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) 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 (Pao2) and carbon dioxide (Paco2) and calculation of alveolo-arterial Pao2 gradient (PA-aO2) and venous admixture (Qva/QT). 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, 5 ± 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 Pa-aO2 (144 ± 46 mmHg) and Qva/QT (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). PA-aO2 (396 ± 116 mmHg) and Qva/QT (29 ± 7%) also were increased. ITBV and PBV remained increased 4 and 20 h postoperatively, 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.)

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 (Pvo2), were presented.

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THORACIC INTRAVASCULAR AND EXTRAVASCULAR FLUID VOLUMES

thus, potential implications of gas exchange of extra-
pulmonary factors are difficult to establish. Intratra-
ch aeic blood volume (ITBV) and pulmonary blood vol-
ume (PBV) also may increase after separation from ECC, 
which can influence both cardiac performance and fil-
tration of fluid into the pulmonary interstitium. How-
ever, 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 EVLV has been tested 
in various experimental conditions. Since the dil-
ution curves for the dye and the thermal indicator are 
measured simultaneously in the descending aorta, cal-
culation of ITBV and PBV is also possible. This tech-
nique 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 EVLV. Finally, we analyzed gas exchange for 
potential correlations with ITBV, PBV, and EVLV.

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 and on data published in the 
literature. 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 EVLV. 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-de-
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 in-
tramuscularly 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 inha-
lation anesthetic (isoflurane 0.5–1.0 MAC). After tra-
cheal intubation, the lungs were ventilated with inter-
mittent positive pressure ventilation. Tidal volume, 
ventilatory frequency, and inspired fraction of oxygen (FiO2) in nitrogen were adjusted to maintain normal 
arterial partial pressure of carbon dioxide (PaCO2) levels 
(PaCO2 35–40 mmHg) and an arterial oxygen saturation 
(SaO2) 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 so-
Dium bicarbonate or potassium was given when neces-
sary. During ECC (duration 84 ± 26 min), body core 
temperature was decreased to 30 ± 0.5°C. Mechanical ventila-
tion was stopped before cardioplegic cardiac ar-
rest (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 un-
clamped and the lungs were ventilated with 100% O2 
with half the minute volume used before ECC. Full 
ventilation was restored before separation from ECC, 
which was performed after sufficient repertusion of the 
heart and reestablishment of a normal core tempera-
ture to obviate postbypass temperature decreases in the 
pulmonary artery. No patient received positive inotropc 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 
bleed loss was noted. In the intensive care unit (ICU), 
mechanical ventilation was maintained in the abovc-
described manner, and the FiO2, was adjusted to maintain 
SaO2 above 95%. All patients were successfully sepa-
rated 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 
troduced into the left or right radial artery for pressure 
measurements and blood sampling. After induction

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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 at-
mospheric pressure were measured. Mean systemic ar-
terial 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 mea-
sured by standard techniques (ABL 3, Radiometer, Co-
penhagen, 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 resis-
tances, alveolo-arterial PO₂ gradient (PA-aQ₂), and ve-
nous admixture (QV/QT) were calculated using stan-
dard formulas. Oxygen saturation of the arterial and
mixed venous blood was measured spectrophotomet-
ically (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 in-
tra- and extravascular volumes. The indicator bolus (in-
docyanine 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 tem-
perature-controlled syringe (fig. 1). The dilution curves
for dye and temperature were recorded simultaneously
in the aorta with the thermistor-tipped fiberoptic cath-
eter. A lung water computer (System Cold Z-021, Par-
tig, München, Germany) determined the mean transit
time for the thermal indicator (MTT T) and for the dye
indicator (MTT d) and calculated total thermal volume,
ITBV, and extravascular thermal volume from the mean
transit time (EVTV T). PBV and extravascular thermal
volume also were determined from the exponential
decay time (EVTV d) for the indicators (see appendix).

