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The Ventilation-Perfusion Relation and Gas Exchange in Mitral Valve Disease and Coronary Artery Disease

Implications for Anesthesia, Extracorporeal Circulation, and Cardiac Surgery

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Background: Patients with mitral valve disease (MVD) are at greater risk for respiratory complications after cardiac surgery compared with patients with coronary artery disease (CAD). The authors hypothesized that ventilation-perfusion (\dot{V}_A/\dot{Q}) inequality is more pronounced in patients with MVD before and after induction of anesthesia and during and after surgery when extracorporeal circulation (ECC) is used.

Methods: In patients with MVD ($n = 12$) or with CAD ($n = 12$), \dot{V}_A/\dot{Q} distribution was determined using the multiple inert gas elimination technique. Intrapulmonary shunt (\dot{Q}_s/\dot{Q}_T) defined as regions with $\dot{V}_A/\dot{Q} < 0.005$ [% of total perfusion (\dot{Q}_T)], perfusion of "low" \dot{V}_A/\dot{Q} areas ($0.005 \leq \dot{V}_A/\dot{Q} < 0.1$, [% of \dot{Q}_T]), ventilation of "high" \dot{V}_A/\dot{Q} regions ($10 \leq \dot{V}_A/\dot{Q} \leq 100$ [% of total ventilation \dot{V}_E]), and dead space ($\dot{V}_A/\dot{Q} > 100$ [% of \dot{V}_E]) were calculated from the retention/excretion data of the inert gases. Recordings were obtained while patients spontaneously breathed air in the awake state, during mechanical ventilation after induction of anesthesia, after separation of patients from ECC, and 4 h after operation.

Results: \dot{Q}_s/\dot{Q}_T was low in the awake state (MVD group, $3\% \pm 3\%$; CAD group, $3\% \pm 4\%$) and increased after induction of anesthesia to $10\% \pm 8\%$ (MVD group, $P < 0.05$) and $11\% \pm 7\%$ (CAD group, $P < 0.01$). \dot{Q}_s/\dot{Q}_T increased further after sepa-

ration from ECC (MVD group, $24\% \pm 9\%$, $P < 0.01$; CAD group, $23\% \pm 7\%$, $P < 0.01$). Similarly, alveolar-arterial oxygen tension difference (P_A-aO_2) increased from 168 ± 54 mmHg (anesthetized state) to 427 ± 138 mmHg after ECC (MVD group, $P < 0.01$) and from 153 ± 65 mmHg to 377 ± 101 mmHg (CAD group, $P < 0.01$). In both groups, P_A-aO_2 was correlated with \dot{Q}_s/\dot{Q}_T . Four hours after operation, \dot{Q}_s/\dot{Q}_T had decreased significantly to $8\% \pm 6\%$ (CAD group) and $10\% \pm 6\%$ (MVD group). P_A-aO_2 and \dot{Q}_s/\dot{Q}_T showed no significant differences between the CAD and MVD groups.

Conclusions: \dot{Q}_s/\dot{Q}_T is the main pathophysiologic mechanism of gas exchange impairment during cardiac surgery for MVD or CAD. Impairment of pulmonary gas exchange secondary to general anesthesia, cardiac surgery, and ECC are comparable for patients undergoing myocardial revascularization or mitral valve surgery. (Key words: Measurement techniques: multiple inert gas elimination technique. Lung: ventilation-perfusion; gas exchange. Surgery, cardiac. Mitral valve. Cardiopulmonary bypass.)

MITRAL valve disease (MVD) frequently is associated with pathologic changes of respiratory function such as decreased lung volumes,^{1,2} reduced pulmonary diffusing capacity for oxygen and carbon monoxide,³ inhomogeneities of regional lung perfusion,⁴ premature closure of peripheral airways,⁴ bronchial hyperresponsiveness causing decreased airway conductance,⁵ increased physiologic dead space ventilation,¹ and decreased static and dynamic lung compliance.²

Mitral valve surgery requires general anesthesia and muscle paralysis, mechanical ventilation, thoracotomy, and in most cases use of extracorporeal circulation (ECC), which may all substantially influence lung function.⁶⁻⁸ Acute respiratory failure and prolonged mechanical ventilation constitute a major complication after cardiac surgery, particularly in patients undergoing mitral valve replacement.⁹⁻¹² Thus a quantitative analy-

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Table 1. Demographic Data

	Mitral Valve Disease (n = 12)	Coronary Artery Disease (n = 12)	Significance
Age (yr)	65 ± 11 (48–78)	67 ± 6 (49–75)	NS
Height (cm)	172 ± 8 (156–183)	172 ± 8 (156–181)	NS
Weight (kg)	73 ± 6 (63–86)	79 ± 15 (62–104)	NS
Duration of anesthesia (min)	271 ± 32 (230–320)	259 ± 51 (165–325)	NS
Duration of surgery (min)	218 ± 30 (175–260)	189 ± 38 (110–260)	NS
Duration of ECC (min)	112 ± 20 (75–140)	89 ± 28 (52–147)	$P < 0.05$
Duration of cardioplegic cardiac arrest (min)	72 ± 18 (48–98)	44 ± 17 (23–71)	$P < 0.01$

NS = not significant. ECC = extracorporeal circulation.

