Intensive Care Med (2000) 26: 1612–1618
DOI 10.1007/s001340000632

ORIGINAL

**M.S. Lourens**
**B. van den Berg**
**J.G.J.V. Aerts**
**A.F.M. Verbraak**
**H.C. Hoogsteden**
**J.M. Bogaard**

# Expiratory time constants in mechanically ventilated patients with and without COPD

Received: 27 January 2000
Final revision received: 29 May 2000
Accepted: 28 June 2000

Supported by the Dutch Asthma Foundation (Nederlands Astma Fonds)

M.S. Lourens (✉) · B. van den Berg ·
J.G.J.V. Aerts · A.F.M. Verbraak ·
H.C. Hoogsteden · J.M. Bogaard
Department of Pulmonary and Intensive Care Medicine, Erasmus Medical Centre Rotterdam, Dr Molewaterplein 40,
3015 6D Rotterdam, The Netherlands
E-mail: lourens@lond.azr.nl
Phone: +31-10-4634891
Fax: +31-10-4634856

**Abstract** *Objective*: In mechanically ventilated patients, the expiratory time constant provides information about the respiratory mechanics and the actual time needed for complete expiration. As an easy method to determine the time constant, the ratio of exhaled tidal volume to peak expiratory flow has been proposed. This assumes a single compartment model for the whole expiration. Since the latter has to be questioned in patients with chronic obstructive pulmonary disease (COPD), we compared time constants calculated from various parts of expiration and related these to time constants assessed with the interrupter method.
*Design*: Prospective study.
*Setting*: A medical intensive care unit in a university hospital.
*Patients*: Thirty-eight patients (18 severe COPD, eight mild COPD, 12 other pathologies) were studied during mechanical ventilation under sedation and paralysis.
*Measurements and results*: Time constants determined from flow-volume curves at 100 %, the last 75, 50, and 25 % of expired tidal volume, were compared to time constants obtained from interrupter measurements. Furthermore, the time constants were related to the actual time needed for complete expiration and to the patient's pulmonary condition. The time constant determined from the last 75 % of the expiratory flow-volume curve (RCfv75) was in closest agreement with the time constant obtained from the interrupter measurement, gave an accurate estimation of the actual time needed for complete expiration, and was discriminative for the severity of COPD.
*Conclusions*: In mechanically ventilated patients with and without COPD, a time constant can well be calculated from the expiratory flow-volume curve for the last 75 % of tidal volume, gives a good estimation of respiratory mechanics, and is easy to obtain at the bedside.

**Key words** Mechanical ventilation · Chronic obstructive pulmonary disease · Respiratory mechanics · Flow-volume curve · Time constant · Airflow obstruction

## Introduction

In chronic obstructive pulmonary disease (COPD) acute respiratory failure is a common and, in many cases, life-threatening complication, requiring ventilatory support. Mechanically ventilated patients with COPD are at risk of difficult weaning and chronic ventilatory dependency. Monitoring respiratory mechanics in these patients is a prerequisite to assess the patient's pulmonary condition, to detect poor patient-ventilator interaction and, consequently, optimise ventilator settings. By appropriately setting the ventilator, hyperinflation, intrinsic PEEP and, consequently, work of breathing can be minimised resulting in a more favourable outcome.

Many studies have addressed the issue of the mechanical properties of the respiratory system during lung inflation. The assessment of respiratory mechanics during relaxed expiration with simple tools, in clinical settings, has been rather unsuccessful.

The expiratory time constant provides information on the mechanical properties of the respiratory system, is a measure of lung emptying, and can be used to predict the minimal time needed for complete exhalation [1, 2]. A generally accepted way to determine the expiratory time constant is by multiplying compliance and resistance, assessed with the interrupter method [3, 4, 5]. However, this method interferes with the relaxed expiration and is not considered a simple tool for bedside use. An easier way to determine the expiratory time constant is based on the slope of the relaxed expiratory flow-volume curve [1, 2, 6, 7, 8, 9, 10, 11]. Brunner et al., proposed to determine the expiratory time constant as the ratio of exhaled tidal volume to peak expiratory flow [1]. This approach assumes a single compartment model for the whole expiration, i.e., a single compartment emptying itself through a constant resistance. This has to be questioned in patients with COPD in view of the presence of ventilatory inhomogeneity and expiratory flow-limitation [12]. However, a linear relationship between flow and volume has been described for the later part of expiration in patients with airway obstruction [7, 13, 14, 15]. Because this linear relationship is inherent in a one-compartment model, we hypothesise that an effective time constant can more appropriately be calculated from the later part of expiration in these patients.

