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A simple method to estimate functional residual capacity in mechanically ventilated patients

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Abstract. *Objective:* The aim of the present study was to evaluate a simplified method for FRC measurement.
Design: Accuracy and precision of the method were assessed in a physical lung model; reproducibility was tested in 10 mechanically ventilated patients. In each patient FRC was measured at three PEEP levels.
Setting: Post-operative intensive care unit in a university hospital.
Measurements and results: Gas flow, CO_2 concentration, and O_2 concentration were measured during in- and expiration by pneumotachography, a mainstream capnometer and a sidestream O_2-analyser. For FRC-measurement inspiratory O_2 concentration was changed by 30%. FRC was determined as mean value of a N_2 washout and N_2 washin procedure. Evaluation of this method in a lung model shows a good correlation between FRC set in the lung model and FRC measured (FRC measured = 1.028*FRC model+22.92 ml; $r^2 = 0.957$; $n = 30$). The mean difference was 4.4% of FRC-reference (range −8.4% to +21.7%). Duplicate determinations in 10 mechanically ventilated patients differed by an average of −2.7% (range −30.1% to +27.3%).
Conclusion: Our results suggest that the proposed method can be used in daily clinical work.

Key words: Mechanical ventilation – Respiration – Functional residual capacity – Lung volume

Functional residual capacity (FRC) is believed to be a key variable in the treatment of hypoxemic patients since the early work of Bergman in 1963 [1]. Therefore, many attempts have been made to measure FRC in mechanically ventilated patients [2–8]. The applied techniques include closed circuit helium dilution, open circuit nitrogen washout and sulphur hexafluoride washout. These are excellent methods which allow accurate determination of FRC. However, none of these methods are suitable for routine measurement since they require bulky instruments, are rather expensive, need technical supervision (mass spectrometer) or require special tracer gases and gas delivery valves (SF6 method).

To overcome these practical problems, a new method was developed to measure lung volume in mechanically ventilated patients. It is based on a rapid mainstream CO_2 analyzer, a pneumotachograph, and a side-stream O_2 analyzer. The purpose of this report is to describe the method, its accuracy and precision in vitro (on a lung model), and the reproducibility in patients.

Material and methods

FRC-estimation

Theory. The proposed method is based on an open nitrogen (N_2) washout/washin procedure and breath-by-breath calculation of the net transfer of nitrogen in and out of the lungs. It requires the application of a step change in nitrogen concentration (FN_2). This is achieved by a 30% change of the inspiratory O_2 fraction. Subsequently, intrabreath nitrogen concentration needs to be calculated and integrated with pneumotachography to yield a breath-by-breath estimate of the difference between in- and expired nitrogen volume. From this, the total N_2-volume which was in- or exhaled during the washin-/washout-procedure is calculated (VN_2-total). Functional residual capacity, or rather, the accessible pulmonary volume can then be derived as

$$FRC = \frac{VN_2\text{-total}}{FN_2(\text{start}) - FN_2(\text{end})} \quad (1)$$

where FN_2(start) and FN_2(end) are the intrapulmonary nitrogen concentrations before and after the washout procedure, respectively.

FRC estimation as proposed here is based on several assumptions. The first is that only oxygen, nitrogen, and carbon dioxide are present in the respired gases. The volume (VN_2), and the in- and expiratory fraction (FN_2) of nitrogen can then be derived from the other volumes during inhalation (i) and exhalation (e) as follows:

$$VeN_2 = Ve\text{-}VeCO_2\text{-}VeO_2 \quad (2)$$

$$ViN_2 = Vi\text{-}ViCO_2\text{-}ViO_2 \quad (3)$$

$$FeN_2 = 1\text{-}FeCO_2\text{-}FeO_2 \quad (4)$$

$$FiN_2 = 1\text{-}FiCO_2\text{-}FiO_2 \quad (5)$$

Thus, it is possible to derive VN_2 from measurements of total in- and expired volume, CO_2 volume (VCO_2) and O_2 volume (VO_2) only. The measurement of VCO_2 and VO_2, however, requires fast gas analy-

sis with a 10–90% rise time of less than 40 ms [9]. Furthermore, the delay time inherent in all gas analysis systems must be accurately compensated with respect to pneumotachography [10]. While these conditions can be met with many mainstream CO_2 analyzers today, only mass spectrometers offer similar performance for O_2 analysis.

However, the proposed method does not need a fast O_2 analyzer. In fact, a "fast" O_2-curve is computed from the measured in- and expiratory O_2-maxima/-minima and the fast CO_2-curve. The assumption is, that the delay-compensated intrabreath CO_2 waveform and the delay-compensated O_2 waveform are congruent (or inversely congruent). Therefore, the proposed method needs a fast mainstream CO_2 analyzer, since this is the basis for the transformation of the O_2 signal. Details are explained in the appendix.

