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TECHNIQUE

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A new method for P0.1 measurement using standard respiratory equipment

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Abstract The airway occlusion pressure, P0.1, is an index for the neuro-muscular activation of the respiratory system. It has been shown to be a very useful indicator for the ability of patients receiving ventilatory support to be weaned from mechanical ventilation. Since the standard measurement technique for P0.1 determination is technically complex, it is not widely available for clinical purposes. For that reason a P0.1 measurement technique was developed as an integrated function in a standard respirator (Evita, Dräger, Lübeck, Germany). This technique is easy to use and does not need any further equipment. We validated this new technique by comparing it to standard P0.1 measurements in a mechanical lung model as well as in ventilated patients. In the lung model we found a correlation between the Evita measurement and standard measurements of $r = 0.99$. In 6 ventilated patients the correlation was $r = 0.78$. Since the Evita P0.1 and the standard measurement had to be performed during two different breaths, this little poorer correlation in patients may be due to a significant breath-by-breath variability in P0.1. Comparing the Evita P0.1 and the standard measurement within one breath resulted in a clearly better correlation ($r = 0.89$). We conclude that this new measurement technique provides an easy and accurate P0.1 measurement using standard respiratory equipment when tested in a lung model. In patient measurements the method is less precise, which is probably due to the variable waveforms of the inspiratory driving pressure seen in patients, for example when intrinsic PEEP is present. However, the new method makes the P0.1 measurement as a "bed-side" method clinically available, although the values should be interpreted cautiously.

Key words Airway occlusion pressure · Mechanical ventilation · Weaning · Respirator technology

Introduction

P0.1 is the negative airway pressure generated during the first 100 ms of an occluded inspiration. This value has been shown to correlate indirectly with the central respiratory drive [1–3]. P0.1 has been proposed as an useful indicator for successful weaning from mechanical ventilation in patients with obstructive lung disease as well as in acute respiratory failure [4–8]. High P0.1 values reflect an increased neuro-muscular activation of the respiratory system and therefore indicate a great likelihood of inspiratory muscle fatigue, whereas low P0.1 values predict a successful weaning. Furthermore a close correlation between P0.1 and the respiratory work was found in patients receiving assist mechanical ventilation [9, 10].

Although these studies suggest the importance of P0.1 measurements during weaning from mechanical ventila-

tion, its clinical use is limited because the measurement requires specialized equipment and is therefore not useful as a 'bed-side' method.

For that reason a method for P0.1 measurement was developed as an integrated function of a standard respirator (Evita, Dräger, Lübeck, Germany). The aim of this study was to validate this new method for P0.1 measurement by comparing it with the standard measurement technique using a mechanical lung model as well as in patients receiving assist mechanical ventilation on the intensive care unit.

Methods

Standard P0.1 measurements

The standard technique employed a pressure transducer and a pneumotachograph (Godart-Statham, Netherlands) with a probe placed in the respiratory tubing between the *Y*-piece of the tubing and the endotracheal tube. The pressure and flow signals were transfered via an analog-digital converter to an IBM-computer for online data sampling using standard communication software (PC-Matlab, Math Works Inc., South Natick, USA). The sampling frequency was 100 Hz, so that every 10 ms one data point for flow and pressure was recorded. The pressure and flow tracings were displayed on the computer screen and after acceptance from the operator stored in columns on the computer disk for later analysis. The operator checked flow and pressure tracings only for artefacts. P0.1 was calculated as the pressure difference between the airway pressure at the onset of inspiration and the pressure 100 ms (10 data points) later. The onset of inspiration was defined graphically as the first data point of the inspiratory pressure drop using a mouse input command for the airway pressure tracings. In order to assure a total occlusion flow had to be zero during the P0.1 measurement. For standard P0.1 measurement we used a Rudolph type valve (Hans-Rudolph-Inc., Kansas City, USA) to occlude the inspiratory limb of the tubing system during the patients expiration. The occlusion was performed silently and invisible for the patient.

