NJH, Clausen JL, Davidson TM: The lung volume at which shunting occurs with inhalation anesthesia. ANESTHESIOLOGY 69:854–861, 1988

30. Leblanc P, Ruff F, Milic-Emili J: The effects of age and body position on "airway closure" in man. J Appl Physiol 28:448–455, 1970

31. Tokics L, Hedenstierna G, Strandberg A, Brismar B, Lundquist H: Lung collapse during general anesthesia: Effects of spontaneous breathing, muscle paralysis, and positive end-expiratory pressure. ANESTHESIOLOGY 66:157–167, 1987

32. Gunnarsson L, Tokics L, Lundquist H, Brismar B, Strandberg A, Berg B, Hedenstierna G: Chronic obstructive pulmonary disease and anaesthesia: Formation of atelectasis and gas exchange impairment. Eur Respir J 4:1106–1116, 1991

33. Hachenberg T, Tenling A, Rothen HU, Nyström SO, Tyden H, Hedenstierna G: Thoracic intravascular and extravascular fluid volumes in cardiac surgical patients. ANESTHESIOLOGY 79:976–984, 1993

34. Byrick RJ, Kay JC, Noble WN: Extravascular lung water accumulation in patients following coronary artery surgery. Can Anaesth Soc J 24:332–345, 1977

35. Gattinoni L, Pesenti A, Bombino M, Baglionmi S, Rivolta M, Rossi F, Rossi GP, Fumagalli R, Marcolin R, Mascheroni D, Torresin A: Relationships between lung computed tomographic density, gas exchange, and PEEP in acute repiratory failure. ANESTHESIOLOGY 69: 824–832, 1988

36. Hedlund LW, Effmann EL, Bates WM, Beck JW, Goulding PL, Putman CE: Pulmonary edema: A CT study of regional changes in lung density following oleic acid injury. J Comput Assist Tomogr 6: 939–946, 1982

37. Anjou-Lindskog E, Broman L, Holmgren A: Effects of nitroglycerin on central haemodynamics and $\dot{V}_A/\dot{Q}$ distribution early after cardiac surgery. Acta Anaesthesiol Scand 26:489–497, 1982

38. Gillespie DJ, Didier EP, Rehder K: Venilation-perfusion distribution after aortic valve replacement. Crit Care Med 18:136–140, 1990

39. Dantzker DR, Covenhagen WM, Willoughby WJ, Kirsh M, Bower JS: Gas exchange alterations associated with weaning from mechanical ventilation following coronary artery bypass grafting. Chest 82:674–677, 1982

40. Hachenberg T, Brüssel T, Roos N, Lenzen H, Möllhoff T, Gockel B, Konertz W, Wendt M: Gas exchange impairment and pulmonary densities after cardiac surgery. Acta Anaesthesiol Scand 36:800–805, 1992

41. Benumof JL: Mechanisms of decreased blood flow to atelectatic lung. J Appl Physiol 46:216–228, 1979

42. Colley PS, Cheney FW, Hlastala MP: Pulmonary gas exchange effects of nitroglycerin in canine edematous lungs. ANESTHESIOLOGY 55:114–119, 1981

43. Marshall BE, Marshall C, Benumof J, Saidman LJ: Hypoxic pulmonary vasoconstriction in dogs: Effects of lung segment size and oxygen tension. J Appl Physiol 51:1543–1551, 1981

44. Bjertnaess LJ: Hypoxia-induced vasoconstriction in isolated perfused lungs exposed to injectable or inhalation anaesthetics. Acta Anaesthesiol Scand 21:133–147, 1977