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The effect of lung volume on transdiaphragmatic pressure

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The effect of lung volume on transdiaphragmatic pressure. C-H. Hamnegård, S. Wragg, G. Mills, D. Kyroussis, J. Road, G. Daskos, B. Bake, J. Moxham, M. Green. ©ERS Journals Ltd 1995.

ABSTRACT: Diaphragm strength can be assessed by measurement of transdiaphragmatic pressure (P_{di}) in response to stimulation of the phrenic nerves. The length-tension relationship of the diaphragm can be studied by measuring twitch P_{di} over the range of lung volume. Previous studies of the relationship between lung volume and diaphragm strength have used the technique of electrical stimulation of the phrenic nerves. In these studies, the phenomenon of twitch potentiation has not been taken into account. It has previously been shown that prior contraction of the diaphragm can greatly enhance the twitch response, thus affecting the measurements.

The aim of this study was to investigate the relationship between unpotentiated twitch P_{di} and lung volume for volumes ranging from residual volume (RV) to total lung capacity (TLC) in normal subjects. Great care was taken to avoid muscle potentiation. For this purpose, we stimulated the phrenic nerves with a magnetic stimulator. In addition, we used positive pressure to inflate the lungs to high lung volumes. The impact of twitch potentiation on the length-tension relationship was investigated by subjects making maximum inspiratory efforts prior to phrenic nerve stimulation.

The unpotentiated twitch P_{di} decreased in a linear fashion with increasing lung volume over the full range of vital capacity by 0.54 kPa·L^{-1}. Potentiation increased twitch P_{di} by 40% at FRC and the effect was similar, in absolute terms, at all lung volumes. In relative terms, the effect of potentiation became greater as lung volume increased, and more than doubled twitch P_{di} at TLC.

With increasing lung volume, there is a linear fall in unpotentiated twitch P_{di} with a slope that is less steep, over the same range of absolute lung volume, than previously reported. When assessing diaphragm strength by the twitch technique, it is essential to control for lung volume and equally important to control for twitch potentiation.

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A knowledge of the length-tension properties of the diaphragm is essential for an understanding of breathing mechanics and this relationship has been investigated in previous studies in man [1–6]. Maximum transdiaphragmatic pressure decreases with increasing lung volume, as diaphragm length shortens.

Several investigators have used voluntary maximum inspiratory efforts to determine the strength of the diaphragm at various lung volumes but it is not always certain that the diaphragm is fully activated during the voluntary contractions [1]. Transcutaneous electrical stimulation of the phrenic nerves permits nonvolitional study of diaphragm function. However, with this technique it is difficult to be sure that stimulation is maximal, particularly at the extremes of lung volume, and repeated breathing manoeuvres and electrical stimulations may be necessary. This may lead to muscle potentiation [2] and variability in the transdiaphragmatic pressure response. Twitch potentiation can increase twitch P_{di} by up to 70% at functional residual capacity (FRC) following a maximal voluntary diaphragm contraction [2, 3]. Previous studies on the relationship between twitch P_{di} and lung volume that have used electrica stimulation have not considered the effect of potentiation. Magnetic stimulation has previously been reported to be an easy, reproducible and well-tolerated technique of phrenic nerve stimulation [4, 5]. Therefore, this technique could be useful in studies in which twitch potentiation is difficult to avoid with electrical stimulation.

The aim of the present study was, therefore, to investigate the relationship between unpotentiated twitch P_{di} and lung volume using the technique of cervical magnetic stimulation, and also to study the effect of potentiation.

Materials and methods

Subjects

Six male subjects aged 30–54 yrs were studied. All were familiar with the purpose of the investigation and had previously participated in studies of respiratory system mechanics. The protocol was approved by the Hospital Ethics Committee and all subjects gave their informed consent.