Injection of the thermal and the
dye indicator

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, TDₚₐ = thermodilution meas-
urement in the pulmonary artery, TDₐorta = thermodilution mea-
asurement in the aorta. The indicator dye is determined si-
multaneously 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 respira-
ory conditions. Then, cardiopulmonary data were
determined, and the intra- and extravascular lung vol-
umes 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 cardiopul-
monary status and intra- and extravascular thoracic
volumes were determined during sedation and me-
chanical 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 Statview sta-
tistical program (Systat, Evanston, IL). Mean values
and standard deviations were calculated. The signifi-
cance 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. 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. After separation from cardiopulmonary bypass, $P_aO_2$ and $Q_{Va/Q_T}$ had increased almost twofold ($P < 0.01$). Four hours after admission to the ICU, $P_aO_2$ and $Q_{Va/Q_T}$ 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 EVLVW were recorded after induction of anesthesia and following sternotomy but increased by 52% after separation from ECC ($P < 0.01$). Four hours postoperatively, EVLVW 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). $Q_{Va/Q_T}$ 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 and of the decay time volumes calculated from the indicator dilution curves (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. In vivo, slightly lower values have been found in clinical studies using double-indicator techniques. Thorvaldson et al. assessed a mean PBV of 3.8–4.2 ml/kg in open-chest dog studies, 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 in normotensive humans. Earlier studies revealed also a good correlation between premortem $\text{EVT}_{\text{MTT}}$ obtained with the fiberoptic-thermistor system and postmortem gravimetric EVLV in oleic acid and hydrostatic edema ($r = 0.97$, $P < 0.01$, $n = 22$). In the present investigation, $\text{EVT}_{\text{MTT}}$ and $\text{EVT}_{\text{MTT}}$ 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...
Table 1. Cardiopulmonary Data

<table>
<thead>
<tr>
<th></th>
<th>After Induction of Anesthesia (Control State)</th>
<th>After Sternotomy</th>
<th>After Separation from Extracorporeal Circulation</th>
<th>4 h after Surgery</th>
<th>20 h after Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (beats/min⁻¹)</td>
<td>55 ± 6</td>
<td>65 ± 9*</td>
<td>74 ± 11*</td>
<td>94 ± 16†</td>
<td>86 ± 12†</td>
</tr>
<tr>
<td>Psa (mmHg)</td>
<td>72 ± 8</td>
<td>82 ± 10*</td>
<td>74 ± 7</td>
<td>85 ± 6*</td>
<td>79 ± 11</td>
</tr>
<tr>
<td>Ppa (mmHg)</td>
<td>17 ± 4</td>
<td>17 ± 3</td>
<td>15 ± 4</td>
<td>21 ± 5</td>
<td>18 ± 2</td>
</tr>
<tr>
<td>Pao (mmHg)</td>
<td>7 ± 3</td>
<td>8 ± 2</td>
<td>7 ± 3</td>
<td>7 ± 4</td>
<td>8 ± 3</td>
</tr>
<tr>
<td>PpaO₂ (mmHg)</td>
<td>8 ± 4</td>
<td>11 ± 2*</td>
<td>10 ± 3</td>
<td>9 ± 4</td>
<td>9 ± 3</td>
</tr>
<tr>
<td>CO (l.min⁻¹)</td>
<td>3.3 ± 0.7</td>
<td>3.4 ± 0.5</td>
<td>4.5 ± 0.9*</td>
<td>4.8 ± 0.9</td>
<td>5.1 ± 0.8</td>
</tr>
<tr>
<td>SVR (dyn.s.cm⁻⁵)</td>
<td>1.579 ± 392</td>
<td>1.720 ± 338</td>
<td>1.242 ± 203*</td>
<td>1.325 ± 269*</td>
<td>1.120 ± 212*</td>
</tr>
<tr>
<td>PVR (dyn.s.cm⁻⁵)</td>
<td>165 ± 58</td>
<td>120 ± 48</td>
<td>103 ± 24*</td>
<td>189 ± 62</td>
<td>127 ± 18</td>
</tr>
<tr>
<td>Pao (mmHg)</td>
<td>154 ± 50</td>
<td>141 ± 39</td>
<td>235 ± 115†</td>
<td>116 ± 26</td>
<td>79 ± 17†</td>
</tr>
<tr>
<td>PaCO₂ (mmHg)</td>
<td>36 ± 2</td>
<td>36 ± 4</td>
<td>34 ± 3</td>
<td>32 ± 3</td>
<td>42 ± 2†</td>
</tr>
<tr>
<td>PVO₂ (mmHg)</td>
<td>33 ± 4</td>
<td>35 ± 3</td>
<td>39 ± 5*</td>
<td>31 ± 5</td>
<td>31 ± 4</td>
</tr>
<tr>
<td>Pa-AO₂ (mmHg)</td>
<td>144 ± 46</td>
<td>154 ± 44</td>
<td>396 ± 116†</td>
<td>132 ± 46</td>
<td>86 ± 43*</td>
</tr>
<tr>
<td>Qva/QO₂ (% CO)</td>
<td>11 ± 4</td>
<td>15 ± 5</td>
<td>29 ± 7†</td>
<td>12 ± 4</td>
<td>16 ± 5</td>
</tr>
</tbody>
</table>

