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Noninvasive method for measuring respiratory system compliance during pressure support ventilation

Zhanqi Zhao, Marcus Eger, Thomas Handzsuj, V. Marco Ranieri, Lorenzo Appendini, Cosimo Micelli, and Knut Möller

Abstract— Purpose: **To date, few methods have been accepted for assessing the respiratory system compliance (C_{rs}) in patients under assisted ventilation at the bedside. The aim of this study was to evaluate our adaptive time slice method (ATSM) to continuously calculate the C_{rs}.** ***Methods:*** **One breath is divided into several time periods (slices). For each slice, a compliance value C_i is calculated. The slice width is adapted according to the confidence interval of C_i. After all C_i values are obtained and the outliers are eliminated, the C_{rs} of this breath is calculated as the mean value of the remainder of C_i's. Seven patients with Chronic Obstructive Pulmonary Disease were evaluated during pressure support ventilation. The results are compared with the values calculated with the transdiaphragmatic pressure (P_{di}).** ***Results:*** **95 ± 4% of the recorded data could be analyzed with ATSM. In 6 patients out of 7, the results delivered with ATSM and with P_{di} had similar variation (standard deviation) and accuracy (difference<20%). They were strongly correlated (weighted correlation coefficient = 0.86, $p<10^{-5}$) with a mean difference of 3.22 ml/mbar.** ***Conclusions:*** **The ATSM is a robust method and able to provide accurate C_{rs} in spontaneously breathing patients during pressure support ventilation noninvasively without extra instrumentation or complicated maneuvers.**

Keywords – respiratory system compliance; transdiaphragmatic pressure; pressure support ventilation; chronic obstructive pulmonary disease

I. INTRODUCTION

ADVANCING spontaneous breathing and reducing the use of controlled mechanical ventilation are recommended to avoid ventilator-induced diaphragm dysfunction [1, 2]. In the presence of spontaneous breathing, the pressure generated by respiratory muscles (P_{mus}), mainly by the activity of the diaphragm, is no longer a negligible driving force. The analysis of such respiratory system is normally based on the linear first order equation of motion where respiratory muscle effort is also considered:

$$P_{aw}(t) = V(t)/C_{rs} + \dot{V}(t) \times R_{rs} + P_0 - P_{mus}(t) \tag{1}$$

where $P_{aw}(t)$ denotes the airway pressure; $V(t)$ is the lung volume integrated by $\dot{V}(t)$, the airway flow; C_{rs} represents the respiratory system compliance; R_{rs} is the airway resistance and P_0 is the pre-existing pressure in the lung. Since the P_{mus} signal varies along the time and shares different shapes among individuals, analysis of respiratory mechanics is very difficult. In order to calculate C_{rs}, additional information about P_{mus} is needed. The transdiaphragmatic pressure (P_{di}) or esophageal pressure (P_{es}) may be used to estimate the respiratory muscle effort during spontaneous breathing [3, 4]. However, measurement of these pressures requires the placement of an esophageal balloon, which is invasive. The airway occlusion pressure at 0.1 second ($P_{0.1}$) reflects the breathing muscle effort [5] but only for a very short period. Other attempts to evaluate patient's respiratory efforts either assume P_{mus} to be linear for a relatively long period of time [6], or assume P_{mus} to have certain pattern [7], or need to interrupt the normal ventilation process [8, 9].

The use of proportional pressure support (PPS) also urgently calls for the evaluation of respiratory mechanics with sufficient precision. PPS, or also called proportional assist ventilation (PAV) delivers assisted ventilation in proportion to patient's breathing effort. It has several physiologic advantages [10] and may translate into clinical benefits with implications for mortality, morbidity, and length of ventilatory support. As a novel, promising ventilation mode, PPS has its inherent limitation: Overestimation of the lung mechanics parameters may trigger the potential risk of so-called "runaways"; Underestimation will not cause a "runaway" but rather under-assist the patient. Either of these problems will hamper the success of ventilatory assistance with PPS [10]. Therefore, an accurate, simple and noninvasive way to monitor R_{rs} and C_{rs} would facilitate the clinical use of PPS and would also make it possible to apply PPS for extended periods of time in order to assess its potential clinical benefits.

