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Thoracic Intravascular and Extravascular Fluid Volumes in Cardiac Surgical Patients

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Background: One possible mechanism of impaired oxygenation in cardiac surgery with extracorporeal circulation (ECC) is the accumulation of extravascular lung water (EVLW). Intrathoracic blood volume (ITBV) and pulmonary blood volume (PBV) also may increase after separation from ECC, which can influence both cardiac performance and pulmonary capillary fluid filtration. This study tested whether there were any relationships between lung fluid accumulation and pulmonary gas exchange during the perioperative period of cardiac surgery and ECC.

Methods: Ten patients undergoing myocardial revascularization were studied. ITBV, PBV, and EVLW were determined from the mean transit times and decay times of the dye and thermal indicator curves obtained simultaneously in the descending aorta. Gas exchange was assessed by arterial and mixed venous partial pressure of oxygen (P_{O_2}) and carbon dioxide (P_{CO_2}), and calculation of alveolo-arterial P_{O_2} gradient ($P_{A-a_{O_2}}$) and venous admixture ($\dot{Q}_{VA}/\dot{Q}_T$). Recordings were made after induction of anesthesia, after sternotomy, 15 min after separation from ECC, and 4 and 20 h postoperatively.

Results: After induction of anesthesia, EVLW (6.0 ± 1.0 ml/kg, $\bar{x}$ ± SD), PBV (3.6 ± 1.3 ml/kg), and ITBV (18.4 ± 2.7 ml/kg) were within normal ranges. Oxygenation was moderately impaired, as indicated by an increased $P_{A-a_{O_2}}$ (144 ± 46 mmHg) and $\dot{Q}_{VA}/\dot{Q}_T$ (11 ± 4%). After separation from ECC, EVLW had increased to 9.1 ± 2.6 ml/kg, which was accompanied by an increase of ITBV (26.0 ± 4.4 ml/kg) and PBV (5.6 ± 1.9 ml/kg). P_{Aa-O_2} (396 ± 116 mmHg) and $\dot{Q}_{VA}/\dot{Q}_T$ (29 ± 7%) also were increased. ITBV and PBV remained increased 4 and 20 h post-operatively, but EVLW decreased to presurgery values. No correlations were found between thoracic intravascular and extravascular fluid volumes and gas exchange.

Conclusions: Cardiac surgery with the use of ECC induces alterations of thoracic intravascular and extravascular fluid volumes. Postoperatively, increased ITBV and PBV need not be associated with higher EVLW. Thus, sufficient mechanisms protecting against lung edema formation or providing resolution of EVLW probably are maintained after ECC. Since oxygenation is impaired during and after cardiac surgery, it is concluded that mechanisms other than or in addition to changes of ITBV, PBV, and EVLW predominantly influence gas exchange. (Key words: Lung: cardiopulmonary bypass; gas exchange; lung water; pulmonary blood volume. Measurement techniques: fiberoptic thermal dye dilution. Surgery, cardiac.)

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CARDIAC surgery with the use of extracorporeal circulation (ECC) frequently is associated with an impaired ability of the lungs to oxygenate blood.[1] The majority of patients present with moderate hypoxia on room air,[2] but respiratory failure occasionally is encountered, necessitating prolonged mechanical ventilation.[3,4] Besides other causes, such as surgical trauma,[5] effects of anesthesia and muscle paralysis,[6] and altered mechanics of the rib cage,[7] the accumulation of extravascular lung water (EVLW) due to capillary leakage has been considered an important pathophysiologic mechanism of impaired lung function.[8–10] However, the injury of the pulmonary capillary endothelium secondary to ECC is probably less severe than previously thought,[11] and formation of lung edema due to alterations of colloidal osmotic pressure or left ventricular filling pressure may be more common.[10,12] Hoeft *et al.* found an unchanged EVLW in cardiac surgical patients, if the priming fluid of the cardiopulmonary bypass was supplemented with 20% albumin.[13] However, gas exchange was impaired to the same extent as that of a group of patients receiving crystalloid pump prime (lactated Ringer's solution), in whom EVLW had increased by 60%. In that study, lung function was determined by blood gases. No further data, such as inspired oxygen fraction, cardiac output, or mixed venous partial pressure of oxygen (P_{O_2}), were presented,

