Relationships between capnogram parameters and respiratory mechanics in ventilated patients

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Summary of PhD Thesis

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List of scientific papers related to this thesis

I. **Csorba Zs,** Czövek D, Bogáts G, Peták F, Babik B. A légzésmechanika hatása a kapnogramra: a légzőrendszer elasztikus tulajdonságának jelentősége. *Aneszteziológia és Intenzív Terápia* 42(2): 77-84, 2012.

II. Babik B, **Csorba Zs**, Balogh Á, Szeti K, Tolnai J, Peták F. Kapnográfia lélegeztetett betegekben. Mindig nézzük, mindent látunk? *Medicina Thoracalis* LXVII:(2) pp. 78-98, 2014.

III. Balogh AL, Petak F, Fodor GH, Tolnai J, **Csorba Zs**, Vigh E, Nevery K, Babik B. Capnogram slope and ventilation dead space parameters: comparison of mainstream and sidestream techniques. *Brit J Anaesth*, 2016 (under review).

1. INTRODUCTION

The bedside estimation of respiratory mechanics, monitoring of in-, and exhaled gas concentrations, assessing of gas exchange, or the different imaging technologies require a broad spectrum of low and high technology. Additionally, the information gained by these techniques about the ventilation, the ventilation perfusion mismatch, the cardiopulmonary interaction, the inflammatory reactions etc. exhibits an impressive physiological and pathophysiological variety.

Capnography is a non-invasive, continuous, on-line, dynamic, effort- and cooperation-independent, numeric and graphic bedside method for monitoring of the exhaled carbon dioxide (CO_2) concentration. The technique is one of the most frequently used monitoring methods in anaesthesia and intensive therapy, because capnography is able to detect vital signs during intentional temporary life-threatening alterations of vital functions with fast responses. However, pathophysiological and clinical information provided by the capnography has not yet been completely elucidated.

In the clinical practice, time capnography is the most reliable method to position endotracheal tube or any supraglottic airway device fast and correctly. Monitoring of exhaled CO_2 help the team recognize over-insertion of endotracheal tube into the right main stem bronchus, ventilation circuit disconnection, leakage, or malfunction of flow control valves of breathing circuit. The end-tidal CO_2 partial pressure (P_{ETCO_2}) value is generally considered as a valuable monitoring tool to recognize absolute or relative minute volume abnormalities, metabolic disturbance, pulmonary embolism**,** or to wean the patient from the respirator. Supplemental monitoring of a ventilated patient with rough qualitative bedside estimation of the S_{III} to assess alveolar emptying can also support clinical decision making. Consequently, international recommendations for standards nowadays require the monitoring of ventilation with capnography in all patients undergoing sedation or general anaesthesia to confirm correct placement of endotracheal tube and to identify abnormalities of minute ventilation.

Nevertheless, CO_2 is an endogenous indicator during expiration, consequently, the capnogram - with arterial blood gas - has a strong potential to reveal complex bedside information about the whole expiratory course and pulmonary microcirculation. Therefore this technique can be used for a lot more than to verify the technical correctness of the airway management and respiratory therapy as a polar question. Capnography also provides important bedside pathophysiological information about the uniformity of lung emptying and adverse changes in the overall airway geometry, and it can serve as a valuable tool for the recognition of pulmonary microcirculatory abnormalities.

Nonetheless, from pathological point of view, capnography nowadays can be considered as the “most frequently monitored, less frequently evaluated bedside modality” in the clinical practice. Characterization of the relationships between standard lung function parameters and capnographic indices may facilitate an understanding of the various shapes of the capnogram. However, the earlier studies demonstrating associations between the capnographic slope factors with the forced expiratory volume in 1 s (FEV_1) and the peak expiratory flow were limited to spontaneously breathing subjects. Despite the particular importance of recognizing adverse alterations in the pulmonary system in mechanically ventilated patients, and the obvious importance of respiratory tissue elastance in determining the expiratory flow and the rate of CO_2 clearance, details as to how the resistive and/or elastic properties of the pulmonary system affect the various indices derived from the capnogram are essentially lacking from the literature.

