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REGIONAL LUNG BLOOD PERFUSION MEASURED WITH LASER DOPPLER METHOD DURING BODY POSITION CHANGE, VALSALVA MANOEUVRE AND CARDIOPULMONARY BYPASS

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Methodological approaches to investigate local regulatory mechanisms of lung blood supply in humans are restricted. We tried a new approach using laser Doppler technique. During bronchoscopy, an angled laser Doppler flow probe was introduced through a biopsy channel and wedged into small bronchus. Laser light penetrated the wall of small bronchus and was reflected from blood cells running through neighbouring capillaries. Regional blood perfusion changes were recorded during body position change from vertical to supine and back to vertical, while performing Valsalva maneuver and during cardiac bypass surgery. Body position change and Valsalva maneuver markedly influenced the blood perfusion signal. During cardiac bypass when lungs were supplied with blood only through bronchial arteries regional blood perfusion dropped substantially on average from 93 ± 42 to 7.3 ± 4.3 perfusion units. We conclude that blood perfusion measured with this method reflect mainly the pulmonary vascular bed and may be used for investigation of its local regulatory mechanisms.

Key words: *pulmonary vascular bed, Laser Doppler technique, cardiac bypass, Valsalva manoeuvre.*

INTRODUCTION

Pulmonary blood circulation differs from systemic circulation in many ways. The whole cardiac output passes the lungs under low hydrodynamic pressure. Significant increase of the cardiac output during physical exercise does not raise pulmonary arterial pressure markedly. Low driving pressure in the blood vessels of pulmonary circulation creates a difference in blood supply to upper and dependent lung regions. Distribution of blood among alveolar capillaries is also widely influenced by alveolar oxygen content. Alveolar hypoxia redistributes blood to better-oxygenated lung regions (Olchewski *et al*., 2002). Both vasoconstricting and vasodilating mediators released from endothelial cells like endothelin, nitric oxyde, and prostacyclin I_2 are involved in the local regulation of lung blood supply (Olchewski *et al.,* 2002). Local regulation interacts with generalised influences realised through the humoral and autonomic nervous systems, activating again both vasoconstricting and vasodilating mechanisms.

The mechanisms underlying blood distribution within pulmonary vessels are still not well understood. One of the reasons is the lack of non-invasive methods allowing real-time measurement of regional pulmonary blood supply.

A Laser Doppler (LD) method allows to record blood perfusion in small volumes of tissue. Laser flow probe may be introduced into small cavities and hollow organs. In the respiratory tract LD technique so far has been used to investigate the blood flow in bronchial mucosa (Baile *et al*., 1988). The dimensions of an angled laser Doppler flow probe allow wedging the probe into small bronchi during bronchoscopy. In such a location laser light penetrates the wall of a small bronchus and is reflected from moving blood cells in the neighbouring capillaries or larger blood vessels, thus providing information about regional blood perfusion. Our pilot studies showed that the signal recorded was sensitive to body position change and to the changes in intrathoracic pressure occurring during the Valsalva manoeuvre (Taivans *et al*., 1999). They demonstrated that the vascular bed, where the signal comes from, is perfused under low pressure as characteristic for the pulmonary circulation. At the same time, it is well known that even small bronchi receive the blood supply from bronchial arteries.

Bronchial arteries anastomose with small branches of pulmonary artery as well as with the pulmonary capillary network (Olchewski *et al*., 2002). This means that the perfusion signal, recorded with laser Doppler flow probe wedged into the small bronchus, should contain some component of bronchial circulation. The overall impact of bronchial circulation into pulmonary blood supply was evaluated by Baile *et al.* (1985) and Agostoni *et al.* (1989). They measured the bronchial-to-pulmonary blood shunt during cardiac bypass surgery when aorta was clamped and the circulation through pulmonary artery arrested. Baile and co-workers found that bronchial-to-pulmonary shunt flow was extremely variable ranging from 8 to 1043 ml/min, or 3.2 ± 4.15 % of pump flow (Baile *et al*., 1985). According to Agostoni *et al.* (1989), shunt flow ranged from 0.32 to 2.76% of the pump flow.