All values represent mean ± standard deviation (range).

sis of factors impeding gas exchange in mitral valve surgery is of both theoretical and clinical value. In a previous study of patients with coronary artery disease (CAD) having cardiac surgery, we found that intrapulmonary shunt increased after separation from ECC.¹³ In the present investigation, our hypotheses were (1) that in the awake state and after induction of anesthesia, \dot{V}_A/\dot{Q} mismatch is more pronounced in MVD than in CAD; (2) that an increase of shunt or perfusion of "low" \dot{V}_A/\dot{Q} regions after cardiopulmonary bypass is more marked in MVD; and (3) that, because of preexisting chronic pulmonary venous hypertension, recovery of \dot{V}_A/\dot{Q} inequality is less complete early after mitral valve surgery than after myocardial revascularization. Using the multiple inert gas elimination technique, we studied the implications of general anesthesia, extracorporeal circulation, and surgical procedure on \dot{V}_A/\dot{Q} relations in a group of patients undergoing mitral valve replacement and in a group of patients subjected to coronary artery bypass graft surgery.

Materials and Methods

We studied 12 patients with MVD and 12 patients with CAD. Table 1 shows the demographic data of both groups. Nine patients in the MVD group had mitral regurgitation, one patient had mitral stenosis, and two patients had a mixed lesion with predominant mitral stenosis. Preoperative lung function tests revealed a forced vital capacity of 3.4 ± 0.9 l (82% ± 12% of predicted value) and a forced expiratory volume in 1 s of 2.7 ± 0.8 l (83% ± 14% of predicted value). Patients with significantly impaired lung function, concomitant ischemic heart disease due to coronary artery stenosis,

or diseases of additional heart valves were excluded from the MVD group. Inclusion criteria for the CAD group were (1) stable angina pectoris, (2) left ventricular ejection fraction greater than 40%, (3) left ventricular end-diastolic pressure less than 15 mmHg, and (4) absence of marked preoperative lung dysfunction.¹⁴ Forced vital capacity was 3.7 ± 1.0 l (85 ± 14% of predicted value) and forced expiratory volume in 1 s was 2.9 ± 0.9 l (84 ± 12% of predicted value). Patients with coexisting cardiac valvular, renal, hepatic, or cerebrovascular diseases or diabetes mellitus type I were excluded from the investigation. 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 were given preoperative medication and anesthesia according to standard procedures at our institution. Morphine (10–15 mg) and scopolamine (0.4–0.6 mg) were given intramuscularly 60 min before the study. General anesthesia was induced with intravenous doses of fentanyl (5–10 µg/kg), thiopental (1.5–2.5 mg/kg), and pancuronium (0.1 mg/kg) and maintained by additional doses of fentanyl and a volatile inhalational anesthetic (halothane or enflurane 0.5–1.0%). The lungs were mechanically ventilated and tidal volume (V_T = 8–10 ml/kg) and ventilatory frequency (f = 8–14 V_T /min) were adjusted to maintain normal levels of arterial carbon dioxide (P_{CO_2} ; P_{aCO_2} , 36–44 mmHg). The Inspired oxygen fraction (F_{IO_2}) in nitrogen was 50% in both groups. Anticoagulation was provided by intravenous doses of acetone-free heparin¹⁵ (initial bolus, 300 IE/kg) and monitored according to the activated clot-

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ting time. The membrane oxygenator (Maxima; Medtronic, Anaheim, CA) was primed with 1,500–2,000 ml acetated Ringer's solution. During ECC, body core temperature was decreased to $30 \pm 0.5^\circ\text{C}$. Mechanical ventilation was stopped and the lungs were maintained in a noninflated state during cold cardioplegic arrest. A left atrial or ventricular vent was used in all patients. After declamping the aorta, the lungs were ventilated with 100% oxygen with one half the minute volume used before ECC, and full ventilation was restored before patients were separated from ECC. No positive end-expiratory pressure was applied before, during, or after cardiopulmonary bypass.¹⁶ Nitroglycerin was given ($0.2\text{--}2.0 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$) to each patient after they were separated from ECC. Mean doses were not statistically different between the groups. Eight patients in the MVD group and five patients in the CAD group required positive inotropic support (dobutamine, $5\text{--}10 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$), and the difference was not statistically significant. Mitral valve replacement was performed in each patient of the MVD group, and the duration of ECC and cardioplegic cardiac arrest were significantly longer compared with the CAD group (table 1). In the intensive care unit, mechanical ventilation was maintained in the manner already described (F_{IO_2} , 50%) until the patient began to breath spontaneously. Adequate analgesia and sedation were achieved according to standard procedures at our institution. All patients were tracheally extubated 6 to 16 h after surgery. The duration of postoperative mechanical ventilation was not significantly different between both the two patient groups.