Moreover, the sensitivity of S_{III} to ventilation and ventilation/perfusion abnormalities suggested its clinical usefulness for the detection of respiratory abnormalities or the subsequent ventilatory and/or pharmacological interventions. Numerous studies have demonstrated that the magnitude of phase III slope of the capnogram (S_{III}) reflects the severity of emphysema or asthma, cystic fibrosis and bronchiectasis, COPD, chronic bronchitis and acute lung injury. Inconsistent associations have been reported in previous attempts to clarify the quantitative relationships between capnographic and lung function indices. Earlier studies reported a strong correlation between FEV_1 and S_{III} merely a modest association or even a lack of correspondence. Furthermore, significant correlations were observed between the total respiratory resistance (Rrs) and S_{III} in mechanically ventilated patients, however S_{III} had limited clinical applicability to predict Rrs. Thus, in consequence of the complex mechanisms affecting S_{III}, its diagnostic and/or monitoring value is far from being clear. The diverse emptying of different lung compartments with various CO_2 levels is determined not only by the airway geometry, but also by the driving pressure governed by the dynamic respiratory compliance (Crs), including the chest wall and the lung. Despite the obvious importance of respiratory tissue elastance in determining the expiratory flow and the rate of CO_2 clearance, the role of the respiratory elastic recoil on the capnogram shape has not been examined to date.

2. AIMS

The goals of the present thesis were to set out various investigations in large cohorts of ventilated patients with normal and diseased lungs during cardiac surgery. Studies focused particularly on the establishment of the connections between the various phase, shape, dead space or pulmonary shunt circulation parameters of the time or volumetric capnogram and those reflecting the airway and lung tissue mechanics, expiratory flow and gas exchange. These measurements were designed to be performed under baseline condition after induction of anaesthesia, and after a complex challenge dominated by elevation of airway resistance performed by cardiopulmonary bypass (CPB).

As a further goal, we also systematically investigated whether S_{III} is affected by changes in both airway caliber and the Crs, in mechanically ventilated patients. We attempted to clarify the contribution of the altered airway properties and tissue mechanics at baseline after induction of anaesthesia and after challenge with increasing positive end-expiratory pressure (PEEP). These measurements were evaluated to assess whether homogeneity or heterogeneity of lung parenchyma indicated by the S_{III} provides suitable information to conclude on the gas exchange as the primary function of lung. We also elucidated whether the reliability of S_{III} depends from the working lung volume, consequently it has to be used only with other parameters referring to lung volume.

3. METHODS

3.1. Patients and anaesthesia

The subjects of both studies presented in this thesis were patients scheduled for elective open heart surgery. The protocols were approved by the Human Research Ethics Committee of Szeged University, Hungary (no. WHO 2788). All the patients received appropriate information about the study protocol and gave their written consent to their participation.

A large cohort of patients scheduled for elective cardiac surgery was enrolled in this thesis. After induction of total intravenous anaesthesia, the patients were intubated and ventilated in volume-controlled mode with descending flow. The ventilator frequency was set to 12-14 breaths/min, with a tidal volume of 7 ml/kg. The fraction of inspired oxygen (FiO_2) was maintained at 0.5 throughout the entire study period.

In *Study 1* one hundred and one patients (71 males, 30 females) 62±9 (mean ± SD) years of age (range: 30-88 yrs.) undergoing elective cardiac surgery were involved in a prospective, consecutive cross sectional manner. Patients were excluded in the event of severe cardiopulmonary disorders and based on earlier medical reports, the patients exhibited wide-ranging variations in pulmonary status. In *Study 2* one hundred and forty-four patients (93 males, 51 females) 62±9 (mean ± SD) years of age (range 39−84 yrs.) undergoing elective coronary bypass surgery were examined in the supine position before the surgical procedure. These patients had various cardiac diseases and also exhibited wide variations in their pulmonary status. In this study, the patients with respiratory symptoms were allocated into three groups, on the basis of their Crs. Group LC comprised patients with Crs in the lowest tenth percentile (Crs<34.5 ml/cmH_2O; n=15), and Group MC patients with Crs between the tenth and the ninetieth percentile (34.5<Crs<69 ml/cmH_2O; n=85), and Group HC patients with Crs above the ninetieth percentile (Crs>69 ml/cmH_2O; n=15). Patients with healthy lungs were regarded as an independent group (Group HL; n=29).