Using the transformed O_2 signal and combining it with pneumotachography the inspired and expired volumes ViO_2 and VeO_2 are obtained. Similarly, $ViCO_2$ and $VeCO_2$ are measured and used to calculate ViN_2 and VeN_2 according to Eqs. 2 and 3. The net transfer of nitrogen per breath (dVN_2) is then derived as the difference ViN_2-VeN_2 and summed over the duration of the washout/washin procedure to yield VN_2-total. Since this calculation is sensible to flow-baseline drift, a drift compensation is necessary. Finally, FRC is calculated (Eq. 1). Two values of FRC are measured: one for a washout procedure (FiO_2 step from 70–100%) and one for a washin procedure (FiO_2 step from 100–70%). The average value between the two is reported.

Measurement-setup. The proposed method requires the measurement of airway gasflow (Screenmate box, Jäger, Würzburg, FRG), CO_2 concentration. (Novametrix 1260, Novametrix, Wallingford, CT, USA), and O_2 concentration (Capnomac, Datex, Helsinki, Finland). Measured data were digitized by an A/D converter (DT 2801, Data Translation, Marlboro, MA) at a rate of 60 samples/s and stored for later analysis (Tandon PCA/12, Moorpark, CA). Before each use the pneumotachograph, O_2- and CO_2-analysers were calibrated. FRC-estimation was then performed by a 30% change of the inspired oxygen fraction.

Calibrations and calculations. Further calculations, which were necessary for drift compensation and computing of FRC were performed with a spread sheet program (Microsoft Excel) and are described in the appendix.

Evaluation in a physical lung model

The proposed method was tested for accuracy and precision using a water-manometer type lung model. The model consisted of two connected plexiglas chambers filled with water. One chamber was closed and fitted to a tube which simulated the anatomical dead space. That chamber represented the lung volume or FRC. The other chamber was open to athmosphere. Compliance of the model was set to 100 ml/cmH_2O, resistance was approximately 2 cmH_2O/l*sec. Details of the model are given elsewhere [11].

The FRC of the model (FRC-reference) was varied from 770 ml to 2580 ml by adding or removing water. The accuracy of FRC-reference was ±25 ml. The model was ventilated with tidal volumes (Vi) ranging from 320–1600 ml in arbitrary steps such as to evenly cover the entire range of Vi/FRC ratios. A total of 30 different combinations of Vi and FRC were assessed. Respiratory rate was constant at 20/min at equal in- and expiratory times. The ventilator (Veolar, Hamilton, Bonaduz, Switzerland) was in pressure controled ventilation mode (PCV).

For each tidal volume and FRC setting, a washout and a washin procedure was performed by changing FiO_2 from 70–100% and, after achieving steady state, from 100–70%, respectively. The signals were analysed as described above. The resulting FRCs were compared with their corresponding reference values by the linear regression technique. Mean difference, standard error of differences, minimal and maximal difference between the reference values and the measured FRC were calculated, both as absolute and relative values.

Evaluation in patients

Ten mechanically ventilated patients for acute respiratory failure ($n = 4$) or post-operative treatment ($n = 6$) were investigated to assess the reproducibility of the method. Age, height, and weight varied between 26 and 72 years, 158 and 187 cm, and 65 and 98 kg, respectively. None of the patients was suffering from chronic obstructive pulmonary disease. All patients were ventilated with PCV (Veolar, Hamilton, Bonaduz, Switzerland) and a level and frequency necessary to achieve normocapnia. Inspiratory and expiratory time were equal. Before each measurement the measurement setup and the patients endotracheal tube were checked for gas leakage. The patients were completely paralyzed and in stable hemodynamic conditions. Duplicate measurements of FRC were taken in each patient at three PEEP levels. This yielded a total of 30 paired FRC measurements (FRC1 and FRC2). FRC measurements lasted for about 20–30 min at each PEEP level. Statistical analysis was done as explained previously.

Results

The measured values of FRC and the set lung volumes on the model (FRC-reference) are plotted against each other in Fig. 1. The regression equation is FRC-measured = 1.03*FRC-reference + 23 ml at an $r^2 = 0.957$. The mean difference was 65 ± 122 ml (range −170 ml to +350 ml) or, expressed as a percentage 4.4 ± 7.8% (range −8.4% to +21.7%). FRC-measured is slightly higher than the reference value. The error, however, is independent of FRC but rather dependent on the ratio between tidal volume (Vi) and FRC (Fig. 2).