Cardiopulmonary Monitoring

Left or right radial arterial pressure was measured using a 20 gauge peripheral catheter. A triple-lumen, thermistor-tipped catheter was introduced transcutaneously through the right jugular vein into a pulmonary artery. Cardiac output was measured by thermodilution. The mean of three measurements was calculated and used for statistical evaluation. Systemic arterial pressure, pulmonary arterial pressure, right atrial pressure, and pulmonary arterial occlusion pressure (P_{PAO}) relative to atmospheric pressure were measured. Mean systemic arterial pressure (\bar{P}_{SA}) and mean pulmonary arterial pressure (\bar{P}_{PA}) were obtained by electric integration of the pressure signal. The electrocardiograph lead II was continuously recorded and used to calculate heart rate. Arterial and mixed venous oxygen tensions (P_{aO_2} , P_{vO_2}) and carbon dioxide tension (P_{aCO_2}) were determined by standard techniques (ABL 3 Radiometer, Copenhagen, Denmark). Arterial and mixed venous oxygen satura-

tions (S_{aO_2} , S_{vO_2}) were measured by spectrophotometry (OSM 3 Radiometer, Copenhagen, Denmark). The alveolar-arterial P_{O_2} gradient ($P_{\text{A-aO}_2}$) was calculated from the alveolar gas equation and measured P_{aO_2} .¹⁷

Measurement of Ventilation-Perfusion Distribution

The \dot{V}_A/\dot{Q} distribution was analyzed according to the multiple inert gas elimination technique described by Wagner *et al.*^{18–20} A mixture of inert gases (sulphur hexafluoride, ethane, cyclopropane, enflurane or halothane, diethylether, and acetone) dissolved in isotonic saline was infused continuously (3 ml/min) into a peripheral vein. A period of 40 min was allowed to ensure equilibration of the infused inert gases. Arterial and mixed venous blood samples and mixed expired gas samples were obtained and analyzed by gas chromatography (5880A, Hewlett Packard, Avondale). Assessment of retention and excretion of the inert gases allowed calculation of perfusion of lung regions with $\dot{V}_A/\dot{Q} < 0.005$ (intrapulmonary shunt [\dot{Q}_s/\dot{Q}_T]), perfusion of lung regions with $0.005 \leq \dot{V}_A/\dot{Q} \leq 0.1$ ("low" \dot{V}_A/\dot{Q} regions), ventilation of lung regions with $10 \leq \dot{V}_A/\dot{Q} \leq 100$ ("high" \dot{V}_A/\dot{Q} regions), and ventilation of lung regions with $\dot{V}_A/\dot{Q} > 100$ (dead space [V_D/\dot{V}_T]). In addition, the mean distribution of ventilation and perfusion (\bar{V}_{mean} of \dot{V}_A/\dot{Q} and \bar{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 ($\log \text{SD}_V$, $\log \text{SD}_Q$) were determined. The technical quality of the \dot{V}_A/\dot{Q} distribution was analyzed using the remaining sum of squared differences between measured and calculated retentions and excretions. The remaining sum of squared differences should not exceed 6 in more than 50% of the tests.²⁰ Based on the calculated \dot{V}_A/\dot{Q} distribution, measured blood flow, mixed venous P_{O_2} , hemoglobin concentration and the slope of the dissociation curve, the expected P_{aO_2} was determined using an iterative procedure^{21,22} and compared with measured P_{aO_2} .

General Protocol

The patients were catheterized in the awake state and the infusion of inert gases was started. After a period of 40 min for equilibration of the inert gases, hemodynamic and respiratory data were determined while the patient was breathing air (1 = control state). General anesthesia was induced and the patient was mechanically ventilated. Another set of data was recorded after

Table 2. Cardiopulmonary Data (mean \pm one standard deviation) in the Mitral Valve Disease Group (MVD; n = 12) and in the Coronary Artery Disease Group (CAD; n = 12)

