

A novel clinical test of respiratory muscle endurance

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A novel clinical test of respiratory muscle endurance. N. Hart, P. Hawkins, C-H. Hamnegård, M. Green, J. Moxham, M.I. Polkey. ©ERS Journals Ltd 2002.

ABSTRACT: Impaired respiratory muscle endurance (RME) could reduce exercise tolerance and contribute to ventilatory failure. The aim of the present study was to develop a clinically-feasible method to measure RME using negative-pressure inspiratory-threshold loading. It was hypothesized that endurance time (t_{lim}) could be predicted by normalizing oesophageal pressure-time product (PTP) per total breath cycle (PTP_{oes}) for maximum oesophageal pressure ($P_{oes,max}$); the load/capacity ratio. The corresponding mouth pressures, PTP_{mouth} and $P_{mouth,max}$ were also measured.

The RME test was performed on 30 healthy subjects exposed to the same target pressure (70% of $P_{oes,max}$). Eight patients with systemic sclerosis/interstitial lung disease were studied to assess the validity and acceptability of the technique.

Normal subjects showed a wide intersubject variation in t_{lim} (coefficient of variation, 69%), with a linear relationship demonstrated between $\log t_{lim}$ and PTP_{oes}/ $P_{oes,max}$ ($r=0.88$). All patients with systemic sclerosis/interstitial lung disease had normal respiratory muscle strength, but six out of eight had a reduction in RME.

In conclusion, endurance time can be predicted from the load/capacity ratio, over a range of breathing strategies; this relationship allows abnormal respiratory muscle endurance to be detected in patients. Oesophageal and mouth pressure showed a close correlation, thus suggesting that the test could be applied noninvasively.

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Sustained excessive load placed on the respiratory muscle pump may cause ventilatory failure or contribute to dyspnoea [1, 2]. Although respiratory muscle strength (RMS) can be readily assessed [3], it is possible that the endurance properties of the muscle may have a greater bearing on the ability of a patient to cope with a prolonged respiratory load. However, reliable tests of respiratory muscle endurance (RME) have proved difficult to establish. The aim of the present study was to develop a clinically-applicable test of RME.

In particular, as constraints on breathing patterns reduce RME [4], the test should avoid preset breathing strategies (e.g. fixed square-wave breathing patterns [5, 6]). In the present study, the authors used constant negative pressure threshold loading and hypothesized that variation in endurance time (t_{lim}) could be predicted during the loading task by normalizing the oesophageal pressure time product for maximal negative oesophageal pressure; this relationship was termed the respiratory load/capacity ratio. This paradigm allows subjects to develop their own breathing strategy in response to the applied pressure, while advances in computer technology allow for rapid calculation of the load/capacity ratio. A secondary aim of this study was to determine whether mouth pressure would accurately reflect oesophageal pressure, as has been shown in previous studies [7, 8], and thus provide a noninvasive method to assess RME.

Methods

Subjects

The protocol was approved by the Ethics Committee of the Royal Brompton Hospital, London, UK, and all participants gave their informed consent.

Study 1 included 30 healthy subjects who underwent RME testing to determine the relationship between t_{lim} and the load/capacity ratio. Study 2 included six of the 30 healthy subjects who underwent RME testing on three separate occasions in order to determine the intrasubject variability of the test. Finally, study 3 included eight patients with interstitial lung disease due to systemic sclerosis (SS/ILD) who underwent RME testing to assess the validity and acceptability of the technique; these patients were compared with eight controls.

Apparatus

Negative pressure threshold loading was performed using a low resistance inspiratory threshold loading (ITL) device, modified from that described by CHEN *et al.* [9]. The device consisted of a cylindrical adjustable pressure chamber, 41×10 cm, which was connected to a two-way nonbreathing valve (PK Morgan Ltd, Rainham, Kent, UK). The negative

pressure (range, -10–135 cmH₂O) was generated by a vacuum cleaner (Numatic International, Chard, Somerset, UK), and pressure in the chamber was measured using a pressure monitor (Magnehelic, Dwyer Instruments Inc., Michigan City, IN, USA). Expiratory flow was measured with a pneumotachograph head (Fleisch, Lausanne, Switzerland) attached to a tube of dimensions 41×3.5 cm connected to an electrospirometer (GM Instruments Ltd, Kilwinning, UK).

