ORIGINAL

Determination of the side-separated pulmonary right-to-left shunt volume

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Abstract : ***Background*** **: With the present method of intrapulmonary right-to-left shunt volume calculation, no differentiation can be made between the shunt volume shares of the right and left lungs. For a better understanding of pathophysiological processes during thorax surgery with side-separated ventilation, a side-separated shunt volume determination would be useful.** ***Materials and Methods*** **: In 14 young female pigs, catheters were implanted into the left atrium after left thoracotomy. After transient clamping of the ipsilateral pulmonary veins, pulmonary venous blood was selectively obtained from the right lung. Cardiac output (CO) and side-separated pulmonary perfusion were determined with flowprobes at the pulmonary trunk and the left pulmonary artery. The shunt volumes were determined before and after thoracotomy during two-lung ventilation (Two-LV), after one-lung (right) ventilation (One-LV) with a continuous positive airway pressure (CPAP) of +7.5, +5.0 cm H_2O, and under atelectasis of the non-dependent left lung (NDL).** ***Results*** **: After thoracotomy in lateral decubitus position and Two-LV, the shunt volumes of the two lungs differ. The right lung holds the major share (11.0 ± 1.7% CO) [mean ± SD]. The share of the left NDL is only 3.3 ± 1.4. Under One-LV (right) and CPAP in the NDL, the total pulmonary shunt volume rises. This is caused by the increase in the NDL shunt volume share to 8.8 ± 5.2 under CPAP +7.5 ($p<0.05$) and to 9.7 ± 2.5 under CPAP +5.0 ($p < 0.05$).** ***Conclusions*** **: The new intraoperative method of side-separated arterial blood gas analysis in conjunction with side-separated perfusion measurement makes side- separated right-to-left shunt volume determination possible and may lead to interesting new pathophysiological insights. J. Med. Invest. 55 : 44-50, February, 2008**

Keywords **:** *pulmonary right-to-left shunt volume, side-separated determination, one-lung ventilation*

INTRODUCTION

The pulmonary right-to-left shunt volume (Qs/Qt) is a measure of the venous admixture in both lungs caused for functional and anatomical reasons. It is calculated by the shunt volume formula acc. to Berggren (1). So far, no differentiated statement about the shunt volume shares of the right and left lungs can be made. For questions related to the optimization of respiration in intensive care practice, the hitherto common shunt volume calculation is sufficient. By contrast, thoracic surgery has important effects on ventilation and perfusion. Due to the lateral position, thoracotomy and side-differentiated ventilation, distribution is disturbed differently in the two lungs (2-6). To better understand the patho-

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physiology of side-separated lung ventilation trying new therapeutical approaches to shunt volume minimization, it would be of advantage to determine the shunt volume share of each lung separately.

Our animal experiment aimed at trying out a new method of intraoperative side-separated right-to-left shunt volume determination.

METHODS

The animal experiments were carried out on 14 young female pigs of the race "Deutsches Landschwein" (weight range : 30-47 kg, average : 37.2 kg), with permission from the Veterinary department of the Thuringian State Authority for Food Protection and Fair Trading, and in compliance with the Animal Protection Act.

Anaesthesia and artificial respiration

Anaesthesia was induced by intramuscular injection of 10 mg kg^{-1} ketamine with 150 IE hyaluronidase. Additionally, 6.25 mg droperidol and 10 mg diazepam were applied after cannulation of an ear vein, and the animals were orotracheally intubated during spontaneous breathing (Magill tube, ID = 8.5 mm). After relaxation with pancuronium bromide (0.2 mg kg^{-1}) and deepening of the anaesthesia by fentanyl (10 μg kg^{-1}), artificial respiration was started with 1.0-1.5 MAC of isofluran in an oxygen/nitrous oxide mix (FIO_2 = 0.3). Anaesthesia and relaxation were maintained by continuous application of isoflurane, fentanyl (0.05-0.08 μg kg^{-1} min^{-1}) and pancuronium bromide (2.5 μg kg^{-1} min^{-1}).

