Abdominal muscle and quadriceps strength in chronic obstructive pulmonary disease

by

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ABSTRACT

Background: Quadriceps muscle weakness is common in chronic obstructive pulmonary disease (COPD), but is not observed in a small hand muscle (adductor pollicis). Although this could be explained by reduced activity in the quadriceps, the observation could also be explained by anatomic location of the muscle or fibre type composition. However the abdominal muscles are of a similar anatomic and fibre type distribution to the quadriceps, though they remain active in COPD. Cough gastric pressure is a recently described technique that more accurately assesses abdominal muscle (and hence expiratory muscle) strength than traditional techniques.

Objective: To test the hypothesis that more severe weakness exists in the quadriceps than the abdominal muscles in patients with COPD compared with healthy elderly controls.

Methods: Maximum cough gastric pressure and quadriceps isometric strength were measured in 43 patients with stable COPD and 25 healthy elderly volunteers, matched for anthropometric variables.

Results: Despite a significant reduction in mean quadriceps strength (29.9 versus 41.2 kg; 95% CI -17.9 to -4.6; p=0.001), cough gastric pressure was preserved in patients with COPD (227.3 versus 204.8 cmH₂O; 95% CI -5.4 to 50.6; p=0.11).

Conclusions: Abdominal muscle strength is preserved in stable COPD outpatients in the presence of quadriceps weakness. This suggests that anatomic location and fibre-type cannot explain quadriceps weakness in COPD. By inference we conclude that disuse and consequent de-conditioning are important factors in the development of quadriceps muscle weakness in COPD patients, or that activity protects the abdominal muscles from possible systemic myopathic processes.

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INTRODUCTION

Although skeletal muscle dysfunction is well recognized in chronic obstructive pulmonary disease (COPD) \(^1\), most research has concentrated on the quadriceps because it is a primary locomotor muscle and readily accessible. Controversy remains as to whether the mechanisms of skeletal muscle dysfunction are local, systemic or both. A predominantly systemic process would result in widely distributed loss of muscle function, whereas chronic inactivity, as a result of breathlessness, and subsequent de-conditioning would result in dysfunction predominantly in the locomotor muscles (e.g. quadriceps). We have previously demonstrated that in stable, non-weight losing patients with COPD, adductor pollicis strength is preserved despite significant weakness in the quadriceps \(^2\). Although this would suggest that inactivity (and subsequent disuse atrophy) is the dominant aetiology, it is possible that a systemic process may have a predilection for certain muscle fibre types. Whereas the adductor pollicis is composed principally of type I fibres, the quadriceps consists of 43% type I fibres and 57% type II fibres \(^3\). Similarly the adductor pollicis is located distally whilst the quadriceps is a proximal muscle. Some myopathic processes, for example steroid myopathy, are known to preferentially affect proximal musculature \(^4\).

The expiratory muscles, of which the most important are those of the anterior abdominal wall, are proximally located and have a similar muscle fibre type distribution to the quadriceps \(^3\). However, whereas the quadriceps muscle is chronically underused, the abdominal muscles contract during coughing (a frequent symptom in COPD), and are recruited during exercise \(^5\), and may often be active at rest \(^6\). Hence, evidence of abdominal muscle weakness in conjunction with quadriceps weakness would support the hypothesis that systemic factors are important in causing weakness, whereas preserved abdominal muscle
strength would by inference support the notion that reduced use is a necessary condition for the development of quadriceps weakness

Several previous studies have measured expiratory muscle strength in COPD, but there is no consensus over whether weakness is present, and few have simultaneously measured quadriceps strength. The differences between studies may reflect patient selection and the matching of appropriate control groups. The choice of test to assess expiratory muscle strength and familiarity of subjects with the test may also be relevant.

In past studies maximum expiratory mouth pressure (PEMAX) has been used to assess expiratory muscle strength. This well-established, non-invasive and reproducible manoeuvre excludes expiratory muscle weakness when normal values are obtained, but care is needed when interpreting low values. In the evaluation of expiratory muscle weakness, PEmax has a positive predictive value of only 58%\(^\text{18}\). The recently introduced test, cough gastric pressure, is a more natural manoeuvre, easier for patients to perform, and has a higher positive predictive value (94%) in detecting abdominal (and hence expiratory) muscle weakness\(^\text{18}\).