We have recently developed a noninvasive method to calculate C_{rs}, named the adaptive time slice method (ATSM). The aim of this study was to introduce ATSM and evaluate its ability to continuously calculate C_{rs}.

II. METHODS AND MATERIALS

A. Patients and measurement

Totally 7 patients with Chronic Obstructive Pulmonary

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Z. Zhao and K. Möller are with the Department of Biomedical Engineering, Furtwangen University, D-78054, VS-Schwenningen, Germany (corresponding author: Z. Zhao. Tel.: +49 7720 307 4395; Fax: +49 7720 307 4210; Email: zhanqi.zhao @ hs-furtwangen.de).

M. Eger and T. Handzsuj are with Dräger Medical, Lübeck, Germany.

V. M. Ranieri is with the Department of Anesthesia and Intensive Care Medicine, University of Turin - S.Giovanni Battista Molinette Hospital, Turin, Italy.

L. Appendini is with the Department of Pneumology, Fondazione S. Maugeri, IRCCS, Istituto Scientifico di Veruno, Veruno, Italy.

C. Micelli is with the KleisTEK, Monopoli, Italy.

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Disease (COPD) were examined retrospectively. The study was approved by the local ethics committee. Written informed consent was obtained from all patients prior to the study. The patients were breathing spontaneously under pressure support ventilation (PSV). Pressure support level varied from 6 to 12 mbar according to the need of patients. Positive end-expiratory pressure (PEEP) level varied from 5 to 8 mbar and fraction of inspired oxygen (F_iO_2) ranged between 35% and 50%. Airway pressure (P_{aw}), flow ($\dot{V}$), esophageal pressure (P_{es}) and gastric pressure (P_{ga}) were measured and recorded at a sampling rate of 200 Hz. Lung volume were integrated from $\dot{V}$. Transdiaphragmatic pressure (P_{di}) was derived by subtraction of P_{es} from P_{ga}.

B. Adaptive time slice method (ATSM)

One breathing cycle is divided into a certain number of slices along the time axis. For slice *i*, the following regression is applied:

$$P_{aw} - \dot{V} \times R_{rs} = V / C_i + k_i + \varepsilon \qquad (2)$$

where k_i and C_i represent intercept and compliance for slice *i*, respectively; ε is the error. Confidence intervals (CI) of k_i and $1/C_i$ are calculated and denoted as CI_k and $CI_{1/C}$. Depending on the quality of the fit, i.e., CI_k and $CI_{1/C}$, the width of the slices are adapted and one or no compliance value is accepted for slice *i*. At the end, totally *n* compliance values are obtained for all slices and the outliers are eliminated according to a modified Z-score [11, 12], C_{rs} of this breathing cycle is calculated as the mean value of the determined compliances C_i ($i \in N = \{1, 2, \ldots, n\}$). For a detail description, see Appendix. The respiratory system compliance calculated with ATSM is denoted as C_{ATSM}.

To apply the ATSM, we assume that P_{mus} is constant within a short time period (slice) and respiratory system resistance R_{rs} is known. R_{rs} can be obtained using different methods [9, 13, 14]. In the present study, P_{di} was used as an approximation of P_{mus}, since they do not significantly differ from each other in our experimental settings [15]. P_{di} serves a comparative purpose in case of compliance and to determine resistance R_{rs} that could be obtained otherwise. Resistance (denoted as R_{Pdi}) and compliance (C_{Pdi}) were calculated using a least-squares-fit (LSF) method [16, 17] based on Eq. 1. Subsequently, R_{rs} in Eq. 2 was substituted by R_{Pdi}. C_{ATSM} was calculated and compared to C_{Pdi} using Bland-Altman analysis [18] and one-tailed t-test. The results are presented in mean ±SD. The absolute difference between C_{ATSM} and C_{Pdi} were compared to 10%, 15% or 20% of maximum C_{Pdi}. A *P* value < 0.05 was considered statistically significant. Since the number of breaths collected in each patient differed, a weighted correlation coefficient was applied to take into account the repeated observations from subjects [19]. The data processing was performed with MATLAB 7.2 (The MathWorks Inc., Natick, MA, USA).