The purpose of this study was to assess the applicability of the expiratory time constant determined from the expiratory flow-volume curve at different percentages of exhaled volume in mechanically ventilated patients both with and without COPD. These time constants were compared to reference time constants obtained from values of compliance and resistance determined with the interrupter method. To evaluate the clinical value of the time constants, we related them to the actual time needed for complete expiration to functional residual capacity and to the presence and severity of airflow obstruction.

## Patients and methods

### Patients

The study was conducted on 38 patients admitted to the respiratory intensive care unit. Patients were included if they fulfilled the following criteria: mechanical ventilation via an endotracheal or tracheostomy tube with an inner diameter ≥ 7 mm, a ventilator-PEEP level < 10 cm $H_2O$, respiratory rate ≤ 20 breaths per minute, and absence of air leaks. Twenty-six patients had a history of COPD. Amongst these, 18 patients suffered from severe COPD and required ventilatory support for respiratory failure due to acute exacerbation of COPD. All these patients fulfilled the criteria of severe COPD according to the ERS consensus: a clinical diagnosis of COPD and previous spirometric data showing an $FEV_1$ < 50 % of predicted (mean 30 % of predicted) [16]. The remaining eight patients had a history of moderate COPD and a previous $FEV_1$ between 50 and 70 % of predicted (mean 59 %) [16]. These patients were ventilated for other conditions than COPD. In 12 patients, underlying diseases included a variety of medical conditions all complicated by respiratory failure and ventilator dependency. Thirty patients were intubated with an endotracheal tube (inner diameter 7.5–9 mm), and eight patients with a tracheostomy tube (inner diameter 7–8.5 mm). All patients were ventilated with a Siemens Servo 900 C ventilator (Siemens-Elema, Solna, Sweden). Ventilator settings were set by the primary physician and remained unchanged during the study, except that if present, ventilator-PEEP was removed. In 32 patients, the volume-controlled mode was used, and in six patients the pressure-controlled mode. The average minute volume was 9.7 l/min, ranging from 6 l to 17.5 l per minute. The average respiratory rate was 16 breaths per minute, ranging from 10 to 20 breaths per minute. At volume-controlled ventilation, the ratio between inspiratory and expiratory time was 35:65. In the pressure-controlled mode, the ratio between inspiratory and expiratory time was 50:50. During the study, all patients were sedated with midazolam (Roche Nederland, Mijdrecht, Holland) and paralysed with vecuronium (Organon Teknika, Boxtel, Holland). Informed consent was obtained from the patient or their next of kin. The study was approved by the local ethics committee.

### Respiratory measurements

A heated pneumotachometer (Lilly, Jaeger, Würzburg, Germany) was connected to the endotracheal tube to measure flow. Volume was obtained by computerised integration of the flow signal. Airway opening pressure was measured proximal to the pneumotachometer using a pressure transducer (Validyne Engineering, Northridge, Calif., USA). Data were stored and analysed using a personal computer (Commodore 486 SX33, Commodore Business Machines, West Chester, Pa., USA) at a sample frequency of 100 Hz.

### Analysis of the flow-volume curve

The time constant was obtained by calculating the quotient of exhaled volume and the corresponding change in flow at different values of exhaled volume. Time constants were calculated for 100 % (RCfv100), the last 75 % (RCfv75), 50 % (RCfv50), and 25 % (RCfv25) of exhaled volume. In the formula for the RCfv50:

RCfv50 = 0.5*Vt/(V’50,ex -V’end,ex)

where RCfv50 is the time constant obtained from flow-volume curve for last 50 % of exhaled tidal volume (s), 0.5*Vt is 50 % of expiratory tidal volume (l), V’50,ex is the flow at 50 % of exhaled volume (l/s), and V’end,ex is the flow at end-expiration (l/s).