However, there are no data available on the relationship between pulmonary and bronchial vascular beds in small lung areas having local autonomous regulation. Vasoconstriction in the response to hypoxia is characteristic for the pulmonary vascular bed. The vessels of systemic circulation, including bronchial arteries, respond to hypoxia by dilation (Olchewski *et al*., 2002). The resulting local perfusion should depend on the impacts of the bronchial and pulmonary components, respectively.

The aim of our study was to evaluate the impact of bronchial circulation into the regional blood perfusion of lungs We performed measurements with a Laser Doppler flow probe wedged into small bronchus in patients during cardiac bypass surgery. Under such conditions the heart was arrested, input from pulmonary artery absent and lungs supplied with blood only from bronchial arteries. In another group of patients we observed changes of regional blood perfusion in response to body position change, and in a third group, in response to intrathoracic pressure changes during the Valsalva manoeuvre.

METHODS

Recordings in awake, spontaneously breathing patients. Laser Doppler measurements were performed on 46 consecutive hospital patients undergoing bronchoscopy for diagnostic purposes. Cases in which bronchial biopsy was indicated were excluded from the test group. Before the procedure patients were premedicated with Sol. Promedoli 2%–1.0 i.m. and Sol. Atropini Sulphas 0.1%–0.5 i.m. Local anaesthesia of the throat was achieved by instillation of Sol. Lidocaini 10%–10.0 and of the bronchi by instillation of up to 50 ml of 3% solution. Patients were sitting in a dentist's chair. A fibreoptic bronchoscope (BF-Olympus LT30) with an endoscopic Laser Doppler probe through the biopsy channel was introduced through the mouth. An angled endoscopic laser Doppler probe, type PF 406 (Perimed, Sweeden) was introduced through the segmental bronchi until wedged into a distal bronchus. To enhance wedging of the probe the patient was asked to hold breath during deep inspiration. The advancement of the probe was stopped as soon as slight resistance appeared. In some patients the probe position was checked on X-ray films (Fig. 1). The most stable probe position could be achieved in the upper lobe segments. It was hard to achieve stability in lower lobe segments due to vertical movement of lungs during the respiratory cycle. Therefore, all further measurements were performed in the 2nd (n = 17) and 3rd (n = 29) lung segments. Blood perfusion was recorded with a Periflux System 4000 (Perimed) emitting laser light with wavelength of 633 nm (red light). The endoscopic flow probe was composed of two flexible silica fibres with a core diameter of 0.125 mm, fibre separation of 0.25 mm. The tip of the angled endoscopic probe was built of bent optic fibres without using any prisms, minimising the tip size. The bandwidth of the instrument was between 20 Hz and 24 kHz, the time constant was set to 0.2 s. The output signals of the instrument (total backscatter, CMBC (the count of moving blood cells), velocity and perfusion were stored in a computer for later analysis by a separate specialised programme (PeriSoft, Perimed). Blood perfusion was expressed in perfusion units (PU) ± confidence interval.

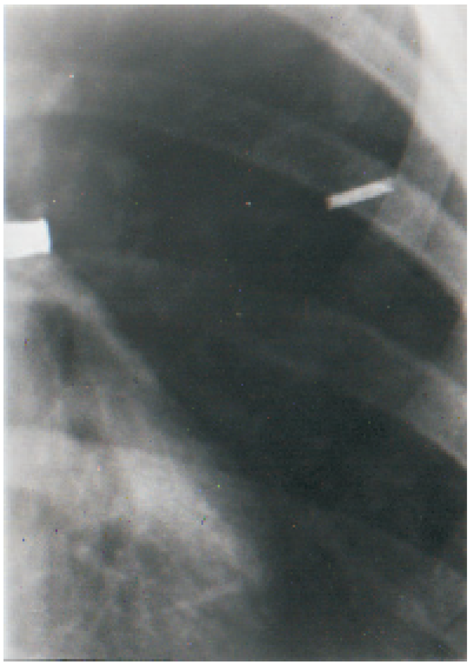

Fig. 1. X-ray image of laser Doppler flow probe inserted into small bronchus.

Recordings with body position change. Measurements were performed in the 2nd lung segment of 17 patients. Recordings were started in the vertical position. After the baseline recording was completed, the patient position was changed to supine and thereafter back to vertical. Recordings in each position lasted around 60 seconds.