Pressure measurements

An oesophageal balloon catheter (Ackrad Laboratories, Cranford, NJ, USA) was inserted and positioned in the standard manner [10]. Oesophageal pressure (P_{oes}) and mouth pressure (P_{mouth}) were measured using differential pressure transducers (Validyne, Northridge, CA, USA) and amplified by carrier amplifiers (Validyne). All signals were passed to an analog-digital board and Power PC (Apple Computers, Cupertino, CA, USA) running Labview 4.1 software (National Instruments, Austin, TX, USA).

Pressure-time product

Oesophageal pressure-time product (PTP) per total breath cycle (PTP_{oes}) and mouth PTP per total breath cycle (PTP_{mouth}) were calculated from P_{oes} and P_{mouth} traces for the whole RME test in each subject. The area subtended by the pressure time curve was determined for each breath using a semi-automated modification of Labview 4.1 software. Average PTP_{oes} and average PTP_{mouth} were used as indicators of the load on the respiratory muscles.

Dynamic compliance

Dynamic compliance (CL_{dyn}) was calculated during resting breathing by dividing tidal volume by the difference in P_{oes} at points of zero flow.

Maximum inspiratory pressure

Before each RME test, all participants performed maximum inspiratory manoeuvres using a mouthpiece attached to a metal tube, which had a small air leak to prevent glottic closure [11]. Efforts were repeated from functional residual capacity (FRC) at least 10 times until three reproducible efforts were obtained. Patients and subjects who were unfamiliar with the manoeuvre had a preliminary session for instruction in order to ensure that maximum pressures were achieved. Peak (rather than the 1-s average) negative oesophageal pressure ($P_{oes,max}$) and peak negative mouth pressure ($P_{mouth,max}$) were determined, and these measurements were used as the capacity of the respiratory muscles.

Inspiratory threshold loading protocol

All subjects and patients were exposed to the same relative target negative pressure (70% of $P_{oes,max}$). No restriction was placed on the pattern of breathing. During the first minute of the test, the threshold pressure was progressively made more subatmospheric from -10 cmH₂O to 70% of $P_{oes,max}$. Subjects had to generate a pressure at the mouth, slightly greater than the chamber pressure, to open the valve in order to initiate and sustain inspiratory flow. The ITL device provided a constant inspiratory pressure when the valve was open [9]. All the subjects underwent 2–5 practice endurance runs, up to 70% $P_{oes,max}$, to become accustomed to the apparatus and the sensation of dyspnoea. It was important for all subjects to familiarize themselves with the equipment and start with low workloads to ensure that the best strategy for handling higher loads was chosen [12]. t_{lim} was defined as the period from when the negative pressure imposed reached 70% of $P_{oes,max}$ to task failure (*i.e.* the incremental loading minute was excluded). Task failure was defined as the inability to generate the target pressure and open the valve. Strong verbal encouragement was given throughout the RME test, and subjects and patients were instructed to stop and come off the mouthpiece when they could no longer open the valve. All subjects continued to exhaustion or until the sensation of dyspnoea was too uncomfortable to tolerate.

Statistical analysis

Due to the curvilinear relationship between t_{lim} and the load/capacity ratio, a single-segment logarithmic conversion of t_{lim} was performed to produce a linear model to describe the relationship between t_{lim} and PTP_{oes}/ $P_{oes,max}$. Furthermore, this variance-stabilizing transformation of the data permitted the definition of 95% confidence bands as well as the establishment of RME values in healthy subjects.

Linear regression analysis was used to determine the relationships between $\log t_{lim}$ and PTP_{oes}/ $P_{oes,max}$; PTP_{oes} and the duty cycle (duration of inspiration/duration of total breathing cycle (t_i/t_{tot})); $\log t_{lim}$ and t_i/t_{tot} ; and $\log t_{lim}$ and PTP_{mouth}/ $P_{mouth,max}$. The relationship between P_{oes} and P_{mouth} data was assessed using a BLAND and ALTMAN plot [13]. An analysis of variance (ANOVA) test for repeated measures was used to evaluate differences between three consecutive RME tests. Differences between controls and patients with SS/ILD were made with an unpaired t-test. A value of $p < 0.05$ was considered statistically significant. Data are presented as mean \pm SD.

Results

Healthy subjects and patients performed and tolerated the RME test well. There were no adverse events.

Study 1: healthy subjects

Thirty subjects (20 males) were studied with a mean±SD age of 38±10 yrs (range 26–65 yrs). Fifteen of these subjects were naïve to the study.