thus, potential implications of gas exchange of extrapulmonary factors are difficult to establish. Intrathoracic blood volume (ITBV) and pulmonary blood volume (PBV) also may increase after separation from ECC, which can influence both cardiac performance and filtration of fluid into the pulmonary interstitium. However, there are few data on the relationship between thoracic intravascular and extravascular fluid volumes during cardiac surgery and possible alterations in the postoperative course. A fiberoptic-thermistor catheter technique for determination of EVLW has been tested in various experimental conditions.[14-16] Since the dilution curves for the dye and the thermal indicator are measured simultaneously in the descending aorta, calculation of ITBV and PBV is also possible.[17] This technique was applied for lung fluid balance studies on cardiac surgical patients. We hypothesized that ITBV and PBV increase after ECC and that increased thoracic intravascular fluid volumes are associated with higher values of EVLW. Finally, we analyzed gas exchange for potential correlations with ITBV, PBV, and EVLW.

Materials and Methods

The study was approved by the Ethical Committee of Uppsala University Hospital, and informed consent was obtained from each patient. Determination of the sample size was based on earlier clinical and experimental studies from our group[18,19] and on data published in the literature.[9,10,20,21] We accepted a type I error of 0.05 and a probability of 80% to detect a difference of 4 ml/kg for ITBV and 2 ml/kg for EVLW.[22] This resulted in a study group of at least nine subjects. Ten patients scheduled for coronary artery revascularization surgery were studied (age 64 ± 7 yr, range 52–71 yr; body weight 77 ± 11 kg, range 60–104 kg; body height 170 ± 6 cm, range 156–176 cm). Inclusion criteria for the investigation were (1) stable angina pectoris due to coronary artery disease; (2) left ventricular ejection fraction greater than 40%; (3) left ventricular end-diastolic pressure less than 15 mmHg; (4) absence of preexisting pulmonary diseases as determined by clinical examination, chest radiography, lung function tests, and blood gas analysis; and (5) absence of renal, hepatic, or cerebrovascular diseases and insulin-dependent diabetes mellitus.

Anesthesia and Mechanical Ventilation

The patients received 0.03 mg/kg flunitrazepam orally on the evening before surgery and 0.15–0.2 mg/

kg morphine and 0.006–0.008 mg/kg scopolamine intramuscularly 1 h before the anesthesia. Anesthesia (duration 300 ± 56 min) was induced with intravenous doses of fentanyl (5–10 μg/kg), thiopental (1–2 mg/kg), and pancuronium (0.1 mg/kg) and maintained with additional doses of fentanyl and a volatile inhalational anesthetic (isoflurane 0.5–1.0 MAC). After tracheal intubation, the lungs were ventilated with intermittent positive pressure ventilation. Tidal volume, ventilatory frequency, and inspired fraction of oxygen ($F_{I_{O_2}}$) in nitrogen were adjusted to maintain normal arterial partial pressure of carbon dioxide (P_{CO_2}) levels (Pa_{CO_2} 35–40 mmHg) and an arterial oxygen saturation (Sa_{O_2}) greater than 95%. The membrane oxygenator (Maxima, Medtronic Anaheim, CA) was primed with 2,000 ml of isotonic crystalloid fluid (acetated Ringer's solution). No colloidal solutions were added, but sodium bicarbonate or potassium was given when necessary. During ECC (duration 84 ± 26 min), body core temperature was decreased to 30 ± 0.5° C. Mechanical ventilation was stopped before cardioplegic cardiac arrest (duration 42 ± 11 min), and no positive end-expiratory pressure was applied during or after ECC. After the bypass surgery was completed, the aorta was unclamped and the lungs were ventilated with 100% O_2 with half the minute volume used before ECC. Full ventilation was restored before separation from ECC, which was performed after sufficient reperfusion of the heart and reestablishment of a normal core temperature to obviate postbypass temperature decreases in the pulmonary artery.[23,24] No patient received positive inotropic drugs for separation from ECC, but nitroglycerin was given in low doses (0.2–0.5 μg·kg^{-1}·min^{-1}) in each case. At the end of surgery (duration 196 ± 41 min), a total balance of 4,130 ± 510 ml for crystalloid fluids and −710 ± 130 ml for blood loss was noted. In the intensive care unit (ICU), mechanical ventilation was maintained in the above-described manner, and the $F_{I_{O_2}}$ was adjusted to maintain Sa_{O_2} above 95%. All patients were successfully separated from intermittent positive pressure ventilation and their tracheas extubated 10–16 h postoperatively. Fluid balance on the first postoperative day was negative for crystalloid fluids (−2,070 ± 890 ml) and positive for colloidal fluids (1,060 ± 790 ml).