	Before Induction of Anesthesia		After Induction of Anesthesia		After Separation from ECC		4 Hours after Cardiac Surgery	
	MVD	CAD	MVD	CAD	MVD	CAD	MVD	CAD
HR (beats \cdot min ⁻¹)	64 \pm 6*	52 \pm 11	67 \pm 10*	54 \pm 10	87 \pm 12*†	68 \pm 15†	92 \pm 11†	89 \pm 13†
P _{SA} (mmHg)	95 \pm 19	101 \pm 14	80 \pm 10‡	85 \pm 10‡	75 \pm 10‡	78 \pm 6‡	78 \pm 6‡	78 \pm 6‡
P _{PA} (mmHg)	30 \pm 8‡	19 \pm 3	24 \pm 7*‡	17 \pm 4	24 \pm 5*‡	19 \pm 4	24 \pm 8*‡	19 \pm 3
P _{RA} (mmHg)	9 \pm 4	9 \pm 4	8 \pm 4	8 \pm 3	11 \pm 4	10 \pm 4	9 \pm 5	9 \pm 3
P _{PAO} (mmHg)	20 \pm 6§	13 \pm 3	16 \pm 4*‡	9 \pm 3	15 \pm 5‡	14 \pm 3	13 \pm 5†	11 \pm 3
CI (l \cdot min ⁻¹ \cdot m ⁻²)	1.9 \pm 0.5	2.0 \pm 0.4	1.7 \pm 0.3	1.8 \pm 0.5	2.3 \pm 0.4‡	2.3 \pm 0.6	2.3 \pm 0.5‡	2.5 \pm 0.9‡
P _{aO₂} (mmHg)	73 \pm 11	76 \pm 6	149 \pm 59†	166 \pm 60†	246 \pm 119†	283 \pm 95†	114 \pm 25†	125 \pm 34†
P _{aCO₂} (mmHg)	42 \pm 3	43 \pm 3	36 \pm 4‡	38 \pm 6‡	37 \pm 3‡	36 \pm 4‡	37 \pm 7‡	36 \pm 4‡
P _{V_{O₂}} (mmHg)	35 \pm 4	33 \pm 3	38 \pm 3‡	40 \pm 6‡	39 \pm 6‡	40 \pm 6‡	35 \pm 5	38 \pm 9
P _{A-aO₂} (mmHg)	33 \pm 15	30 \pm 13	168 \pm 54†	153 \pm 65†	427 \pm 138†	377 \pm 101†	158 \pm 50†	127 \pm 61†

HR = heart rate; P_{SA} = mean systemic arterial pressure; P_{PA} = mean pulmonary arterial pressure; P_{RA} = right atrial pressure; P_{PAO} = pulmonary artery occlusion pressure; CI = cardiac index; P_{aO₂} = arterial oxygen tension; P_{aCO₂} = arterial carbon dioxide tension; P_{V_{O₂}} = mixed venous oxygen tension; P_{A-aO₂} = alveoloarterial P_{O₂} - gradient; ECC = extracorporeal circulation.

* $P < 0.05$.

† $P < 0.01$ (compared with the control state).

‡ $P < 0.05$.

§ $P < 0.01$ (MVD vs. CAD).

a period of 20 min to achieve stable hemodynamic and respiratory conditions (2 = anesthesia). Approximately 45 min after cardiopulmonary bypass and 10 to 15 min after closure of the sternum, ventilatory and hemodynamic measurements were made during stable cardiopulmonary conditions (3 = 45 min after ECC). Four hours after admission to the intensive care unit, cardiopulmonary status was determined during sedation and controlled mechanical ventilation (4 = 4 h after operation). The patients were kept supine before and after induction of anesthesia, during cardiac surgery, and during mechanical ventilation in the intensive care unit.

Statistical Analysis

The data were analyzed on a Systat statistical program (Systat, Evanston, IL) and are presented as mean values \pm standard deviation. Differences between nominal measures were analyzed using the chi squared test. The significance of a difference between two conditions was analyzed using the Wilcoxon signed rank test. The significance of differences among three or more conditions, the influence of more than one factor, or differences between two groups were tested by multiple analysis of variance. Correlations between different parameters were analyzed using the Spearman test.²³ A probability level less than 0.05 was considered significant.

Results

Hemodynamics

Table 2 shows the hemodynamic data. P_{SA} decreased by 16% in both groups after induction of anesthesia and remained decreased after ECC and during the postoperative course. In the MVD group, P_{PA} was abnormally high in the awake state (30 \pm 8 mmHg) and decreased after induction of anesthesia (24 \pm 7 mmHg; $P < 0.05$). P_{PA} was significantly greater compared with the CAD group during all phases of the study. Similarly, in the awake state P_{PAO} was significantly greater in the MVD group (20 \pm 6 mmHg versus 13 \pm 3 mmHg; $P < 0.01$) but decreased by 20% in the anesthetized state. No further significant changes were observed after ECC or 4 h after operation. The cardiac index increased after separation from ECC ($P < 0.05$ in the MVD group) and increased further after the patients were admitted to the intensive care unit ($P < 0.05$ for both groups).

