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Measurement of Pressure–Time Product during Spontaneous Assisted Breathing by Rapid Interrupter Technique

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Background: **Measuring the work of breathing of patients undergoing spontaneous assisted ventilation can be useful to monitor and titrate ventilatory support. The aim of this study was to obtain measurements of the pressure generated by the respiratory muscles (P_{MUSC}) and the derived pressure–time product (PTP; a good indicator of the metabolic work of breathing), performing the rapid interrupter technique with a commercial ventilator.**

Methods: **A Draeger Evita 4 ventilator (Draeger Medical, Lubeck, Germany) was controlled by a personal computer to rapidly interrupt the airway flow at different times and volumes of the respiratory cycle during pressure-support ventilation. From the airway pressure tracing after the occlusion, the authors estimated the alveolar pressure and P_{MUSC}; the integration of P_{MUSC} values over the inspiratory time yields the measurement of PTP. Esophageal pressure measurements were used as a reference. After a bench study of the valves' performance, the authors performed 11 measurement sequences in eight patients.**

Results: **The closure times for the inspiratory and expiratory valves were 74 ± 10 and 61 ± 13 ms, respectively. The interrupter technique provided a reliable estimate of P_{MUSC} ($P_{MUSC,\ occl} = 1.00 \cdot P_{MUSC,\ pes} + 0.19$; $r = 0.88$; 95% confidence interval for agreement, +5.49/−5.32 cm H_2O). PTP_{occl} tightly correlated with PTP_{pes} ($PTP_{occl} = 0.95 \cdot PTP_{pes} + 0.13$; $r = 0.96$; 95% confidence interval, 1.94/−1.61 cm $H_2O \cdot s$).**

Conclusion: **The rapid interrupter technique can be performed by means of a commercial ventilator, providing reliable measurement of PMUSC and PTP.**

SEVERAL acute or chronic lung diseases may determine a mismatch between the work of breathing (WOB) imposed on the patient and the ability of the patient to sustain it, for an increase of the former, a decrease of the latter, or both. In such a condition, mechanical ventilation is often required, but, rather than entirely replacing the respiratory effort of the patient, the ventilator is frequently used to unload the patient from a variable (and seldom known) amount of the WOB. Indeed, the presence of a spontaneous breathing activity has been shown to bear several benefits, such as reopening of previously collapsed lung units,[1] improving ventilation-to-perfusion matching,[2] protecting the diaphragm from atrophy associated with controlled mechanical ventilation, improving cardiovascular function,[3] and decreasing sedation needs.[3] Modern software-controlled mechanical ventilators, combining a wide choice of supportive ventilatory modes with excellent pneumatic performances, allow the use of assisted spontaneous breathing in a widening range of clinical situations.[4] Among the different modes, however, pressure-support ventilation (PSV) remains widely used.[5–7]

Independently of the ventilatory mode, monitoring of the WOB generated by the patient yields important information to monitor the evolution of the patient and to appropriately titrate the ventilatory support. The "gold standard" for the measurement of the patient's inspiratory effort (and WOB) is given by measuring the esophageal pressure (P_{es}) with a balloon-tipped catheter placed in the distal third of the esophagus.[8,9] Specifically, by integrating the pressure developed by the respiratory muscles over the duration of the contraction (*i.e.*, P_{es} − chest wall elastic recoil pressure), it is possible to obtain the respiratory pressure–time product (PTP).[10] Field *et al.*[11] found that the oxygen consumption of the respiratory muscles (often indicated as metabolic WOB) is only weakly correlated with the mechanical WOB (the product $\Delta P \cdot \Delta V$), whereas it is well reflected by the PTP. PTP takes into account the isometric phase of muscle contraction,[10] representing a good indicator of energy expenditure.[12] However, use of an esophageal balloon can be difficult, and it is often excluded from the routine clinical practice. For this reason, several surrogate indexes have been developed and tested.[13,14]

The rapid interrupter technique,[15] a noninvasive technique for punctual measurements of the pressure generated by the respiratory muscles of the patient (P_{MUSC}) at a given moment of the respiratory cycle, has been successfully applied during PSV.[16] So far, the technique has been applied by means of dedicated, ultrafast valves placed in close proximity to the airway opening.

The aim of the current work was to test whether P_{MUSC} could be obtained by the rapid interrupter technique performed through the valves of a commercial ventilator and integrated along the respiratory cycle to estimate the metabolic WOB, similarly to the esophageal-derived PTP.