III. RESULTS

Table 1 shows the compliance values estimated with ATSM and P_{di}. Totally 95±4% of the recorded data could be analyzed with ATSM. In 6 patients out of 7 (except patient Kir), the results delivered with ATSM had similar variation (SD) and accuracy (difference<20%) as with P_{di}.

TABLE 1: Information of the recruited patients and respiratory system compliance. From left to right: the name abbreviation of patients; settings of the ventilators; total number of breaths recorded; number of breaths that could be analyzed with ATSM; Compliance calculated with ATSM; Compliance calculated with P_{di}; absolute difference between C_{ATSM} and C_{Pdi}, percentage of maximum C_{Pdi} and p-value of one-tailed t-test.

Pat.	No. of breaths calculated (available)	C_{ATSM}	C_{Pdi}	Difference, p-value
Bru	134 (138)	93.70±12.83	88.36±7.83	$<10\%$, $p<0.01$
Kir	63 (66)	58.24±16.10	31.93±1.56	$>20\%$, $p>0.05$
Alb	64 (67)	45.75±3.52	41.03±4.95	$<15\%$, $p<10^{-5}$
Teo	71 (83)	60.33±9.91	67.92±14.76	$<15\%$, $p<0.05$
Tsa	133 (141)	110.71±9.67	89.32±11.89	$<20\%$, $p<10^{-5}$
Zab	92 (95)	56.54±16.00	68.77±12.65	$<20\%$, $p<10^{-5}$
Zan	143 (146)	41.04±5.69	50.59±4.45	$<15\%$, $p<10^{-5}$

Fig. 1 is the Bland-Altman analysis of the difference between C_{ATSM} and C_{Pdi}, with the mean of 3.22 and SD of 17.58 ml/mbar. Weighted correlation coefficient was equal to 0.86 ($p<10^{-5}$). In the comparison without patient Kir, the difference was 1.14±16.32 ml/mabr. Weighted correlation coefficient was raised to 0.94 ($p<10^{-5}$).

IV. DISCUSSION

In the present study, the maneuver-free ATSM was introduced to calculate C_{rs} in spontaneously breathing patients under pressure support ventilation. Judging from the preliminary results, the ATSM is robust and able to monitor C_{rs} noninvasively and continuously.

The online estimation of respiratory system mechanics at the bedside is a helpful diagnostic tool to assist therapeutic decisions concerning mechanically ventilated patients. The analysis of respiratory mechanics has been proposed to guide ventilator settings [20-22] and thus improve outcome of critically ill patients on the intensive care unit. Unfortunately, the assessment of lung mechanics is still hard in the presence of respiratory muscle effort, such as during assisted ventilation. Especially in the ventilation mode PPS, knowledge about R_{rs} and C_{rs} is extremely important [14].

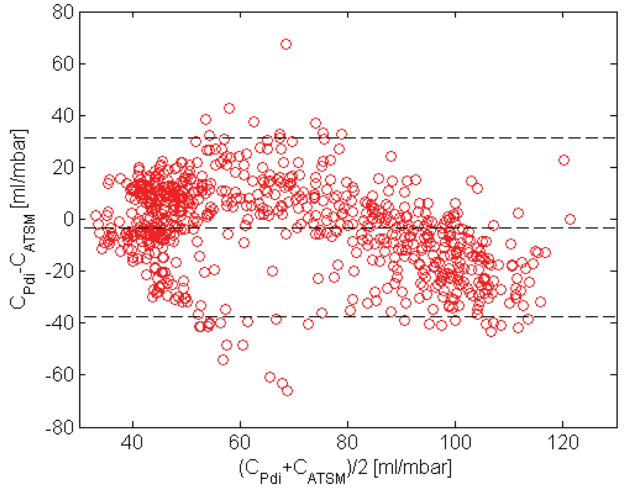

Fig. 1: Bland-Altman plot to compare the respiratory system compliance with ATSM (C_{ATSM}) and with P_{di} (C_{Pdi}). Data from 7 patients, totally 700 breaths were analyzed. Every circle represents one breath from one of the patients. Dashed line at the middle depicts the mean difference between C_{ATSM} and C_{Pdi}. Other two dashed lines represent mean ± 1.96*SD.