Mechanical ventilation was performed with an ICU respirator (Servo 900, Siemens, Germany), using a volume-controlled setting (tidal volume 10 ml kg^{-1}, respiratory rate 16-20 min^{-1}, PEEP = 6 cm H_2O). The endexpiratory pCO_2 was maintained between 35 and 45 mmHg. 4-6 ml/kg/h Ringer's lactate as well as 2-4 ml/kg/h hydroxyethyl starch (HES 10%) were infused as base infusion. The body temperature was maintained between 36-38°C by warming the infusion solution and covering the animals with an isolation sheet.

After tracheotomy, a left-sided Robertshaw double-lumen tube with an extra-long bronchial lane (39 Ch ; special product by Mallinckrodt, Ireland) was inserted. The correct position of the tube was checked by fiber bronchoscopy (BF 3C30 fiber bronchoscope, Olympus, Japan). The animals were placed in the right lateral decubitus posture.

Monitoring

For blood sampling (*arterial and mixed venous blood gas analyses*) and haemodynamic measurements, we placed a pulmonary artery catheter (Swan-Ganz CCO/SvO2 TD Catheter 744 H7.5F, Baxter Healthcare Corp., Irvine, USA) via the right internal jugular vein, and an arterial cannula (18 G ; Vygon, Ecouen, France) into the right common carotid artery.

Cardiac output (CO) and the *left pulmonary arterial blood flow (QLe)* were determined by the ultrasonic transit time method (7). For this purpose, flowprobes were placed around the pulmonary trunk (H20A, size 20mm) and the left pulmonary artery (H10A, size 10mm) (Fig. 1). Both flows were simultaneously recorded with a dual-channel flowmeter (HT207, Transonic Medical Flowmeter, Transonic Systems Inc., Ithaca, New York).

For *side-separated arterial blood taking*, a catheter was introduced into to left atrium of the heart via the cranial pulmonary vein. A short-time clamping (15 seconds) of the left cranial and caudal pulmonary veins by means of vascular clamps made it possible to selectively obtain pulmonary venous blood from the right lung via the left atrial catheter. Pulmonary venous blood gad samples from the left lung were selectively obtained by puncture of the left cranial and caudal pulmonary veins on the peripheral side of the clamps (Fig. 2).

The arterial and mixed venous blood gas samples were analyzed at once (ABL System 625 Radiometer, Copenhagen, Denmark).

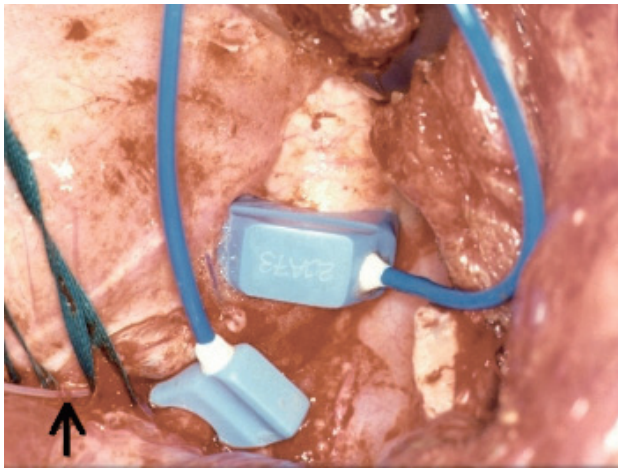

Fig. 1 Intraoperative site : left ventral pulmonary hilum with flowprobes on the pulmonary trunk and the left pulmonary artery, cranial and caudal pulmonary veins surrounded with vessel loops, and left atrial catheter via the cranial pulmonary vein (arrow)