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Table 1. Baseline Patient Characteristics

Patient No.	Age, yr	Sex	Diagnosis	Pao_2/Fio_2, mmHg	PEEP, cm H_2O	Fio_2	RR, breaths/min	PS, cm H_2O	V_T, ml
1	68	F	Postoperative respiratory insufficiency	235	10	0.70	25	16	410
2	52	M	Subarachnoid hemorrhage	305	5	0.40	20	10	510
3	73	M	*Pneumocystis carinii* pneumonia	284	8	0.30	18	10	500
4	64	F	Septic shock	202	5	0.60	15	12	410
5	25	F	Multiple trauma	297	10	0.45	25	8	450
6	71	M	Pneumonia	215	10	0.60	28	14	740
7	63	M	ARDS	210	10	0.70	18	12	400
8	78	M	Septic shock	273	8	0.40	13	14	680
Mean	61.7	3 F	—	253	8.3	0.52	20.2	12	505
SD	16.7	5 M	—	42	2.2	0.15	5.3	2.6	129

Diagnosis column refers to the admission diagnosis in the intensive care unit.

ARDS = acute respiratory distress syndrome; Fio_2 = inspired oxygen fraction; Pao_2 = arterial oxygen tension; PEEP = positive end-expiratory pressure; PS = pressure support above PEEP; RR = respiratory rate; V_T = tidal volume.

Materials and Methods

Experimental Protocol

We enrolled eight nonconsecutive patients admitted to our intensive care unit, with acute respiratory failure from various primary etiologies (table 1) and undergoing PSV. The investigational protocol was approved by our institution's ethical committee (Università degli Studi Milano Bicocca, Ospedale San Gerardo, Monza, Italy); informed consent was obtained according to the committee recommendations.

We used an Evita 4 ventilator (Draeger Medical, Lubeck, Germany) controlled by a personal computer through the serial communication port (MEDIBUS protocol).

Once enrolled in the study, the patients were suctioned if necessary, while their ventilatory settings were kept unmodified from those set by the attending physician (table 1). Throughout the study procedure, the patient's electrocardiogram, arterial invasive pressure, peripheral oxygen saturation (Spo_2), and expired carbon dioxide partial pressure ($ETco_2$) were continuously monitored. An esophageal balloon was placed in the distal third of the esophagus and secured, after correct placement was assessed according to standardized procedures.[17] The absence of intrinsic positive end-expiratory pressure (PEEP) was carefully checked at enrollment and throughout the study procedure by the simultaneous evaluation of the esophageal and airway pressure tracings. After a stabilization period, in the first 5 min of undisturbed PSV ventilation, we measured the average tidal volume (V_T) of the patient. The V_T was then divided in 25-ml intervals.

One occlusion maneuver (see below) was then programmed at each of these target volumes, in random order, to encompass the entire V_T range, during both the inspiratory and expiratory phases. After an occlusion command, when the target volume was reached, the ventilator closed the inspiratory or expiratory valve as rapidly as possible. After 2 s, the occlusion was released, and the ventilator was switched back to the baseline ventilation. A safety mechanism would immediately open the expiratory valve if, at any time, the airway pressure exceeded 40 cm H_2O. Twenty to 30 undisturbed breaths were allowed before the next occlusion of the programmed sequence was performed.

In three patients, at the end of the measurement series, we increased the pressure support level by 5 cm H_2O and performed a new measurement sequence. We thus obtained a total of 11 measurement sequences.

Airflow was measured by a pneumotachograph (Fleisch No. 2; Lausanne, Switzerland), connected to a differential pressure transducer (Baroscan PC-100; Hoffrichter, Germany). The signal was calibrated at the inspired oxygen fraction in use. The volume was obtained by integration of the flow signal. Airway and esophageal pressures were measured by an F-497 transducer array (Special Instruments, Nordlinger, Germany). A voltage signal, switching from 0 V during the normal ventilation to +5 V during the occlusion, was also recorded, to provide a precise marker in the waveform file for the detection of the occlusions. All of the signals were digitized with a frequency of 125 Hz (NI-DAQ; National Instruments, Houston, TX), displayed on a personal computer monitor in real time, and stored on the hard drive for the off-line data analysis.