Comparison between data recorded in each position was performed using paired Student t-test.

Recordings during Valsalva manoeuvre. 29 patients were involved in this study. In all cases the flow probe was wedged into a small bronchus of the 3rd segment. A specially designed mouthpiece was used, which allowed introducing a catheter for oral cavity pressure measurements and enabling to seal hermetically the outlet during the test. The catheter was connected to manometer for mouth pressure control. In some patients an oesophageal balloon was introduced for simultaneous recording of intrathoracic pressure. After one minute of quiet breathing the patient's nose was squeezed with a nose clip and patient was asked to perform forced expiratory effort against the closed mouthpiece for at least five seconds. Valsalva manoeuvre was considered successful if the pressure within the oral cavity exceeded 40 mmHg. After the cessation of the manoeuvre recordings were followed up for at least one minute. Mean blood perfusion changes before, during and after the manoeuvre were compared using the paired Student t-test.

Measurements during cardiac bypass surgery. Investigations were performed on nine patients (four men and five women; 50 to 71 years old). Six patients were scheduled for coronary surgery, three for mitral valve replacement due to valvular disease. Patient characteristics are given in Table 1. Total cardiopulmonary bypass (CPB) was conducted with a standard circuit and membrane oxygenator at mild hypothermia. For coronary artery bypass grafting (CABG) a two stage venous cannula (Medtronic MC2 extracorporeal cannula, 36/46 Fr) was introduced into the right atrium with tip directed into inferior vena cava. For mitral valve replacement two single-stage venous cannulas (DLP 36 Fr) were introduced bicavally. Blood from venous cannulas flowed to an oxygenator (Dideco, Italy) with heat exchanger (Stockert, Germany), to the cardiopulmonary bypass pump (Stockert) and then through the aortic cannula (Medtronic select series wirewound arterial cannula, 24 F) back to aorta. The aorta was clamped proximally to aortic cannula.

During total cardiopulmonary bypass the patients were not ventilated. The lungs were kept inflated.

Anaesthesia was induced with etomidate, fenthanyl and cisatracurium and was maintained with cisatracurium, phentanyl, sevoflurane and propofol at standard doses in all patients.

During CPB blood flow was 2.0–2.4 L/m^2, rectal temperature was 34.0 ^{o}C and esophageal temperature was 34.5 ^{o}C.

Invasive blood pressure was measured from the radial artery by a pressure transducer. An Edwards Lifesciences Swan-Ganz CCO/SvO_2 thermodilution catheter was introduced into jugular vein and advanced through the right atrium and ventricle into a branch of the pulmonary artery that was sufficiently small for pulmonary artery wedge pressure measurements. Pulmonary arterial pressure and lung blood perfusion was recorded during the whole surgical procedure. The mean values of perfusion before the onset of CPB, after aortal cross clamping, and after the full restoration of cardiac output were used for calculations. Pulmonary wedge pressure was measured in eight patients.

The study protocol was approved by the Ethics Committee of Pauls Stradiņš Clinical University Hospital, Latvia. Informed consent to both the surgical and experimental procedures was obtained from all patients.

Table 1

DIAGNOSES AND REGIONAL LUNG PERFUSION RATES IN PATIENTS DURING THE CHANGE OF BODY POSITION FROM SITTING TO SUPINE AND BACK TO SITTING

Patient No	Diagnosis	Sitting	Supine	Again sitting
1	Pneumonia	54.75	85.36	113.31
2	Pneumonia	78.70	213.06	238.14
3	Pneumonia	39.51	33.51	30.86
4	Mild COPD	74.14	88.11	92.00
5	Asthma	48.75	42.36	27.77
6	Pneumonia	68.16	58.10	41.73
7	Chronic bronchitis	91.21	92.68	43.20
8	Pleuritis	85.22	94.49	79.14
9	Normal	37.17	55.28	32.76
10	Normal	59.04	136.78	120.31
11	Normal	90.30	194.64	106.04
12	Normal	58.75	70.37	70.03
13	Mild COPD	101.53	91.61	73.26
14	Mild COPD	127.58	133.11	123.17
15	Normal	47.70	57.03	101.66
16	Acute bronchitis	164.49	169.56	187.27
17	Acute bronchitis	38.27	37.44	43.55
	MEAN	**74.40**	**97.30**	**89.70**
	DELTA	**17.50**	**28.00**	**29.40**