Baseline static inspiratory pressures. $P_{oes,max}$ and $P_{mouth,max}$ before testing were 126±23 cmH₂O and 125±22 cmH₂O, respectively.

Endurance time. Intersubject variability in t_{lim} was wide, with mean t_{lim} of 370±255 s (coefficient of variation, 69%).

Relationship between endurance time and respiratory load/capacity ratio. The t_{lim} showed a curvilinear relationship with $PTP_{oes}/P_{oes,max}$ (fig. 1a). A linear relationship was demonstrated between $\log t_{lim}$ and $PTP_{oes}/P_{oes,max}$ ($r=0.88$, $p<0.0001$; fig. 1b).

Breathing strategy. There was a linear relationship between $PTP_{oes}/P_{oes,max}$ and tI/t_{tot} (fig. 2a; $r=0.87$, $p<0.0001$) and also between $\log t_{lim}$ and tI/t_{tot} (fig. 2b; $r=0.77$, $p<0.0001$).

Comparison of oesophageal and mouth load/capacity ratio. BLAND and ALTMAN plot [13] demonstrated

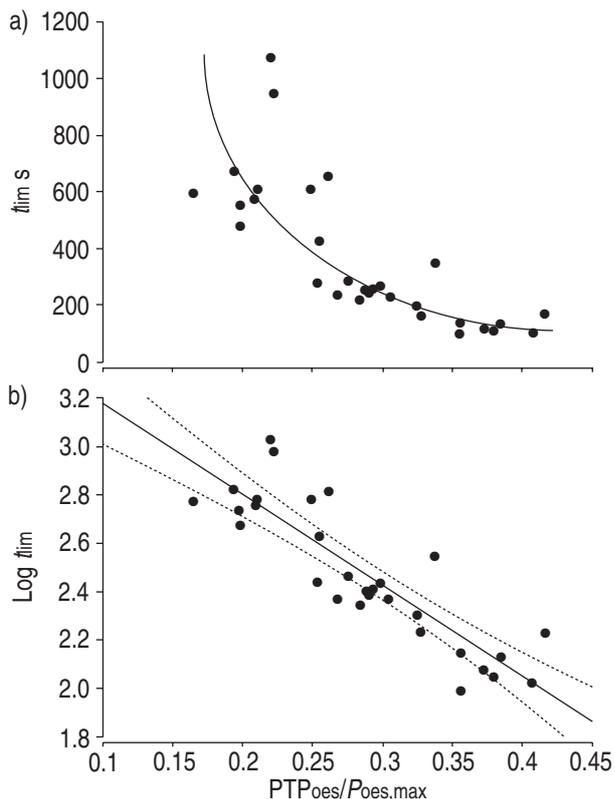


Fig. 1. – a) "Best-fit" plot of the curvilinear relationship between endurance time (t_{lim}) and oesophageal load/capacity ratio (oesophageal pressure-time product per total breath cycle (PTP_{oes})/maximum negative oesophageal pressure ($P_{oes,max}$)) in normal subjects ($n=30$). b) Regression analysis with the 95% confidence bands of the linear relationship between $\log t_{lim}$ and $PTP_{oes}/P_{oes,max}$ in normal subjects ($n=30$; $r=0.88$, $p<0.0001$).