Interrupter Technique Data Analysis

The rapid interrupter technique relies on the principle of the pressure equilibration within the respiratory system in the absence of flow. Figure 1 shows a representative inspiratory occlusion maneuver. Immediately after the occlusion (vertical dashed line), the flow ceases, and, ideally, the airway pressure equilibrates with alveolar pressure. Further changes in airway pressure are due to

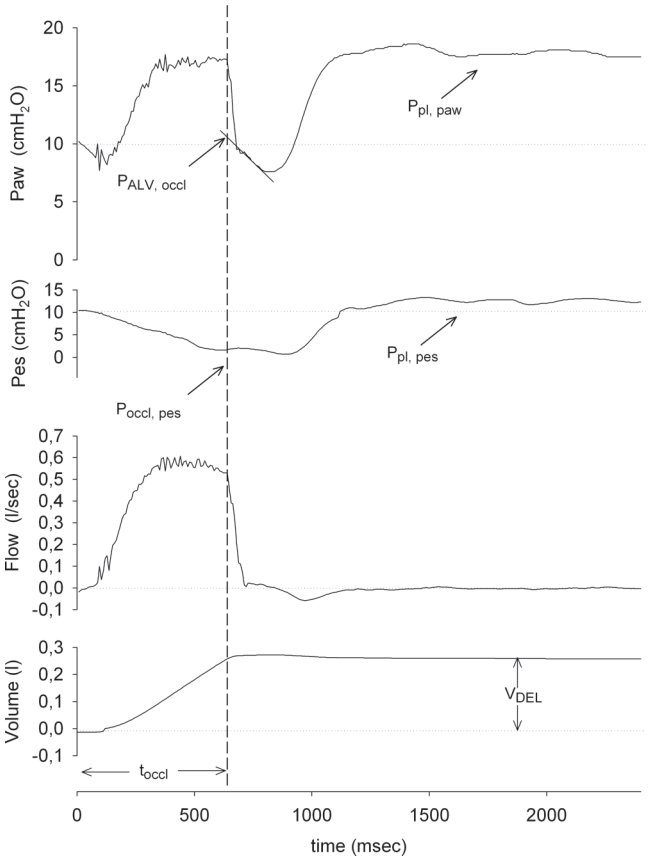

Fig. 1. Representative tracing of airway pressure (P_{aw}), esophageal pressure (P_{es}), and airway flow and volume, from one interruption performed during the inspiration. After the interruption (*dashed vertical line*), the airway pressure decreases, equaling the alveolar pressure. The value of alveolar pressure at the time of the interruption ($P_{ALV, occl}$) can be derived by back-extrapolating the linear portion on the P_{aw} tracing (*solid line*); after the patient has relaxed his muscles, a plateau can be seen on the P_{aw} and P_{es} tracings, due to the elastic recoil of the respiratory system and of the chest wall, respectively. $P_{occl, pes}$ = esophageal pressure at the time of occlusion; $P_{pl, paw}$ = airway plateau pressure; $P_{pl, pes}$ = esophageal plateau pressure; t_{occl} = time elapsed between the beginning of the inspiration and the occlusion; V_{DEL} = volume effectively delivered to the patient from the beginning of inspiration to the time of occlusion. See text for further details.

the persisting patient's respiratory effort; finally, the effort ceases and, if the patient relaxes his or her muscles, a plateau develops on the airway pressure tracing ($P_{pl, aw}$). However, because the occlusion is rapid but not instantaneous, and because the occlusion gives rise to a pressure noise in the signal for a period of 50–100 ms, the value of alveolar pressure at the time of occlusion ($P_{ALV, occl}$) cannot be read directly and must be back-extrapolated, by linearly fitting the points from the most linear portion of P_{aw} after the noise ceases (fig. 1, solid line), back to the moment of the interruption.[18]

The pressure generated by patient's respiratory muscles ($P_{MUSC, occl}$) was calculated as $P_{MUSC, occl} = P_{el, rs} - P_{ALV, occl}$, where $P_{el, rs}$ represents the elastic recoil of the respiratory system (*i.e.*, at any time, the alveolar pressure equals the sum of the elastic recoil pressure of the respiratory system and the pressure generated by the respiratory muscles). For each occlusion, on the assumption of a linear compliance throughout the V_T range, $P_{el, rs} = (V_{DEL}/C_{rs}) + PEEP$, where V_{DEL} represents the volume effectively delivered to the patient from the beginning of inspiration to the time of the occlusion, and C_{rs} represents the respiratory system compliance.

The value of C_{rs} in each patient was obtained averaging the values of $V_{DEL}/(P_{pl, aw} - PEEP)$ for those occlusions in which a flat plateau (at least 500 ms long) in the airway pressure tracing was seen. During expiration, the same equations were applied.