Data are mean ± SD; n = 10.
HR = heart rate; Psa = mean arterial pressure; Ppa = mean pulmonary arterial pressure; Pao = mean arterial pressure; CO = cardiac output; SVR = systemic vascular resistance; PVR = pulmonary vascular resistance; PaO₂ = partial pressure of oxygen; PaCO₂ = partial pressure of carbon dioxide; Pao = partial pressure of oxygen; Qva/QO₂ = venous admixture.
* P < 0.05 compared with the control state.
† P < 0.01 compared with the control state.

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. In noncardiac surgical patients, we observed a decreased ITBV after induction of anesthesia but an unchanged EVLV. Thoracic blood volume is significantly affected by airway

Table 2. Thoracic Intravascular and Extravascular Fluid Volumes

<table>
<thead>
<tr>
<th></th>
<th>After Induction of Anesthesia (Control State)</th>
<th>After Sternotomy</th>
<th>After Separation from Extracorporeal Circulation</th>
<th>4 h after Surgery</th>
<th>20 h after Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>ITBV (ml)</td>
<td>1,417 ± 208</td>
<td>1,671 ± 265</td>
<td>2,002 ± 343*</td>
<td>1,986 ± 378*</td>
<td>1,832 ± 393</td>
</tr>
<tr>
<td>(ml·kg⁻¹)</td>
<td>16.4 ± 2.7</td>
<td>21.7 ± 3.7</td>
<td>26.0 ± 4.4*</td>
<td>25.8 ± 4.9*</td>
<td>23.8 ± 5.2</td>
</tr>
<tr>
<td>PBV (ml)</td>
<td>277 ± 103</td>
<td>323 ± 115</td>
<td>431 ± 146*</td>
<td>393 ± 117*</td>
<td>331 ± 85</td>
</tr>
<tr>
<td>(ml·kg⁻¹)</td>
<td>3.6 ± 1.3</td>
<td>4.2 ± 1.5</td>
<td>5.6 ± 1.9*</td>
<td>5.1 ± 1.5*</td>
<td>4.3 ± 1.1</td>
</tr>
<tr>
<td>EVLV (ml)</td>
<td>462 ± 78</td>
<td>470 ± 115</td>
<td>701 ± 203†</td>
<td>493 ± 162</td>
<td>477 ± 117</td>
</tr>
<tr>
<td>(ml·kg⁻¹)</td>
<td>6.0 ± 1.0</td>
<td>6.1 ± 1.5</td>
<td>9.1 ± 2.6†</td>
<td>6.4 ± 2.1</td>
<td>6.2 ± 1.5</td>
</tr>
</tbody>
</table>

Data are mean ± SD; n = 10.
ITBV = intrathoracic blood volume; PBV = pulmonary blood volume; EVLV = extravascular lung water.
* P < 0.05 compared with the control state.
† P < 0.01 compared with the control state.
THORACIC INTRAVASCULAR AND EXTRAVASCULAR FLUID VOLUMES

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. 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. In addition, pulmonary arterial occlusion pressure increased slightly, which also can influence PBV. 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. Thus, redistribution of interstitial fluid into the intravascular compartment after separation from ECC may explain the increased thoracic intravascular 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.