Measurements

Pressure at the mouth (P_{ao}) was measured from a side port on a mouthpiece. Transdiaphragmatic pressure (P_{di}) was defined as the difference between gastric (P_{gas}) and oesophageal (P_{oes}) pressures and was recorded from conventional balloon catheters (P.K. Morgan, Rainham, Kent, UK). One balloon was positioned in the oesophagus, 10 cm above the cardiac sphincter, and the other in the stomach. They were filled with 0.5 and 2 mL of air, respectively. The position of the oesophageal balloon was adjusted until the difference in transpulmonary pressure (P_{ao}-P_{oes}) was less than 0.2 kPa during inspiratory manoeuvres against an occluded airway [6]. Twitch P_{di}, twitch P_{oes} and twitch P_{gas} were measured as the difference between baseline pressures immediately before the twitch and the peak pressures.

The balloon catheters and the mouthpiece catheter were connected to differential pressure transducers (Validyne, MP-45-1±150 cmH_2O), carrier amplifiers (Validyne Co., Northridge, CA, USA), a 12-bit NB-MIO-16 analogue-to-digital board and a Macintosh Centris 650 computer (Apple Computer, Inc., Cupertino, CA, USA) running LabView® software (National Instruments™, Austin, TX, USA). Lung volumes were recorded using an Ohio 840 dry spirometer. Pressure and volume signals were sampled at 100 Hz.

Phrenic nerve stimulation

The phrenic nerve roots were stimulated bilaterally with cervical magnetic stimulation using a Magstim 200 (Magstim Co. Ltd, Whitland, Dyfed, Wales, UK) and a circular 90 mm coil (P/N 9784-00). The neck was flexed to allow the positioning of the coil. Several stimulations at 80% of maximum magnetic stimulator output were performed over the spinous processes in the midline between C5-C7 until the maximum response was determined. Thereafter, all stimulations were performed with the coil in that position, and at maximal magnetic stimulator output, to achieve supramaximal diaphragm activation [5]. Phrenic stimulation was shown to be supramaximal in five subjects, as judged by a plateau of twitch P_{di} and diaphragm electromyography activity (EMG) in response to maximum magnetic stimulation.

Experimental protocol

The subjects were seated during the study. Inspiratory capacity, expiratory reserve volume and vital capacity (VC) were measured at body temperature, and atmospheric pressure, saturated with water vapour (BTPS). The static elastic properties of the chest wall and the lungs were determined between total lung capacity (TLC) and residual volume (RV). For this purpose, each subject was instructed to inspire to TLC and then relax against a closed valve at the mouthpiece, which was intermittently opened to the spirometer. The pressure volume data was used during the study to assess the adequacy of respiratory muscle relaxation.

To avoid twitch potentiation the subjects were rested for 20 min before each study and were instructed to breath quietly and to remain silent. Ten twitch P_{di} responses were obtained at FRC to establish a baseline. The subjects were then instructed to gently expire from FRC by a volume equal to 5% of their vital capacity, relax against a closed valve, and a magnetic stimulus was given. The valve was then reopened to the spirometer, the subject breathed normally for a few breaths and FRC was checked. This sequence was repeated five times at each lung volume of interest. Twitch responses at FRC were obtained to assess whether any potentiation was present, defined as an increase of twitch P_{di} of more than 5% above baseline. This occurred occasionally but only at lung volumes close to RV and TLC, following these manoeuvres, twitch P_{di} was checked at FRC after every measurement and if increased by more than 5% the preceding measurement was deleted and the subject was rested for 20 min before further measurements were obtained. To avoid potentiation at high lung volumes, the subjects were passively inflated with a volume-cycled mechanical ventilator (Brompton Pac). Only those twitch responses where the subject was able to relax, as assessed from the pressure volume relationship for the lung (P_{ao}-P_{oes}), the chest wall (P_{oes}) and the diaphragm (P_{di}), were analysed.