3.2. Forced oscillatory measurements

In *Study 1* airway and tissue mechanical properties were assessed by measuring the low-frequency forced oscillatory input impedance of the pulmonary system (ZL). The common side of a T-piece was attached to a distal ET tube. The other sides of the T-piece containing two collapsible segments were connected to the respirator and the forced oscillatory measurement apparatus. Before the oscillatory measurements, the lungs were inflated to a pressure of approximately 30 cmH_2O to standardize the volume history. During short (15-s) apnoeic periods, this equipment allowed switching the patient from the respirator to the forced oscillatory system while pseudorandom pressure excitations were generated into the trachea. The pressure forcing signal contained 15 integer-multiple components in the frequency range 0.4-6 Hz. ZL was computed from the power spectra of the airway opening pressure (Pao) and tracheal airflow (V’). Pao was measured with a pressure transducer, and V’ was measured with a screen pneumotachograph connected to the identical pressure transducer. A well-validated 4-parameter model containing a frequency-independent airway resistance (Raw) and inertance (Iaw) and a constant-phase tissue compartment characterized by the coefficients of damping (G) and elastance (H) was fitted to the mean ZL data by minimizing the weighted differences between the measured and modelled impedance values:

$$ZL = Raw + j\omega Iaw + (G - jH)/\omega^{\alpha}$$

where ω is the angular frequency ($2\pi f$) and $\alpha = 2/\pi \cdot \arctan(H/G)$. The tissue resistive component (Rti) at the ventilation frequency (0.2 Hz) was calculated from the parenchymal damping coefficient ($Rti = G/\omega^{\alpha}$). The total lung resistance (RL) was determined as the sum of the airway resistance (Raw) and the Rti ($RL = Raw + G/\omega^{\alpha}$). In *Study 2* the input impedance of the respiratory system (Zrs) was measured, and the forcing signal contained 30 integer-multiple components of the 0.2-Hz fundamental frequency, in the frequency range 0.2-6 Hz.

3.3. Recording and analyses of the expiratory capnogram

In *Study 1* a mainstream capnograph and another central airflow meter were connected into the ventilatory circuit at the Y-piece, and 15-s CO_2 and ventilator flow traces were recorded simultaneously. The CO_2 and ventilator flow traces were digitized and imported into custom-made signal analysis software. The slopes of phase III of the capnogram in the time ($S_{III,T}$) and in the volumetric ($S_{III,V}$) domains were determined by fitting a linear regression line to the last two-thirds of each phase-III traces. The phase-II slopes of the time ($S_{II,T}$) and volumetric ($S_{II,V}$) capnograms were determined by calculating the slopes of the best-fitting line around the inflection point (±20%). Each slope was divided by the average corresponding CO_2 concentration in the mixed expired gas to obtain normalized time ($Sn_{II,T}$ and $Sn_{III,T}$) and volumetric ($Sn_{II,V}$ and $Sn_{III,V}$) phase II and III slopes. This normalization was made only for the slope indices, as performed earlier before and after CPB. The angle (α_{cap}) formed by the phase II and III limbs of the expiratory time capnogram was also calculated by using a standard monitoring speed of 12.5 mmHg/s. The transition rates of change from phase II to phase III in the time (D_{2min}) and volumetric (D_{2Vmin}) capnograms reflecting the curvature were calculated as the minima of the second-order time and volumetric derivatives.

Dead space parameters were also derived from the volumetric capnogram. The Fowler dead space (V_{DF}) was determined by calculating the expired gas volume until the inflection point of phase II was reached in the volumetric capnogram. The physiological dead space was assessed by the Bohr method and referred as Bohr dead space (V_{DB}):

$$V_{DB} = (P_{ACO_2} - P_{\bar{E}CO_2}) / P_{ACO_2}$$

where P_{ACO_2} is the mean alveolar CO_2 concentration located at the midpoint of the phase III in the expired CO_2 curve, and $P_{\bar{E}CO_2}$ is the mixed partial pressure of CO_2 during the entire expiration. The latter is calculated as the ratio of the tidal elimination of V'_{CO_2} obtained by integrating the flow and CO_2 signals over the entire breath and the tidal volume. The dead space according to Enghoff's modification (V_{DE}) was calculated as:

$$V_{DE} = (P_{aCO_2} - P_{\bar{E}CO_2}) / P_{aCO_2}$$

where P_{aCO_2} is the partial pressure of CO_2 in the arterial blood. We also calculated the differences between the Enghoff and Bohr dead space parameters ($V_{DE} - V_{DB}$) representing the pulmonary shunt circulation. The intrapulmonary shunt blood flow (Qs/Qt) was additionally assessed via the Fick equation.