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. After induction

of anesthesia, a triple-lumen, thermistor-tipped 7.5-French pulmonary artery catheter was transcutaneously introduced 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 electrical integration of the pressure signal. The ECG lead V5 was recorded continuously and used for heart rate calculation. Arterial and mixed venous oxygen and carbon dioxide tensions were measured by standard techniques (ABL 3, Radiometer, Copenhagen, Denmark). Cardiac output was measured by thermodilution technique. Ten milliliters of ice-cold 0.9% saline solution was injected rapidly into the right atrium, the dilution being 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, systemic and pulmonary vascular resistances, alveolo-arterial P_{O_2} gradient $(P_A\text{-}a_{O_2})$, and venous admixture $(\dot{Q}_{VA}/\dot{Q}_T)$ were calculated using standard formulas. Oxygen saturation of the arterial and mixed venous blood was measured spectrophotometrically (OSM 3, Radiometer).

Measurement of Thoracic Intra- and Extravascular Fluid Volumes

A fiberoptic thermistor catheter was advanced *via* the right or left femoral artery into the descending aorta. The bolus injection described for the determination of cardiac output also was used to measure thoracic intra- and extravascular volumes. The indicator bolus (indocyanine green (an intravascular marker)) mixed in ice-cold 5% glucose (a thermal intra- and extravascular indicator) to assess intravascular and extravascular spaces was injected into the right atrium with a temperature-controlled syringe (fig. 1). The dilution curves for dye and temperature were recorded simultaneously in the aorta with the thermistor-tipped fiberoptic catheter. A lung water computer (System Cold Z-021, Partig, München, Germany) determined the mean transit time for the thermal indicator (MTT_T) and for the dye indicator (MTT_{dye}) and calculated total thermal volume, ITBV, and extravascular thermal volume from the mean transit time $(EVTV_{MTT})$. PBV and extravascular thermal volume also were determined from the exponential decay time $(EVTV_{DT})$ for the indicators (see appendix).
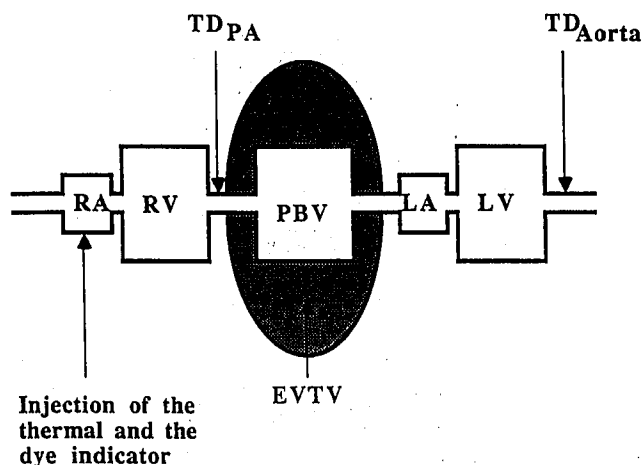

Fig. 1. Schematic diagram of the cardiopulmonary system. RA = right atrium, RV = right ventricle, PBV = pulmonary blood volume, EVTV = extravascular thermal volume, LA = left atrium, LV = left ventricle, TD_{PA} = thermodilution measurement in the pulmonary artery, TD_{aorta} = thermodilution measurement in the aorta. The indicator dye is determined simultaneously at the corresponding point in the descending aorta.

All measurements were made in triplicate, and the mean was calculated and used for statistical evaluation.