A similar protocol was used to determine the relationship between the potentiated diaphragm and lung volume. In order to potentiate the diaphragm, the subject was instructed to perform a maximal inspiratory manoeuvre against a closed airway at FRC for 4 s. Twitch measurements were obtained 30 s later. Twitch responses at FRC were obtained initially to find the baseline values for potentiated twitch P_{di}. Potentiated twitch responses at FRC were obtained regularly to verify the constancy of the twitch response and to detect any possible diaphragm fatigue. When twitch amplitude decreased more than 10% all measurements were terminated, thus explaining the fewer data points for some subjects.

The relationships between lung volume on the one hand and twitch P_{di}, twitch P_{oes} and twitch P_{gas} on the other, was analysed by linear regression analysis.

Table 1. – Characteristics of the six normal subjects

Sub No.	Age yrs	Height cm	Weight kg	VC L	VC % pred
1	33	200	95	5.9	88
2	33	175	80	6.6	122
3	54	175	70	5.0	102
4	39	185	83	6.6	114
5	38	181	68	6.2	111
6	31	170	68	5.2	100

Predicted normal vital capacity according to BERGLUND *et al.* [7]. Sub: subject; VC: vital capacity; % pred: percentage of predicted.

Results

Characteristics of the subjects are shown in table 1. Magnetic stimulation was well-tolerated by all subjects and the amplitude and waveform of twitch Pdi was reproducible at all lung volumes studied. An example of the pressure changes during magnetic stimulation at a lung volume 1 L above FRC is shown in figure 1. The amplitude of the unpotentiated Pdi twitch is about 2/3 of the potentiated one.

Figure 2 shows the results of all measurements of unpotentiated and potentiated twitch Pdi responses in each subject. The amplitude of the unpotentiated twitches decreased with increasing lung volume in an almost linear fashion in all subjects. The potentiated twitch Pdi appeared less reproducible than unpotentiated twitch Pdi. Mean values for twitch Pdi are shown in figure 3a. Unpotentiated twitch Pdi decreased from a mean of 4.1 kPa at volumes close to RV to a mean of 0.9 kPa at TLC. At FRC (approximately 30% VC) mean unpotentiated twitch Pdi was 3.1 kPa. The relationship between unpotentiated twitch Pdi and lung volume was linear (r=0.99) with a slope of 0.033 kPa/%VC (0.54 kPa·L^{-1}). The reduction in twitch Pdi was due mainly to a fall in twitch Poes. As lung volume increased from RV to TLC, the contribution of Poes to Pdi decreased considerably (figure 3b), from about 75 to 0%. The unpotentiated twitch Pgas tended to remain constant at all lung volumes, whereas Poes fell in an almost linear fashion with a mean slope of 0.035 kPa/% VC. We observed a positive twitch Poes at lung volumes close to TLC in all subjects.