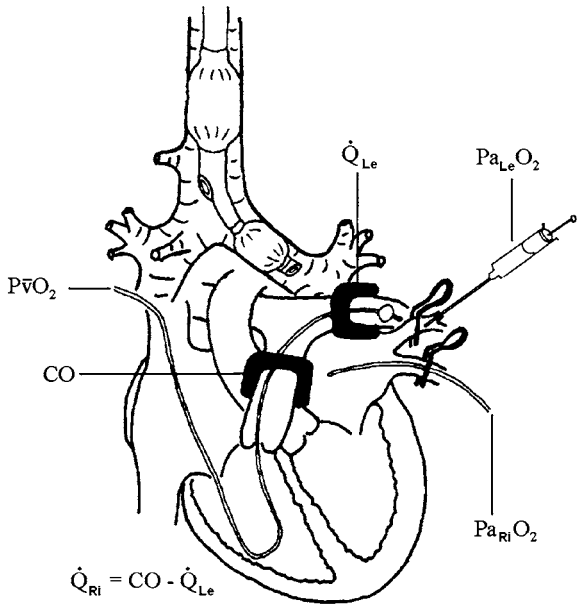

Fig. 2 Schematic diagram illustrating the side-separated blood gas and blood flow measurement ; pulmonary arterial catheter, left atrial catheter, flowprobes on the pulmonary trunk and the left pulmonary artery ; cardiac output (CO), pulmonary arterial blood flow of left lung (QLe), mixed venous partial oxygen pressure (PvO_2), arterial partial oxygen pressure of the left lung ($PaLeO_2$), arterial partial oxygen pressure of the right lung ($PaRiO_2$) ; clamping of the left pulmonary vein

Shunt volume calculation

- Pulmonary right-to-left shunt volume (8) :

$$Qs/Qt = \frac{AaDO_2 \times 0.0031}{AaDO_2 \times 0.0031 + (CaO_2 - CvO_2)}$$

- Side-separated pulmonary right-to-left shunt volume:

Right lung : Qs/Qt (Ri)

$$= \frac{AaDO_2 \times 0.0031}{AaDO_2 \times 0.0031 + (Ca_{Ri}O_2 - CvO_2)}$$

O_2 content of the arterial blood of the right lung :

$Ca_{Ri}O_2 = Pa_{Ri}O_2 \times 0.0031 + (Hb \times 1.39 \times Sa_{Ri}O_2\%)$

Mixed venous O_2 content :

$CvO_2 = PvO_2 \times 0.0031 + (HB \times 1.39 \times SvO_2\%)$

Alveolo-arterial O_2 difference :

$AaDO_21.0 = (Bp - Pa_{Ri}CO_2 - {}_PH_2O) - Pa_{Ri}O_2$

Because of the uneven perfusion of the two lungs, the calculated value needs to be corrected making allowance for the perfusion of the respective side :

$$Qs_{Ri}/Qt = \frac{Qs/Qt\ (Ri) \times Q_{Ri}}{CO}$$

Left lung :

Same as right, using $Pa_{Le}O_2$, $Sa_{Le}O_2\%$, $Pa_{Le}CO_2$, Q_{Le}

Experimental procedure

The parameters were measured before left-lateral thoracotomy under two-lung ventilation (pre-THT/ Two-LV), after thoracotomy under two-lung ventilation (post-THT/ Two-LV), one-lung ventilation with a continuous positive airway pressure of 7.5 cmH_2O (One-LV+CPAP 7.5), one-lung ventilation with a continuous positive airway pressure of 5.0 cmH_2O (One-LV+CPAP 5.0), and one-lung ventilation with atelectasis of the left lung (One-LV+atelectasis).

20 min before the beginning of thoracotomy, the FIO_2 was increased to 1.0.

The respirator setting was left unchanged throughout the experiment. With One-LV of the right lung, the only change was the connection of a CPAP system to the left leg of the double-lumen tube. Via the CPAP system, a CPAP of 7.5 cmH_2O and subsequently a CPAP of 5.0 cmH_2O with a FIO_2=1.0 were applied to the left lung for 20 minutes each. Then the endobronchial leg of the tube was finally disconnected, and we waited for spontaneous atelectasis.

Statistical analysis

Results are expressed as mean (SEM) values.

For assessing the differences between the stages of the experiment we used the Wilcoxon signed ranks test. Differences having a p-value of < 0.05 were considered statistically significant. The following experimental stages were compared with each other :

1 Pre-THT/Two-LV vs. Post-THT/Two-LV
2 Post-THT/Two-LV vs. One-LV+CPAP 7.5, One-LV+CPAP 5.0 and One-LV + atelectasis (* = significant)
3 One-LV+CPAP 7.5 vs. One-LV+CPAP 5.0 and One-LV+CPAP 5.0 vs. One-LV + atelectasis (# = significant)