Experimental Procedure

A period of 30 min was allowed after induction of anesthesia to achieve stable hemodynamic and respiratory conditions. Then, cardiopulmonary data were determined, and the intra- and extravascular lung volumes were assessed. These values served as control. The patients were studied 10 min after sternotomy and 15 min after separation from ECC. The operation was terminated, and the patient was transferred to the ICU. Four hours after admission to the ICU, another cardiopulmonary status and intra- and extravascular thoracic volumes were determined during sedation and mechanical ventilation. Finally, the patients were studied on the first postoperative day (approximately 20 h after cardiac surgery) during spontaneous breathing in the awake state.

Statistical Analysis

All data were sampled and analyzed on a Systat statistical program (Systat, Evanston, IL). Mean values and standard deviations were calculated. 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. The relationship between two or more variables was tested by Spearman's rank test and multiple regression analysis to obviate a potential patient effect.[22] A level of $P < 0.05$ was considered as significant.

Results

Systemic and Central Hemodynamics

The data are presented in table 1. No gross hemodynamic abnormalities were observed before and during surgery or in the postoperative course. Cardiac output increased by 36% after separation from ECC ($P < 0.05$) and was stable after admission of the patient to the ICU and on the first postoperative day. Mean systemic arterial pressure and pulmonary arterial occlusion pressure showed small but significant increases after sternotomy. Systemic vascular resistance decreased significantly after separation from ECC and remained within the lower part of the normal range postoperatively. There were no significant changes of mean systemic arterial pressure, pulmonary vascular resistance, or pulmonary arterial occlusion pressure 4 h after admission to the ICU and on the first postoperative day.

Gas Exchange

The data are presented in table 1. Oxygenation was impaired after induction of anesthesia to the same extent as reported earlier.[25] After separation from cardiopulmonary bypass, $PA-a_{O_2}$ and $\dot{Q}_{VA}/\dot{Q}_T$ had increased almost twofold ($P < 0.01$). Four hours after admission to the ICU, $PA-a_{O_2}$ and $\dot{Q}_{VA}/\dot{Q}_T$ had improved rapidly and were not statistically different from those values obtained after induction of anesthesia. However, on the first postoperative day, during spontaneous breathing all patients revealed an impaired oxygenation and reduced carbon dioxide removal.

Thoracic Intravascular and Extravascular Fluid Volumes

The data are presented in table 2. Normal values of EVLW were recorded after induction of anesthesia and

following sternotomy but increased by 52% after separation from ECC ($P < 0.01$). Four hours postoperatively, EVLW had decreased to presurgery values and remained at this level on the first postoperative day. ITBV and PBV tended to increase after sternotomy ($P = 0.09$). After separation from ECC, ITBV and PBV were significantly increased and remained increased postoperatively (fig. 2). $\dot{Q}_{VA}/\dot{Q}_T$ tended to increase with higher levels of lung water; however, there was no significant correlation between the parameters ($r = 0.41$, $P = 0.075$; fig. 3). Likewise, we found no correlation between ITBV, PBV, and oxygenation during the different phases of the study.

Discussion

Methodologic Aspects

The technique used in the present study for determination of thoracic intravascular and extravascular fluid volumes is based on the measurement of the mean transit times for thermal and dye indicators[26-29] and of the decay time volumes calculated from the indicator dilution curves[30] (see appendix). To our knowledge, a direct comparison between ITBV or PBV as determined with the indicator dilution technique and *in situ* ITBV or PBV has not been published. However, Backmann and Hartung estimated a mean PBV of 508 ml in postmortem normal adult lungs.‖ The methodologic and clinical implications of this finding have been discussed in detail by Harris and Heath.[31] *In vivo*, slightly lower values have been found in clinical studies using double-indicator techniques.[31,32] Thorvaldson *et al.* assessed a mean PBV of 3.8–4.2 ml/kg in open-chest dog studies,[20,33] which is well in accordance with our results before cardiopulmonary bypass. Likewise, an ITBV of approximately 1,400 ml in the control state (table 2) agrees with data published by London *et al.*, who found a mean cardiopulmonary blood volume of 741 ml/m² ($\approx 1,445$ ml) in normotensive humans.[34] Earlier studies revealed also a good correlation between premortem $EVTV_{MTT}$ obtained with the fiberoptic-thermistor system and postmortem gravimetric EVLW in oleic acid and hydrostatic edema ($r = 0.97$, $P < 0.01$, $n = 22$).[35] In the present investigation, $EVTV_{DT}$ and $EVTV_{MTT}$ were closely correlated ($r^2 = 0.91$, $P < 0.01$), supporting the accuracy of the method. Despite its inclusion of some nonpulmonary tissue due to the distribution of the thermal indicator to the heart chambers, pulmonary artery, and aorta, extravascular