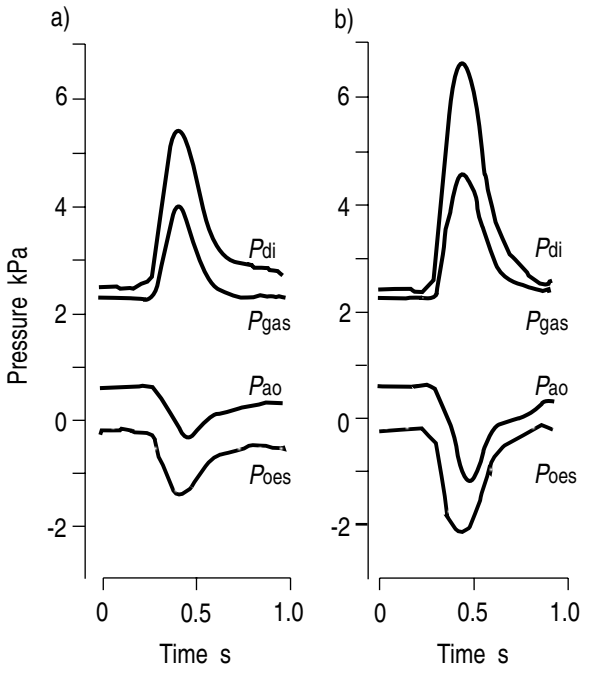

Fig. 1 – Example of twitch pressures in one subject at a lung volume 1 L above FRC. a) Unpotentiated twitch pressures; and b) potentiated twitch pressures. The relaxed pressures immediately prior to the twitch are similar, showing that the twitches are performed at the same lung volume during relaxation. The amplitude of the unpotentiated Pdi is about 2/3 of the potentiated one. Pdi: diaphragmatic pressure; Pgas: gastric pressure; Pao: pressure at airway opening (mouth); Poes: oesophageal pressure.

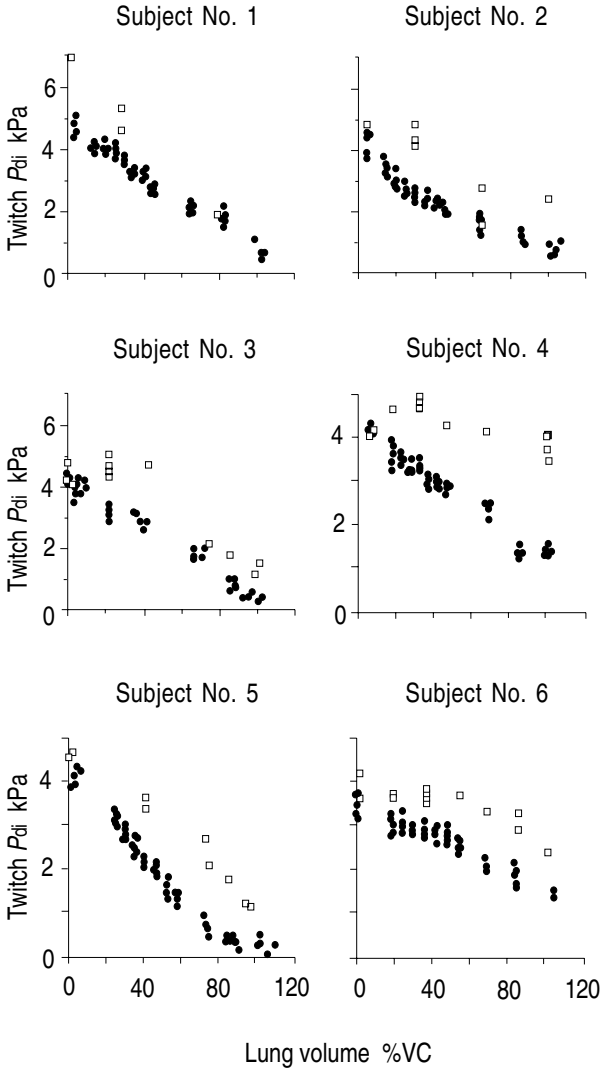

Fig. 2 – All measurements of unpotentiated (●) and potentiated (❑) twitch transdiaphragmatic pressure (Pdi) *versus* lung volume expressed as % of vital capacity.