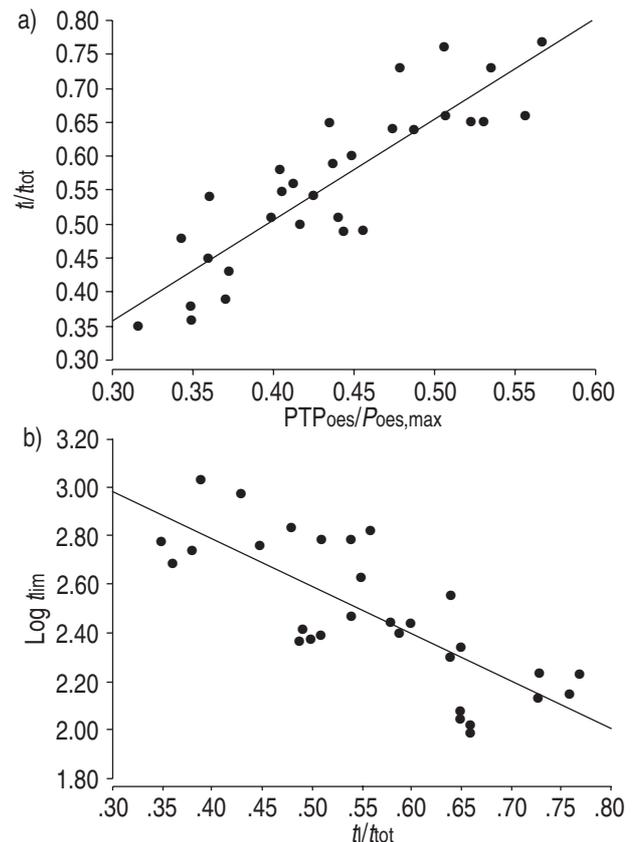


Fig. 2. – a) Regression analysis of the linear relationship between duty cycle (duration of inspiration/duration of total breathing cycle (tI/t_{tot})) and oesophageal load/capacity ratio (oesophageal pressure-time product per total breath cycle (PTP_{oes})/maximum negative oesophageal pressure ($P_{oes,max}$)) in normal subjects ($n=30$; $r=0.87$, $p<0.0001$). b) Regression analysis of the linear relationship between the log endurance time ($\log t_{lim}$) and duty cycle (tI/t_{tot}) in normal subjects ($n=30$; $r=0.77$, $p<0.0001$).

agreement between $PTP_{oes}/P_{oes,max}$ and $PTP_{mouth}/P_{mouth,max}$ (fig. 3a). The r -value for the linear relationship between $\log t_{lim}$ and $PTP_{mouth}/P_{mouth,max}$ was 0.82 ($p\leq 0.0001$; fig. 3b).

Study 2: reproducibility in healthy subjects

Six subjects (four male) were studied on three separate occasions. Mean time between each test was 78±82 days.

Baseline static respiratory pressures. Mean $P_{oes,max}$ for the group before each RME test was 118±25, 122±22 and 123±21 cmH₂O, respectively ($p=0.2$).

Endurance time. Intrasubject variability in t_{lim} was wide, with mean t_{lim} of 236±79 s, 321±195 s and 416±248 s for the first, second and third RME test, respectively. There was a trend for t_{lim} to increase, but no difference was demonstrated between RME tests ($p=0.2$); subjects 1 and 2 had a reduction in t_{lim} from baseline, whereas subjects 3–6 had progressive increases in t_{lim} . (table 1).

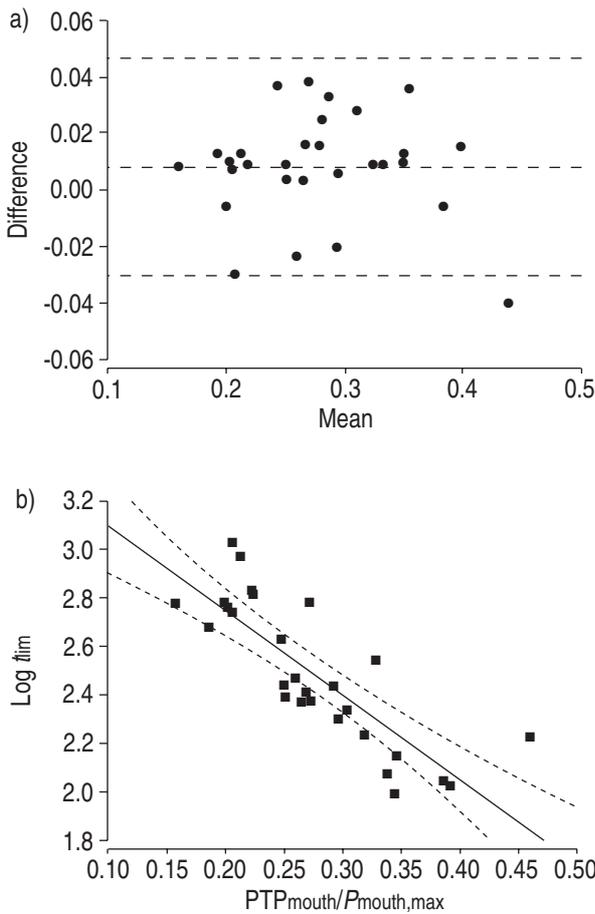


Fig. 3. – a) BLAND and ALTMAN plot [13] of the difference in oesophageal pressure-time product per total breath cycle ($PTP_{oes}/P_{oes,max}$) and mouth pressure-time product per total breath cycle ($PTP_{mouth}/P_{mouth,max}$) against the mean of $PTP_{oes}/P_{oes,max}$ and $PTP_{mouth}/P_{mouth,max}$ in normal subjects ($n=29$). b) Regression analysis with 95% confidence bands of the linear relationship between log endurance time ($\log t_{lim}$) and mouth load/capacity ratio ($PTP_{mouth}/P_{mouth,max}$) in normal subjects ($n=29$; $r=0.82$, $p<0.0001$).