After the experimental protocol was completed, the tracings of airway pressure, flow, and volume during each occlusion were analyzed with dedicated software. Whereas one marker was automatically placed at the beginning of the occlusion, we manually placed one marker at the beginning of the inspiration (defined as the beginning of the deflection in the P_{aw} tracing), two markers encompassing the P_{aw} tracing portion to be fitted after the occlusion, and two markers encompassing the plateau phase, if present. Provided with these markers, the software performed the aforementioned calculations. The time elapsed between the beginning of the inspiration and the occlusion (t_{occl}) was also measured.

We then plotted each value of $P_{MUSC, occl}$ over its respective t_{occl}, obtaining the time course of the inspiratory effort, sampled over different breaths at different times and volumes. The integral of $P_{MUSC, occl}$ over the duration of inspiration is analogous to the PTP and was computed with the trapezoidal rule.

The maximum $P_{MUSC, occl}$ value observed was also recorded ($P_{MAX, occl}$).

Esophageal Pressure Measurements

Esophageal pressure measurements were used as reference. From the occlusions showing a flat plateau in the esophageal pressure tracing ($P_{pl, pes}$), chest wall compliance was calculated as $C_{cw} = V_{DEL}/(P_{pl, pes} - PEEP_{pes})$. The expected chest wall elastic recoil pressure ($P_{el, cw}$), for each occlusion, similarly to the above-mentioned calculation, was computed as $P_{el, cw} = (V_{DEL}/C_{cw}) + PEEP_{pes}$. Therefore, the alveolar pressure at the time of the occlusion can be calculated as $P_{ALV, pes} = P_{occl, pes} + P_{el, l}$, where $P_{el, l}$ is the elastic recoil pressure of the lungs (equal to $P_{el, rs} - P_{el, cw}$), and $P_{occl, pes}$ equals the esophageal pressure at the time of the occlusion. $P_{MUSC, pes}$ was finally calculated as $P_{occl, pes} - P_{el, cw}$.

The pressure–time product (PTP_{pes}) was calculated as the area subtended by P_{es} and the chest wall static recoil pressure, averaging 10 undisturbed V_Ts. From the same V_Ts, the maximum deflection in P_{es}, another index on respiratory work, was obtained and averaged ($P_{MAX, pes}$).

Bench Valve Evaluation Protocol

With the ventilator connected to a passive model of the respiratory system (compliance, 25 ml/cm H_2O; resistance, 12 cm $H_2O \cdot l^{-1} \cdot s^{-1}$), we performed a series of occlusions during volume-controlled mechanical ventilation. We used three different levels of PEEP (5, 10, 15 cm H_2O) and three different flow rates ($\dot{V}$ = 0.5, 0.75, 1 l/min) to investigate the influence of the airway pressure and flow rate on the valve behavior. For each combination, we performed interruptions along a V_T of 500 ml, during both the expiratory and the inspiratory phases. Because the model exhales passively, performing occlusions at different volumes during expiration allowed us to obtain different flow rates at the moment of the occlusions.

Statistics

Data are expressed as mean ± SD unless otherwise specified. Relations between two series of variables were assessed by linear regression. Ninety-five percent limits of agreement between esophageal- and occlusion-derived variables were calculated as suggested by Bland and Altman.[19]

Results

Bench Performance of the Valves

The average time closures for the inspiratory and expiratory valves were 74 ± 10 and 61 ± 13 ms, respectively. Both valves exhibited longer closure times at increasing flow rates ($t_{cl} = 13 \cdot \dot{V} + 64$, $r = 0.48$, $P < 0.01$ and $t_{cl} = 18 \cdot \dot{V} + 47$, $r = 0.46$, $P < 0.001$ for inspiratory and expiratory valves, respectively). The volumes delivered during the closure of the valves averaged 34 ± 17 and 26 ± 16 ml, and they positively correlated with the closure time of the valve ($r = 0.48$ and $r = 0.46$, $P < 0.01$, data now shown). We could not disclose any effect of the airway pressure level on the valve closing time.

Patient Measurements

A total of approximately 400 occlusions were obtained in the 11 measurement series. Measurement series were well tolerated in all patients without the development of desaturation or hemodynamic instability. A mild increase in the respiratory rate (21 ± 5%, $P < 0.05$) was observed between the beginning and the end of the measurement sequence.