Gas Exchange

Table 2 shows data for gas exchange. P_{A-aO₂} was slightly increased in the awake state in both groups and increased significantly after induction of anesthesia ($P < 0.01$) and further after patients were separated from ECC ($P < 0.01$). Four hours after operation, P_{A-aO₂} had

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Table 3. Gas Exchange Data (mean \pm standard deviation) Derived from the Multiple Inert Elimination Technique in the Mitral Valve Disease Group (MVD; n = 12) and Coronary Artery Disease Group (CAD; n = 12)

	Before Induction of Anesthesia (control state)		After Induction of Anesthesia		After Separation from ECC		4 Hours after Cardiac Surgery	
	MVD	CAD	MVD	CAD	MVD	CAD	MVD	CAD
RSSD	1.42 \pm 0.88	1.40 \pm 1.20	1.37 \pm 1.02	1.76 \pm 1.60	2.57 \pm 1.85	2.60 \pm 2.80	1.79 \pm 1.20	1.41 \pm 0.94
\dot{Q}_{mean} of \dot{V}_A/\dot{Q}	0.80 \pm 0.21	0.71 \pm 0.25	1.10 \pm 0.43	1.06 \pm 0.35	1.06 \pm 0.23	1.24 \pm 0.60	1.22 \pm 0.62	1.09 \pm 0.51
log SD _Q	0.86 \pm 0.29	0.85 \pm 0.38	1.31 \pm 0.53*	1.11 \pm 0.47*	0.97 \pm 0.43	0.90 \pm 0.46	0.96 \pm 0.41	0.88 \pm 0.39
\dot{V}_{mean} of \dot{V}_A/\dot{Q}	1.24 \pm 0.37	1.10 \pm 0.42	2.09 \pm 0.73*	2.12 \pm 0.75*	1.89 \pm 0.96	2.22 \pm 1.34	1.94 \pm 0.83	1.71 \pm 0.59
log SD _V	0.51 \pm 0.12	0.56 \pm 0.15	0.56 \pm 0.09	0.61 \pm 0.09	0.48 \pm 0.10	0.60 \pm 0.34	0.55 \pm 0.09	0.64 \pm 0.13
F \dot{Q} low \dot{V}_A/\dot{Q} units	0.03 \pm 0.03	0.03 \pm 0.04	0.06 \pm 0.05	0.07 \pm 0.08	0.03 \pm 0.03	0.04 \pm 0.05	0.03 \pm 0.04	0.02 \pm 0.05
\dot{Q}_S/\dot{Q}_T	0.03 \pm 0.03	0.03 \pm 0.04	0.10 \pm 0.08*	0.11 \pm 0.07†	0.24 \pm 0.09†	0.23 \pm 0.07†	0.10 \pm 0.05*	0.08 \pm 0.06*
F \dot{V} high \dot{V}_A/\dot{Q} units	0.03 \pm 0.02	0.03 \pm 0.02	0.05 \pm 0.03	0.05 \pm 0.03	0.03 \pm 0.03	0.05 \pm 0.03	0.03 \pm 0.03	0.06 \pm 0.07
\dot{V}_D/\dot{V}_T	0.42 \pm 0.06	0.40 \pm 0.10	0.28 \pm 0.06†	0.27 \pm 0.10†	0.34 \pm 0.07†	0.29 \pm 0.10†	0.32 \pm 0.09†	0.28 \pm 0.08†
\dot{Q}_T (l \cdot min ⁻¹)	3.7 \pm 1.0	3.9 \pm 1.0	3.1 \pm 0.7	3.5 \pm 1.2	4.3 \pm 0.7*	4.4 \pm 1.4*	4.3 \pm 1.0*	4.7 \pm 1.3*
\dot{V}_E (l \cdot min ⁻¹)	6.4 \pm 1.2	5.9 \pm 1.0	6.8 \pm 0.9	7.4 \pm 1.4	6.4 \pm 0.5	7.5 \pm 1.4	7.7 \pm 2.1*	8.3 \pm 1.9*

RSSD = remaining sum of squared differences, \dot{Q}_{mean} of \dot{V}_A/\dot{Q} = mean ventilation – perfusion ratio of perfusion distribution, log SD_Q = log standard deviation of perfusion, \dot{V}_{mean} of \dot{V}_A/\dot{Q} = mean ventilation – perfusion ratio of ventilation distribution, log SD_V = log standard deviation of ventilation, F \dot{Q} of low \dot{V}_A/\dot{Q} units = fraction of blood \dot{V}_D/\dot{V}_T = inert gas dead space, \dot{Q}_T = total blood flow [cardiac output], \dot{V}_E = expired minute ventilation, ECC = extracorporeal circulation.

* $P < 0.05$.

† $P < 0.01$ (compared with the control state).

decreased and was not statistically different from the values obtained after induction of anesthesia. $P_A\text{-}a\text{O}_2$ was not significantly different between patients with MVD or CAD throughout the study. In both groups, was slightly decreased while patients were awake and increased after anesthesia was induced ($P < 0.05$). After operation, $P_{v\text{O}_2}$ was not statistically different from values before anesthesia was induced.