The results of the reproducibility study in patients is given in Fig. 3. The regression equation is FRC2 = 0.92*FRC1 + 226 ml and r^2 was 0.779. The mean difference between two FRC-measurements was −2.7 ± 13.8% (range −30.1% to +27.3%).

Discussion

The aim of this study was to test accuracy, precision and reproducibility of a simplified procedure for estimation of functional residual capacity. The evaluation of the proposed method shows that FRC may indeed be calcu-

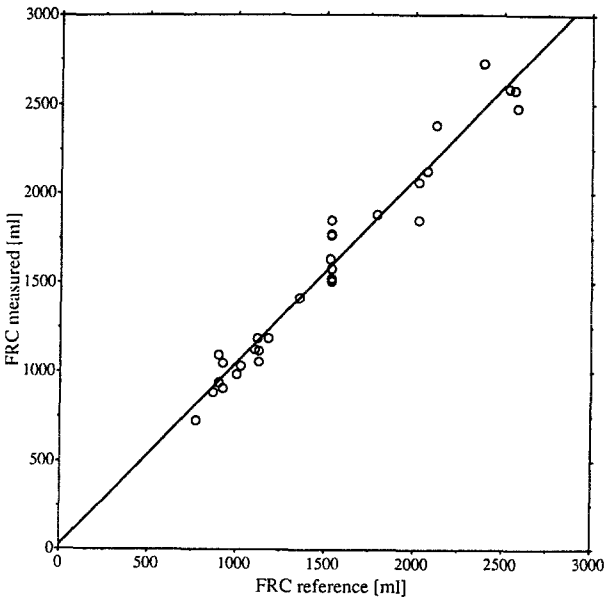

Fig. 1. Measured FRC plotted against FRC set in the lung model (FRC reference) ($n = 30$). Line is regression line (equation see text)

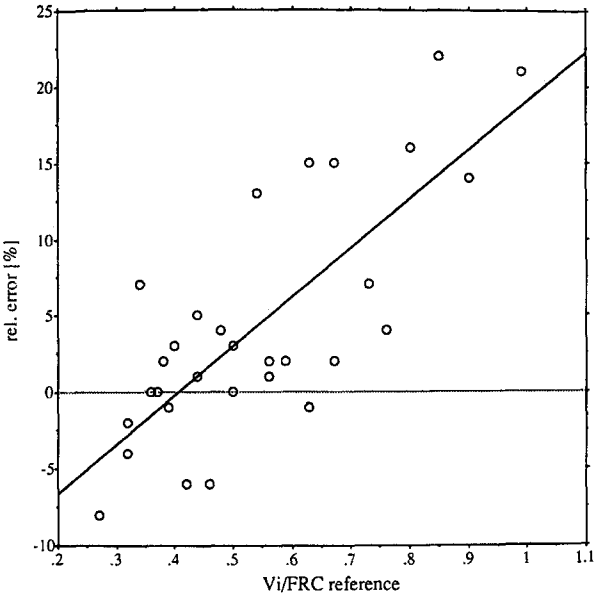

Fig. 2. Relative error (FRCmeasured-FRCreference)/FRCreference expressed as percentage (rel. error), is plotted against Vi/FRCreference ($n = 30$). Solid line is regression line ($y = 32.1 \cdot x - 13$; $r^2 = 0.593$) Results of lung model measurements

lated rather accurately in this simplified way. If the relation between tidal volume and FRC does not change, a difference of 20% between two measurements, may be regarded as a real change of FRC. Thus measurements are expected to be precise enough for clinical practice, i.e. to diagnose low FRC in mechanically ventilated patients and to control respiratory therapy, especially the application of positive end expiratory pressure.

The simplification of the proposed method is based first, on the combined use of a "rapid" CO_2-analyser and a "slow" oxygen analyser and second, on the computation of a "fast" responding O_2-waveform from the in- and expiratory extreme O_2 values and the course of the rapidly measured CO_2-concentration-curve. Thus, the equipment needed for FRC-measurement is modest. This will allow FRC to become a routinely measured parameter in mechanically ventilated patients. Though calculation procedures are extensive, they are easily performed by a computer. Only the measuring time which is about three times longer than with other techniques may be regarded as disadvantageous.