Evita P0.1 measurement

In the Evita-respirator (Dräger, Lübeck, Germany) the P0.1 measurement is integrated as one of the respirators menu functions for assisted spontaneous breathing. Activation of this function causes the inspiratory valve to remain closed during the first 104 ms of the next inspiratory cycle. The time of 104 ms is due to the respirators sampling frequency of 125 Hz. The airway pressure during the occlusion is measured by the respirators inbuilt pressure transducer (SCX01, SZ75120), Sensym Inc., Sunnyvale, USA) in the expiratory limb just before the exhalation valve. The pressure difference between the onset and the end of occlusion is then calculated as the P0.1 value and displayed on the respirators screen. In order to avoid artefacts the airway pressure must drop 0.5 cm H_2O to define the onset of inspiration. The 104 ms occlusion starts only after this initial pressure drop. After the 104 ms occlusion the inspiratory valve opens and inspiratory flow is delivered.

Simultaneous P0.1 measurement

Since the Evite P0.1 measurement and the standard P0.1 measurement have to be performed during two different breaths, we also recorded the flow and pressure tracings during the Evita occlusion maneuver using the above described online data sampling method for pressure and flow measured at the endotracheal tube site. The simultaneous P0.1 was determined exactly as during the standard P0.1 measurement, with the only difference that the occlusion was not performed manually but by the Evita. Using this setup we could determine both, the Evita P0.1 and the manually analysed P0.1 within one breath.

Lung model

For validation of the P0.1 measurement we used a mechanical lung model (LS 4000, Dräger, Germany). This lung model consists of a motor driven piston. By feed back control of the pressure as well as of the displacement and the velocity of the piston the compliance and resistance of the system can be freely adjusted. To simulate spontaneous breathing of the patient there are inputs for the time course of the patients muscular effort or the spontaneously breathed volume, respectively. So this model can be used to simulate ventilation ranging from purely spontaneous breathing to controlled ventilation. The lung model was connected to the Evita respirator using standard respiratory tubing (Dräger, Lübeck, Germany). The Rudolph valve was inserted in the inspiratory limb of the tubing system in order to occlude the inspiration manually. Pressure and flow tracings were recorded using a probe placed at the endotracheal tube site of the tubing system. With different adjustements for tidal volume, breathing frequency, resistance and compliance of the lung model we generated P0.1 values ranging from 0.6 – 11.8 cm H_2O. For a given adjustement we performed 2 Evita and 2 manual occlusion maneuvers. For each Evita occlusion maneuver a simultaneous pressure tracing was recorded in order to manually analyse the P0.1 for that breath.

With the same setup, we tested the effect of a heated humidifier (Concha Therm III with Aerodyne humidification column, Kendall, Neustadt, Germany) mounted in the inspiratory limb of the tubing. The humidification column had a volume of 250 ml. In a second set of lung model experiments we measured Evita P0.1 and simultaneous P0.1 twice for a given adjustement of the lung model without and twice with the heated humidifier mounted in the respiratory system. Standard P0.1 was also measured twice for one adjustement of the lung model, but not with and without the humidifier. For these measurements we generated P0.1 values ranging from 0.7 – 12.3 cm H_2O.

Patients

We investigated 6 patients receiving mechanical ventilatory support. The diagnosis leading to respiratory failure included multiple trauma (twice), sepsis, pneumonia and ARDS (twice). All patients were ventilated with inspiratory pressure support ventilation (10 – 20 cm H_2O) and PEEP (5 – 10 cm H_2O) using the Evita respirator with standard tubing system (Dräger, Lübeck, Germany). In each patient 5 Evita and 5 manual occlusion maneuvers were performed in random order for the given adjustement of the respirator. In order to generate a range of P0.1 values the inspiratory pressure support was then decreased minus 5 cm H_2O and another 5 Evita and manual occlusion maneuvers were performed in random order. All other respirator settings remained unchanged. The manual occlusion was performed using a Rudolph valve in the inspiratory limb of the tubing system which was closed during the patients expiration. Again

for each Evita occlusion a simultaneous pressure and flow tracing was recorded at the endotracheal tube site for determination of the simultaneous P0.1 analysis. All occlusion maneuvers were performed silently and invisible for the patient.