The Ventilation-Perfusion Relation

Table 3 shows data for the ventilation-perfusion relation. The retention and excretion data of the inert gases resulted in technically adequate \dot{V}_A/\dot{Q} distributions, and the remaining sum of the squared differences remained less than 6 in 90 of 96 individual measurements. Before anesthesia was induced, a small inert gas shunt (0.03 ± 0.03 [MVD group], 0.03 ± 0.04 [CAD group]) and very little perfusion of "low" \dot{V}_A/\dot{Q} regions (0.03 ± 0.03 [MVD group], 0.03 ± 0.04 [CAD group]) were observed. However, a slightly increased dispersion of "low" \dot{V}_A/\dot{Q} ratios was seen, as evident by an increased log SD_Q in both groups, compared with healthy persons of the same age.²⁴ After anesthesia was induced, shunt increased significantly in the MVD group to 0.10 ± 0.08 ($P < 0.05$). Perfusion of "low" \dot{V}_A/\dot{Q} regions was also higher, but the difference was not significant. \dot{V}_A/\dot{Q} mismatching worsened, as indicated by an increase of log SD_Q to 1.31 ± 0.53 ($P < 0.05$).

In patients with CAD, similar changes were observed. Shunt increased to 0.11 ± 0.07 ($P < 0.01$) and log SD_Q increased to 1.11 ± 0.47 ($P < 0.05$). The differences compared with the MVD group were not statistically significant. After separation from ECC, there was a marked increase of shunt to 0.24 ± 0.09 (MVD group, $P < 0.01$) and to 0.23 ± 0.07 (CAD group, $P < 0.01$). Only a small fraction of cardiac output was distributed to "low" \dot{V}_A/\dot{Q} areas. $P_A\text{-}a\text{O}_2$ was correlated with \dot{Q}_S/\dot{Q}_T (MVD group: $r^2 = 0.67$, $P < 0.05$; CAD group: $r^2 = 0.58$, $P < 0.05$). Four hours after operation, \dot{Q}_S/\dot{Q}_T had decreased to presurgical values, which was associated with an improvement of $P_A\text{-}a\text{O}_2$. \dot{Q}_S/\dot{Q}_T was not significantly different in the MVD group (0.10 ± 0.05) compared with that in the CAD group (0.08 ± 0.06). Log SD_Q was not significantly different from baseline values.

In the MVD group, but not in the CAD group, a consistent difference between predicted (calculated) and measured $P_A\text{-}a\text{O}_2$ (ΔP_{O_2}) was observed (6 ± 6 mmHg, $P < 0.05$) in the awake state (fig. 1). There was no correlation between \bar{P}_{PA} and ΔP_{O_2} . There was a larger variation in the relationship between measured and calculated $P_A\text{-}a\text{O}_2$ during anesthesia and after operation, possibly attributable to an imprecise estimation of F_{IO_2} . Because small differences of F_{IO_2} will interfere significantly with ΔP_{O_2} , statistical calculations were made only for the data obtained while patients breathed air.

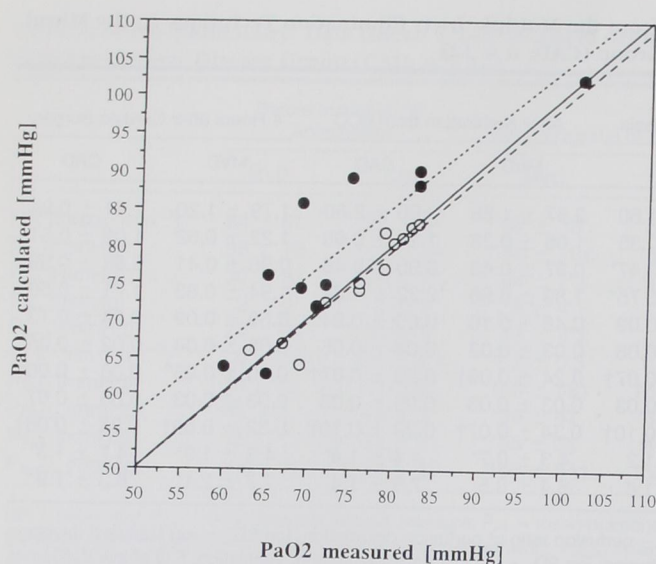


Fig. 1. Comparison between measured arterial oxygen partial pressure (P_{aO_2}) and that calculated from the \dot{V}_A/\dot{Q} distributions in patients with coronary artery disease (CAD; $n = 12$, open circles) and mitral valve disease (MVD; $n = 12$, solid circles). Data were obtained while the patients were awake and spontaneously breathing air. Note the similarity between the regression line (broken line) for measured and calculated P_{aO_2} values ($y = -0.508 + 1.0003x$, $r^2 = 0.90$, $P < 0.001$) in the CAD group and the identity line (solid line). In the MVD group, calculated P_{aO_2} was systematically higher than measured P_{aO_2} , as indicated by a shift of the regression line (broken line; $y = 10.753 + 0.923x$, $r^2 = 0.77$, $P < 0.01$). One patient with mitral regurgitation showed remarkably well-preserved oxygenation despite pulmonary hypertension.