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. Despite these changes, no patient revealed clinical or radiologic signs of pulmonary congestion.

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. 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 Hoefl et al. 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. According to the Starling equation, a decrease of intravascular colloid osmotic pressure should enhance hydraulic fluid movement into the in-


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Fig. 3. Relationship between extravascular lung water (EVLW) and venous admixture (Qva/Qt). Qva/Qt tended to increase with higher levels of lung water, but the correlation was not statistically significant.

\[ \tau = 0.416 \quad p = 0.075 \]
terstitial space even if the conductance and reflection coefficients of the alveolocapillary membrane are unchanged.\textsuperscript{46} Also, an increased permeability due to endothelial cell injury may lead to lung edema after cardiopulmonary bypass,\textsuperscript{3,8-10,45} although the relevance of the latter mechanism has been challenged by MacNaughton et al.\textsuperscript{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.\textsuperscript{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 $\dot{Q}_{\text{VA}}/\dot{Q}_T$ 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.\textsuperscript{45} In critically ill patients, no correlation between EVLW and $P_a-O_2$ was found in a differential analysis of lung water below or above 9 ml/kg.\textsuperscript{46} In the present study, $\dot{Q}_{\text{VA}}/\dot{Q}_T$ 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, $\dot{Q}_{\text{VA}}/\dot{Q}_T$ was also influenced by the infusion of nitroglycerin after ECC and in the postoperative course.\textsuperscript{47} Nitroglycerin may directly impair oxygenation in edematous lungs by release of hypoxic pulmonary vasoconstriction.\textsuperscript{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.\textsuperscript{49} Possibly, formation of atelectasis after induction of anesthesia\textsuperscript{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.\textsuperscript{29} Accordingly, two distribution volumes can be calculated:

\[
\text{ITBV}_{\text{MRT}} = Q_{\text{dy}}, \text{MTT}_{\text{dy}}
\]

\[
\text{TTV}_{\text{MRT}} = Q_T, \text{MTT}_{\text{T}}
\]

In equation 1, ITBV\textsubscript{MRT} is the ITBV (intravascular volume from the point of injection of the indicator to detection in the descending aorta), and $Q_{\text{dy}}$ and MTT\textsubscript{dy} represent the flow and the mean transit time of the indicator dye, respectively. In equation 2, a total thermal distribution volume TTV\textsubscript{MRT} is obtained by means of the thermolysis flow ($Q_T$) and MTT\textsubscript{T}. TTV\textsubscript{MRT} represents the sum of ITBV\textsubscript{MRT} and the extravascular heat exchangeable volume. Thus, ETV\textsubscript{MRT} is defined as the difference between TTV\textsubscript{MRT} and ITBV\textsubscript{MRT}:

\[
\text{ETV}_{\text{MRT}} = \text{TTV}_{\text{MRT}} - \text{ITBV}_{\text{MRT}}
\]

ETV\textsubscript{MRT} is regarded as a reliable estimate of EVLW, provided the perfusion of the pulmonary vessels is not significantly impaired.\textsuperscript{29,29,51} Using the diffusion curve decay approach,\textsuperscript{38} the pulmonary thermal decay volume (PTV\textsubscript{MRT}) is calculated:

\[
\text{PTV}_{\text{MRT}} = Q_T, t_{\text{expon}}
\]

where $t_{\text{expon}}$ is the exponential decay time for the thermal indicator.
measured in the descending aorta. Likewise, PBV_{es} is obtained for
the indicator dye:

$$PBV_{es} = Q_e \cdot \tau_{tot}.$$  (5)

where PBV_{es} constitutes the PBV and \(\tau_{tot}\) 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 deter-
mined predominantly by the largest chamber. Thus, EVTV_{es} is cal-
culated:

$$EVTV_{es} = PTV_{es} - PBV_{es}.$$  (6)

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References

1. Braun SR, Birmbaum ML, Chopra PS: Pre- and postoperative pul-
monary function abnormalities in coronary artery revascularization

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. LoCicero J, McCann B, Missad M, Joob WA: Prolonged ventilatory

respiratory distress syndrome following cardiopulmonary bypass: In-

function after coronary artery surgery using the internal mammary
artery and the saphenous vein. Thorax 44:209-211, 1989