Relationship between endurance time and respiratory load/capacity ratio. Log t_{lim} was plotted against $PTP_{oes}/P_{oes,max}$ for three RME tests in each subject. These serial data were compared to log t_{lim} and $PTP_{oes}/P_{oes,max}$ data obtained from the 30 healthy

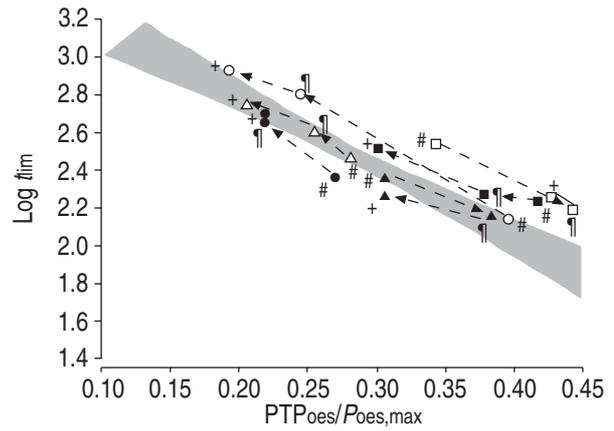


Fig. 4. – Plot of log endurance time ($\log t_{lim}$) and oesophageal load/capacity ratio (oesophageal pressure-time product per total breath cycle (PTP_{oes})/maximum negative oesophageal pressure ($P_{oes,max}$)) for three separate respiratory muscle endurance (RME) runs in six normal subjects. The arrows indicate 1st (#), 2nd (†) and 3rd (‡) RME test. The shaded area represents the simple regression analysis with 95% confidence bands from figure 1b. □: subject 1; ▲: subject 2; ○: subject 3; ■: subject 4; △: subject 5; ●: subject 6.

subjects (fig. 4). Although the results of t_{lim} and $PTP_{oes}/P_{oes,max}$ for each subject changed between each successive test (table 1), figure 4 shows that log t_{lim} and $PTP_{oes}/P_{oes,max}$ data remain within, or close to, the normal values determined by study 1.

Breathing strategy. Linear relationships were demonstrated between $PTP_{oes}/P_{oes,max}$ and t_{tot} for first ($r=0.95$, $p=0.004$), second ($r=0.97$, $p=0.001$), and third ($r=0.89$, $p=0.02$) RME tests.

Study 3: patients with interstitial lung disease due to systemic sclerosis

Characteristics of the patients are summarized in table 2. Eight patients underwent RME testing and were compared with eight controls (table 3). Log t_{lim} , less than predicted from the $PTP_{oes}/P_{oes,max}$ when compared with normal RME values in study 1 (fig. 1b), was taken as a reduction in RME. All patients had normal cardiac function on echocardiogram and evidence of interstitial lung disease on computed tomography.

Table 1. – Endurance time (t_{lim}), maximum negative oesophageal pressure ($P_{oes,max}$) and oesophageal load/capacity ratio for six healthy subjects who performed three consecutive respiratory muscle endurance (RME) tests

Subject no.	1st RME test			2nd RME test			3rd RME test		
	t_{lim} s	$P_{oes,max}$ cmH ₂ O	$PTP_{oes}/P_{oes,max}$	t_{lim} s	$P_{oes,max}$ cmH ₂ O	$PTP_{oes}/P_{oes,max}$	t_{lim} s	$P_{oes,max}$ cmH ₂ O	$PTP_{oes}/P_{oes,max}$
1	352	145	0.34	155	149	0.44	173	151	0.43
2	234	109	0.31	137	118	0.36	187	126	0.31
3	135	99	0.39	625	97	0.24	833	99	0.19
4	169	143	0.42	185	143	0.38	321	136	0.31
5	293	85	0.28	395	98	0.26	521	97	0.21
6	235	129	0.27	433	129	0.22	465	130	0.22

PTP_{oes} : oesophageal pressure-time product per total breath cycle.