Discussion

The main findings of this study were (1) that no significant differences for gas exchange and \dot{V}_A/\dot{Q} distribution could be demonstrated between awake patients with MVD or CAD, (2) that induction of anesthesia caused comparable degrees of intrapulmonary shunt in patients with MVD or CAD, (3) that \dot{Q}_s/\dot{Q}_T was aggravated by ECC to the same extent in mitral valve surgery and myocardial revascularization, and (4) that recovery of gas exchange impairment and \dot{V}_A/\dot{Q} inhomogeneity early after cardiac surgery were seen to the same extent in both groups of patients.

Moderate pulmonary venous hypertension may be associated with an increased blood flow to the apex of the lungs.²⁵ Concomitantly, ventilation of nondependent lung areas is increased at the expense of dependent regions,²⁶ which may improve \dot{V}_A/\dot{Q} distribution in MVD. McEvoy *et al.*²⁷ studied the \dot{V}_A/\dot{Q} relation in five patients with mitral stenosis before, during, and

after submaximal exercise. At rest, little \dot{V}_A/\dot{Q} mismatching was observed, as indicated by normal $\log SD_{\dot{Q}}$ and $\log SD_{\dot{V}}$ and absence of hypoxemia. In our patients with MVD, an increased $\log SD_{\dot{Q}}$ reflects more extensive dispersion of \dot{V}_A/\dot{Q} ratios. However, we noted a similar increase in the patients with CAD without pulmonary hypertension. More likely causes to the \dot{V}_A/\dot{Q} mismatch are reduced functional reserve capacity promoting airway closure, and increased airway resistance (spirometry showed mild reductions of vital capacity and forced expiratory volume in 1 s).

Gas exchange was impaired after induction of anesthesia in the MVD group, but these changes were not statistically different from changes in the CAD group. Thus general anesthesia did not induce a more marked \dot{V}_A/\dot{Q} mismatch in patients with pulmonary venous hypertension. The alterations of lung function in the anesthetized and paralyzed state are well in accordance with data published earlier by others^{7,28} and by our group.^{13,29} P_{a-aO_2} correlated with \dot{Q}_s/\dot{Q}_T , but not with perfusion of "low" \dot{V}_A/\dot{Q} regions. Thus perfusion of nonventilated lung areas is an important component of gas exchange impairment in anesthetized patients who have MVD or CAD. Considerable \dot{V}_A/\dot{Q} inhomogeneity was reflected by $\log SD_{\dot{Q}}$, which had increased to a mean of 1.31 in the MVD group and 1.11 in the CAD group. Although the relative changes were comparable, the underlying mechanisms causing an increased degree of pulmonary blood flow dispersion may differ between both groups of patients. Pulmonary hypertension in mitral valve stenosis or insufficiency may be a consequence of structural alterations of the capillaries, but hypoxic pulmonary vasoconstriction elicited by alveolar hypoxia can also be important. \bar{P}_{PA} decreased by 20% in the MVD group when anesthesia was induced and with mechanical ventilation. No such alterations occurred in the CAD group. It has been shown that an increased pulmonary vascular tone improves \dot{V}_A/\dot{Q} distribution in lung diseases (e.g., in obliterative pulmonary hypertension³⁰), whereas an abnormally low vascular reactivity (e.g., in liver cirrhosis³¹) interferes with pulmonary gas exchange. Alternatively, the decrease in \bar{P}_{PA} may be caused by decreased intrathoracic blood volume secondary to induction of anesthesia and mechanical ventilation. In earlier studies, Rehder *et al.*³² and Landmark *et al.*³³ observed minor \dot{V}_A/\dot{Q} inequality in anesthetized and paralyzed younger healthy persons. This may be due in part to differences in ages between our older patients and these other two studies. A correlation between \log

$SD_{\dot{Q}}$ and age has been shown in patients while they were awake and during anesthesia.²⁴