Data analysis

Data are expressed as mean±SD. Correlation between the different methods was determined by linear regression analysis. All Evita P0.1 measurements were correlated to the standard measurement procedere as well as to the simultaneously recorded manually analysed P0.1 values. Statistical significance was considered at $p < 0.05$. Furthermore, data were analysed according to the method suggested by Bland and Altman [11].

Results

Lung model

The mechanical lung model was used to generate P0.1 values ranging from 0.6–11.8 cm H_2O. The mean P0.1 value for all measurements was 5.7±3.3 cm H_2O with the Evita measurement, 5.4±3.1 cm H_2O with the standard method and 5.1±2.9 cm H_2O with the simultaneous P0.1 recording. The Evita measurement correlated very well with the standard method ($r = 0.99$, $y = 1.04 \pm 0.03 * x + 0.12 \pm 0.21$, $p < 0.01$). The mean difference between all Evita measurements and the standard method was 0.3±0.5 cm H_2O, with a minimum of −0.3 cm H_2O and a maximal difference of 1.4 cm H_2O (Fig. 1). The Evita P0.1 correlated also well with the simultaneous P0.1 recordings ($r = 0.99$, $y = 1.13 \pm 0.03 * x - 0.09 \pm 0.17$, $p < 0.01$). The mean difference for all Evita and simultaneous P0.1 measurements was 0.6±0.5 cm H_2O, with a minimum of −0.5 cm H_2O and a maximal difference of 1.4 cm H_2O (Fig. 2).

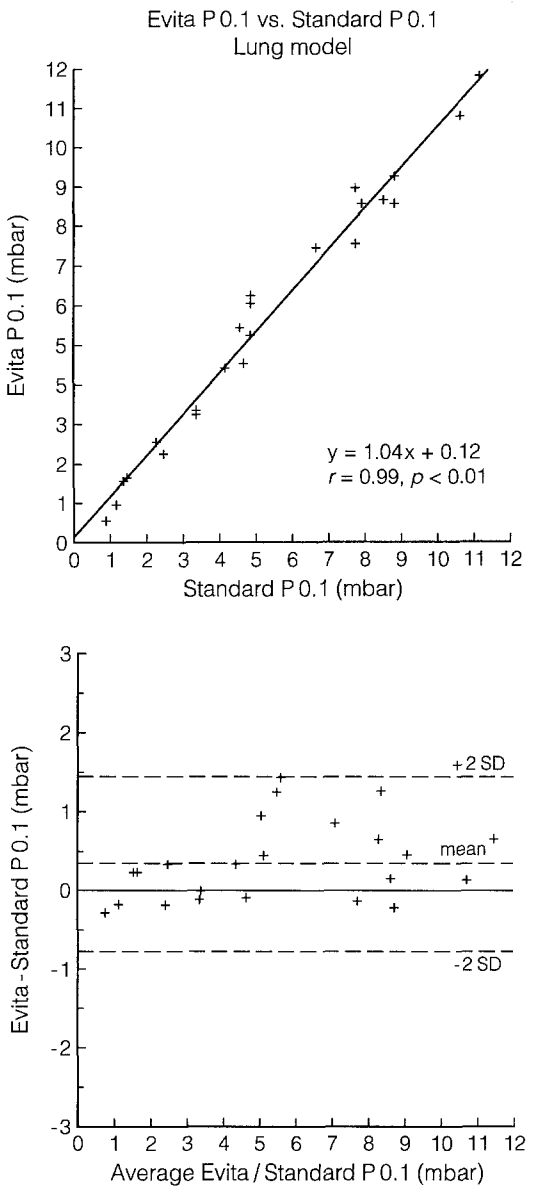

Fig. 1 Correlation between Evita P0.1 and Standard P0.1 (upper part) in a mechanical lung model. In the *lower plot* individual differences between Evita and standard P0.1 measurements are plotted as a function of the average between the two methods. Each data point reflects a single measurement. A total number of 24 measurements were performed for each method

