Use of twitch mouth pressure to assess diaphragm strength in patients with chronic obstructive pulmonary disease

Dong-ming Hua, Yi-hua Liang, Yu-kun Xie, Qi-Liu, Ze-guang Zheng, Rong-chang Chen*, Nan-shan Zhong

Guangzhou Institute of Respiratory Disease, First Affiliated Hospital of Guangzhou Medical College, No. 151 Yajiang Road, Guangzhou, China

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ABSTRACT

This study was undertaken to determine whether twitch mouth pressure (TwPmo) can reliably assess diaphragm strength in patients with chronic obstructive pulmonary disease (COPD) using fully automatic trigger techniques.

Fifteen patients with COPD were recruited. TwPmo, twitch oesophageal pressure (TwPes) and twitch transdiaphragmatic pressure (TwPdi) were generated by phrenic nerve stimulation and were measured using an inspiratory flow trigger (40 ml/s, Experiment 1) using an inspiratory pressure trigger (−5 cmH₂O, Experiment 2) and using no trigger at functional residual capacity (Experiment 3).

The correlation between TwPmo and TwPes was as follows: r = 0.832; P < 0.0001 (Experiment 1), r = 0.900; P < 0.0001 (Experiment 2); there was no significant correlation in Experiment 3. A Bland–Altman plot of the difference between TwPmo and TwPes showed the limits of agreement in Experiment (1) bias (range) 0.18 cmH₂O (−2.05 to 2.41) and Experiment (2) bias (range) 0.32 cmH₂O (−1.69 to 2.32).

Measuring TwPmo using a fully automatic technique is a simple and convenient method for assessing diaphragm strength.

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1. Introduction

Respiratory muscles play an important role in human life and provide us with the power to breathe. Dysfunction of the diaphragm may induce dyspnea or even respiratory failure (Fitting, 2012; Mccool and Tzelepis, 2012; Wilcox and Pardy, 1989). There is increasing interest in respiratory medicine in assessing respiratory muscle function (Hamnegard et al., 1994; Hughes et al., 1999; Kabitz et al., 2007a,b; Man et al., 2004; Mills et al., 2001; Syabhalo, 1998).

Measuring twitch mouth pressure (TwPmo) has been recognised as a convenient, non-invasive and non-volitional method, but this method may be hindered by glottic closure (Anon, 2002; Similowski et al., 1993; Steier et al., 2007). To overcome this hindrance, a fully automated and controlled trigger technique has been established (Kabitz et al., 2007a,b; Windisch et al., 2005). Previous studies suggest that an inspiratory pressure trigger was more suitable for clinics than was an inspiratory flow trigger (Kabitz et al., 2007a,b; Windisch et al., 2005). However, in both studies, only healthy subjects were included. Kabitz et al. (2007a,b) have determined in three COPD patients that the correlation between TwPmo and twitch oesophageal pressure (TwPes) is excellent when a controlled inspiratory trigger is used. However, it remains unclear which trigger mechanisms were more suitable for assessment of diaphragmatic strength in COPD patients.

The purpose of this study was to test the hypothesis that diaphragmatic muscle strength can be measured reliably using non-invasive twitch mouth pressures in COPD patients.

2. Materials and methods

The protocol for this study was approved by the Research Ethics Committee of the Guangzhou Medical College. Informed written consent was obtained for all subjects.

2.1. Subjects

Fifteen patients with COPD according to GOLD guidelines (mean age ± SD was 69.0 ± 6.70 years) took part in this study (Vestbo et al., 2012). All of the patients were stable with no episodes of exacerbation within the previous 2 months. Patients were not currently being treated with oral corticosteroids. The characteristics of the patients are shown in Table 1.

* Corresponding author. Tel.: +86 13602440132.
E-mail addresses: crc2012bh@126.com, Chenc@vip.163.com (R.-c. Chen).

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2.2. Pressure and flow recordings

Lung function parameters were measured (Pony FX; COSMED; Italy). TwPmo was measured using a mouthpiece connected to a fully automatic trigger device.