RESULTS

Recordings in spontaneously breathing awake patients. The laser Doppler perfusion signals recorded from peripheral bronchi showed fluctuations, synchronous with the pulse rate and respiration (Fig. 2). The perfusion signal increased during inspiration when the intrathoracic pressure became more negative and decreased during expiration when the pressure rose. The baseline perfusion level differed markedly among patients ranging from several PU to 400 PU. Mean baseline perfusion recorded from a small bronchus of the 2nd segment was 74.4 ± 17.2 PU.

Figure 3 demonstrates changes of regional lung perfusion in response to body position change from vertical to supine

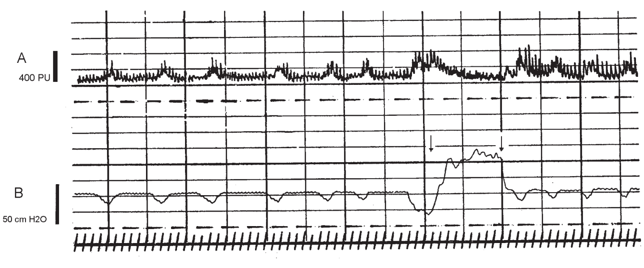

Fig. 2. Laser Doppler perfusion signal recorded from small bronchus (A) and intrathoracic pressure (B) during spontaneous breathing followed by Valsalva manoeuvre. Arrows indicate the start and the end of the Valsalva manoeuvre.

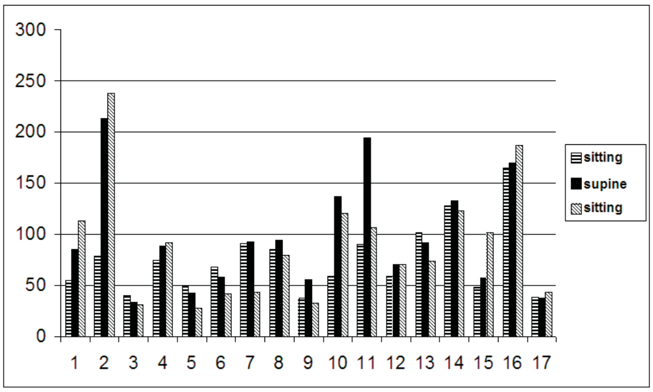

Fig. 3. Individual blood perfusion values recorded from small bronchus of the 2nd lung segment during body position change from sitting to supine and back to sitting position.

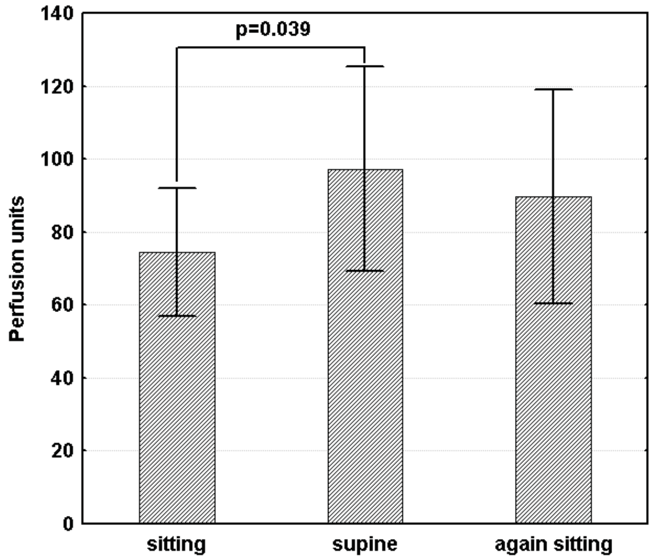

Fig. 4. Mean blood perfusion recorded from small bronchus of the 2nd lung segment in response to body position change (n = 17, bars represent the confidence interval of the mean).

and back to vertical in individual patients. In 12 of 17 patients in supine position the perfusion increased. With the return back to vertical position in the majority of patients the perfusion tended to return back to the initial level, however in four patients it increased. In five persons perfusion did not change with body position change or tended to decline in supine position (Table 2).