RESULTS

Mean (SEM) values with significance indicators for each parameter are shown in Table 1. Under different ventilation conditions, the CI was stable between 3.8 and 4.4 l/min/m^2 body surface. CI, PaO_2, PvO_2, $PaCO_2$ and Qs/Qt displayed no relevant changes after THT. After THT and Two-LV, 35.9% of the CO circulated through the left, 64.2%

through the right lung. Under One-LV + CPAP, perfusion slightly decreases in the left lung and slightly increases in the right one. A distinct difference in perfusion is found in case of One-LV + atelectasis (QLe/Qt : 13.8 ±7.5% CO vs. Two-LV, $p < 0.05$; QRi/Qt : 86.3 ± 7.5% CO vs. Two-LV, $p < 0.05$) (Fig. 3).

The PaO_2 drops by 65.1 mmHg ($p > 0.05$) under One-LV + CPAP 5.0, and by 262.4 mmHg ($p < 0.05$) under One-LV + atelectasis, compared to post-THT/Two-LV. The post-THT+Two-LV $PaLeO_2$ is distinctly higher than the $PaRiO_2$ (524.1 versus 488.3 mmHg). Under One-LV + CPAP and atelectasis, however, the ratio distinctly changes at the cost of the left lung. With atelectasis of the left lung, the $PaRiO_2$ increases significantly (501.0 ± 49.6 vs. 425.8 ± 67.0 mmHg, $p < 0.05$) (Fig. 4).

The total pulmonary shunt volume (Qs/Qt) does not change after THT + Two-LV, but distinctly increases after One-LV + CPAP 5.0 (21.0 ± 1.9 vs.

Tab. 1 Cardiac index (CI), arterial and mixed venous blood gas levels (PaO_2, PvO_2, $PaCO_2$; left lung : $PaLeO_2$; right lung : $PaRiO_2$), pulmonary arterial blood flow (left lung : QLe/Qt ; right lung : QRi/Qt), total pulmonary and side-separated right-to-left shunt volume (Qs/Qt ; left lung : QsLe/Qt ; right lung : QsRi/Qt) in right lateral decubitus position before THT and two-lung ventilation (pre-THT/Two-LV), after thoracotomy and two-lung ventilation (post-THT/Two-LV), after one-lung ventilation at a continuous positive airway pressure of +7.5 and +5.0 cmH_2O (One-LV+CPAP 7.5 and One-LV+CPAP 5.0, resp.), and under one-lung ventilation plus atelectasis (One-LV+atelectasis). The table shows mean values and standard deviations obtained from 14 animals.
CI = CO / m^2 body surface (l/min/m^2 bs),
Statistical comparison of each stage of the experiment under One-LV with postTHT/Two-LV (* $p < 0.05$) ; statistical comparison of the four postTHT stages with each other (# $p < 0.05$)

Variable		pre- ThT	post- ThT			
		Two-LV	Two-LV	One-LV + CPAP 7.5	One-LV + CPAP 5.0	One-LV + atelectasis
CI	(l/min/m^2 bs)	4.4 ± 0.7	3.8 ± 0.8	4.1 ± 0.8	4.3 ± 0.6	4.2 ± 0.9
QLe/Qt	(% CO)		35.9 ± 9.4 *	30.0 ± 8.8	33.8 ± 8.1	13.8 ± 7.5 *
QRi/Qt	(% CO)		64.2 ± 9.4 *	70.1 ± 8.9	66.3 ± 8.1	86.3 ± 7.5 *
PaO_2	(mmHg)	469.9 ± 42.5	473.5 ± 69.4 *	460.0 ± 102.6	408.4 ± 73.5 * #	211.1 ± 69.7 #
PvO_2	(mmHg)	43.0 ± 3.2	46.8 ± 6.3	50.6 ± 5.8	51.4 ± 6.9	41.2 ± 7.0
$PaCO_2$	(mmHg)	40.8 ± 4.1	42.3 ± 3.3	40.7 ± 3.4	40.3 ± 3.6	37.8 ± 3.6
$PaLeO_2$	(mmHg)		524.1 ± 51.5 *	399.7 ± 116.3 *	337.0 ± 133.4 * #	47.0 ± 8.2 #
$PaRiO_2$	(mmHg)		488.3 ± 39.5	444.5 ± 50.6	425.8 ± 67.0 #	501.0 ± 49.6 #
Qs/Qt	(% CO)	15.0 ± 4.1	15.0 ± 3.8 *	18.0 ± 3.4	21.0 ± 1.9 * #	26.5 ± 7.3 * #
QsLe/Qt	(% CO)		3.3 ± 1.4 *	8.8 ± 5.2 *	9.7 ± 2.5 * #	13.8 ± 7.5 * #
QsRi/Qt	(% CO)		11.0 ± 1.7	10.0 ± 4.7	12.0 ± 3.8	12.0 ± 4.4