‖ Backmann R, Hartung W: Differentiating measurements of blood volumes in isolated human lungs. Progr Respir Res 5:327–337, 1970.

Table 1. Cardiopulmonary Data

	After Induction of Anesthesia (Control State)	After Sternotomy	After Separation from Extracorporeal Circulation	4 h after Surgery	20 h after Surgery
HR (beats/min^{-1})	55 ± 6	65 ± 9*	74 ± 11*	94 ± 16†	86 ± 12†
Psa$_{mean}$ (mmHg)	72 ± 8	82 ± 10*	74 ± 7	85 ± 6*	79 ± 11
Ppa$_{mean}$ (mmHg)	17 ± 4	17 ± 3	15 ± 4	21 ± 5	18 ± 2
Pra (mmHg)	7 ± 3	8 ± 2	7 ± 3	7 ± 4	8 ± 3
Ppao (mmHg)	8 ± 4	11 ± 2*	10 ± 3	9 ± 4	9 ± 3
CO (l·min^{-1})	3.3 ± 0.7	3.4 ± 0.5	4.5 ± 0.9*	4.8 ± 0.9*	5.1 ± 0.6*
SVR (dyn·s·cm^{-5})	1,579 ± 392	1,720 ± 338	1,242 ± 203*	1,325 ± 269*	1,120 ± 212*
PVR (dyn·s·cm^{-5})	165 ± 58	120 ± 46	103 ± 24*	189 ± 62	127 ± 18
Pa$_{O_2}$ (mmHg)	154 ± 50	141 ± 39	235 ± 115†	116 ± 26	79 ± 17†
Pa$_{CO_2}$ (mmHg)	36 ± 2	37 ± 2	36 ± 4	36 ± 3	42 ± 2†
P$\bar{v}_{O_2}$ (mmHg)	33 ± 4	35 ± 3	39 ± 5*	31 ± 5	31 ± 4
PA-a$_{O_2}$ (mmHg)	144 ± 46	154 ± 44	396 ± 116†	132 ± 46	86 ± 43*
$\dot{Q}_{VA}/\dot{Q}_T$ (% CO)	11 ± 4	15 ± 5	29 ± 7†	12 ± 4	16 ± 5

Data are mean ± SD; n = 10.

HR = heart rate; Psa$_{mean}$ = mean systemic arterial pressure; Ppa$_{mean}$ = mean pulmonary arterial pressure; Pra = right atrial pressure; Ppao = pulmonary artery occlusion pressure; CO = cardiac output; SVR = systemic vascular resistance; PVR = pulmonary vascular resistance; Pa$_{O_2}$ = arterial oxygen tension; Pa$_{CO_2}$ = arterial carbon dioxide tension; P$\bar{v}_{O_2}$ = mixed venous oxygen tension; PA-a$_{O_2}$ = alveoloarterial oxygen tension gradient; $\dot{Q}_{VA}/\dot{Q}_T$ = venous admixture.

* $P < 0.05$ compared with the control state.

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

thermal volume is regarded as a reliable estimate of EVLW.[29,35-37] The possibility exists, however, that insufficient time for equilibration of the thermal indicator with pulmonary extravascular space or vascular derecruitment influence EVTV$_{MTT}$ and EVTV$_{DT}$. Although this has no effect on determination of ITBV and PBV, lung water and potential correlations with gas exchange consequently may be underestimated.