To clarify whether expiratory muscle strength is preserved or reduced in the presence of quadriceps weakness, we measured cough gastric pressure and quadriceps maximum voluntary contraction force in a group of COPD patients and age-matched healthy controls. Data obtained from some of the healthy elderly controls contributed to the normal values of cough gastric pressure reported in a previous study\(^\text{18}\), and data obtained from some of the COPD patients contributed to baseline measurements reported in previous studies\(^\text{19,20}\).
METHODS

Forty-three stable patients with COPD referred to a pulmonary rehabilitation programme, with no infective exacerbation in the preceding four weeks, were recruited. All had been cigarette smokers for at least 20 pack-years with a clinical course consistent with the British Thoracic Society criteria for diagnosis \(^{21}\), and complained of significant functional limitation due to dyspnoea. Twenty-five healthy active elderly volunteers, with no history of respiratory disease, were also recruited. Study participants were free from co-morbidities that could limit mobility or reduce muscle strength. The local research ethics committee of King’s College Hospital approved the study, and all participants gave informed consent.

In each participant, expiratory muscle strength was assessed by recording the cough gastric pressure (Cough Pga). Quadriceps muscle strength was measured by recording the isometric quadriceps maximum voluntary contraction of the dominant leg. Fat free mass (FFM) was estimated using bioelectrical impedance analysis, and disease- and age- specific regression equations \(^{22,23}\). FFM was normalized to height by calculating the fat free mass index (FFMI = FFM (kg) / Height (m\(^2\)). Spirometry, and lung volumes obtained from body plethysmography were measured in the COPD patients.

Cough Pga was measured, as previously described \(^{18}\), using a balloon catheter passed per nasally, following local anaesthesia of the nasal mucosa and pharynx. The tip of the balloon was placed at 70cm from the nostril, and correct placement in the stomach was confirmed by a positive deflection during a sniff manoeuvre. Seated subjects were asked to perform maximal single coughs at 30-second intervals until no further increase of cough Pga was observed. The investigator gave verbal encouragement throughout the study, and cough Pga manoeuvres were displayed on a computer screen to provide visual feedback for the subject.
Isometric quadriceps maximum voluntary contraction (QMVC) was studied using the technique previously described by Polkey and colleagues \(^{24}\) with a specially designed chair from which the back was removed and laid flat. All subjects were studied supine or semi-supine (based on subject comfort), keeping the knee flexed at 90° over the end of the chair. An inextensible strap was placed around the ankle and connected to a strain gauge, mounted to the back of the chair so that the strap ran perpendicular to the ankle and gauge. A restraining belt was used to fix the pelvis and lower trunk to minimize unwanted movement. Subjects were asked to extend their knee maximally against the strap. Consecutive efforts were made at 30-second intervals, with visual feedback and verbal encouragement from the investigator, until no further increase in QMVC occurred.

Statistical analysis was performed using SPSS 11.5 for Windows. As data were normally distributed, differences between the COPD and control groups were compared using unpaired t-tests.
RESULTS

Anthropometric data for the COPD patients (n=43) and healthy elderly control subjects (n=25) are summarized in Table 1. The two groups were well matched for gender, height, weight, BMI, FFM and FFMI. 25 of the COPD patients had received oral prednisolone in the preceding year with a mean daily dose of 3.26mg (4 patients were on maintenance oral corticosteroids, and 21 patients had received corticosteroid-burst regimens for an infective exacerbation). 7 patients were receiving domiciliary long term oxygen therapy. Nutritional depletion was considered to be present if FFMI <15 for females or <16 for males. Based on these criteria, 15 of the 43 patients were nutritionally depleted.