For the calculation of the RCfv100 the peak flow was considered as 100 % flow-level (Fig. 1). To compare our time constants with the method proposed by Brunner et al., the time constant was also calculated as the ratio of exhaled volume and peak flow (RCfvp) [1]. To estimate the actual time needed for lung emptying, the expiratory line of the ventilator circuit was disconnected from the ventilator at end-inspiratory pause and the patient was allowed

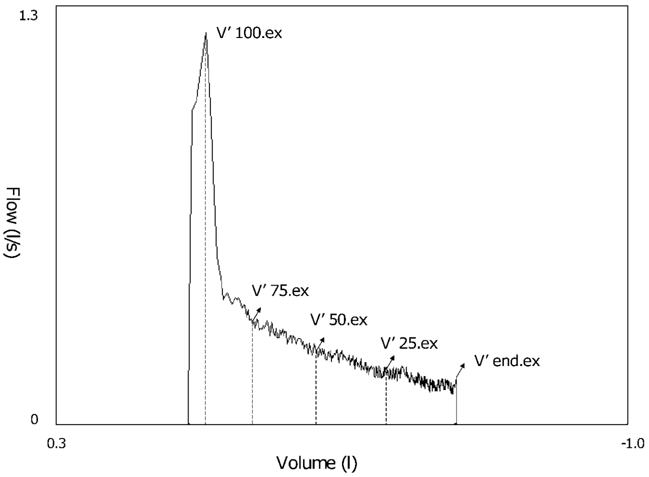

**Fig. 1** Flow-volume curve of a patient with COPD. V'100,ex, V'75,ex, V'50ex, V'25,ex and V'end,ex are indicated

to expire completely ($n = 27$). Taking into account the noise in the flow recording, expiration was considered complete when the flow was ≤0.04 l/s. The time needed for complete expiration was measured (Tact). All measurements were performed in triplicate and the average was calculated.

### Interrupter measurements

A pneumatic interrupter installed distal to the pneumotachometer in the ventilator circuit, was used for repeated occlusions of the upper airway during expiration. The valve was computer-controlled. Opening and closing of the valve was alternated at a cycle time of 500 ms. The interrupter procedure was performed throughout the expiration. Pressure and flow signals were stored on a computer for subsequent analysis. Values of the post-interruption plateau in tracheal pressure, of preceding flow, and of corresponding volume were obtained for all subsequent occlusions during one expiration. Volume-pressure (V/P) and pressure-flow (P/V') curves were plotted from these values. Using a least squares linear regression method, a line was fitted through the data from the second interruption till a volume was expired equal to the pre-set tidal volume. Compliance and resistance were determined for this tidal volume range from the slope of the V/P and P/V' curve, respectively. During flow limitation the resistance behaviour is complex and resistance has to be considered as effective resistance. The time constant (RCint) was calculated by multiplying compliance- and resistance-values. All measurements were performed in triplicate and the average was calculated.

### Data analysis

Time constants obtained from the flow-volume curve and from the interrupter method were compared using the method of Bland and Altman for assessing agreement between two methods of clinical measurement [17]. Differences between RCint and RCfv were plotted against the means of the corresponding values of RCint and RCfv, and limits of agreement were estimated as ± 2 SD of the differences.

To assess the differences in time constants between the groups with mild COPD, severe COPD, and other pathologies, the Kruskal-Wallis test was performed. A $P$-value $< 0.05$ was considered significant.

To evaluate the sensitivity and specificity of the time constant as measure for COPD, receiver operating characteristic (ROC) curves were computed for the time constants obtained with the interrupter and flow-volume method at different percentages of exhaled volume [18, 19]. An $FEV_1 < 70\%$ of predicted value prior to ventilatory support was used as a standard for discrimination between patients with other pathologies and COPD (moderate and severe). The area under the ROC curve represents the combined sensitivity and specificity behaviour of the index used.