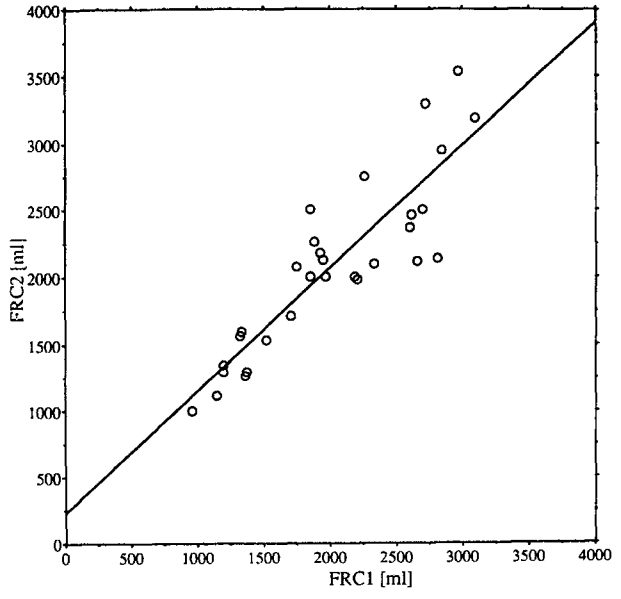

Fig. 3. Results of duplicate measurements in 10 patients at 3 PEEP levels each ($n = 30$). First measurement (FRC1) plotted against second measurement (FRC2). Line is regression line (equation see text)

The congruency of O_2- and CO_2-waveforms is a major assumption for the proposed method. In 1954 Bartels and Severinghaus [12] measured respiratory dead space by single breath analysis of O_2, CO_2, N_2 and He. Using mass spectrometry and a nitrogen analyser, they described that the concentrations of nitrogen, oxygen and carbon dioxide described virtually the same curve. Differences of intrabreath gas concentrations were negligible so that there was no measurable difference in dead space volume. Bartels' experiment is no proof that the N_2- and O_2-waveforms remain congruent throughout the washout procedure. In fact it is known, that the shape of the N_2-curve may change dramatically towards the end of a washout [13]. Such effects are neglected by the current method. If present, they probably contribute little to the net transfer of nitrogen in normal lungs, in the above mentioned extreme example much less than 5%. However, this very question was not addressed explicitely in this study and might require further investigations, in particular with COPD patients.

Because functional residual capacity is calculated from in- and expiratory volume, oxygen fraction, and carbon dioxide fraction, respectively, errors in these measurements and their cumulation will influence the calculated FRC markedly. One effect that leads to errors in FRC measurement is associated with the application of the O_2 stepchange and the assumption that FO_2 remains constant during inhalation (see appendix). Let us assume that a ventilator without internal tank is used for the experiment (for example a PB 7200). In such a ventilator, any change in O_2 concentration will be immediately effective at the ventilator outlet and a "front" is formed between previous and new O_2 concentration. As the inhalation process continues, this front travels through the inspiratory hose towards the airway opening of the patient. The front might get slured by long tubing and a humidifier, but it does not disappear. Eventually it will reach the airway opening, yet one does not know a priori if this happens at the beginning, the end, or sometimes during the inhalation. Thus, in the first breath of the washout the assumption of constant FiO_2 during inhalation is violated and this can lead to gross errors. This error will be reduced if a respirator with internal tank is used. The tank will act as a mixing chamber and smooth the O_2 step. A 30% change in FiO_2 will then not be measurable within the first inhalation but be partitioned over the first few breaths.

The ratio between inspiratory tidal volume and the preset FRC of the lung model (Vi/FRC), influences the accuracy of FRC estimation. With high Vi/FRC values the nitrogen of the lung model is washed out rapidly

within the first few breaths, causing big differences between in- and expiratory fractions of oxygen and nitrogen, respectively. Obviously, under these circumstances FRC is overestimated (Fig. 2), which may be caused by an overestimation of the total expired nitrogen volume. On the other hand, FRC is underestimated if Vi/FRC is low and differences between in- and expiratory fractions of oxygen and nitrogen are low (Fig. 2).

Furthermore, the accuracy of the method is limited by the rise time of the oxygen sensor. If inspiratory or expiratory time will become too short, maximal and minimal oxygen fractions during in- and expiration will be measured wrong. This results in a false calculation of in- and expiratory nitrogen concentration. Evaluating CO_2 analysers, Brunner and Westenskow [9] found a close relation between the rate of ventilation and the error of end tidal CO_2 concentration measurement. The Datex Capnomac oxygen analyser has a 10–90% rise time T90 of about 470 ms. As T90 is about twice the 10–70% rise time [9] the measurement error of the Capnomac and of a CO_2 analyser with a T70 of 220 ms may be approximately the same. With equal in- and expiratory time a carbon dioxide analyser with a T70 of 220 ms showed an error of end tidal CO_2 measurement of 2% at a respiratory rate of 40/min and an error of 8% at a respiratory rate of 60/min, respectively. Assuming the same relative slope of the alveolar plateau for O_2 and CO_2, the measurement error of a CO_2 analyser and an O_2 analyser are the same, if the rise times of the two gas sensors are equal. Accepting an error of oxygen measurement of 2%, in- and expiratory time, therefore, should last longer than 0.75 s if FRC is determined with the above described method.