Figure 2 shows the individual relations between V_{DEL} and ($P_{pl,\ aw}$ − PEEP) for the occlusions where a flat plateau had been identified. For each patient, a linear relation was present between V_{DEL} and ($P_{pl,\ aw}$ − PEEP), suggesting that muscle relaxation was achieved (fig. 2; average $r = 0.95 \pm 0.064$; range, 0.79–0.99). The estimated compliance averaged 35 ± 9 ml/cm H_2O; in the three patients studied at two pressure support levels, the pairs of compliance measurements obtained from the two series (pressure support low–pressure support high) were 22–23, 35–34, and 46–45 ml/cm H_2O.

$P_{ALV,\ occl}$ showed a tight correlation with $P_{ALV,\ pes}$ ($P_{ALV,\ occl} = 1.11 \cdot P_{ALV,\ occl} - 2.47$, $r = 0.88$, $P < 0.001$).

Figure 3 shows the comparison of $P_{MUSC,\ occl}$ with $P_{MUSC,\ pes}$. Although the slope is equal to one and the intercept is close to zero, the experimental points are quite scattered. The 95% confidence interval for agreement between the two measures was +5.49 and −5.32, with a bias of 2.7 cm H_2O.

PTP_{pes} and PTP_{occl} averaged 6.29 ± 3.07 and 6.47 ± 3.08 cm $H_2O \cdot s$, respectively. PTP_{occl} was tightly correlated with PTP_{pes}: $PTP_{occl} = 0.95 \cdot PTP_{pes} + 0.13$; the bias between the two techniques was negligible (0.16 cm $H_2O \cdot s$), with a 95% confidence interval between the two measures of 1.94 and −1.61 cm $H_2O \cdot s$ (fig. 4). $P_{0.1}$ averaged 3.15 ± 1.75 cm H_2O (range, 1.3–7.9 cm H_2O), and the values correlated with PTP_{pes} ($r = 0.76$, $P < 0.05$).

Finally, $P_{MAX,\ occl}$ was tightly correlated with, but tended to overestimate, $P_{MAX,\ pes}$: $P_{MAX,\ occl} = 1.32 \cdot P_{MAX,\ pes} - 0.81$ ($r = 0.96$, $P < 0.001$); the confidence interval for the two techniques was between 3.65 and −10.13 cm H_2O.

Discussion

During spontaneous assisted breathing, measuring the patient's respiratory work can help in setting the mechanical support. In the current study, we reappraised the rapid interrupter technique as proposed by Pesenti *et al.*[16] to estimate the muscular pressure developed by patients during PSV. Particularly, we tested the feasibility of applying the rapid interrupter technique by means of a commercial ventilator, and we obtained reliable measurements of respiratory system compliance and of P_{MUSC}. When these P_{MUSC} measurements were integrated into an index similar to the PTP, the latter was closely related to the esophageal-derived PTP.

The first result we describe is the measurement of C_{rs} during assisted spontaneous breathing, achieved by averaging the C_{rs} values of the occlusion bearing a flat plateau tracing after the occlusion. When trying to measure the compliance value in a patient undergoing assisted spontaneous breathing, adequate muscle relaxation during the plateau phase is mandatory to obtain reliable data. We could not compare the compliance measurements that we obtained during PSV with those obtained during sedation and paralysis. Previous studies have shown, however, that the presence of a satisfactory plateau after the occlusion allows an accurate estimate of $C_{pl,\ rs}$ when compared with the data obtained in controlled mechanical ventilation.[16] In the current study, we