Figure 1 demonstrates individual data and group means for Cough Pga and QMVC. Mean [SD] QMVC was reduced in the COPD patients (QMVC: 29.9 [13.2] versus 41.2 (13.3) kg; 95% CI -17.9 to -4.6; p = 0.001). When stratified for gender, QMVC remained significantly reduced in both male and female COPD patients compared with their healthy counterparts (Female: 23.2 [10.2] versus 29.6 [6.0] kg, p = 0.03; Male: 32.8 [13.4] versus 47.7 [11.8] kg, p = 0.0006). There was a trend for cough Pga to be increased in the COPD group, although this did not reach statistical significance (227.3 [54.2] cmH2O versus 204.8 [58.3] cmH2O; 95% CI -5.4 to 50.6; p = 0.11). This was not affected by stratification for gender (Female: 197.5 [50.4] versus 167.0 [44.3] kg, p = 0.16; Male: 240.3 [51.2] versus 226.0 [55.4] kg, p = 0.39).

There was no linear relationship between FFMI and either QMVC ($r^2 < 0.01; p=0.53$) or Cough Pga ($r^2 = 0.02; p=0.41$) in the COPD patients. No significant relationship was found between % predicted total lung capacity and Cough Pga ($r^2 < 0.001; p=0.85$).
DISCUSSION

The principal finding of this study is that cough gastric pressure is normal in COPD patients compared with healthy elderly controls matched for age and fat free mass, despite substantial reduction in quadriceps strength. These data support the hypothesis that a systemic process alone is not responsible for quadriceps weakness in non-weight losing patients with COPD. Before enlarging on these points, it is appropriate to discuss the methodology.

Cough Gastric Pressure as an Index of Expiratory Muscle Strength

In this study, cough gastric pressure (cough Pga) was used as an index of expiratory muscle strength rather than the more traditional maximum expiratory mouth pressure (PE\text{MAX}). PE\text{MAX} is the only commonly used test for assessment of expiratory muscle strength, and has many advantages. It is non-invasive, reproducible and normal values are well described. When high values of PE\text{MAX} are obtained, expiratory muscle weakness can be excluded \cite{18}. However care is required in interpreting low values, as many subjects may under-perform this manoeuvre. In a recent study of 293 patients referred for respiratory muscle testing, over 40% of patients with a low PE\text{MAX} had a normal cough Pga \cite{18} demonstrating that PE\text{MAX} commonly underestimates true expiratory muscle strength. Measurement of cough Pga offers an alternative to PE\text{MAX} as the principal expiratory muscles, the abdominal muscles, are strongly recruited in cough. Whilst not a non-volitional technique, an advantage is that as a natural dynamic manoeuvre, cough is technically easier to perform than PE\text{MAX}, whilst retaining similar between occasion reproducibility \cite{18}. The obvious disadvantage of the technique is that it is invasive, requiring the placement of balloon catheter. However, in this clinical research study, all participants tolerated the procedure well, and there were no adverse events. The expiratory muscles, like the quadriceps, can be assessed non-volitionally.
by magnetic stimulation of the lower thoracic nerve roots. However, this technique, unlike stimulation of the femoral nerve or phrenic nerves, is not supramaximal, and hence less useful when precisely quantifying expiratory muscle strength.

A possible confounding factor is increased lung volume, and the effect on the length-tension relationship of the abdominal muscles. Cough Pga were performed at or near total lung capacity (TLC), and one would expect the COPD patients, with their increased TLC, to produce higher gastric pressures during the manoeuvres. However previous studies from our laboratory have shown that lung volume exerts only a relatively modest effect upon Pga. Using paired magnetic stimuli of the thoracic nerve roots, Pga only increases about 17% from functional residual capacity to TLC. In this study, no significant relationship was found between TLC and cough Pga.

**Patient Selection**

The patients recruited for this study were sedentary, clinically stable, moderate to severe COPD patients as commonly seen in respiratory outpatient clinics. Mean FEV1 was 35% predicted (range 12 – 58%), and all had been referred to a pulmonary rehabilitation programme. Although the BMI, FFM and FFMI of our patients were not significantly lower than our control group, 35% of our patients met standard criteria for nutritional depletion, supporting previous observations of body composition in stable COPD patients. A limitation of our study is that we did not make formal objective measurements of daily activity levels. However, we believe it is reasonable to assume our patients were more sedentary than their healthy counterparts. All patients complained of exertional dyspnoea and reduced exercise tolerance (hence their referral to pulmonary rehabilitation), while all the healthy elderly controls were either in part or full time employment or led active social lives.
Previous Studies of Expiratory Muscle Strength in COPD