Table 2.—Characteristics for patients with systemic sclerosis and interstitial lung disease

Patient no.	Sex M/F	Age yrs	FEV1/FVC %	$T_{L,CO,c}$ mmol·min ⁻¹ ·kPa ⁻¹ ·L ⁻¹
1	M	39	83.9	35.3
2	M	58	78.9	50.0
3	F	30	93.8	44.6
4	F	37	90.8	37.1
5	F	55	87.5	66.3
6	F	38	84.7	23.3
7	M	64	87.1	26.5
8	F	42	93.0	25.8

M: male; F: female; FEV1: forced expiratory volume in one second; FVC: forced vital capacity; $T_{L,CO,c}$: transfer factor of the lung for carbon monoxide: corrected for haemoglobin.

Respiratory muscle strength and endurance. There was no difference in mean $P_{oes,max}$ between the SS/ILD group and the controls. $\log t_{lim}$ and $PTP_{oes}/P_{oes,max}$ were calculated for the patients and compared to the $PTP_{oes}/P_{oes,max}$ and $\log t_{lim}$ values obtained from the 30 normal subjects (fig. 5). The $\log t_{lim}$ value was less than predicted from the $PTP_{oes}/P_{oes,max}$ value in patients 1, 2, 4, 6–8, indicating a reduction in RME. Patients 3 and 5 had a value for $\log t_{lim}$ that would be predicted from the $PTP_{oes}/P_{oes,max}$, indicating normal RME.

Dynamic compliance, duty cycle, load/capacity ratio. Patients with SS/ILD (table 3) had a reduction in CL_{dyn} ($p < 0.0001$). This was associated with an increase in tI/t_{tot} ($p = 0.001$) and $PTP_{oes}/P_{oes,max}$ ($p = 0.04$).

Discussion

The present study confirms previous data that there is wide inter- as well as intrasubject variability in t_{lim} when loading tasks are performed with unconstrained breathing patterns. However, the data shows that this variation in t_{lim} can be explained by variations in breathing strategy, which in the present model is

Table 3.—Comparison of patients with systemic sclerosis and interstitial lung disease (SS/ILD) and age-matched controls

	SS/ILD	Controls	p-value
Age yrs	45.4±12.0	41.5±10.7	0.50
$P_{oes,max}$ cmH ₂ O	96.2±37.9	110.4±26.9	0.40
Target pressure cmH ₂ O	67.4±26.5	77.3±18.8	0.40
tI/t_{tot}	0.67±0.09	0.48±0.09	0.001
$PTP_{oes}/P_{oes,max}$	0.31±0.07	0.24±0.03	0.04
t_{lim}	122±99	611±288	0.0005
CL_{dyn} L·cmH ₂ O ⁻¹	0.056±0.04	0.148±0.03	<0.0001

Data are presented as mean±SD. $P_{oes,max}$: maximum negative oesophageal pressure; tI/t_{tot} : duration of inspiration/duration of total breathing cycle (duty cycle); PTP_{oes} : oesophageal pressure-time product per total breath cycle; $PTP_{oes}/P_{oes,max}$: oesophageal load capacity ratio; t_{lim} : endurance time; CL_{dyn} : dynamic compliance.

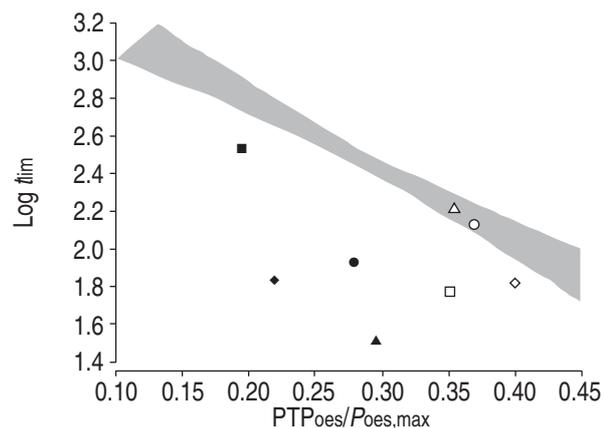


Fig. 5.—Plot of log endurance time ($\log t_{lim}$) and oesophageal load/capacity ratio (oesophageal pressure-time product per total breath cycle (PTP_{oes})/maximum negative oesophageal pressure ($P_{oes,max}$)) for eight patients with systemic sclerosis and interstitial lung disease, compared directly with that of the 30 healthy normals in figure 1b. □: patient 1; ▲: patient 2; ○: patient 3; ■: patient 4; △: patient 5; ●: patient 6; ◇: patient 7; ◆: patient 8.

principally tI/t_{tot} . If the PTP (load) during the RME test is normalized for the maximum negative pressure (capacity), then t_{lim} becomes more predictable and abnormal RME can be identified. This relationship also holds true for P_{mouth} , which suggests that it is possible to use this method as a noninvasive test of RME.