Average values showed a statistically significant increase of regional blood perfusion in supine position with an insignificant tendency to return back to the values observed during the initial vertical position.

The mean perfusion value measured from the 2nd segment in vertical position was 74.4 ± 17.2 PU, in supine 97.2 ± 28.4 PU (difference significant, compared to baseline, $P < 0.05$), but after the return to vertical position—89.6 ± 28.9 PU (difference insignificant, $P > 0.05$, Fig. 4.)

Figure 2 shows the LD recording from individual patients when performing the Valsalva manoeuvre. As intrathoracic pressure increased the perfusion gradually declined reaching the lowest point by the end of the straining. During the post-manoeuvre phase, perfusion rose gradually, exceeding significantly the pre-manoeuvre level.

On average, the blood perfusion during Valsalva manoeuvre dropped to 40.5 ± 7.8% of the baseline (n = 29, $P < 0.05$) and increased to 255.3 ± 77.8% above baseline after the cessation of the manoeuvre (n = 27, $P < 0.05$, Fig. 5.).

Recordings in patients undergoing cardiac bypass surgery. Laser Doppler perfusion signals recorded in anaesthetised and artificially ventilated patients also showed fluctuations synchronous with the pulse rate. However, the perfusion decreased during inspiration, when the alveolar pressure became more positive and increased during expiration, as the alveolar pressure dropped. The baseline perfusion levels differed markedly among patients. Both high and low perfusion rates were observed in both ischemic

Table 2

HAEMODYNAMIC INDICES AND REGIONAL LUNG BLOOD PERFUSION BEFORE AND DURING CARDIAC BYPASS

Patient ID	Age	Sex	Diagnosis	Pulmonary wedge pressure, mmHg	Probe tip position	Haemodynamic changes						
						before bypass		during aortic occlusion		during reperfusion		
						PAP	RPP	RPP	RPP%	PAP	RPP	RPP%
VV	63	M	IHD	8	L3	17	87±0.1	10.3±0.02	11.8	17	99.1±0.3	114
MR	68	F	IHD		L3	12	107±0.4	0.1±0.0	0.1	17	96.0±0.3	90
AG	67	M	IHD	12	L3	17	67±0.2	8.2±0.06	12.2	16	64.6±0.4	96
LV	44	M	IHD		L3	14	136±0.3	17.5±0.04	12.9	6	234.0±0.8	172
MV	60	M	IHD	16	L3	47	40±0.1	1.1±0.01	2.75	28	30.0±0.1	75
UA	71	F	MS	12	L4	12	43±0.4	13.2±0.05	30,7	27	442.5±0.8	1029
SJ	64	F	IHD	8	L3	11	172±1.7	5.9±0.01	3.4	21	186.1±0.5	108
KV	50	F	MS	17	L3	17	21±0.1	4.0±0.04	9,0	23	100.41±0.6	478
LB	52	F	MS		L3	21	164±0.2	5.2±0.03	3.2	10	58.9±0.3	36
Mean							93±42	7.3±4.3*	9.6±7.1		145±98	244±247

IHD, ischemic heart disease; MS, mitral stenosis; PU, perfusion units; L3, third segment of left lung, L4, fourth segment of left lung; PAP, pulmonary artery pressure (mmHg); RPP, regional pulmonary perfusion (in perfusion units, PU); RPP% - regional pulmonary perfusion in percentages of pre-bypass level