Several previous studies have measured expiratory muscle strength in COPD \(^{7-17}\), but no consensus has been reached over whether weakness is present. Some investigators have described significant expiratory muscle weakness \(^{8-10,13-16}\), whereas others have shown normal strength \(^{11,17}\) or indeed, increased strength \(^{7}\). These differences may be due to patient selection, the absence of appropriate healthy control groups or differences in nutritional status. An alternative explanation may, in part, be the choice of PEMAX as the test of expiratory muscle strength, and this study is novel in that it is the first to measure cough Pga in both COPD patients and healthy controls. Only one other study has used the cough manoeuvre to measure expiratory muscle strength in COPD. In 1968, Byrd and Hyatt measured cough oesophageal pressures in 31 patients with chronic obstructive lung disease \(^{7}\), and demonstrated, as in our study, higher cough pressures than corresponding mouth static pressures, although no measurements in controls were made, nor measurements of quadriceps strength in their patients.

Few studies have directly compared the expiratory muscles with the quadriceps muscle in COPD patients. Gosselink and colleagues measured respiratory muscle, handgrip and quadriceps strength as well as exercise capacity in 41 patients with COPD, demonstrating similar reductions in PEMAX and isometric quadriceps force \(^{9}\). However fat free mass measurements were not made and the muscle strength data were compared with historical normal values. The same group later quantified respiratory and peripheral muscle strength in 40 COPD patients and 22 healthy elderly controls \(^{10}\). Although they concluded that muscle weakness did not affect all muscles to a similar extent, the reduction in strength in the expiratory muscles was similar to the reduction seen in knee extension. However their
patients were not matched to the controls in terms of weight or body mass index, and hence the influence of nutritional status and fat free mass as confounding factors on expiratory muscle strength could not be excluded. In contrast, the patients in the current study had normal cough Pga values, but significantly reduced quadriceps maximum voluntary contraction force compared with controls matched for fat free mass.

**Significance of Findings**

In the present study, it was observed that cough Pga in the COPD group was preserved compared with pressures obtained from a group of healthy active elderly subjects matched for age, gender, and anthropometric values despite a significant reduction in quadriceps strength. This supports the hypothesis that local, rather than systemic, factors have a principal role in initiating muscle dysfunction. An obvious local factor is inactivity and subsequent muscle de-conditioning due to the sedentary lifestyles of patients locked in a downward spiral of breathlessness. Dysfunction would be expected to be greatest in the muscles that are least used (e.g. the locomotor muscles such as the quadriceps). Unlike the quadriceps muscle, the abdominal muscles are not chronically underused, and are frequently recruited during rest and exercise.

This hypothesis is supported by previous studies showing the unequal distribution of muscle weakness in COPD, in particular the strength of the upper extremity muscles being relatively preserved compared with those of the lower extremity. Using the non-volitional technique of supramaximal magnetic nerve stimulation to exclude the confounding effects of patient motivation, we have previously demonstrated that both twitch adductor pollicis tension and twitch transdiaphragmatic pressures are normal in COPD patients compared with healthy elderly controls, despite a 30% reduction in twitch quadriceps force. One potential criticism
of that study is that the adductor pollicis and quadriceps muscles vary in their fibre type distribution: the adductor pollicis is composed principally of type I fibres (80%), whereas the quadriceps consists of 43% type I fibres and 57% type II fibres. The present study largely addresses this criticism as the abdominal muscles have a similar fibre type distribution to the quadriceps, comprising 46% type I fibres and 54% type II fibres.

Although it has been postulated that inactivity may play a major factor in skeletal muscle dysfunction in COPD patients, there is some evidence that this may not explain all observed abnormalities. Maltais and colleagues have demonstrated modifications in the myosin heavy chain profile in the vastus lateralis of patients with COPD compared with healthy subjects despite only modest differences in physical activity. Studies on emphysematous hamsters have shown reduced oxidative capacity of their hind-limb muscles despite the absence of a reduction in their level of activity compared with control animals. Other local factors, such as local exercise induced oxidative stress, may also be possibly involved in initiating muscle dysfunction.