Critique of method

Lung volume. $P_{oes,max}$ was measured at FRC; whereas during loaded breathing, the end expiratory lung volume is likely to decrease [14] and decreasing would have the effect in the present study of increasing the load/capacity ratio, as the numerator will be increased. However, for the test to be clinically practical it was not feasible to correct for volume. Moreover, since the change in $P_{mouth,max}$ between residual volume and FRC is ~14% [15] and not all of this range is covered by expiratory phase abdominal muscle recruitment, the authors predict that volume considerations would not be a major source of variance.

Why use constant submaximal threshold loading rather than other inspiratory loading protocols to measure respiratory muscle endurance? Several tests of RME have been reported [12, 16–21], many of which have used incremental loading methods [12, 19–21]. Although normal reference range data have been published [20], there is still uncertainty as to whether breathing pattern affects incremental loading. More recent studies suggest that incremental threshold loading is not affected by changes in breathing pattern [12, 22], whereas previous studies showed that pressure load [5, 6], flow rate [23], duty cycle [24] and lung volume [25] all affect RME. Furthermore, poor reproducibility of the incremental test has limited its clinical use. In one of the first studies using threshold loading to determine RME [18], the maximum sustainable inspiratory

pressure increased in subsequent tests, and these results differed from those reported by MARTYN *et al.* [12] who repeated a similar protocol. Thus, the learning effect that accompanies all volitional tests [26], combined with the fact that incremental tasks reflect the strength rather than the endurance of the respiratory muscles [14], could contribute to the poor reproducibility. In study 2, the authors found a significant learning effect with wide variability in t_{lim} between occasions. However, when t_{lim} is compared to the load/capacity ratio, the RME was shown to be unchanged (fig. 4).

Why set the threshold pressure level at 70% of maximal? The threshold pressure level of 70% of maximum was determined from pilot work. The present authors found that this pressure was acceptable to normal subjects and patients, in terms of the sensation of dyspnoea and duration of the test. It was hypothesized that maximal acceptability would minimize the impact of central factors, particularly motivation. Nevertheless, the authors acknowledge that for patients with a substantial intrinsic load imposed by their cardiorespiratory disease, a level of 70% of $P_{oes,max}$ may be too high to allow them to achieve a meaningful t_{lim} . For such patients, it may be necessary to use a lower level; however, by expressing t_{lim} as a function of the respiratory load/capacity ratio, the test should still yield useful results.

Respiratory load/capacity ratio to assess respiratory muscle endurance

Previous investigators have evaluated the endurance properties of the respiratory muscles and the effect of pressure and timing on diaphragm [5] and ribcage muscle [6] fatigue. These studies used pressure time index ($PTI = (\text{mean pressure generated}/\text{maximum pressure generated}) \times (\text{inspiratory time}/\text{duty cycle})$) to determine when fatigue is likely to occur. The present authors found the calculation of PTI to be problematic, even with the modern software available. To calculate PTI, according to the method of BELLEMARE and GRASSINO [5], a square-wave breathing pattern must be maintained throughout inspiration, and the plateau pressure is recorded as the mean pressure generated. However, untrained healthy subjects and patients find it difficult to breathe with a square-wave breathing pattern and, in fact, breathe with much more "smoothed-out" patterns, so that it is difficult to accurately determine the plateau pressure. Furthermore, this type of breathing pattern is associated with a more gradual fall and rise in the negative intrathoracic pressure, which is not accommodated by PTI. Even if a nonsquare wave breathing pattern is used, the computation would require an algorithm such that,

$$\text{Mean pressure} = \sum_0^n P/n \quad (1)$$

where P is the pressure generated per breath and n is the number of P points sampled throughout the inspiration [27]. A much simpler method uses PTP. APPENDINI and DONNER [28] recently re-evaluated PTI

and suggested that PTI is the PTP developed over the total breath cycle (PTP/t_{tot}) expressed as a percentage of the maximum pressure that can be generated. This modified version of PTI, or load/capacity ratio, was used in the present study to determine the relationship between ($P_{oes,tp} \cdot \text{total breath cycle}^{-1}/P_{oes,max}$) and t_{lim} in subjects breathing with an unrestricted pattern. Interestingly, in the healthy normals, the mean $PTP_{oes} \cdot \text{cycle}^{-1}/P_{oes,max}$ was 0.29, which is close to the 0.30 threshold value for PTI reported by ZOCCHI *et al.* [6], above which ribcage muscle fatigue occurred in four highly-trained subjects performing square-wave breathing.