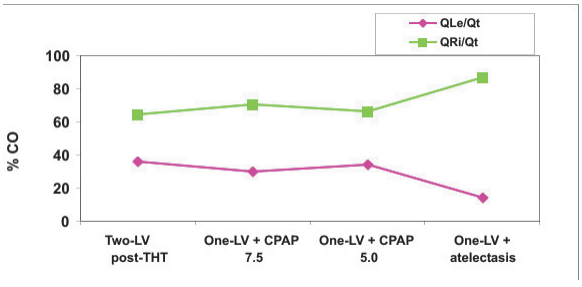

Fig. 3 Side-separated pulmonary arterial blood flow (left lung : QLe/Qt ; right lung : QRi/Qt % CO) after thoracotomy and two-lung ventilation (post-THT/Two-LV), after one-lung ventilation at a continuous positive airway pressure of +7.5 and +5.0 cmH_2O (One-LV+CPAP 7.5 and One-LV+CPAP 5.0, respectively), and under one-lung ventilation plus atelectasis (One-LV+atelectasis). Mean values obtained from 14 animals

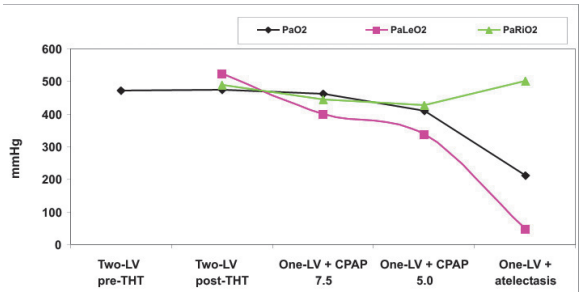

Fig. 4 Arterial and side-separated pulmonary venous (arterial) partial oxygen pressure (PaO_2 ; left lung : $PaLeO_2$; right lung : $PaRiO_2$ mmHg) after thoracotomy and two-lung ventilation (post-THT/Two-LV), after one-lung ventilation at a continuous positive airway pressure of +7.5 and +5.0 cmH_2O (One-LV+CPAP 7.5 and One-LV+CPAP 5.0, resp.), and under one-lung ventilation plus atelectasis (One-LV+atelectasis). Mean values obtained from 14 animals

15.0 ± 3.8% CO, $p < 0.05$). Under atelectasis of the left lung, a further increase in Qs/Qt is observed (26.5 ± 7.3 vs. 21.0 ± 1.9% CO, $p < 0.05$). After thoracotomy and Two-LV, the shunt volumes of the two lungs differ. The major share is taken by the right lung, which lies below (QsRi/Qt : 11.0 ± 1.7% CO). The share of the left lung lying on top (QsLe/Qt) is only 3.3 ± 1.4% CO. After One-LV + CPAP, an increase in the shunt volume share of the left lung up to 9.7 ± 2.5% CO ($p < 0.05$) can be registered. Under atelectasis, QsLe/Qt further increases compared to One-LV + CPAP 5.0 (13.8 ± 7.5 vs. 9.7 ± 2.5% CO, $p < 0.05$), whereas the QsRi/Qt shows no significant change (Fig. 5).