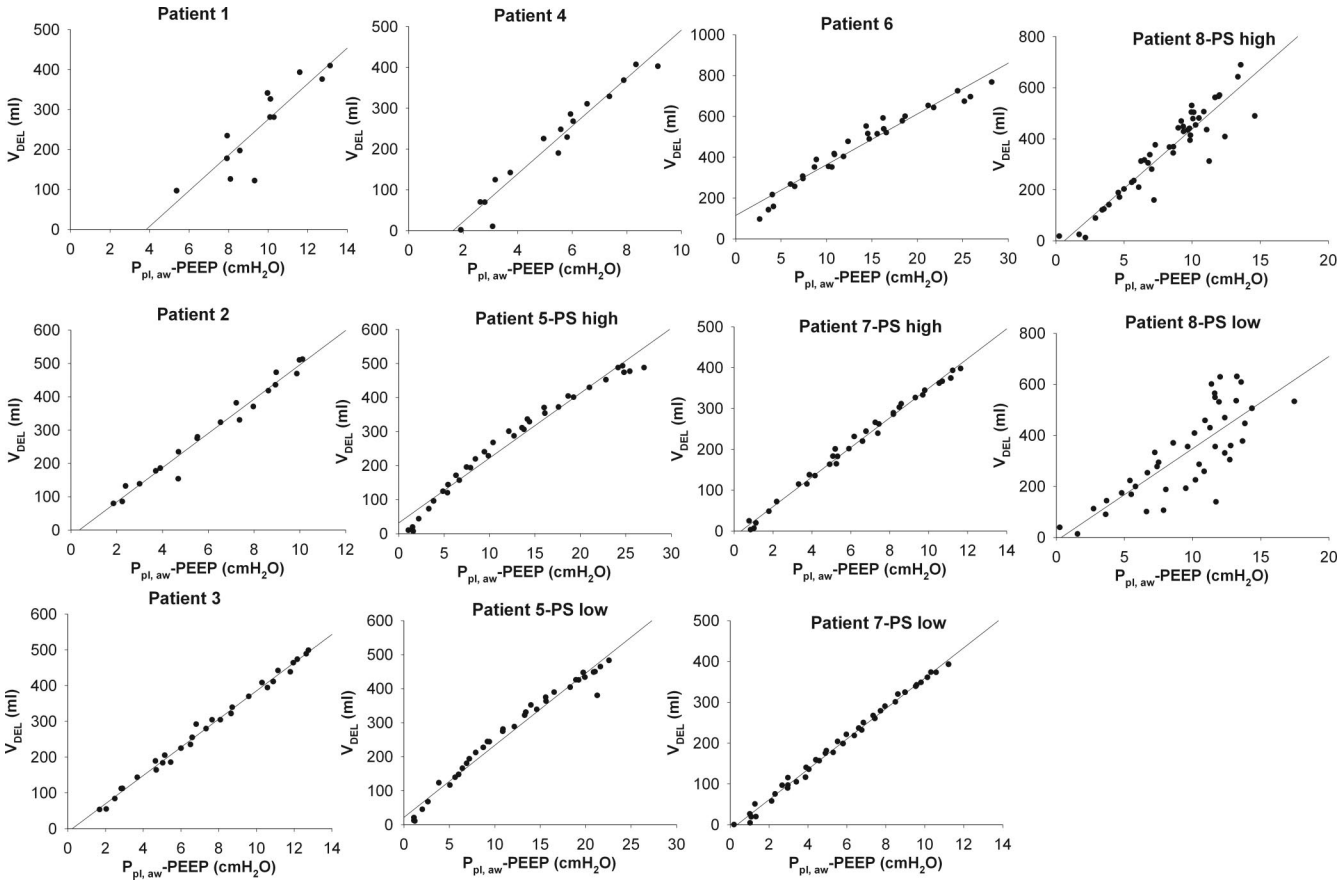

Fig. 2. Pressure–volume relations obtained in each measurement sequence. Each point represents the data obtained in one occlusion where a flat plateau tracing was seen. The volume delivered to the patient is plotted as a function of the difference between the airway pressure during the plateau phase and the positive end-expiratory pressure ($P_{pl, aw}$ − PEEP), *i.e.*, the elastic recoil pressure of the respiratory system. In each measurement sequence, a good linear relation could be disclosed, suggesting that effective muscle relaxation had been achieved. PS = pressure support; V_{DEL} = volume effectively delivered to the patient from the beginning of inspiration to the time of occlusion.

rely on the intrasubject reproducibility of the measurement and on the tight pressure–volume relation to claim that the compliance measurements we obtained are accurate.

By subtracting $P_{ALV, occl}$ from $P_{el, rs}$ we obtained a measurement of P_{MUSC}, which was well correlated with the reference esophageal measurement. For the calculation of $P_{MUSC, occl}$, we did not take into account the plateau pressure of each occlusion; rather, we calculated the expected value of $P_{el, rs}$. This approach offers two advantages: The first is that the noise possibly present in the single occlusions tends to be canceled when an average value of compliance is calculated. Second, it is possible to obtain estimates of P_{MUSC} also from those occlusions in which an adequate muscle relaxation cannot be achieved or if the patient activates his or her expiratory muscles. The population we studied showed relatively low $P_{0.1}$ values, averaging 3.15 cm H_2O, although some subjects showed values up to 8; this might have favored the achievement of muscle relaxation during the occlusions. In this respect, however, it is worth noting that complete muscle relaxation of both the inspiratory and expiratory muscles is not crucial for every occlusion, as far as the compliance values (from which $P_{el, rs}$ is calculated) are adequately computed (as demonstrated by the pressure–volume relations). Moreover, after the compliance value has been adequately estimated on a few occlusions, it could be possible to perform "mini-invasive" occlusions of short duration. These occlusions would only be used to estimate the value of alveolar pressure, whereas the value of the elastic recoil pressure is calculated after the compliance value has been measured. This would reduce the invasiveness of the technique for the patients, particularly if right after the inspiratory occlusions the ventilator could switch back to the preset pressure-support level rather than cycling to exhalation.