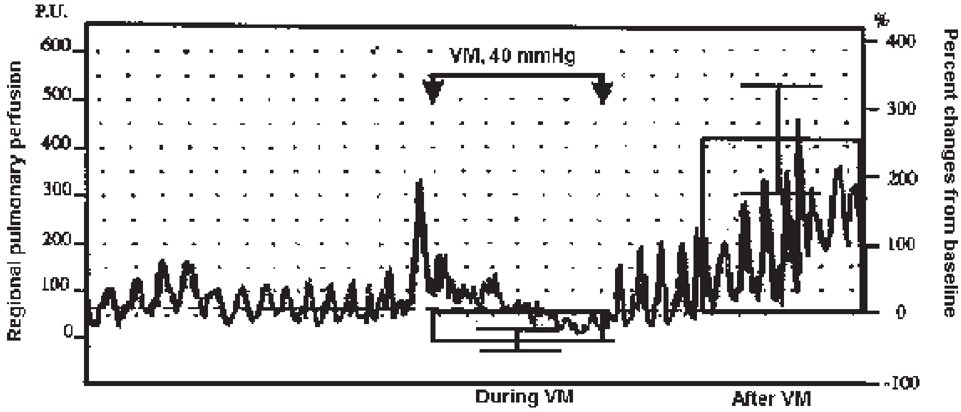

Fig. 5. Mean changes of regional pulmonary perfusion during (n = 29) and after (n = 27) the Valsalva manoeuvre (VM). PU, perfusion units, bars represent the confidence interval of the mean.

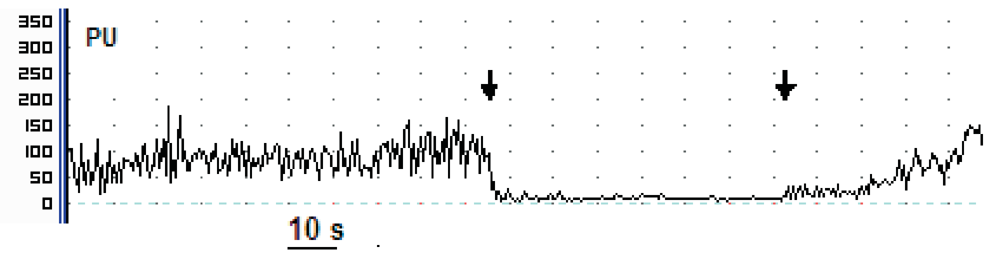

Fig. 6. Real-time recording of blood perfusion from small bronchus of the 2nd lung segment during cardiac bypass surgery. Arrows indicate the onset and the termination of the aortic clamping period.

heart and valvular disease patients Regional pulmonary perfusion (RPP) was neither correlated with pulmonary arterial pressure (PAP), nor depended on the patient's diagnosis (Table 1).

Introduction of cardiac bypass led to a marked decrease of regional pulmonary perfusion. After the cross-clamping of the aorta and the cardiac arrest, pulse waves in the LD recording disappeared and became a straight line (Fig. 6). Bronchial arteries provided the only remaining blood supply to lungs, and the pulmonary perfusion depended on the magnitude of broncho-pulmonary anastomotic connections. Under these conditions the individual differences in RPP were great. In patients MR and MV (Table 1) RPP dropped to almost zero. In some other patients after the aortic cross-clamping RPP dropped less markedly.

The individual and mean values of the regional pulmonary perfusion and the pulmonary arterial pressure before, during and after the aortic cross-clamping are given in the Table 1.

DISCUSSION

The obtained results show that the signal recorded with an angled laser Doppler probe wedged into small bronchus reflects mainly the circulation in the pulmonary capillary network. Changes of blood perfusion synchronous with the respiratory rate represent the influence of intrathoracic pressure on the pulmonary capillary filling. Changes in blood perfusion influenced by the change of body position are also characteristic for the pulmonary vascular bed, which is fed under low arterial pressure. Likewise, a voluntary increase of the intrathoracic pressure during the Valsalva manoeuvre, leading to almost total arrest of the regional lung perfusion, indicates features of a low-pressure vascular bed.

The tendency to increased regional blood perfusion after the return to vertical position from supine evidently demonstrate the recruitment of previously closed pulmonary capillaries of this vascular bed in response to increased driving pressure in supine position. The opposite reaction of a decrease of blood perfusion in supine position in individuals with high initial perfusion in vertical position possibly reflects the local vasoconstriction that occurs during the overfilling of the particular local pulmonary vascular bed.

The measurements performed during a cardiac bypass show that pulmonary capillary network is supplied with blood both from pulmonary and bronchial arteries. When the heart is arrested and a pump supports systemic blood perfusion, the bronchial artery remains the only source of blood supply to lungs. It has been established that bronchial arteries have anastomoses with pulmonary arterioles and pulmonary capillary networks (Verloop, 1948, Deffebach *et al.*, 1987, Olchewski *et al.*, 2002). The impact of the bronchial circulation in the regional pulmonary perfusion measured in our observations showed large variations. A high bronchial component in our measurements could simply represent the spatial inhomogeneity of lung blood supply as well as the inhomogeneity of the distribution of pulmonary and bronchial component. It may also represent the greater impact of bronchial circulation into total pulmonary blood supply in some individuals.