Learning effect with endurance testing

Previous studies have demonstrated learning effects with the different tests of RME [26]. This has contributed to the difficulty in determining a set of normal values for RME, as a healthy subject would have to undergo a number of endurance trials to achieve a reliable result. In study 2, there was wide intra- and intersubject variability in t_{lim} (table 1).

The results from these repeated tests raises two relevant points: 1) repeated tests of RME may not always result in an increased t_{lim} ; individuals can actually adopt breathing strategies that reduce t_{lim} (subjects 1 and 2); and 2) variations in t_{lim} between RME tests in the same individual can be explained if t_{lim} is related to the respiratory load/capacity ratio such that a decrease in $PTP_{oes}/P_{oes,max}$ correlates with an increase in $\log t_{lim}$ (fig. 4). This is advantageous when assessing sequential clinical or experimental data.

Load/capacity ratio and endurance time

The curvilinear relationship between t_{lim} and the respiratory load/capacity ratio (fig. 1a) is similar to that described in previous studies [5, 6]. The present approach recognizes and utilizes this relationship without the need for a fixed breathing strategy and expresses RME as a function of the relationship between t_{lim} and $PTP_{oes}/P_{oes,max}$. To have a more clinically-useful measure of RME and to establish normal values, logarithmic conversion of t_{lim} was performed as a variance-stabilizing transformation (fig. 1b). This allows a simple, direct comparison of patient data with normal values (fig. 5).

It could be argued that t/t_{tot} is sufficient to explain the variance in $\log t_{lim}$, but comparison of figures 1b and 2b shows that the correlation between $\log t_{lim}$ is better for the load/capacity ratio ($r=0.88$) than for t/t_{tot} ($r=0.77$). Thus, t/t_{tot} has a good, but not invariable, relationship with the load/capacity ratio (fig. 2a).

Assessment of respiratory muscle endurance from mouth pressures

A BLAND and ALTMAN plot [13] confirmed the close agreement between the P_{mouth} and P_{oes} measurements

during ITL (fig. 3a), with $\log t_{\text{lim}}$ being linearly related to $\text{PTP}_{\text{mouth}}/P_{\text{mouth,max}}$ ($r=0.82$; fig. 3b). Thus, measurements based on P_{mouth} would permit a noninvasive assessment of RME.

Assessment of respiratory muscle endurance in patients with systemic sclerosis and interstitial lung disease

RMS in patients with ILD is reported as normal [29], but these patients suffer from severe breathlessness and impaired exercise performance. The authors hypothesized that reduction in exercise performance and increased breathlessness is due to increased intrinsic elastic load, resulting in an imbalance in the load/capacity ratio and a reduction in RME. Indeed, all the patients with SS/ILD had normal RMS and six of the patients had a reduction in RME (fig. 5). The increased load in the patients with SS/ILD imposed a different respiratory pattern, with an increased $t_{\text{I}}/t_{\text{tot}}$, which was reflected in a higher load/capacity ratio than for the controls (table 3). However, this load/capacity ratio could not be sustained, and t_{lim} was reduced. Interestingly, in the patient group, those with reduced RME had a trend for the CL_{dyn} to be lower ($0.05 \text{ L}\cdot\text{cmH}_2\text{O}^{-1}$) than in those with normal RME ($0.09 \text{ L}\cdot\text{cmH}_2\text{O}^{-1}$; $p=0.1$). Thus, the reduction in RME could result from the combination of the intrinsic elastic load in series with the imposed extrinsic threshold load.

In summary, endurance time can be expressed as a function of the respiratory load/capacity ratio over a range of breathing strategies, using constant submaximal negative pressure threshold loading. The use of this relationship can detect abnormal respiratory muscle endurance in patients with cardiorespiratory disease. Furthermore, mouth pressure accurately reflects oesophageal data, and the noninvasive assessment of respiratory muscle endurance will allow normal values to be established in a large population, against which patients can be evaluated.

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