The time constants obtained from flow-volume curves were correlated with the actual time needed for complete expiration. According to the concept of a single compartment model, passive lung emptying is described by the following exponential equation:

$$V(t) = V(0)*e^{(-t/\tau)}$$

with V(0) and V(t) as, respectively, the lung volume at the start (time t = 0) and at t (time = t) s from the onset of expiration and $\tau$ as the expiratory time constant [7, 8, 9, 10]. According to this equation, three times the time constant is needed to achieve exhalation down to 5% of the initial volume. The time constants determined from the flow-volume curve were multiplied by three and correlated to 95% of the actual time needed for complete expiration, using Pearson's correlation. To show the relationship between RCfv and Tact the Bland and Altman method was used. The differences between 3*RCfv and Tact were plotted against their means. Limits of agreement were estimated as ± 2 SD of the differences.

## Results

In all patients, both relationships between volume and pressure and between pressure and flow obtained from interrupter measurements were found to be approximately linear for the volumes studied ($r^2 = 0.99$, SD 0.01 and $r^2 = 0.97$, SD 0.02, respectively).

The values of the time constants obtained from flow-volume curves and interrupter measurements are shown in Table 1. Comparing the time constants of the three patient groups within one method, significant differences were found between the groups with moderate and severe COPD and between the groups with

**Table 1** Time constants obtained from flow-volume curves and interrupter measurements. For abbreviations and definitions see text

| | | Severe COPD | Moderate COPD | Other pathologies |
|---|---|---|---|---|
| Rcint | Mean (SD) | 2.88 (1.61)[a] | 1.02 (0.40)[b] | 0.65 (0.28) |
| Rcfvp | Mean (SD) | 0.75 (0.20) | 0.70 (0.19) | 0.60 (0.10) |
| RCfv100 | Mean (SD) | 0.85 (0.18) | 0.79 (0.22) | 0.63 (0.12) |
| RCfv75 | Mean (SD) | 2.84 (1.53)[a] | 1.05 (0.32)[b] | 0.72 (0.18) |
| RCfv50 | Mean (SD) | 3.42 (1.61)[a] | 1.25 (0.44) | 0.84 (0.39) |
| RCfv25 | Mean (SD) | 4.20 (1.99)[a] | 1.47 (0.57) | 1.06 (0.63) |

[a] Significant difference between time constants of severe and moderate COPD

[b] Significant difference between time constants of moderate COPD and other pathologies