Controversy remains over whether a systemic inflammatory response is a major aetiological factor in the skeletal muscle dysfunction commonly seen in COPD. Indirect evidence supporting this hypothesis comes from the observation that TNFα levels are elevated in patients who fail to gain weight during a rehabilitation and re-feeding program, while IL-8 levels are inversely related to quadriceps strength in patients admitted with an exacerbation of COPD. Elevated IL-6 levels are also associated with radiological evidence of quadriceps wasting in COPD, and with reduced lean body mass. Levels of inflammatory cytokines were not measured in this study, and hence a systemic inflammatory process cannot be excluded. However the results from this study suggest that activity protects the muscles
against any putative systemic process. Even in situations of increased systemic inflammation, such as soon after the onset of an acute exacerbation, increased activity in the form of a pulmonary rehabilitation programme can lead to highly significant improvements in exercise capacity and health status. Available data suggest that any future therapeutic interventions targeted at the inflammatory process will need to be accompanied by exercise training.

In summary, cough gastric pressures are normal in stable COPD patients despite the presence of significant weakness of the quadriceps. This observation supports the hypothesis that disuse is necessary for the development of skeletal muscle weakness in COPD patients.
References


Table Legend

**Table 1:** Anthropometric and lung function measurements in study participants. Data expressed as mean (standard deviation) or mean difference (95% confidence interval). Unpaired t-tests used throughout except * Chi-square test. M = Male, F = Female. BMI = Body Mass Index, FFM = Fat free mass, FFMI = Fat free mass index, FEV1% = Forced Expiratory Volume in one second per cent predicted. TLC = Total Lung Capacity.

Figure Legend

**Figure 1:** Scatterplots showing individual data and group means of expiratory muscle and quadriceps strength in healthy elderly controls and COPD (chronic obstructive pulmonary disease) patients. Cough Pga = Cough Gastric Pressure, Quadriceps MVC = Isometric quadriceps maximum voluntary contraction.
<table>
<thead>
<tr>
<th></th>
<th>Healthy Elderly</th>
<th>COPD</th>
<th>Mean Difference (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (M/F)</td>
<td>16/9</td>
<td>30/13</td>
<td>-</td>
<td>0.62*</td>
</tr>
<tr>
<td>Age (years)</td>
<td>67.6 (14.1)</td>
<td>64.6 (10.1)</td>
<td>-3.0 (-8.9, 2.9)</td>
<td>0.31</td>
</tr>
<tr>
<td>Height (meters)</td>
<td>1.69 (0.10)</td>
<td>1.68 (0.08)</td>
<td>-0.01 (-0.06, 0.03)</td>
<td>0.58</td>
</tr>
<tr>
<td>Weight (kilograms)</td>
<td>74.3 (13.1)</td>
<td>69.0 (16.1)</td>
<td>-5.3 (-12.9, 2.2)</td>
<td>0.16</td>
</tr>
<tr>
<td>BMI (kg / m²)</td>
<td>25.8 (3.0)</td>
<td>24.5 (5.8)</td>
<td>-1.3 (-3.8, 1.2)</td>
<td>0.29</td>
</tr>
<tr>
<td>FFM (kg)</td>
<td>50.3 (12.6)</td>
<td>46.7 (7.0)</td>
<td>-3.6 (-8.4, 1.1)</td>
<td>0.13</td>
</tr>
<tr>
<td>FFMI (kg/m²)</td>
<td>17.3 (2.6)</td>
<td>16.5 (2.2)</td>
<td>-0.8 (-1.9, 0.4)</td>
<td>0.20</td>
</tr>
<tr>
<td>FEV1% Predicted</td>
<td>-</td>
<td>35.4 (18.2)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>TLC % Predicted</td>
<td>-</td>
<td>125 (20)</td>
<td>-</td>
<td>-</td>
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</table>
FIGURE 1
Competing Interest Statement

All authors declare that the answer to the questions on your competing interest form (http://bmj.com/cgi/content/full/317/7154/291/DC1) are all No and therefore have nothing to declare.

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