Effect of the heated humidifier

In this second set of lung model experiments the Evita P0.1 was 5.6±3.4 cm H_2O without the humidifier and 5.4±3.4 cm H_2O with the humidifier. The mean difference between the measurements with and without humidifier was −0.2±0.3 cm H_2O. The correlation between Evita P0.1 with and without humidifier was $r = 0.99$, $y = 1.01 \pm 0.02 * x + 0.14 \pm 0.12$ ($p < 0.01$, Fig. 3). Standard P0.1 was 5.6±3.5 cm H_2O. The mean difference between Evita P0.1 and standard P0.1 was 0.04±0.61 cm H_2O without and −0.1±0.6 cm H_2O with the humidifier. The simultaneous P0.1 was 5.1±3.5 cm H_2O without and 4.8±3.2 cm H_2O with humidifier. The mean difference between Evita P0.1 and simultaneous P0.1 was 0.6±0.4 cm H_2O without and 0.7±0.4 cm H_2O with the humidifier.

Patients

The mean P0.1 value for the 60 individual measurements was 3.4±1.6 cm H_2O with the Evita measurement, 2.9±1.1 cm H_2O with the standard method and 2.7±1.2 cm H_2O with the simultaneous P0.1 recordings. Correlation analysis between the Evita P0.1 and the standard method revealed $r = 0.78$, $y = 1.07 \pm 0.11 * x + 0.19 \pm 0.35$ ($p < 0.01$, Fig. 4). The mean difference be-

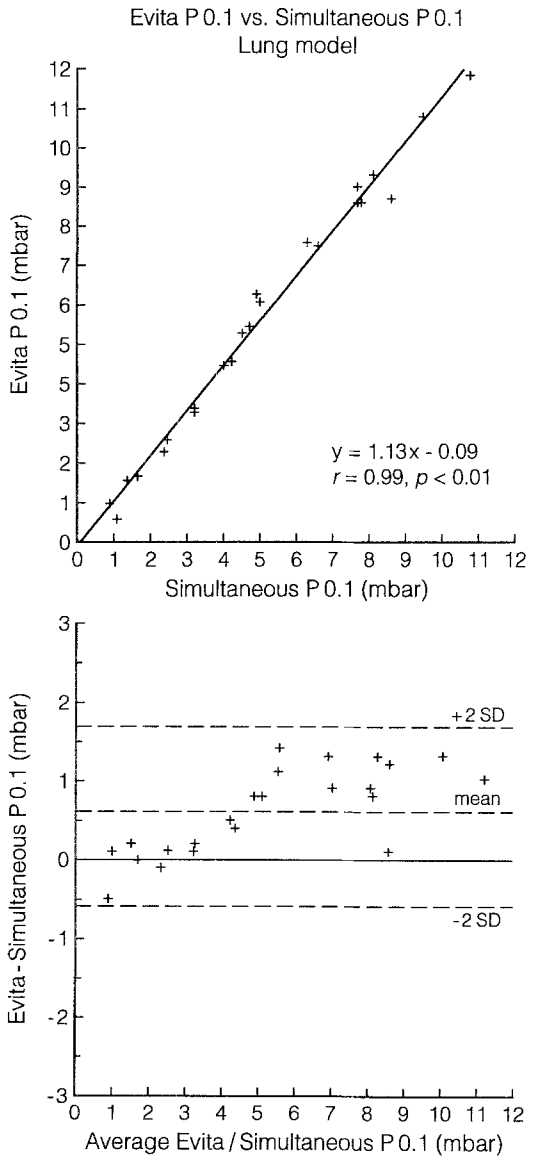

Fig. 2 Correlation between Evita P0.1 and simultaneous P0.1 (*upper part*) in a mechanical lung model. In the *lower plot* individual differences between Evita and simultaneous P0.1 measurements are plotted as a function of the average between the two methods. Each data point reflects a single measurement. A total number of 24 measurements were performed for each method