After cardiopulmonary bypass, oxygenation was significantly impaired and \dot{Q}_s/\dot{Q}_T had more than doubled. Extracorporeal circulation imposes considerable trauma to the lung, presumably due to the production and release of biologically active mediators from damaged blood cells, complement activation, platelet aggregation, pulmonary sequestration of granulocytes and monocytes, lung collapse, and disturbances of surfactant.^{8,34-36} In addition, infusion of vasodilators may have contributed to an increased shunt. Extravascular lung water increases after ECC,³⁷ and this could also aggravate formation of atelectasis in dependent lung areas. However, Davies *et al.*³⁸ described significantly reduced ^{113m}In — labeled transferrin accumulation in lungs of patients with severe mitral stenosis, indicating reduced microvascular permeability. Whether a decreased transcapillary fluid conductance prevents or attenuates formation of pulmonary edema during mitral valve surgery remains to be determined. Bedside assessment of extravascular lung water using a double-indicator technique (and the mean transit time approach) is questionable in the presence of MVD, and noninvasive techniques such as positron emission tomography or magnetic resonance tomography are not applicable during cardiac surgery. Despite a longer aortic cross-clamping time and duration of cardiopulmonary bypass, \dot{V}_A/\dot{Q} mismatch was comparable in the patients in the MVD and CAD groups. Indices of perfusion dispersion even decreased and no perfusion of lung areas with $0.005 \leq \dot{V}_A/\dot{Q} \leq 0.1$ was observed in either group. Thus more severe impairment of oxygenation was caused by increased shunt rather than by maldistribution of pulmonary blood flow. Our data show that these effects of ECC persisted for a short time, because oxygen exchange and \dot{V}_A/\dot{Q} matching improved significantly during the first hours after cardiac surgery. In fact, \dot{Q}_s/\dot{Q}_T , "low" \dot{V}_A/\dot{Q} , and log $SD_{\dot{Q}}$ values were not significantly different compared with the anesthetized state before surgery. The decrease in \dot{Q}_s/\dot{Q}_T may be explained by recruitment of collapsed alveoli, reabsorption of lung edema, or a combination of both mechanisms. The reasons for an improved \dot{Q}_s/\dot{Q}_T cannot be differentiated by our multiple inert gas elimination technique data, because they describe overall gas exchange properties of the lung rather than topographical distribution of ventilation and perfusion. It should be noted that we excluded patients with MVD and severely impaired lung function or poorly compensated congestive heart failure. Thus addi-

tional studies are warranted to disclose the pathophysiology of shunt in patients having cardiac surgery.

In the MVD group, but not in the CAD group, P_A-aO_2 calculated from the \dot{V}_A/\dot{Q} relation was systematically higher than measured P_A-aO_2 (fig. 1). In absolute terms, breathing air at rest, the difference between predicted and measured P_A-aO_2 (ΔP_{O_2}) values averaged 6 mmHg or 18% of the actual P_A-aO_2 . Histologic studies in patients with chronic pulmonary venous hypertension have found substantial thickening of the layer between the capillary lumen and the alveolar wall, which may cause diffusion limitation of oxygen.³⁹⁻⁴¹ Traditional techniques for assessing diffusion capacity for oxygen are also influenced by the \dot{V}_A/\dot{Q} distribution. The determination of ΔP_{O_2} by the multiple inert gas elimination technique assumes (1) that no diffusion limitation exists for the six inert gases, (2) absence of postpulmonary shunt, (3) that the weights of the inert gases have no effect on their elimination, and (4) absence of intravascular inert gas gradients.⁴² There is no evidence that the technical conditions of the present investigation interfere with these assumptions. A good fit of the derived \dot{V}_A/\dot{Q} relation to the retention data (small remaining sum of squared differences) was found and an equally low mean error for heavy inert gases (e.g., enflurane) or light gases (e.g., ethane). An increased perfusion of bronchial or Thebesian vascular channels could produce an increased postpulmonary shunt. However, left ventricular end-diastolic pressure is typically increased in mitral insufficiency and this can rather be assumed to decrease postpulmonary shunt blood flow. In patients with idiopathic pulmonary fibrosis who breathed air at rest, Agusti *et al.*⁴³ observed a mean difference between predicted and measured P_A-aO_2 of 6 mmHg, which compares favorably with our data. In interstitial lung disease, ΔP_{O_2} may contribute approximately 30% to P_A-aO_2 during exercise.⁴⁴ The results of the present study give some support to the concept of a diffusion limitation for oxygen in mitral stenosis described by Blount *et al.*⁴⁵ more than 40 yr ago. The small ΔP_{O_2} indicates that \dot{V}_A/\dot{Q} inequality is the main mechanism of gas exchange impairment in MVD, at least as long as the lung is normoxic and capillary transit time or P_{vO_2} are not significantly reduced.

In conclusion, in awake or anesthetized and paralyzed patients with MVD or CAD, nearly the same \dot{V}_A/\dot{Q} distribution was observed before, during, and after cardiac surgery. Intrapulmonary shunt and, to a lesser extent, perfusion of "low" \dot{V}_A/\dot{Q} regions and decreased P_{vO_2} contributed to impaired gas exchange. These alterations

were aggravated by ECC but improved after surgery. Because \dot{V}_A/\dot{Q} distribution is not significantly different between patients with CAD and MVD, the higher incidence of pulmonary complications in the latter group may be caused by other or additional mechanisms.

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