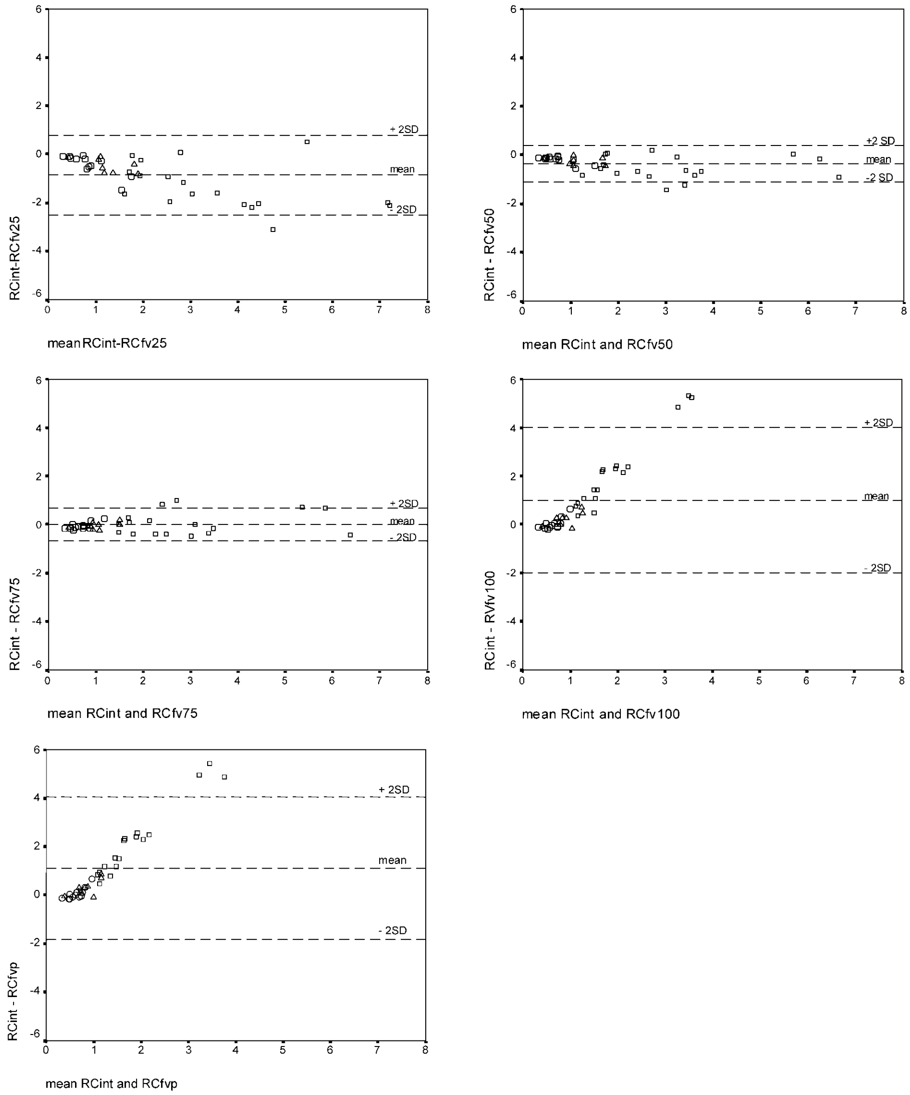

**Fig. 2** Bland and Altman analysis of differences (RCint –RCfv) plotted against the means of RCint and RCfv. Mean and standard deviations are indicated. □, patients with severe COPD; △, patients with moderate COPD; ○, patients with other pathologies

severe COPD and other pathologies for the RCint, RCfv75 RCfv50, and RCfv25 (all $P < 0.001$). The difference found between the group with moderate COPD and the group with other pathologies was only significant for the RCint ($P = 0.034$) and the RCfv75 ($P = 0.017$).

The agreement between the time constants obtained from flow-volume curves and interrupter measurements is shown in the Bland and Altman analyses (Fig. 2). The differences between RCint and RCfv are plotted against their means. Mean difference and limits of agreement are indicated.

ROC-curves were computed for all time constants. The area under the curve was 0.93 for the RCint, 0.75 for the RCfvp, 0.82 for the RCfv100, 0.94 for the RCfv75, 0.92 for the RCfv50, and 0.89 for the RCfv25. The RCfv75 with a cut-off level of 0.82 combines the highest sensitivity (0.96) and specificity (0.83) as measure of airway obstruction.

The mean difference between actual times needed for complete expiration and 3*RCfv was 0.5 s (sd 2.8) for the RCint, 2.9 s (sd 4.2) for the RCfvp, 2.8 s (sd 4.2) for the RCfv100, 0.4 s (sd 2.4) for the RCfv75, –0.5 s (sd 3.1) for the RCfv50, and –1.6 s (sd 3.6) for the RCfv25. Pearson's test yielded the following correlations between Tact and the respective time constants: RCint: 0.81 ($P < 0.001$), RCfvp: 0.26 ($P > 0.1$), RCfv100: 0.38 ($P = 0.052$), RCfv75: 0.85 ($P < 0.001$), RCfv50: 0.79 ($P < 0.001$), and RCfv25: 0.82 ($P < 0.001$). In Fig. 3, the Bland and Altman plot of 3*RCfv75 and Tact is shown.

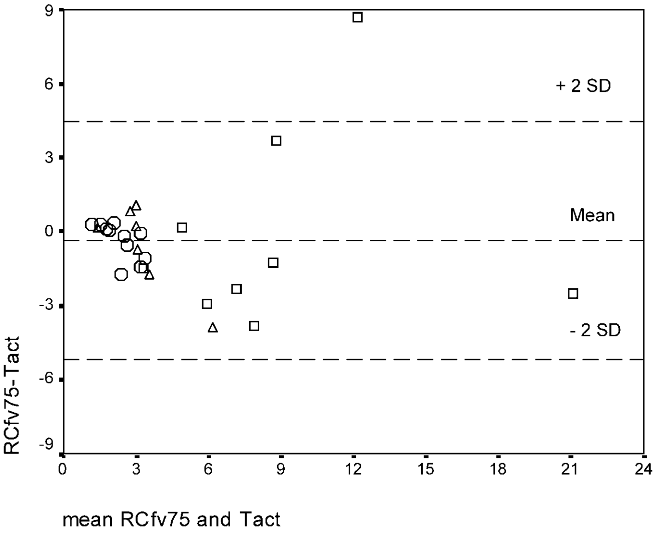

**Fig. 3** Bland and Altman analysis of the differences between 3* the time constant obtained from the last 75 % of tidal volume of the flow-volume curve (3*RCfv75) and the time needed for complete exhalation (Tact) against the means of 3*RCfv75 and Tact, in seconds. Mean and standard deviations are indicated. □, patients with severe COPD, △, patients with moderate COPD, ○, patients with other pathologies