TwPes and twitch gastric pressure (TwPga) were recorded with 2 balloon catheters positioned 10 cm above the cardia and in the stomach (Hamnegaard et al., 1995). Twitch transdiaphragmatic pressure (TwPdi) is defined as the difference between TwPga and TwPes. The mouthpiece and the two balloon catheters were linked to three pressure transducers (P-300B, Jinsanjiang Sensitive Technology Co., Ltd; Beijing, China). The magnetic valve was connected to a pressure differential pneumotachograph (MLT300L, AD Instruments; Australia). A steel tube of 1 mm in internal diameter was placed near the magnetic valve to avoid glottic closure during the manoeuvre (Fig. 1).

2.3. Phrenic nerve stimulation

The phrenic nerve was stimulated using a Magstim 200 stimulator (Magstim Co. Ltd., Wales, UK). The precise position of the coil should be between C5 and C7 (Hamnegaard et al., 1995). We first measure the pressure at C5, C6 and C7 and then chose the location with the highest pressure. That location was consistently used throughout all the Experiments.

### Table 1

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<th>Patients No.</th>
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Mean: 68 | 53 | 165 | 19.78 | 1.04 | 39.9 | 85.3 | 50.8 | 226.0 | 112.2
S.D.: 8 | 6 | 6 | 2.03 | 0.34 | 10.0 | 18.2 | 9.3 | 60.5 | 18.9

FEV₁, forced expiratory volume in one second; FVC, forced vital capacity; RV, residual volume; TLC, total lung capacity.

2.4. Experimental study design

The stimulations were performed 30 s apart to avoid twitch potentiation. In Experiments 1 and 2, the twitch pressures were recorded using two different triggering techniques. In Experiment 3, no trigger device was used at relaxed FRC. For each Experiment, the twitches were recorded until five acceptable mouth pressures achieved the trigger criteria that are defined below. The highest and lowest mouth pressures were rejected and the remaining three values were accepted. All the subjects were required to breathe quietly.

**Experiment 1:** To assess diaphragmatic strength during inspiratory flow triggering at 40 ml/s (TwPm), the magnetic valve closed at the beginning of inspiration. The trigger was released when the inspiration flow reached 40 ml/s. Because the time interval of occlusion of the magnetic valve (2w–20 K Yongchuang Co Ltd, China) lasts approximately 160 ms, a delayed magnetic stimulation of 200 ms was delivered to the phrenic nerve.

**Experiment 2:** To assess diaphragmatic strength during an inspiratory pressure trigger of −5 cmH₂O, the magnetic valve was closed at the beginning of inspiration. Magnetic stimulation (100%) was released when pressure in the mouth reached −5 cmH₂O. Furthermore, the trigger was accepted when the inspiratory flow was higher than 10 ml/s to avoid development of static pressure alone (Topeli et al., 1999).

**Experiment 3:** To assess diaphragmatic strength in the current gold standard, no trigger device (TwPn) was used at relaxed FRC.
correlation was used for correlation analysis. Data were analysed using an F-test when more than two groups were compared. Linear regression analysis and Bland and Altman plots were used when appropriate. A P value of less than 0.05 was considered to be significant.

4. Results

Demographic data and parameters of lung function are shown in Table 1.

4.1. Experiment 1

The $\text{Twpmo}_{\text{InP}}$ and $\text{Twpes}_{\text{InP}}$ were correlated with a regression line of $\text{Twpes}_{\text{InP}} = 0.855 \times \text{Twpmo}_{\text{InP}} - 1.061$ ($r = 0.832; P < 0.0001$) (Fig. 4). The correlation between $\text{Twpmo}_{\text{InP}}$ and $\text{Twpdi}_{\text{InP}}$ was statistically significant ($r = 0.502; P < 0.0001$). The limits of agreement between $\text{Twpmo}_{\text{InP}}$ and $\text{Twpes}_{\text{InP}}$ ranged from $-2.05$ to $2.41 \text{cmH}_2\text{O}$ with the mean of the difference being $0.18 \text{cmH}_2\text{O}$. In aggregate, 37% of twitch values failed to achieve the triggering criteria.