Further error may stem from hemodynamic or metabolic instability during FRC measurement, as a marked increase or decrease in O_2 consumption may lead to a wrong calculation of expired N_2 volume and FRC. However, if hemodynamic and metabolic stability is guaranteed the change of the inspiratory oxygen fraction will not influence FRC measurement. If the increase of FiO_2 improves arterial oxygenation, which appears as O_2 uptake, the N_2 washin will decrease O_2 uptake in the same range. FRC calculated as mean value of both maneuvers, therefore, may not be affected by the change of FiO_2. However, the change of FiO_2 may cause atelectases in lung spaces with low ventilation/perfusion relationship at high FiO_2, and hypoxemia in patients requiring ventilation with pure O_2 at low FiO_2 (e.g. 70% in this study). Therefore, in the latter case, continuous measurement of arterial oxygen saturation should be available during the washin/washout procedure for monitoring purposes.

Our simplified method shows less precision and less reproducibility compared with nitrogen washout, helium dilution or sulfur hexafluoride measurements [11, 14]. In particular, with the present method small changes of nitrogen concentration late in the washin/washout procedure may get lost in the noise of the O_2 and CO_2 signals. Sparsely ventilated lung spaces, which may be present in patients suffering from severe obstructive pulmonary disease may therefore not be measured with this method.

We conclude that functional residual capacity can be estimated after a change in FiO_2 using the method described in this paper. This method is simpler than other techniques but also less precise. It has not yet been applied to patients with obstructive pulmonary disease. However, our results suggest that the method can be used for clinical routine work, i.e. to support clinical decision-making and control of ventilatory therapy. Actual application of the method in daily clinical work is needed to evaluate its usefulness.

Appendix A: Transformation of the O_2 waveform

The following paragraphs describe a method to obtain a fast responding O_2-concentration-waveform by combining a slow O_2 analyzer (10–90% rise time 500 ms) with a fast CO_2 analyzer. The transformation is done in 3 steps:

1. step: Determine extreme O_2 value during inhalation and exhalation (EiO_2, EeO_2).
2. step: Determine extreme CO_2 value during inhalation and exhalation ($EiCO_2$, $EeCO_2$)
3. step: Calculate the O_2 curve ($FO_2(t)$) as a function of the fast CO_2 curve ($FCO_2(t)$): Manipulate the amplitude of the CO_2 curve such that $EiCO_2$ becomes EiO_2 and $EeCO_2$ becomes EeO_2.

Mathematically, step 3 can be described as follows, with $FO_2(t)$ and $FCO_2(t)$ being the O_2 and CO_2 concentration as function of time:

$$FO_2(t) = \frac{EiO_2 - EeO_2}{EiCO_2 - EeCO_2} \cdot FCO_2(t) + \frac{EeO_2 \cdot EiCO_2 - EeCO_2 \cdot EiO_2}{EiCO_2 - EeCO_2}$$

The assumptions for this method are manyfold and include:

- Same series dead space for CO_2, N_2, and O_2
- Same relative slope of the alveolar plateau for CO_2, N_2, and O_2, and
- no phase IV

Appendix B: Drift compensation

The assumption is that the net transfer of nitrogen is zero prior to, and after completion of the washout. This is expressed in equations:

$$dVN_2 \text{ (prior)} = 0$$
$$dVN_2 \text{ (completion)} = 0$$

Drift and asymmetry of sensors, however, cause the measured values of dVN_2 to be different from zero. This leads to gross errors in FRC determination. Our drift compensation forces the above equations in order to reduce drift and asymmetry errors. This is done by taking the average dVN_2 of the ten breaths before the washout starts as the baseline B1, and the average dVN_2 after the washout is completed as the baseline B2. Analogously, the average expiratory nitrogen concentration before and after completion of the washout/washin are calculated as F1 and F2, respectively. B1, B2, F1 and F2, are then used to correct the breath-by-breath estimations of dVN2 as follows:

$$dVN_2^* = dVN_2 - B2 - (B1 - B2) \cdot \frac{FeN_2 - F1}{F1 - F2}$$

where dVN_2^* is the corrected net transfer volume of nitrogen in a given breath, dVN_2 is the actually measured volume of N_2, and FeN_2 is the expiratory nitrogen concentration of that breath. Beginning and end of the washout are determined by hand.

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