Thoracic Intravascular Fluid Volumes

The assessment of ITBV has been put into experimental and clinical perspective for the estimation of volume status and as a tool providing optimal therapy in critically ill patients.[15,21,38] In noncardiac surgical patients, we observed a decreased ITBV after induction of anesthesia but an unchanged EVLW.[19] Thoracic blood volume is significantly affected by airway

Table 2. Thoracic Intravascular and Extravascular Fluid Volumes

	After Induction of Anesthesia (Control State)	After Sternotomy	After Separation from Extracorporeal Circulation	4 h after Surgery	20 h after Surgery
ITBV					
(ml)	1,417 ± 208	1,671 ± 285	2,002 ± 343*	1,986 ± 378*	1,832 ± 393
(ml·kg^{-1})	18.4 ± 2.7	21.7 ± 3.7	26.0 ± 4.4*	25.8 ± 4.9*	23.8 ± 5.2
PBV					
(ml)	277 ± 103	323 ± 115	431 ± 146*	393 ± 117*	331 ± 85
(ml·kg^{-1})	3.6 ± 1.3	4.2 ± 1.5	5.6 ± 1.9*	5.1 ± 1.5*	4.3 ± 1.1
EVLW					
(ml)	462 ± 78	470 ± 115	701 ± 200†	493 ± 162	477 ± 117
(ml·kg^{-1})	6.0 ± 1.0	6.1 ± 1.5	9.1 ± 2.6†	6.4 ± 2.1	6.2 ± 1.5

Data are mean ± SD; n = 10.

ITBV = intrathoracic blood volume; PBV = pulmonary blood volume; EVLW = extravascular lung water.

* $P < 0.05$ compared with the control state.
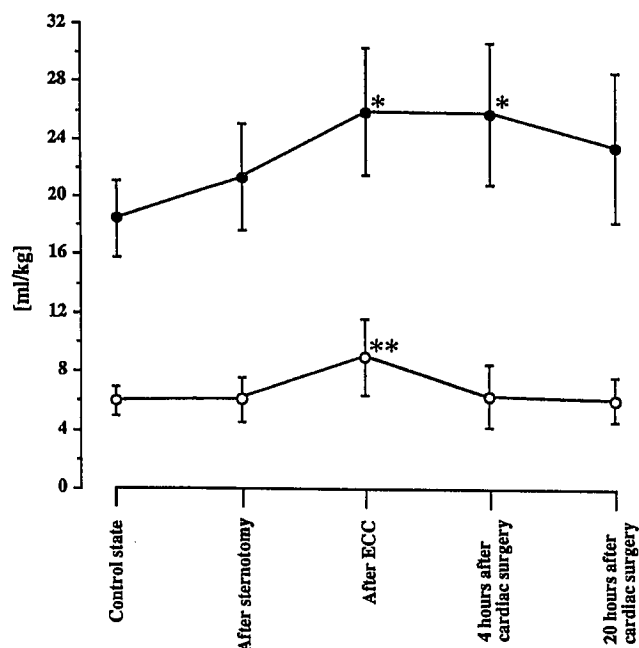
† $P < 0.01$ compared with the control state.

Fig. 2. Alterations of intrathoracic blood volume (closed circles) and extravascular lung water (open circles) in cardiac surgical patients (n = 10). For clarity, pulmonary blood volume is not shown. ECC = extracorporeal circulation. *$P < 0.05$. **$P < 0.01$.

pressure and by the tone of the capacity vessels.[20,39] Thus, positive pressure ventilation and the vasodilating effect of general anesthesia can induce a blood volume shift, which may decrease both ITBV and PBV.

After sternotomy, PBV and ITBV tended to increase, which may be due to a higher functional residual capacity# and lower pulmonary vascular resistance.[20] In addition, pulmonary arterial occlusion pressure increased slightly, which also can influence PBV.[33] However, the most impressive changes were observed after separation from ECC. ITBV and PBV increased by 41% and 60%, respectively. Koller et al. estimated a mean transfer of 34 ml/min between plasma and the interstitium during 60–90 min of ECC providing a total filtered volume of 3,000 ml in a normothermic 70-kg subject.[40] Thus, redistribution of interstitial fluid into the intravascular compartment after separation from ECC may explain the increased thoracic intravascular

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fluid volume, which remained elevated 4 h after cardiac surgery. Cardiac output also increased, but changes of blood flow probably have little effect on PBV in normal lungs.[33]