4.2. Experiment 2

The $\text{Twpmo}_{\text{InP}}$ and $\text{Twpes}_{\text{InP}}$ were strongly correlated ($r = 0.900; P < 0.0001$) with a regression line of $\text{Twpes}_{\text{InP}} = -0.262 \times \text{Twpmo}_{\text{InP}} + 1.009$ (Fig. 4). The correlation of $\text{Twpmo}_{\text{InP}}$ and $\text{Twpdi}_{\text{InP}}$ was acceptable ($r = 0.605; P < 0.0001$). The correlation of $\text{Twpmo}_{\text{InP}}$ and $\text{Twpdi}_{\text{InP}}$ is shown in Fig. 5. The mean of the difference between $\text{Twpmo}_{\text{InP}}$ and $\text{Twpes}_{\text{InP}}$ was $0.32 \text{cmH}_2\text{O}$ and the limits of agreement were from $-1.69$ to $2.32 \text{cmH}_2\text{O}$. Approximately 24% of events did not meet the established criteria.

4.3. Experiment 3

There was no correlation between $\text{Twpmo}_{\text{NT}}$ and $\text{Twpes}_{\text{NT}}$ or $\text{Twpdi}_{\text{NT}}$ ($P > 0.53$ and $P > 0.97$) (Fig. 6).

For each Experiment, the mean and standard deviation values of $\text{Twpmo}$, $\text{Twpes}$, $\text{Twpdi}$, $\text{P}_{\text{Trig}}$, $\text{PTP}_{\text{Trig}}$, $\text{PTP}_{\text{Shut}}$, $	ext{Tshut}$ and $\text{Vtrig}$ are shown in Table 2.

There was no difference between $\text{Twpes}$ and $\text{Twpdi}$ in Experiments 1 and 3 ($P = 0.179$). There was also no difference between $\text{Twpmo}$ and $\text{Twpdi}$ in Experiments 2 and 3 ($P = 0.253$). However, the $\text{Twpmo}$ obtained using a trigger (Experiments 1 and 2) was lower, and the $\text{Twpes}$ was larger than that obtained without the use of a trigger (Experiment 3) (all values of $P < 0.0001$). In none of the three experiments was there a correlation between $\text{Twpmo}$ and $\text{Twpdi}$ ($P > 0.1$).

The variances of $\text{PTP}_{\text{Shut-trig}}$ and $\text{Tshut}$ obtained using a trigger were large in Experiments 1 and 2 because the subjects reached the triggering threshold at varying rates and degrees (Windisch et al., 2005). However, this would not have influenced the variance in $\text{Twpmo}$, $\text{Twpes}$ and $\text{Twpdi}$ because there was no significant difference between $\text{Twpmo}$ ($P = 0.84$), $\text{Twpes}$ ($P = 0.59$) and $\text{Twpdi}$ ($P = 0.75$) when these were compared between the Experiments using a trigger system (Experiments 1 and 2).

5. Discussion

Although measurements of $\text{Twpes}$ and $\text{Twpdi}$ that require insertion of two balloon catheters can precisely assess diaphragm function (Anon., 2002), this invasive method may cause discomfort for the subjects and may have limited clinical applications. Previous studies (Kabitz et al., 2007a,b; Windisch et al., 2005) show that $\text{Twpmo}$ can reliably predict $\text{Twpes}$ achieved by a fully automatic trigger manoeuvre in healthy subjects and in a subgroup...
of patients (only 3 samples). Ours is the first study to evaluate TwPmo compared with TwPes TwPga and TwPdi using an automatic inspiratory trigger manoeuvre and to find the most useful trigger technique in a representative sample of COPD patients. We have found that TwPmo could most reliably predict TwPes using an inspiratory pressure trigger (Experiment 2).

Previous studies have clearly shown that TwPmo can be used to predict TwPes attributable to complete glottic opening under controlled trigger conditions in healthy subjects, (Kabitz et al., 2007a,b; Laghi and Tobin, 1997; Topeli et al., 1999; Windisch et al., 2005). Furthermore, TwPmo could also reliably predict TwPes in patients with COPD when mouth twitches influenced by glottic closure were excluded (Similowski et al., 1993). In this study, TwPes and TwPdi generated using a trigger were not different from those generated without a trigger. Therefore, we clearly show that this trigger system should not influence TwPes and TwPdi values.