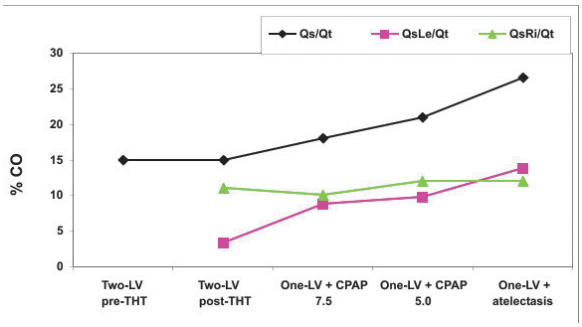

Fig. 5 Total pulmonary and side-separated right-to-left shunt volume (Qs/Qt ; left lung : QsLe/Qt ; right lung : QsRi/Qt % CO) after thoracotomy and two-lung ventilation (post-THT/Two-LV), after one-lung ventilation at a continuous positive airway pressure of +7.5 and +5.0 cmH_2O (One-LV+CPAP 7.5 and One-LV+CPAP 5.0, resp.), and under one-lung ventilation plus atelectasis (One-LV+atelectasis). Mean values obtained from 14 animals

DISCUSSION

Our results show that side-separated right-to-left shunt volume determination in the opened thorax is possible in animal experiments on two conditions : side- separate collection of pulmonary venous blood from the right and left lung, and measurement of side-separated pulmonary perfusion. To solve that problem, the ipsilateral pulmonary veins were temporarily clamped. By puncture of the pulmonary veins on the peripheral side of the clamps we selectively obtained pulmonary venous blood from the non-dependent lung (NDL). Blood from the contralateral dependent lung (DL) can be collected separately via an atrial catheter. We used an atrial catheter, as the left atrial pressure was to be measured continuously anyhow for a different purpose. Alternatively, blood can be collected by puncture of the pulmonary veins resp. left atrium on the central side of the clamps. The clamp time was 15 seconds. This is enough time to wash out left pulmonary venous blood from the left atrium to take blood exclusively from the right lung. There should be no influence on the examined left pulmonary venous blood because the gas exchange of the blood in this section was finished at the time of punction. Mixed venous blood can also be obtained by puncture of the pulmonary artery. Thus, the method can be applied during thorax surgery in everyday clinical practice with no great effort.

As the perfusion of the two lungs is unequal, it is necessary to measure blood flow in the ipsilateral pulmonary artery in addition to CO. By means of a flowprobe applied on the stem of the left pulmonary artery, the pulmonary arterial blood flow can be determined separately for each lung. The shunt volume calculated has to be corrected allowing for the perfusion of the respective lung. This yields the true shunt volume share of each lung.

In thorax surgery performed in lateral decubitus position with differentiated ventilation of the two lungs, complex changes of the pulmonary blood circulation and oxygenation are known to occur. Therefore, we chose just these conditions for testing the new method of side-separated right-to-left shunt volume determination. From the test we gained interesting new insights. In agreement with Brown, *et al.* (9), THT in Two-LV (PEEP +6 cmH_2O) does not deteriorate oxygenation (PaO_2 : 473.5 ± 69.4 vs. 469.9 ± 42.5 mmHg) nor Qs/Qt (15.0 ± 3.8 vs. 15.0 ± 4.1% CO). The distribution of perfusion between NDL and DL in lateral position with Two-LV of the closed thorax is reported in the literature to be 43/57% CO (6). After thoracotomy we recorded a perfusion ratio of 36/64% CO. Presumably, compliance of the NDL increases due to the missing abutment of the intact thoracic wall, so that the NDL receives an even greater share of the tidal volume and the PEEP. This results in an increased resistance of the pulmonary vessels, which leads to a redistribution of blood to the DL. For the same reason CPAP 7.5 caused an increased vascular resistance with decrease of pulmonary blood flow in comparison to CPAP 5.0 (QLe/Qt CPAP 7.5 : 30.0 ± 8.8 %CO vs. CPAP 5.0 : 33.8 ± 8.1 %CO). The blood flow in the NDL during Two-LV is higher than One-LV+CPAP 7.5 (QLe/Qt : 35.9 ± 9.4 %CO vs. 30.0 ± 8.8 %CO) by reason of intermittent ventilation with PEEP (+6.0 cmH_2O).

Contrary to Benumof (10), we found that the post-THT Qs/Qt under Two-LV was not distributed evenly

to the two lungs. Our method made it possible for the first time to separately determine the shunt volume share of each lung (QsLe/Qt : 3.3 ± 1.4 ; QsRi/Qt : 11.0 ± 1.7% CO). The shunt volume of the NDL is distinctly lower than that of the DL, as the NDL gets better ventilation.