Finally, the single values of P_{MUSC} were integrated over the contraction time, obtaining a reliable estimate of the PTP. When pooling in one single time course P_{MUSC} values sampled from different V_Ts, it must be kept in mind that each point bears a certain experimental error, in estimation of both P_{MUSC} and t_{occl}; moreover, the respiratory efforts of each V_T are likely to differ from each other. For these reasons, integrating over time the P_{MUSC} measurement in one index (PTP_{occl}) serves the

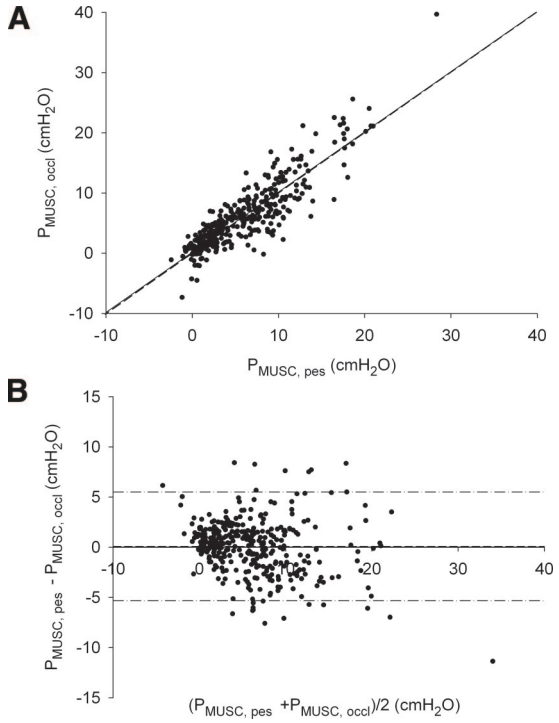

Fig. 3. Comparison between occlusion-derived ($P_{MUSC, occl}$) and esophageal pressure–derived ($P_{MUSC, pes}$) measurements of the pressure generated by respiratory muscles (P_{MUSC}). All of the occlusions obtained in the different measurement sequences are included. (*A*) Linear regression analysis yielded the following equation: $P_{MUSC, occl} = 1.00 \cdot P_{MUSC, pes} + 0.19$; $r = 0.88$, $P < 0.001$. (*B*) Ninety-five percent confidence intervals for agreement between the two measurements.

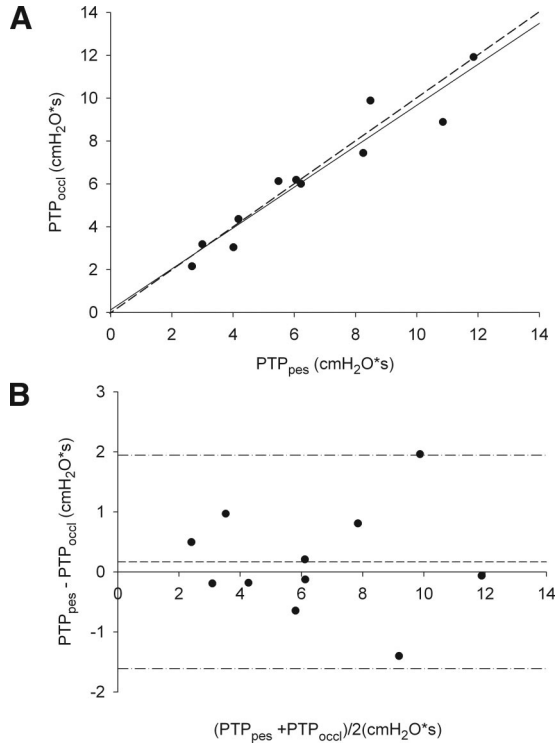

Fig. 4. Each point in the plot represents the pressure–time product (PTP) values obtained in the 11 measurement sequences. A tight correlation was found between the values derived from esophageal pressure (PTP_{pes}) and occlusion (PTP_{occl}), as shown both by the regression analysis (*A*; $PTP_{occl} = 0.95 \cdot PTP_{pes} + 0.13$, $r = 0.96$, $P < 0.001$) and by the Bland and Altman plot (*B*; 95% confidence interval, 1.94 and −1.61 cm $H_2O \cdot s$)