Differences between lung perfusion measured before and after the cardiac bypass in the same area show significant differences. In some patients blood perfusion after the bypass increased dramatically, in one case even tenfold, whereas in some other patients it decreased.

During cardiopulmonary bypass, due to surgical trauma and blood contact with synthetic surfaces, systemic circulation accumulates different vasoactive substances such as bradykinin, activated complement components, and arachidonic acid metabolites that partially are metabolised in lungs (Cugno *et al*., 2001; Downing *et al*., 1992). These substances induce both systemic and pulmonary vasodilatation.

The opposite changes occur after the cardiopulmonary bypass, tending to constrict the pulmonary vascular bed. Pulmonary vascular response to vasodilator agents become dampened (Angdin *et al*., 1998) and levels of strong vasoconstricting substances like endothelin-1 rise in peripheral blood. This is observed immediately after the removal of aortic cross clamp, when blood from lungs enters the systemic circulation. The endothelin-1 level was correlated positively with the mean pulmonary arterial pressure (Angdin *et al*., 1998).

The interaction of generalised vasodilatory and local vasoconstrictive influences may result in the spatial inhomogeneity of lung blood supply after the bypass cessation. Indeed, immediately after the separation from exracorporeal circulation a large increase of lung blood shunting was observed, which parallel with an alveolo-arterial PO_2 difference indicating disproportion between regional lung perfusion and ventilation (Hachenberg *et al*., 1994). There may be several causes of the rearrangement of blood distribution. During the absence of ventilation hypoxic vasoconstriction may occur in some lung regions, which decreased local blood perfusion. If the hypoxic vasoconstriction occurred in large lung areas, it resulted in an increase of pulmonary artery pressure, as observed in several patients. Relative lung ischaemia during cardiac bypass surgery might result in diminished vasodilatory response, as it was observed by Angdin *et al*., 1998) in patients after cardiac bypass surgery.

The conclusions from the presented results are:

1. Laser Doppler recordings performed with angled endoscopic probe reflect lung regional perfusion supplied from both pulmonary and bronchial arteries.

2. Blood perfusion recorded by laser Doppler probe inserted into small bronchus reflects mainly the pulmonary vascular bed.

3. The impact of the bronchial component in regional perfusion is widely variable among individuals and does not depend on pulmonary arterial pressure, pulmonary wedge pressure, nor on overall regional perfusion.

4. Laser Doppler technique can be used for the investigation of regional lung blood perfusion regulatory mechanisms.

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REĢIONĀLĀS PLAUŠU PERFŪZIJAS PĒTĪJUMS AR LĀZERA DOPLERA METODI, ĶERMENIM ATRODOTIES DAŽĀDĀS POZĀS, VEICOT VALSALVA MANEVRU UN MĀKSLĪGĀS ASINSRITES LAIKĀ

Plaušu asinsrites regulācijas mehānismi cilvēkam līdz šim maz pētīti, jo trūkst atbilstošu metožu. Pētījumā izmantota oriģināla pieeja, kas ļāva reģistrēt plaušu reģionālo asinsriti, iekīlējot lāzera Doplera leņķa zondi vienā no sīkajiem bronhiem bronhoskopijas laikā. Mērījumi tika veikti, cilvēkam atrodoties dažādās ķermeņa pozās, kā arī veicot Valsalva manevru un sirds operācijās mākslīgās asinsrites laikā. Ķermeņa pozu maiņa un Valsalva manevrs būtiski ietekmē asins perfūziju plaušās. Mākslīgās asinsrites laikā plaušu asinsriti uztur tikai reģionālā perfūzija bronhiālo artēriju līmenī, un tad perfūzija mazinās no 93 ± 42 līdz 7,3 ± 4,3 perfūzijas vienībām. Secināts, ka, izmantojot šādu metodiku, galvenokārt iegūst signālu no mazā asinsrites loka. Šādu metodiku var izmantot, lai pētītu lokālos asinsrites regulācijas mehānismus plaušās.