The new method makes it possible also to better assess the extent of hypoxic pulmonary vasoconstriction (HPV). We found that, under One-LV+atelectasis of the left lung, 67.8% of the blood flow not taking part in the shunt flow to the left lung (32.6% CO with Two-LV) are diverted to the right lung (QRi/Qt : 86.3 ±7.5 vs. 64.2 ± 9.4% CO). Before, the assumption was that intact HPV would curb circulation in the non-ventilated lung (NVL) by 50%. (11).

Re-routing the blood does not cause any appreciable rise in the shunt volume in the DL (QsRi/Qt : 12.0 ± 4.4 vs. 11.0 ± 1.7% CO). The shunt volume increase during One-LV+atelectasis compared to Two-LV (Qs/Qt : 26.5 ± 7.3 vs. 15.0 ± 3.8% CO, $p < 0.05$) is only due to the shunt volume in the NVL (QsLe/Qt : 13.8 ± 7.5% CO), which corresponds to the residual perfusion. Benumof *et al*. (12) showed that the PaO_2, at a FIO_2 of 1.0 under One-LV, drops from 484 mmHg to 116 mmHg while the shunt volume rises from 14% to 44%. With One-LV under the same conditions, Alfery, *et al*. (13) found a PaO_2 of only 61 mmHg, a shunt volume of 50% and a perfusion of the NVL of 41%. The nearly unchanged perfusion of the NVL found by the authors explains the greater decline in PaO_2 or the rise in shunt volume as an indication of incomplete HPV.

With differentiated application of CPAP and PEEP it is possible to distinctly improve oxygenation with One-LV as compared to One-LV+atelectasis of the NDL (14). We can confirm this. Our results also show, however, that CPAP +7.5 and especially CPAP +5.0 cannot prevent a rise in shunt volume compared to Two-LV (Qs/Qt : 18.0 ± 3.4 or 21.0 ± 1.9 vs. 15.0 ± 3.8% CO, $p < 0.05$). CPAP at the level applied seems no adequate substitute for ventilation with PEEP. Even with CPAP +7.5 we observed a macroscopically visible volume reduction and the formation of dystelectases of the NDL. The results show that no sufficient ventilation of the alveoli can be achieved with a CPAP of +5 cmH_2O to the NDL. A greater CPAP (>10 cmH_2O), which Alfery (14) found to have a positive effect with dogs, or the use of high-frequency jet ventilation might be helpful. We were able to show that the increase in shunt volume under One-LV +CPAP compared to Two-LV, with approximately equal blood flow and constant shunt volume in the right lung, is caused exclusively by the poorer oxygenation of the left lung (QsLi/Qt : 8.8 ± 5.2 or 9.7 ± 2.5 vs. 3.3 ± 1.4% CO, $p < 0.05$).

With constant One-LV, an increase in perfusion in the ventilated DL does not lead to a rise in the right-to-left shunt volume in this lung. QsRi/Qt did not change significantly under atelectasis of the left lung compared to Two-LV (12.0 ± 4.4% CO vs. 11.0 ± 1.7% CO) despite a distinct increase in perfusion (QRi/Qt : 86.3 ± 7.5% CO vs. 64.2 ± 9.4% CO, $p < 0.05$). One-LV +CPAP with at least +7.5 of the NDL seems to be a good alternative of Two-LV during thoracic surgery. In this way only a minimal decrease in oxygenation (PaO_2 : 460.0 ± 102.6 vs 473.5 ± 69.4 mmHg) occurs. The lung volume under CPAP 7.5 makes no problems in open thoracic surgery, but thoracoscopic operations are more difficult.

Even with the new method of side-separated blood gas analysis, no differentiation between functional and anatomical shunt volume shares can be made. The venous extra-alveolar admixture to the pulmonary venous blood via thebesian veins, pulmonary arterio-venous anastomoses or bronchial veins cannot be avoided.

In summing up it can be said that the determination of the side-separated pulmonary right-to-left shunt volume in the opened thorax is possible in animal experiments. This may lead to interesting new insights into the pathophysiology of differentiated ventilation of the opened thorax.

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