## Discussion

This study demonstrates that in mechanically ventilated patients with and without COPD the expiratory time constant determined from the expiratory flow-volume curve for the last 75 % of tidal volume is in closest agreement with the time constant obtained with interrupter measurements. The RCfv75 is a good prognosticator for the actual time needed for complete exhalation and is discriminative for the severity of COPD.

In the present study, time constants obtained from the flow-volume curves and time constants obtained with the interrupter technique were compared. The interrupter method is based on the assumption that a rapid equilibration occurs between alveolar and airway opening pressures during a brief period of airway occlusion [3, 4, 5]. In this study, the airways were occluded intermittently for 250 ms. In COPD patients with airway obstruction, pressure equilibration may be delayed because of regional differences in mechanical properties within the lungs [3, 4]. However, we observed pressure plateaus during airway closure within 250 ms in all patients. This is comparable to the findings of others, describing a plateau in airway opening pressure within 300 ms during expiratory interruptions [3]. In the present study, the presence of an endotracheal tube or a tracheal cannula eliminated the influence of the upper airway. Therefore, no delay in pressure equilibration occurred related to the compliance of the extrathoracic airways [20].

On the other hand, the presence of the endotracheal tube might have influenced the time constant. The design of the study precluded removal of the endotracheal tube since all patients were on controlled ventilation with sedation and paralysis. However, a previous study showed that in patients with COPD the presence of the endotracheal tube did not appreciably affect the slope of the later part of the expiratory flow-volume curve, due to the low flow-rates in these patients [21]. In the patient group with other pathologies, the average flow-rate during expiration is usually higher. The endotracheal tube can cause a minor decrease in flow in these patients, resulting in a slightly higher time constant [21]. With respect to the exhalation valve of the ventilator, it has been described that this valve significantly decreases the peak flow, but does not affect the slope of the flow-volume curve during the later part of expiration [21].

The passive expiratory flow-volume relationship can be divided into an early rapid component, which reflects resistive behaviour of predominantly extrathoracic resistive elements, and a consecutive slower component, mainly reflecting viscous and elastic properties of the lungs and chest wall [2, 22, 23]. The transition point between these components has been referred to as the inflection point, determined as the point of maximum slope following the peak expiratory flow [2]. In this study, we found that the time constants calculated from the part of the flow-volume curve beyond the inflection point more closely approached the values determined with the interrupter method, especially in patients with COPD. The RCfv75 and RCfv50 were found to be in good agreement with the RCint. The results of the RCfv25 were less favourable, and this is most likely due to an increase in the noise-signal ratio because of the low flow-rates at end-expiration. The RCfv100 and RCfvp gave a systematic underestimation of the time constant, particularly in patients with COPD. In these patients the peak flow only minimally contributes to the exhalation, and the rate of lung emptying is predominantly determined by the slope of the flow-volume curve beyond the inflection point (Fig. 1). Therefore, the method to determine the time constant as the ratio of exhaled volume to peak flow, proposed by Brunner et al., is less appropriate in COPD patients [1]. As the part of the expiratory flow-volume relationship beyond the inflection point approaches linearity, both in patients with COPD and with other pathologies, it is more suitable for calculation of the time constant. This linearity has also been described by others [7, 13, 14, 15]. We chose to use the RCfv75 instead of the RCfv50 for several reasons: the RCfv75 was in closest agreement with the RCint, it was the best discriminator for the severity of COPD, and it represented a greater part of the expiratory flow-volume curve.