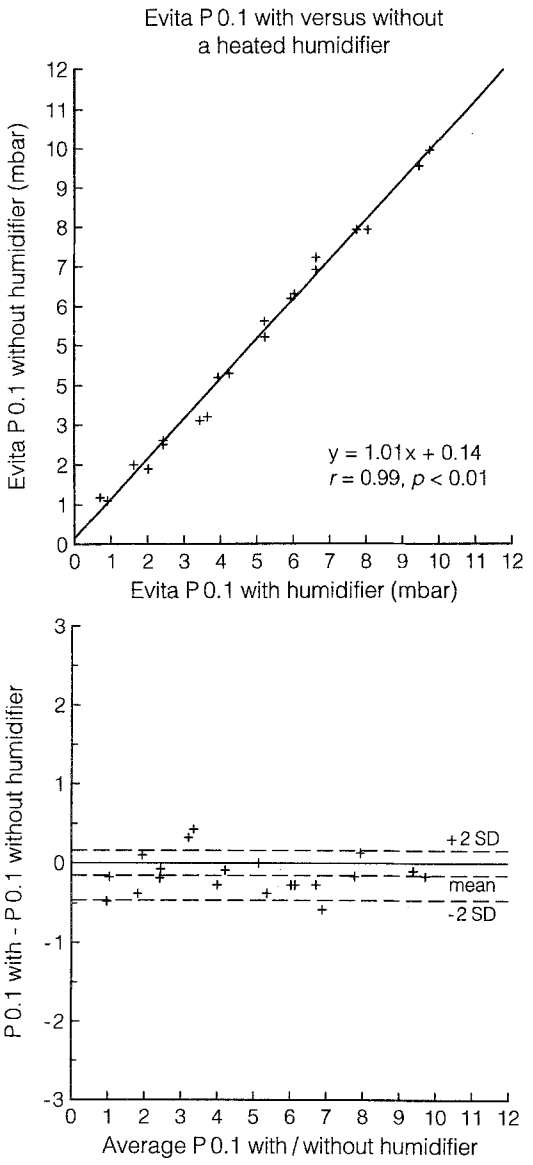

Fig. 3 Correlation between the Evita P0.1 with and without a heated humidifier in the respiratory circuit (*upper part*). In the *lower plot* the individual difference between Evita P0.1 with and without humidifier are plotted as a function of the average between these two measurements. Each data point reflects a individual measurement. A total of 22 measurements were performed for each method

tween the Evita and the standard measurement was 0.4 ± 1.0 cm H_2O, with a minimum of 2.1 cm H_2O and a maximal difference of 2.4 cm H_2O. The correlation between the Evita P0.1 and the simultaneous P0.1 recording was $r = 0.89$, $y = 1.20 \pm 0.08 * x + 0.11 \pm 0.24$ ($p < 0.01$, Fig. 5). The mean difference for all Evita and simultaneous P0.1 measurements was 0.6 ± 0.7 cm H_2O, with a minimum of -0.8 cm H_2O and a maximal difference of 2.2 cm H_2O.

Discussion

The aim of this study was the validation of a new respirator-integrated P0.1 measurement by comparing it with the standard measurement technique. The presented data show a good correlation and precision between this new P0.1 measurement and the standard technique in a mechanical lung model and a poorer correlation and precision in patients receiving assisted mechanical ventilation.