In *Study 2* Changes in partial CO_2 pressure in the exhaled gas during mechanical ventilation were measured with a calibrated side-stream capnograph. Since capnograms are displayed in clinical routine in the time domain, time capnography was applied in each patient to record CO_2 changes. To minimize the possible drawback of this time domain analyses, we paid attention to involve only the linear part of the CO_2 trace in the readings of S_{III}. Nevertheless, volumetric capnography may allow a better distinction between the phases and thus, in a subgroup including the last 68 patients, the flow during mechanical ventilation was simultaneously recorded with the CO_2 traces by introducing an additional pneumotachograph into the ventilation circuit. This allowed the analyses of volumetric capnograms in 20, 7, 32 and 9 patients in the Groups HL, HC, MC and LC, respectively. The 15-s CO_2 and respiratory flow traces were imported into commercial signal analysis software. Assessing the slopes of phase III of the capnogram in time ($S_{III,T}$) and in volumetric ($S_{III,V}$) domains and their normalizations were performed similar to those applied in *Study 1*. In both studies, and at every experimental condition, 3 to 5 expiratory traces in each recording were analyzed, resulting in the ensemble-averaging of 10-12 values for further analysis in each patient.

3.4. Analysis of the expiratory flow

In *Study 1,* in order to characterize the expiratory flow pattern, the expiratory phases of each V' recordings were analyzed by fitting an exponential function to the elevating limb.

3.5. Calculating intrapulmonary shunt based on the classic shunt equation

In *Study 1,* the ratio of the shunted cardiac output (Qs) to total cardiac output (Qt) is referred to classic shunt equation and can be calculated as.

3.6. Measurement protocols

In *Study 1* two sets of measurements were made under the open-chest condition 5 min before the CPB and 5 min after the patient was weaned from the CPB. Recruitment manoeuvres were performed before the weaning from the CPB. Each data collection period started with recordings of 3 to 5 capnogram traces. During this period, an arterial blood gas sample was taken to measure Pa_{O_2} and Pa_{CO_2} for the calculation of HQ and V_{DE}, respectively. The total lung resistance (R_{vent}) and compliance (C_{vent}) displayed by the respiratory monitor of the ventilator were registered at this stage of the protocol. The data collections under both conditions were supplemented by recordings of 3 to 5 ZL data epochs at 1-min intervals.

In *Study 2*, when stable hemodynamic and respiratory mechanical conditions had been reached while PEEP was maintained at 3 cmH_2O, an arterial blood gas sample was taken, and dynamic compliance (Crs) was recorded from the display of the respirator. The first capnogram trace was then collected followed by recording of the first Zrs data epoch. Two more capnographic and Zrs measurements were then made in alternating sequence at 60-s intervals. PEEP was next elevated to 6 and then 9 cmH_2O, a 3-min equilibration period being permitted after each step, and the data collection procedure was repeated.