This is in agreement with the findings of Galbusera et al., who also studied expiratory time constants during mechanical ventilation at different percentages of exhaled volume [11]. However, in their calculation of the time constant, the end-expiratory flow is not taken into account. In mechanically ventilated patients with flow limitation, expiration is usually terminated before the end-expiratory flow reaches zero l/s. Therefore, the end-expiratory flow should also be included in the calculation.

The present study shows that the time needed for complete expiration was approximately three times the calculated time constant for all patient groups, in which the RCfv75 correlated best with the Tact. This indicates that the time constant can be a useful tool in setting the ventilator. Recently, the expiratory time constant determined over the last 75 % of expiratory tidal volume has even been implemented in the software of the Hamilton ventilator "Galileo" (Hamilton Medical, Rhäzüns, Switzerland), giving information about the suitable respiratory rate. In patients with severe COPD, however, it may be impossible to set the expiratory time at three times the time constant in view of the minimum respiratory rate required for sufficient ventilation. In these patients, the time constant is informative on the patient's pulmonary condition and can be used to optimise patient-ventilator interaction.

The time constant was found to discriminate between patients with and without COPD. These findings are in line with previous studies, in which the time constant and the FEV1 were closely related both in spontaneously breathing and in mechanically ventilated patients with COPD [7, 14].

The present study was performed on paralysed patients. During paralysis, exhalation is passively driven by the elastic recoil of the total respiratory system. In mechanically ventilated patients without paralysis, muscle activity may interfere during expiration. Several studies have described the presence of inspiratory muscle activity during the first part of expiration, opposing emptying of the lungs [24, 25, 26]. It has, however, been shown in spontaneously breathing patients with COPD that the measured flow-volume relationship closely followed the course of the flow-volume curve predicted on the basis of the passive time constant during late expiration [24]. Another study reported activity of the diaphragm for only the first 50 % of expiration [26]. In patients with COPD an even faster decline in inspiratory muscle activity has been described during expiration [27, 28]. Therefore, it is likely that a time constant can be determined from the later part of expiration in mechanically ventilated patients without paralysis. Further studies are required to validate the feasibility of the expiratory time constant in non-paralysed patients.

In conclusion, in mechanically ventilated patients an expiratory time constant can best be calculated from the expiratory flow-volume curve for the last 75 % of exhaled tidal volume. Both in patients with COPD and in patients with other pathologies, RCfv75s are in good agreement with time constants assessed with interrupter measurements. Furthermore, the RCfv75 is found to be a good prognosticator for the actual time needed for complete expiration and to be an indicator of the severity of COPD. Thus, a time constant calculated from the last 75 % of the expiratory flow-volume curve is an easy method to assess respiratory mechanics at the bedside in artificially ventilated patients.

## References

1. Brunner JX, Laubscher TP, Banner MJ, Iotti G, Braschi A (1995) Simple method to measure total expiratory time constant based on the passive flow-volume curve. Crit Care Med 23: 1117–1122
2. Guttmann J, Eberhard L, Fabry B, Bertschmann W, Zeravik J, Adolph M, Eckart J, Wolff G (1995) Time constant/volume relationship of passive expiration in mechanically ventilated ARDS patients. Eur Respir J 8: 114–120
3. Gottfried SB, Higgs BD, Rossi A, Carli F, Mengeot PM, Calverly PMA, Zocchi L, Milic-Emili J (1985) Interrupter technique for measurement of respiratory mechanics in anesthetized humans. J Appl Physiol 59(2):647–652
4. Gottfried SB, Rossi A, Higgs BD, Calverly PMA, Zocchi L, Bozic C, Milic-Emili J (1985) Noninvasive determination of respiratory system mechanics during mechanical ventilation for acute respiratory failure. Am Rev Respir Dis 131: 414–420
5. Reinoso MA, Gracey DR, Hubmayr RD (1993) Interrupter mechanics of patients admitted to a chronic ventilator dependency unit. Am Rev Respir Dis 148: 127–131
6. McIlroy MB, Tierney DF, Nadel JA (1963) A new method for measurement of compliance and resistance of lungs and thorax. J Appl Physiol 18: 424–427
7. Aerts JGJV, van den Berg B, Lourens MS, Bogaard JM (1999) Expiratory flow-volume curves in mechanically ventilated patients with chronic obstructive pulmonary disease. Acta Anaesthesiol Scand 43: 322–327
8. Zin WA, Böddener A, Silva PRM, Pinto TMP, Milic-Emili J (1986) Active and passive respiratory mechanics in anesthetized dogs. J Appl Physiol 61: 1647–1655
9. Zin WA, Pengelly LD, Milic-Emili J (1982) Single-breath method for measurement of respiratory mechanics in anesthetized animals. J Appl Physiol 52: 1266–1271
10. Behrakis PK, Higgs D, Baydur A, Zin WA, Milic-Emili J (1983) Respiratory mechanics during halothane anesthesia and anesthesia-paralysis in humans. J Appl Physiol 55: 1085–1092
11. Galbusera C, Cortis G, Olivei M, Tosi PF, Via G, Ciccone R, Verde G, Iotti G, Braschi A (1999) Breath-by-breath evaluation of the expiratory time constant during mechanical ventilation. Am Rev Respir Crit Care Med 159(3):A366