6. Ducek 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

7. Locke TJ, Griffiss, Mourl H, Gibson: Rib cage mechanics after

8. Royston D, Minist BD, Higenbotiam TW, Wallwork J, Jones JG:
The effect of surgery with cardiopulmonary bypass on alveolar-cap-
illary barrier function in human beings. Ann Thorac Surg 40:139-
143, 1985

Schulfsfried F: Intraoperative changes in extravascular lung water: A
study involving cardiosurgical patients. Anesthesia 34:593-599, 1985

10. Byrick RJ, Kay JC, Noble WN: Extravascular lung water ac-
cumulation in patients following coronary artery surgery. Can Anaesth

11. MacNaughton PD, Braude S, Hunter DN, Denison DM, Evans
TW: Changes in lung function and pulmonary capillary permeability

12. Lougic B, Gonzalez, E, Jamart J, Bulliard G, Schoevaerts JC: Post-
cardio pulmonary lung edema. Chest 103:86-95, 1993

cardiopulmonary bypass with human albumin or ringer lactate:

Effect on colloid osmotic pressure and extravascular lung water. Br

central blood volume and extravascular lung water. Thorac Cardio-

Effects of prolonged surgical trauma on the extravascular lung water
and central blood volume in the dog. Acta Anaesthesiol Scand 30:
309-313, 1986

stierna G: Does PEPP facilitate the resolution of extravascular lung
water experimental hydrostatic pulmonary oedema? Eur Respir J:
1053-1059, 1991

P, Zeravik J, Zimmermann G: A fiberoptics based system for inte-
grated monitoring of cardiac output, intrathoracic blood volume, extrava-
cular lung water, O2-saturation, and a+ v differences. Practical Ap-
lications of Fiberoptics in Critical Care Monitoring. Edited by Lewis

son L, Tokics L: Functional residual capacity, thoracoabdominal di-
dimensions, and central blood volume during general anesthesia with
muscle paralysis and mechanical ventilation. Anesthesiology 62:247-
254, 1985

extravascular lung water by thermal-dye dilution technique: Mechanisms of cardiac output dependence. Intensive Care Med
16:115-120, 1990

20. Thorvaldsd J, Hebeek A, Kilii F: Determinants of pulmonary
blood volume: Effects of acute changes in airway pressure. Acta Phys-

volume accurately reflects circulatory volume status in critically ill
patients with mechanical ventilation. Intensive Care Med 18:142-
147, 1992

334, 664-673

23. Joachimsson PO, Nyström SO, Tveden H: Postoperative vita-
minatory and circulatory effects of extended rewarming during cardi-

24. Bazary MG, Petre J, Novoa R: Errors in thermomelization cardiac
output measurements caused by rapid pulmonary artery temperature
decreases after cardiopulmonary bypass. Anesthesiology 77:31-37,
1992

25. Nunn JF, Bergman NA, Coleman AJ: Factors influencing the
arterial oxygen tension during anaesthesia with artificial ventilation.
Br J Anaesth 37:897-914, 1965

26. Steward GN: The pulmonary circulation time, the quantity of
blood in the lungs, and the output of the heart. Am J Physiol 58:20-
44, 1921

method for measurement of blood flow and volume. J Appl Physiol
6:731-744, 1954

28. Effros RM: Lung water measurements with the mean transit

29. Lewis FR, Elings VB, Hill SL, Christensen JM: The measurement of
extravascular lung water by thermal-green dye indicator dilution. Ann
N Y Acad Sci 384:394-410, 1982

Mceever WP: The dye dilution method for describing the central
31. Harris P, Heath D: The Human Pulmonary Circulation. Edin-
burgh, Churchill Livingstone, 1986, pp 114–121
39. Versprille A, Jansen JRC, Fritzman RC, Hulsman AR, van der Klauw MM: Negative effect of insufflation on cardiac output and pul-
41. Pistolesi M, Miniati M, Milne ENC, Guinteri C: The chest roent-
47. Anjou-Lindskog E, Broman L, Holmgren A: Effects of nitro-