Formerly, Younes *et al.* have proposed a so-called "run away" technique to assess lung mechanics [10]. In the situation when a "run away" happens, the whole respiratory system becomes unstable and the patient feels very uncomfortable. Although this technique may provide satisfactory results, it is not used at the bedside. Later Younes and his colleagues have suggested a noninvasive method to calculate C_{rs} [23]. Phasic expiratory activity and behavioral responses are the major uncertainties of this method, and therefore, the occlusion time is uncertain. Besides, this method is not suitable for continuous monitoring on a breath by breath basis.

The ATSM assumes constant P_{mus} in short time period, and calculates the compliance with LSF. Compared to two-point compliances, compliance estimated with LSF is less sensitive to noise. Resistance is considered as prior knowledge to reduce the uncertainty in the linear regression. A confidence interval is applied in compliance calculation in ATSM to assure the reliability of the estimates. Since breath-by-breath estimation with ATSM could be achieved in 95% of recorded data, it is suitable for clinical use at the bedside without complicated maneuvers.

Potential error sources of ATSM include the accuracy of resistance and activity of respiratory muscles. In this preliminary study, transdiaphragmatic pressure was used to calculate respiratory system compliance for comparison and resistance. Since P_{di} is only an approximation of P_{mus}, the compliance and resistance calculated accordingly may be inaccurate in certain patients where P_{di} measurement is problematic. In the presence of strong activity of respiratory muscles, the assumption in ATSM (constant P_{mus} within a short time period) may be violated. Therefore, the ATSM is suitable for patients under assisted ventilation (such as PPS and PSV) but not for those without ventilator support. Although C_{rs} is not constant over the whole vital capacity [24], we assume it to be constant sometime within tidal breathing. A limitation of the ATSM is that a fixed threshold θ is used to determine the slice width. The threshold was obtained by trial and error and has only been evaluated on the preliminary data available. In further studies, more patients will be included and different thresholds will be examined.

V. CONCLUSION

Respiratory system compliance in spontaneously breathing patients can be calculated by means of "slicing" the time axis and applying a LSF separately for each slice. The process to determine the slice width benefits from the confidence interval of the fitting parameters. Therefore, this slice width selection is adapted to the noise level of the signals and the time variation of P_{mus}. The ATSM method takes advantage of the selection process and – based on the preliminary data available – provides satisfactory results.

APPENDIX

Detail description of the ATSM:

Step 1: Determination of the number and the beginning of slices. In the present study, the sampling frequency of the data is 200 Hz and the whole breathing cycle is divided into 40 steps. The number of steps depends on the sampling frequency so that not too few samples are included in every step (at least more than 10 samples). Each step is treated as the beginning of one slice.

Step 2: Determination of the slice width for every slice. Given a threshold value θ we proceed as follows. The slice width is initialized with a length of one step for each slice. With the regression Eq. 2, let $\beta=1/C_i$. The relative CI of β, i.e. CI_β/β, is calculated for each slice. Then every slice width grows individually step by step until $CI_\beta/\beta < \theta$ or no more steps can be recruited. If the growing process stops because of $CI_\beta/\beta < \theta$, the β ($1/C_i$) and k are counted for this slice. Otherwise this slice will be ignored.

Step 3: Outliers elimination and the overall C_{rs} calculation. Normally, the CI_β will decrease when the length of the slice is increased in most of the cases. And the ranges of CI_β/β are between 1 and 0.1 in most of the cycles. Outliers of β might be hidden in the slices where CI_k/k is large. Therefore using an outlier detection to avoid errors is needed. Here a modified Z-score is applied and performed twice for both $1/C_i$ and C_i.

- First, the median over the data sample is calculated: $x_m = \text{Median}(x_i)$; ($i \in N = \{1, 2, \ldots, n\}$, number of valid slices; $x = 1/C_i$ or $x = C_i$)
- Then the median of the absolute differences is needed: $\text{MAD} = \text{Median}(|x_i-x_m|)$
- The modified z-score heuristic is defined as: $z_i = 0.6745\times(x_i-x_m) / \text{MAD}$
- An outlier is defined as: $|z_i| > 3.5$

After the outliers are eliminated, for the remaining C_i, $C_{rs} = \text{mean}(C_i)$, $i \in N = \{1, 2, \ldots, n\}$.

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