3.7. Statistical analyses

In both studies, scatters in measured variables are expressed as SEM values. The Pearson test was applied to analyze the correlations between the different variables. Values $p<0.05$ were considered to be statistically significant. All reported p values are two-sided. The statistical tests were performed with a SigmaPlot statistical software package except the Steiger's Z-test. In *Study 1* the necessary sample size estimation was applied to involve sufficient number of patients for the detection of clinically relevant significances. In the event of passing the normality test, paired t-tests were used to examine the statistical significance of the changes induced in the parameters by the CPB. Wilcoxon signed-rank tests were applied otherwise to verify the significance of the changes in the mechanical, capnographic or gas exchange parameters. The comparison of Pearson correlation coefficients was made by Steiger's Z-test; these tests were performed between the particular and the nearest r values. Subgroups of patients were formed based on the initial HQ level (high and low 25 percentile), and based on the extremity of changes after surgery (top 25 percentile increase and bottom 25 percentile decrease in HQ, respectively). Time domain capnogram slope indices and Raw and C_{vent} and their changes after the surgery were also correlated in these subgroups and were compared to the results obtained from the pooled population. In *Study 2* the normality of the data was tested with the Kolgomorov-Smirnov test with Lilliefors correction. Two-way repeated measures analysis of variance (ANOVA) with including an interaction term was used with the variables PEEP (3, 6 and 9 cmH_2O) and the group allocation (Groups HL, LC, MC and HC) to establish the effects of lung volume and Crs on the respiratory mechanical, blood gas and capnographic variables. This statistical method was utilized to test the hypothesis that the level of Crs affects the PEEP-dependent changes in the respiratory mechanical and capnogram variables. Multiple linear regression analysis was performed to establish whether the levels of BMI and EF affect Crs. The Holm-Sidak multiple comparison procedure was adopted to compare the variables in the various study groups under different conditions. Chi-square test was used to assess whether there is a significant difference between the expected and the observed frequencies of gender, obesity, pulmonary and cardiac diseases in the protocol groups.

4. RESULTS

Study 1: Capnographic parameters: correspondence with airway and tissue mechanics

All the resistive parameters, including those reflecting the flow resistance of the airways (Raw), or of the lung tissues (Rti), or the combination of these compartments (R_{vent} and RL), exhibited marked and statistically significant increases after CPB ($p<0.0001$ for each). Conversely, more moderate, but still highly significant decreases were observed following

CPB in the compliance parameters determined at end-expiratory lung volume by the oscillometry (CL) or at end-inspiratory lung volume by the ventilator (C_{vent}) ($p<0.0001$ for both). Marked and statistically significant increases were observed in the time and volumetric parameters reflecting the phase III slope of the expired CO_2 ($p<0.0001$ for $S_{III,T}$, $Sn_{III,T}$, $S_{III,V}$ and $Sn_{III,V}$) after the CPB. The slopes of phase II revealed significant decreases following CPB ($p<0.0001$ for both $S_{II,T}$ and $S_{II,V}$), whereas these drops were no longer detectable after normalization to the CO_2 concentration in the mixed expired gas ($p=0.4$ and 0.9 for $Sn_{II,T}$ and $Sn_{II,V}$, respectively). CPB increased the curvature representing the transition from phase II to phase III ($p<0.0001$ for both D_{2min} and D_{2Vmin}). Uniform decreases were detected in V_{DF} and V_{DB} ($p<0.0001$) after the CPB, whereas V_{DE} increased significantly ($p<0.0001$). These changes in the dead space parameters resulted in significant elevations in the shunt parameters reflecting the alterations in lung ventilation ($p=0.02$ and $p<0.0001$ for $V_{DB} - V_{DF}$ and $V_{DE} - V_{DB}$, respectively) and perfusion (Qs/Qt, $p<0.0001$).

The strengths of the correlations between the lung mechanical parameters and the time and volumetric capnographic parameters, reflecting the slopes, transitions, dead space and shunt fractions were also investigated. The lung resistive parameters exhibited the closest associations with the phase III slope capnographic parameters ($p<0.0001$), particularly after the CPB, when all the indices reflecting the resistive properties of the pulmonary system were markedly elevated ($p<0.0001$). Significant, but somewhat weaker correlations were observed between the lung resistive parameters and the ventilation dead-space parameters V_{DF} ($p<0.0001$) and V_{DB} ($p<0.0001$). More specifically, the mechanical parameter representing the flow resistance of the airways (Raw) correlated best ($p<0.0001$) with the $S_{III,T}$ ($r=0.63$ and 0.68 for $S_{III,T}$ before and after the CPB, respectively; $p<0.0001$). Moreover, Raw correlated significantly with $S_{III,V}$ ($r=0.43$ and 0.55 for $S_{III,V}$ before and after CPB, respectively, $p<0.0001$). Normalization of the phase III slopes to the CO_2 concentration in the mixed expired gas did not affect these relationships noticeably ($p=0.71$). Conversely, the mechanical parameters characterizing lung tissue elasticity (H and C_{vent}) showed the closest ($p=0.006$) relationships with the time capnographic parameters describing the phase II ($r=0.65$ and 0.41 between H and $S_{II,T}$ before and after the CPB, respectively; $p<0.0001$). The pulmonary elastance and compliance parameters also revealed close associations with the capnographic indices reflecting the curvatures of the transitions between the phases, particularly before the CPB ($r=-0.57$ between H and D_{2min}; $p<0.0001$).