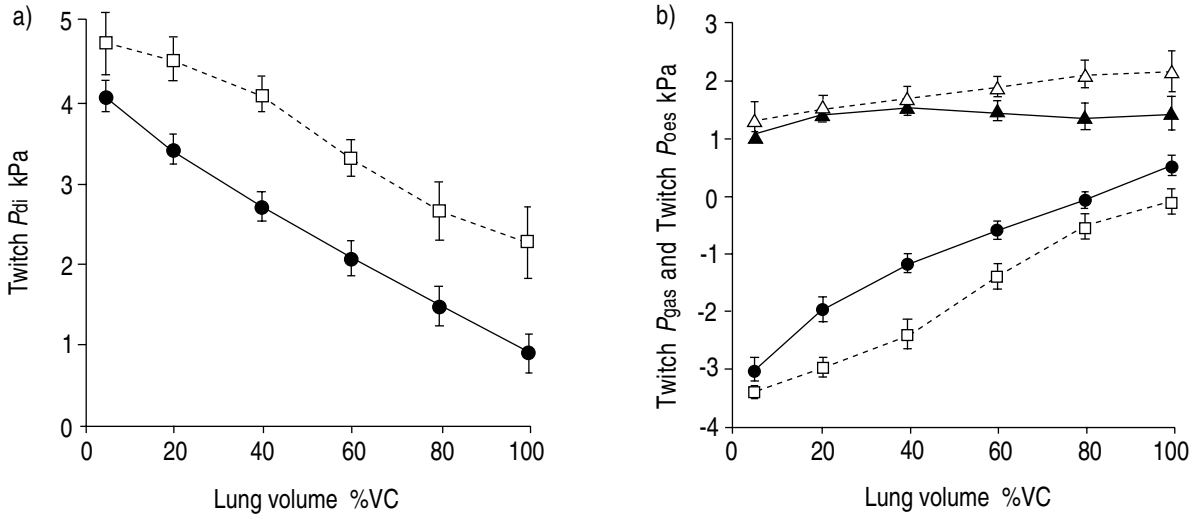

Fig. 3. – a) Mean (SEM) group values (n=6) for unpotentiated (—●—) and potentiated (—□—) twitch P_{di} *versus* lung volume expressed as % of vital capacity (%VC). The linear regression equation for unpotentiated twitch P_{di}=4.13–0.033×%VC (r=0.99). b) Mean (SEM) group values (n=6) for unpotentiated and potentiated twitch P_{oes} and twitch P_{gas} *versus* lung volume expressed as % of vital capacity (%VC). The linear regression equation for unpotentiated twitch P_{oes}=-2.84+0.035×%VC (r=0.98). VC: vital capacity. For further abbreviations see legend to figure 1. ---△--- : P_{gas} potentiated; —▲— : P_{gas} unpotentiated; —●— : P_{oes} unpotentiated; ---□--- : P_{oes} potentiated.

Discussion

In this study, there was a linear fall in unpotentiated twitch P_{di} with increasing lung volume. The slope was 0.54 kPa·L^{-1} (0.033 kPa/%VC). These results are consistent with previous reports [8–10] in that twitch P_{di} decreased with increasing lung volume, reflecting shortening of the diaphragm. However, the magnitude of the decrease in twitch P_{di} with increasing lung volume varies between reports. MIER *et al.* [9] and HUBMAYR *et al.* [10], both of whom did not study the extremes of VC, reported a slope of 0.70 and 0.78 kPa·L^{-1}, respectively. Calculated data from the study of SMITH and BELLEMARE [8] shows a slope of 0.93 kPa·L^{-1} for lung volumes between 50% expiratory and 50% inspiratory capacity.

The present study and that of SMITH and BELLEMARE [8] examined the relationship between twitch P_{di} and lung volume over the full range of lung volumes. If lung volume is expressed as a percentage of VC the slopes seen in the SMITH and BELLEMARE [8] study are very similar to those for the potentiated data points in the present study.

The twitch response of skeletal muscle is known to be affected by prior voluntary efforts. This phenomenon is known as twitch potentiation and the mechanism responsible is not certain [11]. WRAGG *et al.* [2] have shown that after an inspiratory voluntary contraction the P_{di} twitch height can increase by up to 70%. Submaximal contractions also resulted in a substantial increase of twitch P_{di}. A voluntary contraction of 50% of maximum resulted in a mean increase in twitch P_{di} of 28% (range 13–43%). Furthermore, it seems that the magnitude of the effort is the major determinant of the degree of potentiation, rather than the duration [2]. Thus, a brief inspiratory manoeuvre, such as a sniff, can significantly influence twitch P_{di}.