On the first postoperative day, ITBV and PBV were still increased, which can reflect an increased circulating volume status. However, these data were obtained during spontaneous breathing. A lower mean airway pressure as compared with mechanical ventilation may have contributed to the higher thoracic intravascular fluid volumes.[20,39] Despite these changes, no patient revealed clinical or radiologic signs of pulmonary congestion.[41]

Extravascular Lung Water

In the control state and after sternotomy, average EVLW was 6.0 ml/kg, which corresponds well with data published by other investigators.[10,29] EVLW increased by 52% after ECC but decreased rapidly in the postoperative course despite elevated ITBV and PBV. These results are also in accordance with the study by Hoeft et al.[13] The increment of EVLW may be explained partly by the fluid load due to the priming volume of the cardiopulmonary bypass, which has been shown to reduce intravascular colloid osmotic pressure by 10 mmHg or more.[10,40] According to the Starling equation, a decrease of intravascular colloid osmotic pressure should enhance hydraulic fluid movement into the in-
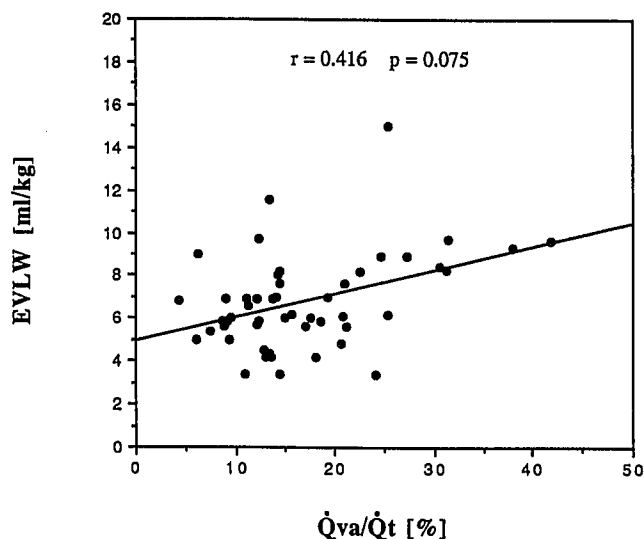

Fig. 3. Relationship between extravascular lung water (EVLW) and venous admixture ($\dot{Q}_{VA}/\dot{Q}_T$). $\dot{Q}_{VA}/\dot{Q}_T$ tended to increase with higher levels of lung water, but the correlation was not statistically significant.

terstitial space even if the conductance and reflection coefficients of the alveolocapillary membrane are unchanged.[42] Also, an increased permeability due to endothelial cell injury may lead to lung edema after cardiopulmonary bypass,[4,8-10,43] although the relevance of the latter mechanism has been challenged by MacNaughton *et al.*[11] Resolution of pulmonary edema may depend not only on Starling forces and lymphatic drainage but also on active transport of sodium and water out of the alveolar and interstitial compartments.[44] An intact epithelial barrier function seems to be an important factor for this mechanism; however, no clinical data are available after separation from ECC. In our study, the increased levels of ITBV or PBV were not correlated with higher EVLW. Thus, mechanisms providing lung water homeostasis probably are maintained after cardiopulmonary bypass surgery.

Gas Exchange and Thoracic Intravascular and Extravascular Fluid Volumes

No correlations were found between $\dot{Q}_{VA}/\dot{Q}_T$ and thoracic intravascular or extravascular fluid volumes during the different phases of the study. Although accumulation of lung water may significantly impair oxygenation, EVLW has not been shown to be closely related to gas exchange in pulmonary edema secondary to increased alveolocapillary permeability.[45] In critically ill patients, no correlation between EVLW and $PA-a_{O_2}$ was found in a differential analysis of lung water below or above 9 ml/kg.[46] In the present study, $\dot{Q}_{VA}/\dot{Q}_T$ was increased during anesthesia before surgery and tended to deteriorate further after sternotomy, whereas extravascular thermal volume was unchanged. More importantly, lung water had returned to baseline values postoperatively, but gas exchange was still significantly impaired. Possibly, $\dot{Q}_{VA}/\dot{Q}_T$ was also influenced by the infusion of nitroglycerin after ECC and in the postoperative course.[47] Nitroglycerin may directly impair oxygenation in edematous lungs by release of hypoxic pulmonary vasoconstriction.[48] In the present study, lung water levels were normal before and shortly after cardiac surgery. Therefore, mechanisms other than or in addition to changes of lung water may cause intrapulmonary shunt in cardiac surgical patients, which is potentially aggravated by potent vasodilators. In a preliminary clinical investigation using computed tomography, we were able to demonstrate bilateral basal pulmonary densities after coronary artery revascularization surgery, which correlated highly with intrapulmonary venous admixture.[49] Possibly, formation of atelectasis