As concerns the relationships between the CPB-induced changes in the lung mechanical and capnographic indices, the marked elevations in Raw correlated best (p=0.001) with the decreases in the phase II slope parameters of the time capnogram (r=-0.72 and -0.70 for $S_{II,T}$ and $Sn_{II,T}$, respectively; p<0.0001). The CPB-induced airway narrowing was also reflected in the elevated phase III slope parameters of the time and volumetric capnograms (r=0.49 for both $S_{III,T}$ and $S_{III,V}$; p<0.0001), and the curvature of the transition between the phases in the time domain (r=0.6 for D_{2min}; p<0.0001). The changes in the other mechanical parameters reflecting the tissue damping (G) or total lung resistance (RL or R_{vent}) displayed similar relationships with the alterations in the various capnographic indices after the CPB. Assessment of the mild CPB-induced stiffening of the lung tissue also revealed statistically significant correlations between the changes in C_{vent} and those in the phase III slope parameters in both the time and volumetric capnograms (r=-0.48 for both $Sn_{III,T}$ and $Sn_{III,V}$; p<0.0001).

The relationships between the initial fundamental lung mechanical and capnographic indices for the subgroups of patients based on starting HQ were also investigated. Strong positive significant correlations were observed between Raw and phase III slope parameters (p=0.002) and between C_{vent} and phase II slope parameters independently of the subgroup allocation (p=0.001). The initial C_{vent}-$S_{III,T}$ relationship was not significantly correlated (p=0.20), while the Raw-$S_{II,T}$ correlation appeared significant only for the pooled patient population (p=0.0045). The changes in Raw correlated to those in both slope variables (p<0.0001), whereas the alterations in C_{vent} were significantly related with those in phase III slopes (p=0.023).

Study 2: Respiratory mechanics and the capnogram phases: importance of dynamic

The statistical analyses revealed significant interactions between the group allocation and PEEP, demonstrating that the respiratory compliance exerted significant effects on the responses to PEEP in the forced oscillatory mechanical parameters (p<0.001 for Raw, G and H), for the Crs displayed by the respirator (p<0.001), P_{aO2} (p=0.04), and the capnogram third phase slope variables (p<0.001 for $S_{III,T}$ and $Sn_{III,T,}$ p=0.003 for $S_{III,V}$, and p=0.002 and $Sn_{III,V}$). Time and volumetric capnogram variables exhibited similar Crs and PEEP dependences, which is also reflected in the significant correlations between $S_{III,T}$ and $S_{III,V}$ in

Groups HL ($R=0.4$, $p=0.002$), HC ($R=0.79$, $p<0.001$), LC ($R=0.45$, $p=0.02$) and MC ($R=0.79$, $p<0.001$).

The greatest Raw, G, H and the lowest Pa_{O_2} were observed for the patients in Group LC, and these patients generally exhibited the greatest response to PEEP. The patients in Group MC still exhibited elevated Raw, G and H with a more moderate, but still significant response to PEEP changes. The lowest forced oscillatory airway and tissue parameters and the greatest P_{aO2} were obtained in the patients in Groups HL and HC, and their changes with PEEP were generally mild. The capnogram third phase indices were highest in Group HC and somewhat lower in Group MC, with both groups exhibiting marked decreases with increasing PEEP. The variables characterizing the third phase slopes from the capnogram were lowest in the patients in Group HL.

In all patients, Raw and $S_{III,T}$ underwent concomitant monotonous decreases with increasing PEEP, but marked differences were observed between the protocol groups in the relationships of these parameters. The marked decreases in the high initial Raw values were associated with substantially smaller drops in S_{III} in the patients in Group LC, whereas the PEEP-induced decreases in S_{III} were more pronounced than those in Raw in the patients in Group HC. The patients in Group MC exhibited an intermediate Raw– $S_{III,T}$ relationship. This trend of association was observed in the patients in Group HL at markedly lower levels of Raw and S_{III}.