Unpotentiated diaphragm responses were achieved by asking the subjects to rest for 20 min. This period was considered suitable because we have previously shown that the effect of maximal diaphragm contractions on subsequent twitch pressures is negligible after 20 min [2]. Furthermore, throughout the study we performed check stimulations at FRC in order to identify any twitch potentiation. Potentiation was sometimes detected after subjects had been studied at the extremes of lung volume, even when we used positive pressure to passively inflate the lungs. In such cases, the subject was requested to rest for 20 min before further measurements.

We went on to investigate the effect of twitch potentiation on the twitch volume relation by repeating our measurements having first fully potentiated the diaphragm. This was achieved by asking the subjects to make a maximal inspiratory effort of 4 s duration against a closed airway at FRC prior to each stimulation [2]. We were concerned that repeated maximal inspiratory efforts could induce diaphragm fatigue, which would then offset the effect of potentiation. Frequent checks of twitch P_{di} at FRC served to confirm whether or not the diaphragm remained fully potentiated. When P_{di} was reduced, no further measurements were made.

At FRC potentiation increased twitch P_{di} by 40%. The potentiating effect relatively increased with increasing lung volume from RV to TLC. This is consistent with the results of VANDERVOORT *et al.* [11] who showed that the degree of potentiation increased with muscle shortening. Thus, the effect of potentiation on the diaphragm is relatively small at RV, whereas at TLC it increases twitch P_{di} by a factor of 2.5.

The mechanisms that determine the relationship between lung volume and twitch P_{di} have been discussed in previous reports [1, 8, 12, 13]. It is almost certain that isometric conditions are not fulfilled during the twitch [12, 13]. Therefore, the lung volume/twitch P_{di} relationship cannot be interpreted simply in terms of the length-tension relationship. Furthermore, the relaxation manoeuvre at RV and TLC involve considerable shape changes,

which complicate the interpretation at the extremes of lung volume. This is not a problem when the maximal voluntary effort technique is used. However, during these manoeuvres it is not always certain that the diaphragm is fully activated [1].

As lung volume approached RV, the unpotentiated twitch P_{di} did not reach a plateau value. It is likely that the shape change caused by the relaxation manoeuvre at RV affects the length of the diaphragm such that it shortens. Thus, we have probably not measured twitch P_{di} at the longest possible diaphragm length, as obtained during a maximum voluntary expiratory effort to RV.

Close to TLC we frequently found twitch P_{oes} to be positive and, therefore, expiratory in action. We have considered the possibility of this effect being due to contraction of muscles in the upper thorax caused by the magnetic stimulation. At least two observations are against this interpretation. Firstly, we have not observed a positive oesophageal pressure in any of the many patients with bilateral phrenic paralysis investigated by magnetic stimulation in our laboratory. Secondly, we have observed similar results during more selective electrical stimulation. SMITH and BELLEMARE [8] have reported similar findings in one subject. Thus, the expiratory twitch P_{oes} close to TLC is almost certainly not due to magnetic stimulation being less selective. A more probable explanation is that the contraction of the low flat diaphragm pulls the lower rib cage inwards.

In this study, we found that changes in lung volume of ±0.5 L around FRC resulted in ±10% changes in twitch P_{di}. However, much greater variability in twitch height can result from twitch potentiation. The effect of potentiation was a mean increase in twitch P_{di} of 40% at FRC. At higher lung volumes, the effect of potentiation is even larger. Thus the efforts necessary for subjects to voluntarily alter lung volume could potentiate the diaphragm and cause changes in twitch pressure that may be greater than those due to changes in muscle length.

In conclusion, we have found a linear fall in unpotentiated twitch P_{di} with increasing lung volume with a slope that is less steep than previously reported. When assessing diaphragm strength by the twitch technique, it is essential to control for lung volume, but it may be even more important, to avoid twitch potentiation.

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