after induction of anesthesia[50] or during cardiac surgery largely influences oxygenation. Likewise, an improvement of gas exchange in the postoperative course may be related to aeration of collapsed lung tissue. Whether increased lung water influences development of atelectasis in these patients remains to be established.

In conclusion, ITBV, PBV, and EVLW undergo significant alterations during and after cardiac surgery. EVLW increases after separation from ECC but decreases almost to normal values 4 h postoperatively. ITBV and PBV increase after sternotomy and ECC and remain elevated in the early postoperative course. The lung probably is able to maintain sufficient mechanisms protecting against formation of edema or providing resolution of lung water after cardiopulmonary bypass surgery. Gas exchange is impaired during and after cardiac surgery, but this is not correlated with changes of thoracic intravascular and extravascular fluid volumes.

Appendix

The product of mean transit time (MTT) and total flow represents the distribution volume of an indicator between the point of injection (*e.g.*, right atrium) and detection (*e.g.*, descending aorta). MTT constitutes the time point until the first indicator particle has reached the detector and the mean time difference between the appearance of the first and all subsequent indicator particles. The cold indicator diffuses and is convected into the extravascular compartment depending on time, heat conductivity, heat capacity, and vascular surface area, whereas the dye indicator binds rapidly to plasma proteins. Thus, the dye indicator is confined to the intravascular compartment during one passage through heart, pulmonary vessels, and aorta, although its molecular weight is low.[29] Accordingly, two distribution volumes can be calculated:

$$ITBV_{MTT} = Q_{dye} \cdot MTT_{dye} \qquad (1)$$

$$TTV_{MTT} = Q_T \cdot MTT_T. \qquad (2)$$

In equation 1, $ITBV_{MTT}$ is the ITBV (intravascular volume from the point of injection of the indicator to detection in the descending aorta), and Q_{dye} and MTT_{dye} represent the flow and the mean transit time of the indicator dye, respectively. In equation 2, a total thermal distribution volume TTV_{MTT} is obtained by means of the thermodilution flow (Q_T) and MTT_T. TTV_{MTT} represents the sum of $ITBV_{MTT}$ and the extravascular heat exchangeable volume. Thus, $EVTV_{MTT}$ is defined as the difference between TTV_{MTT} and $ITBV_{MTT}$:

$$EVTV_{MTT} = TTV_{MTT} - ITBV_{MTT}. \qquad (3)$$

$EVTV_{MTT}$ is regarded as a reliable estimate of EVLW, provided the perfusion of the pulmonary vessels is not significantly impaired.[28,29,51] Using the dilution curve decay approach,[30] the pulmonary thermal decay volume (PTV_{DT}) is calculated:

$$PTV_{DT} = Q_T \cdot t_{DT}, \qquad (4)$$

where t_{DT} is the exponential decay time for the thermal indicator

measured in the descending aorta. Likewise, PBV_{DT} is obtained for the indicator dye:

$$PBV_{DT} = Q_T \cdot t_{DT_{dye}}, \qquad (5)$$

where PBV_{DT} constitutes the PBV and $t_{DT_{dye}}$ represents the exponential decay time for the indicator dye measured fiberoptically. This method is based on two assumptions: (1) for a single mixing chamber with complete mixing of the indicator and constant fluid flow, the dilution curve decays exponentially with time, and (2) for a number of different serial mixing chambers constituting different mixing volumes but identical chamber flow, the decay of the dilution curve is determined predominantly by the largest chamber. Thus, $EVTV_{DT}$ is calculated:

$$EVTV_{DT} = PTV_{DT} - PBV_{DT}. \qquad (6)$$

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