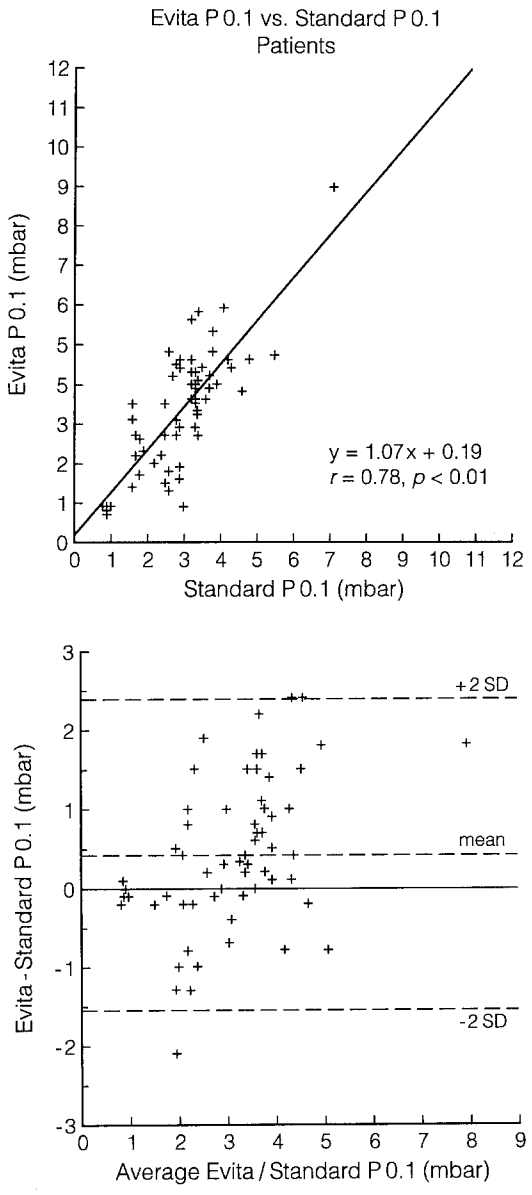

Fig. 4 Correlation between Evita P0.1 and standard P0.1 (*upper part*) in six ventilated patients. In the *lower plot* individual differences between Evita and standard P0.1 measurements are plotted as a function of the average between the two methods. Each data point reflects a single measurement. In each individual patient a total of 10 measurements were performed for each method ($n = 60$)

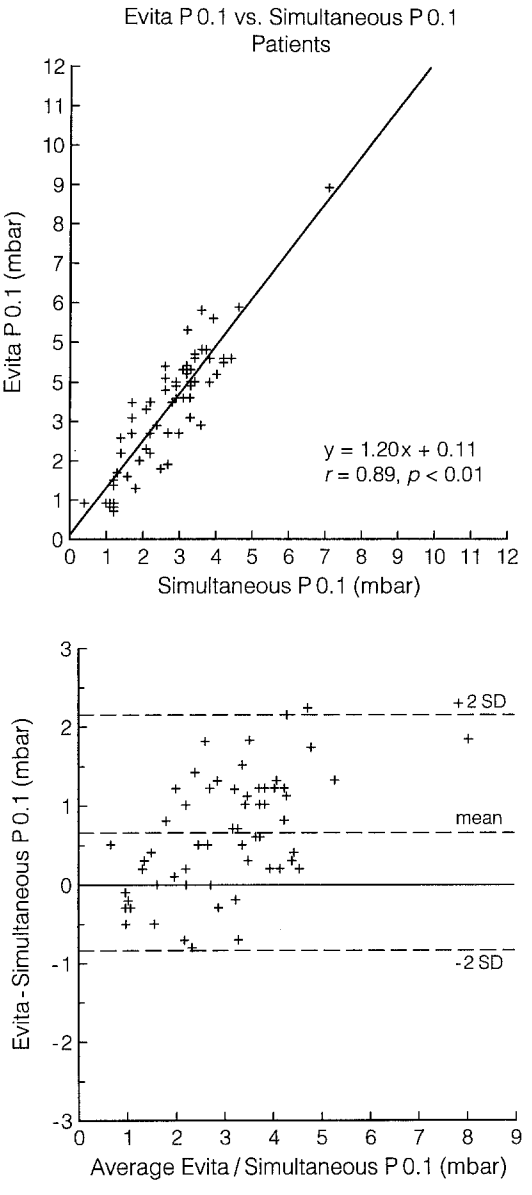

Fig. 5 Correlation between Evita P0.1 and simultaneous P0.1 (*upper part*) in six ventilated patients. In the *lower plot* individual differences between Evita and simultaneous P0.1 measurements are plotted as a function of the average between the two methods. Each data point reflects a single measurement. In each individual patient of total of 10 measurements were performed for each method ($n = 60$)