12. Peslin R, Felicio da Silva J, Chabot F, Divivier C (1992) Respiratory mechanics studied by multiple linear regression in unsedated ventilated patients. Eur Respir J 5: 871–878
13. Rossi A, Polesi G, Brandi G, Conti G (1995) Intrinsic positive end-expiratory pressure (PEEP). Intensive Care Med 21: 522–536
14. Morris MJ, Madgewick RG, Collyer I, Denby F, Lane DJ (1998) Analysis of expiratory tidal flow patterns as a diagnostic tool in airflow obstruction. Eur Respir J 12: 1113–1117
15. Williams EM, Madgewick RG, Morris MJ (1998) Tidal expired airflow patterns in adults with airway obstruction. Eur Respir J 12: 1118–1123
16. Siafakas NM, Vermeire P, Pride P, Paoletti P, Gibson J, Howard P, Yernault JC, Decramer M, Higenbottam T, Postma DS, Rees J (1995) Optimal assessment and management of chronic obstructive pulmonary disease. Eur Respir J 8: 1398–1420
17. Bland JM, Altman DG (1986) Statistical method for assessing agreement between two methods of clinical measurement. Lancet 8: 307–310
18. McNeil B, Keeler E, Adelstein SJ (1975) Primer on certain elements of medical decision making. N Engl J Med 293: 211–215
19. Zweig MH, Campbell G (1993) Receiver-operating characteristics (ROC) plots: a fundamental evaluation tool in clinical medicine. Clin Chem 39: 561–577
20. Jaeger MJ (1982) The effect of the cheeks and the compliance of alveolar gas on the measurement of respiratory variables. Respir Physiol 47: 325–340
21. Lourens MS, van den Berg B, Hoogsteden HC, Bogaard JM (1999) Flow-volume curves as measure of respiratory mechanics during ventilatory support: the effect of the exhalation valve. Intensive Care Med 25: 799–804
22. Chelucci GL, Brunet F, Dall'Ava-Santucii J, Dhainaut JF, Paccaly D, Armaganidis A, Milic-Emili J, Lockhart A (1991) A single compartment model cannot describe passive expiration in intubated, paralysed humans. Eur Respir J 4: 458–464
23. Bates JHT, Decramer M, Chartrand D, Zin WA, Boddener A, Milic-Emili J (1985) Volume-time profile during relaxed expiration in the normal dog. J Appl Physiol 59: 732–737
24. Shee CD, Ploy-song-sang Y, Milic-Emili J (1985) Decay of inspiratory muscle pressure during expiration in conscious humans. J Apppl Physiol 58: 1859–1865
25. Agostoni A, Citterio G, D'Angelo E (1979) Decay rate of inspiratory muscle pressure during expiration in man. Respir Physiol 36: 269–285
26. Agostoni A, Citterio G (1979) Relative decay rate of inspiratory muscle pressure during expiration in man. Respir Physiol 38: 335–346
27. Morris MJ, Madgwick RG, Frew AJ, Lane DJ (1990) Breathing muscle activity during expiration in patients with chronic airflow obstruction. Eur Respir J 3: 901–909
28. Citterio G, Agostoni E, Del Santo A, Marazzini L (1981) Decay of inspiratory muscle activity in chronic airway obstruction. J Appl Physiol 51: 1388–1397