purpose of providing a "global" measurement of the inspiratory effort, which is more interpretable than the punctual P_{MUSC} values decreasing at the same time the experimental error. Increasing the number of occlusions obtained in each patient might be a path to more reliable results by decreasing the impact of possible outliers. The interrupter technique that we have tested during PSV is conceptually applicable to other forms of assisted spontaneous breathing in which the patients are likely to exploit a greater breath-to-breath variability of the respiratory efforts, such as proportional assist ventilation or airway pressure release ventilation.[20] Under these conditions, the interrupter technique could still provide an "average" measurement of the metabolic WOB, provided that a sample of occlusions adequately representative of the different respiratory efforts is obtained; yet further studies would be necessary to address this issue. The PTP is usually computed over a minute, taking the effect of the respiratory rate into account.[10] However, we chose not to perform this operation because multiplying PTP_{pes} and PTP_{occl} for the same number (the respiratory rate) would have introduced a mathematical coupling, spuriously increasing the correlation between the two variables.

The patients tolerated the procedure well, without developing desaturation or hemodynamic instability. The respiratory rate tended to increase compared with baseline. However, we are unable to separate the effect of the occlusions from the effect of the additional dead space because of the presence of the pneumotachograph, which was, unfortunately, quite bulky.

Although the use of a commercial ventilator bears significant advantages in performing the interrupter technique, at least two main limitations of such an approach must be considered. The valve is located inside the ventilator, rather than at the airway opening. In this way, a relatively large volume of gas (the ventilator circuit) is interposed between the valves and the alveoli, representing a compressible volume that can damp the high-frequency oscillations. Even if the valve is closed, the respiratory system volume is not necessarily constant: The pressure swings generated by the patient's respiratory muscles can displace some gas from the lungs to the circuit and *vice versa*. Particularly, when the patient relaxes the respiratory muscles, some gas volume can move out of the respiratory system into the tubing. However, the low compliance of the ventilator circuit should minimize the impact of this phenomenon.

Another limitation of using a commercial ventilator, rather than a dedicated valve system, is the closure time of the valves. The valves of a modern commercial venti-

lator have very high-level performance. The speed of opening and closing is often a compromise between acceptable performance and the wear of the valve itself. The closure times (approximately 70 ms to completely zeroing the gas flow) that we report are greater than those reported in the literature for the rapid interrupter technique (between 5 and 30 ms), and a "long" closure time could affect the measurements. There is a delay between the occlusion and the P_{aw} tracing portion suitable for the slope analysis. During this time, the patient might change his or her effort, making the linear back-extrapolation of the curve unreliable. However, the very fast valves tend to generate oscillations in the pressure signals, making the first period of the occlusion not easily interpretable anyway. Moreover, it has been shown that the reaction time in humans to an airway occlusion is between 200 and 300 ms.[21,22] Indeed, the $P_{0.1}$ measurement relies on the assumption that during a 100-ms occlusion, the decrease in the airway pressure is linear.[23] If the flow interruption is not instantaneous, the volume of the system changes during the occlusion process: The volume in the respiratory system after the occlusion is greater (during the inspiration) or smaller (during the exhalation) than before the start of the occlusion. This translates the entire P_{aw} tracing after the occlusion upward or downward compared with the theoretical one. In our bench study, the volume delivered during the occlusions were relatively small, averaging 34 $\pm$ 17 and 26 $\pm$ 16 ml during inspiration and expiration, respectively.

Our study population, although with a common diagnosis of acute respiratory failure, was quite heterogeneous for primary diagnosis and severity, and it did not include patients with chronic obstructive pulmonary disease or with a relevant intrinsic PEEP. Indeed, the validity of the technique in patients with long and/or heterogeneous time constants as well as in patients with increased respiratory drive or a very high respiratory rate is questionable and would require specific investigation.

In conclusion, this work shows that the rapid interrupter technique can be performed by means of a commercial ventilator, offering reliable measurement of respiratory system compliance, of P_{MUSC}, and of the derived parameter PTP. Although further studies are required to verify the robustness and usefulness of the technique in a general intensive care unit population, we suggest that the advantage of performing the interrupter technique without the need for a dedicated apparatus is likely to balance some of its limitations and bears the potential to make the estimate of the metabolic WOB easily obtainable at the bedside.

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