To examine the possible roles of obesity and lung congestion in the increased level of Crs, the effects of BMI and EF were considered. The patients in Group LC had significantly higher BMI ($p<0.001$) and/or lower EF ($p<0.001$) than those in Groups HL or HC, indicating that the low Crs was a consequence of restrictive changes resulting from obesity and/or heart failure leading to pulmonary congestion (multiple linear regression coefficient of $R=0.58$). The important effects of BMI and EF on the group allocation was confirmed by the presence of a significant correlation ($R=0.53$, $p=0.005$ and $p<0.0001$ for EF and BMI, respectively).

5. SUMMARY AND CONCLUSION

Capnography is an often used, but not completely utilized monitoring method in the clinical practice. The data presented in this thesis revealed that the capnogram shape indices in ventilated patients are specifically influenced by the resistive and elastic parameters of the lungs or the respiratory system.

Study 1: Capnographic parameters: correspondence with airway and tissue mechanics

We characterized the relationships between the time or volumetric capnographic parameters and the lung mechanical indices reflecting the airway and the lung tissue viscoelastic properties in cardiac surgery patient underwent open heart surgery. Since the elastic forces are maximal at high lung volumes at early exhalation, the lung tissue stiffness predominantly determines the capnographic parameters in the early phase of expiration. Thus, in the vast majority of the cases, the phase II slope of the capnogram is predominantly determined by pulmonary elastic recoil. Conversely, the resistive properties of the lungs become increasingly important during the later phase of expiration at lower lung volumes, and thus, the phase III slope is shaped overwhelmingly by the airway resistance. However, markedly elevated lung resistance additionally worsens the capnogram phase II slope. Similarly, severely compromised lung elastance also distorts the capnogram phase III slope.

Study 2: Respiratory mechanics and the capnogram phases: importance of dynamic compliance

The dual effect of the resistive and elastic forces on phase III slope was further investigated under closed chest conditions before CPB with increasing PEEP as a challenge. Detailed analysis of the time capnogram revealed a strong association between Raw and $S_{III,T}$ when the respiratory mechanics was altered by increasing PEEP. However, due to the substantial inter-individual variability in this relationship, $S_{III,T}$ provides useful information about alterations in the airway calibre only within an individual patient. The assessment of $S_{III,T}$ during mechanical ventilation may be of value for bedside monitoring of the changes in airway resistance, but its sensitivity depends on the elastic recoil of the respiratory system. $S_{III,T}$ exhibits high sensitivity to detect changes in the airway resistance in case of high Crs, when the lung emptying is governed primarily by the small airway and alveolar geometry. In cases of stiff respiratory tissues, however, $S_{III,T}$ displays low sensitivity in indicating changes in airway caliber, when the lung emptying is determined by the high elastic recoil and depends less on the small airway geometry. The relatively low $S_{III,T}$ may result from homogenous alveolar emptying of an overinflated, but decreased fraction of lung parenchyma and may coincide with the compromised Pa_{O_2} in these patients. Indeed, in patients with low Crs, the S_{III} was similar than that in the healthy patients, but their oxygenation was the worst. The relative homogeneous open alveoli of the lung parenchyma are emptying heterogeneously in HC group patients. In contrast, the relative heterogeneous open part of the alveolar compartment is emptying homogeneously in patients in the LC group.

Therefore, low S_{III} does not predict appropriate oxygenation alone in patients with low Crs, because it only reflects the alveolar emptying of the working lung. In such cases, $S_{III,T}$ appears to be normal, therefore it can serve as a pitfall of the ventilation monitoring. A low and apparently physiological $S_{III,T}$ does not predict appropriate oxygenation alone. Thus, the shape of the capnogram should always be evaluated bedside in conjunction with Crs. The joint assessment of the capnogram and the respiratory mechanics is of particular importance in clinical situations when patients with a high BMI and/or a compromised left ventricular function are anesthetized and ventilated.

Since computational methods could be incorporated into the modern anaesthesia machines to quantify capnographic shape factors, these parameters together with the traditional bedside mechanical indices has the promise to improve differential diagnoses and advance guiding respiratory therapy. Overall, our results suggest that all the important clinical capacity of the capnography can be exploited during ventilation the patients in the anaesthesia and intensive therapy.

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