Although P0.1 has been shown to be an important parameter during weaning from mechanical ventilation [4–8] its clinical use has been limited by a technically complex measurement procedure. The standard P0.1 measurement employes a flow and pressure measurement device at the endotracheal tube site connected to a recording device. The inspiratory occlusion is usually performed by a Hans-Rudolph valve mounted in the inspiratory limb of the respiratory tubing. The valve is closed during the patients expiration in order to occlude the next inspiration. The airway pressure tracing during this occluded inspiration is then analyzed and the P0.1 value is calculated as the pressure difference between the onset of inspiration and 100 ms later. This occlusion has to be performed silently and invisible for the patient and it should be reopened quickly after the 100 ms, so that the patient can continue to breathe. To make this complex measurement more easy and useful for routine clinical application, a

new P0.1 measurement was developed as an integrated function of a standard respirator (Evita, Dräger, Lübeck, Germany). After activation of the P0.1 function in the respirators software menu the inspiratory valve remains closed for the first 104 ms after the onset of the triggered inspiration. The P0.1 value is then calculated from the pressure drop in the system within these 104 ms, recorded by the inbuilt pressure transducers of the respirator.

The results from the lung model show an excellent correlation between the standard and the Evita measurement, suggesting that the measurement procedure itself reveals reliable data and that there was no significant dumping of the pressure signal due to the compliance of the respiratory tubing. Also, the measurement seems to be sufficiently precise, as can be seen from the small systematic difference of 0.3 ± 0.5 cm H_2O. According to the method described by Bland and Altman [11], the limits of agreement are ± 1 cm H_2O (2*SD), which means that for a measured Evita P0.1 the true P0.1 could be 1 cm H_2O lower or higher.

In the six investigated patients the correlation between standard and Evita measurement was less accurate ($r = 0.78$). Also the precision mas much less with a systematic error of 0.4 ± 1.0 cm H_2O, indicating limits of agreement of ± 2 cm H_2O. This finding may be explained by the significant breath-by-breath variability of P0.1 during spontaneous breathing, as it was shown in a very recent paper by Larrson et al. [12]. They found a 30% variability of P0.1 in healthy volunteers. Since the standard and the Evita measurement had to be performed during two different breaths, this variability could be the reason for the poorer correlation and precision observed in ventilated patients. Therefore we also recorded the flow and pressure tracings during an Evita occlusion maneuver at the endotracheal tube site and calculated P0.1 values exactly as with the standard measurement. With this setup we obtained an Evita P0.1 value and a simultaneously recorded "quasi" standard P0.1 value within one occluded inspiration. The correlation between this simultaneous P0.1 and the Evita P0.1 was clearly closer ($r = 0.89$) for the patient measurements. Also the precision as assessed by the limits of agreement was clearly better (± 1.4 cm H_2O), although the systematic error between Evita P0.1 and simultaneous P0.1 was a little higher (0.6 ± 0.7 cm H_2O). These data suggest that the patients breath-by-breath variability at least in part accounted for the poorer correlation and precision with the standard P0.1 measurement. In the lung model there was no difference between the standard P0.1 and the simultaneously recorded P0.1, since the lung model generated a constant breathing pattern without any variability for a given adjustment.

In all lung model and patient measurements there was a small but consistent difference in the absolute P0.1 values obtained with the Evita measurement compared to the standard or simultaneous measurement. This may be explained by the fact, that in the Evita the respirators software starts the P0.1 calculation only after an initial pressure drop of 0.5 cm H_2O in order to avoid artefacts. Furthermore, the occlusion in the Evita is not exactly 100 ms but, due to the respirators sampling frequency of 125 Hz, 104 ms long. With the standard measurement the time period for P0.1 calculation was exactly the first 100 ms of the occluded inspiration without any initial pressure drop. The first data point on the pressure tracing below the end expiratory pressure level was taken as the onset of inspiration and P0.1 was calculated from the pressure difference exactly 100 ms later. These differences should not affect the P0.1 determination as long as the inspiratory pressure decline shows a linear curve with one negative slope for longer than 100 ms. This assumption may not always be true, as some of the original pressure tracings we obtained show an inspiratory pressure decline with a lower negative slope at the beginning and a steeper slope after 20–50 ms. Since we did not measure intrinsic PEEP in this study, we can only speculate whether this could be due to a small amount of intrinsic PEEP [13]. However, the mean P0.1 difference between the Evita and the standard measurement was not more than 0.4 cm H_2O, and it should therefore not affect the clinical significance of the Evita P0.1 measurement.