There was no correlation between TwPmo and TwPes or TwPdi using no trigger at FRC (Experiment 3), which we attribute to the occurrence of glottic closure (Anon., 2002; Hamnegaard et al., 1995; Similowski et al., 1993; Windisch et al., 2005).

During inspiratory flow when a pressure trigger was used (Experiments 1 and 2), Vtrig was approximately 26 and 30 ml, respectively, reflecting a small change in lung volume (<1.1% of FVC). In support of our findings, the values of TwPes and TwPdi were not different when comparing Experiments 1 and 2 to Experiment 3. These findings suggest that triggered (Experiment 1 and 2) TwPmo was generated very close to FRC.

TwPmo and TwPga were not correlated in any of our Experiments because of the influence of stomach contents and thoracoabdominal configuration (Chen et al., 2000; Man et al., 2004).

Fig. 4. Correlation between twitch mouth (TwPmo) and oesophageal pressure (TwPes) during phrenic nerve stimulation in Experiments 1–3 (n = 15). Experiment 1 inspiratory flow trigger; Experiment 2 inspiratory pressure trigger; Experiment 3 No trigger at FRC. The regression line is also given.

Fig. 5. Correlation between twitch mouth (TwPmo) and transdiaphragmatic pressure (TwPdi) during phrenic nerve stimulation in Experiment 2. The regression line was also shown.
However, these factors most likely do not affect the reliability of TwPmo and TwPes (Chen et al., 2000; Man et al., 2004). The measurement of TwPmo using an automatic trigger manoeuvre could well make up the shortcomings of the traditional test technique (no trigger at relaxed FRC) such as the glottic closure and changes the meaning of results of an inspiratory or an expiratory effort at FRC (Kabitz et al., 2007a,b; Windisch et al., 2005). However, the challenges of equilibrating pressure in TwPmo during a very rapidly changing pressure response such as a diaphragm twitch still exist, particularly in the context of airway obstruction (Anon., 2002; Similowski et al., 1993). Therefore, in the present study, the correlation between TwPmo and TwPes was lower in COPD patients than in normal subjects in previous studies (Hamnegaard et al., 1995; Kabitz et al., 2007a,b; Laghi and Tobin, 1997). Whatever the underlying mechanism, the significant correlation between TwPmo and TwPes by controlled and automated trigger techniques may have useful implications for assessing diaphragm strength in COPD patients. Therefore, the measuring of TwPmo using an inspiratory trigger is a convenient, non-invasive and reliable method to assess diaphragm strength in healthy subjects and patients with COPD.

However, the failure to reach the trigger threshold was approximately 37% in Experiment 1 and 24% in Experiment 2, respectively, and we suspect that the reject rate would increase markedly if a greater number of twitches were recorded. Therefore, it was essential to indicate that the values of the trigger threshold were appropriate for healthy subjects (Kabitz et al., 2007a,b; Windisch et al., 2005) but not for patients with COPD. That is to say, sometimes it is difficult to utilise a trigger technique with COPD patients. However, in this study, we could not achieve the complete closing time of approximately 160 ms required for lowering the trigger threshold. In further studies, differing trigger threshold levels with better controlled techniques should be included to find the best trigger criteria for subjects with or without lung diseases.

In conclusion, TwPmo could be reliably predicted by TwPmo when using an automatic trigger system in patients with COPD. Furthermore, this study suggests that a fully automatic triggering technique with a trigger delay optimised for use in patients with obstructive lung disease, may provide a reliable method to assess the strength of inspiratory muscles.

### References


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Table 2

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<tr>
<th></th>
<th>TwPmo(cmH2O)</th>
<th>TwPes(cmH2O)</th>
<th>TwPga(cmH2O)</th>
<th>TwPdi(cmH2O)</th>
<th>PTrig(cmH2O)</th>
<th>FTrig(ml/s)</th>
<th>PTPshut-trig(cmH2O’s)’s</th>
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![Fig. 6. Bland–Altman plot of the difference between TwPmo and TwPes and the mean values, with the limits of agreement in Experiments 1 and 2.](image-url)