Another explanation for the differences between Evita P0.1 and standard measurements could be the different amount of compressible gas volume in the respiratory circuit. Therefore, we tested the effect of a heated humidification column mounted in the inspiratory limb of the tubing system which added another 250 ml compressible gas to the circuit. In this set of experiments we found a very small systematic error of -0.2 ± 0.3 cm H_2O for the Evita P0.1 with or without humidifier. The Evita P0.1 without humidifier was consistently higher compared to the values with humidifier (5.6 ± 3.4 versus 5.4 ± 3.4 cm H_2O). This small difference may be explained by the increased compressible gas volume with consecutive dumping of the pressure signal. Consistently, the absolute values for the simultaneous P0.1 were also higher without and lower with the humidifier (5.1 ± 3.5 versus 4.8 ± 3.2 cm H_2O), and the mean difference between Evita and simultaneous P0.1 was higher with (0.7 ± 0.4 cm H_2O) and lower without (0.6 ± 0.4 cm H_2O) the humidifier. From these data can be concluded that the additional 250 ml compressible gas volume accounted for not more than a 0.2 cm H_2O underestimation of P0.1.

As discussed by Bland and Altman [11], the given limits of agreement have to be evaluated according to the clinical meaning of their magnitudes. From that point of view, a good performance of the new method can only be claimed for the lung model experiments, where the differences between standard measurements and the new method were in the range of ± 1 cm H_2O, which should be sufficiently precise for clinical purposes. In the patient measurements the differences between these methods

were in the range of ± 2 cm H_2O, which is rather high for clinical application of the new method, when it is used as a single point measurement. When the significant breath-by-breath variability of P0.1 is taken into account, the precision of the new method is clearly better, although the limits of agreement are still ± 1.4 cm H_2O, which may be misleading for clinical interpretation of a single measurement. Therefore, multiple measurements with the new method are recommended. From the presented data it can be concluded that there might be a small overestimation of P0.1 with the Evita measurement of approximately 0.5 cm H_2O when measured repeatedly, which should be taken into account. For the clinical interpretation of P0.1 measurements one should not only be aware of potential measurement mistakes, but also of the fact, that P0.1 is a complex parameter, which is influenced by a variety of conditions. One of the major determinants of P0.1 is the shape of the pressure wave during the occluded inspiration, which may contribute to changes in P0.1 without a proportional change in overall central respiratory drive [13]. This holds true for all methods of P0.1 measurement and therefore can also attribute to differences between methods.

In conclusion, the presented data show that the P0.1 measurements in the Evita respirator correlates very well with standard P0.1 measurements in the mechanical lung model. For patient measurements the correlation is much less precise. Part of this lower precision may be due to a significant breath-by-breath variability of P0.1. Furthermore, the amount of intrinsic PEEP affects the waveform of the inspiratory pressure decline and therefore, it influences all P0.1 measurements. Since we did not measure intrinsic PEEP in the patient series, we can only speculate, whether this was true for our patients. The extent to which the different amount of compressible gas accounts for differences in the tested P0.1 measurements was also investigated in the lung model and found to be not more than 0.2 cm H_2O.

Although the measurement itself seems to result in reliable P0.1 values, its application at the bed-side should be viewed critically. However, the advantage of an integrated P0.1 measurement technique without the need for any further equipment opens the possibility for clinical determination of P0.1 on a routine basis.

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