

Available online at [www.sciencedirect.com](http://www.sciencedirect.com)

SciVerse ScienceDirect

journal homepage: [www.elsevier.com/locate/rmed](http://www.elsevier.com/locate/rmed)

# Pain in people with chronic obstructive pulmonary disease (COPD)

Bahareh HajGhanbari <sup>a,\*</sup>, Liisa Holsti <sup>b</sup>, Jeremy D. Road <sup>c</sup>, W. Darlene Reid <sup>a</sup>

<sup>a</sup> Department of Physical Therapy, Muscle Biophysics Laboratory, Vancouver Coastal Health Research Institute, University of British Columbia, Canada V6T 1Z3

<sup>b</sup> Department of Occupational Science and Occupational Therapy, University of British Columbia, Child and Family Research Institute, Vancouver, BC, Canada

<sup>c</sup> Respiratory Division, Department of Medicine, Vancouver General Hospital, University of British Columbia, Canada

Received 6 December 2011; accepted 7 March 2012

Available online 22 April 2012

## KEYWORDS

Pain;  
Chronic obstructive  
pulmonary disease;  
Physical exertion;  
Exercise

## Summary

**Introduction:** The prevalence and characteristics of pain are not known in COPD patients. The purposes of this study were to determine if pain is more common in COPD patients than in healthy people and if it was related to self-reported physical activity, health related quality of life (HRQoL) and comorbidities.

**Methods:** Participants returned a mailed survey package that contained: 1) McGill Pain Questionnaire (MPQ) and Brief Pain Inventory (BPI) to evaluate pain severity and how pain interferes with activities; 2) Tampa Scale for Kinesiophobia (TSK) to evaluate fear of movement related to pain; 3) Short Form-36 (SF-36), to measure HRQoL; 4) Community Health Activities Model Program for Seniors (CHAMPS) to evaluate physical activity; 5) a form to list medications and comorbidities.

**Results:** Forty-seven COPD patients and 47 age- and gender-matched healthy people responded. People with COPD demonstrated more pain (MPQ and BPI,  $p = 0.000$ ), a greater pain-related interference in their lives (BPI,  $p = 0.000$ ), a higher pain-related fear of movement, and lower frequency and energy expenditure of physical activities (CHAMPS,  $p = 0.000$ ) than healthy people (TSK,  $p < 0.001$ ). Pain severity (MPQ and BPI) was indirectly correlated to the Physical Component Score of the SF-36. COPD patients identified pain in the neck and trunk 3.1 times more often than healthy people. The number of comorbidities was the most consistent independent correlate of pain in COPD patients.

**Conclusions:** COPD patients demonstrate more pain which interferes with activities more so than healthy people of similar age. Pain is also negatively associated with HRQoL in COPD.

© 2012 Elsevier Ltd. All rights reserved.

\* Corresponding author. Department of Physical Therapy, University of British Columbia, 600, 828 West 10th Ave, Vancouver, BC, Canada V5Z 1M9. Tel.: +1 604 875 4111x62574, +604 771 2273 (mobile); fax: +1 604 875 4376.

E-mail address: [baharehg@interchange.ubc.ca](mailto:baharehg@interchange.ubc.ca) (B. HajGhanbari).

## Introduction

COPD is a major health burden worldwide and is estimated to be the third leading cause of death by 2020.<sup>1</sup> The recent guidelines note the multi-systemic effects of COPD including its impact on peripheral muscle dysfunction, right heart failure, malnutrition, depression, and decreased exercise tolerance.<sup>2</sup> These guidelines and other statements provide solid evidence to support the therapeutic benefit of exercise and maintaining an active lifestyle.<sup>1</sup> However, exercise prescription and lifelong adherence to physical activity for people with COPD is limited. Reasons for the lack of adherence to physical activity programs require further exploration.

Most commonly, lower extremity (LE) fatigue alone or in combination with dyspnea has been reported to be major limiting symptoms during exercise tests and is considered to limit physical activity of COPD patients.<sup>3</sup> Recent reports suggest that pain may be of equal or greater concern. Pain was a significant contributor to reduced health related quality of life as demonstrated by the Health Utility Index and SF-36 evaluations of people with severe emphysema who underwent lung volume reduction surgery.<sup>4</sup> It has also been reported in COPD patients toward the end of life<sup>5,6</sup> in stable COPD patients who experienced pain,<sup>6,7</sup> and as components of quality of life.<sup>8</sup> However, the characteristics of pain such as fear of movement due to pain, and its relationship with comorbidities and physical activity has not been examined.

In addition to an increasingly sedentary lifestyle, several factors related to the manifestations of the disease may contribute to pain in people with COPD. Firstly, the activation of cytokines has a major role in the development of inflammatory pain.<sup>9</sup> It is therefore tenable that the systemic inflammatory process contributes to the generation of chronic and neuropathic pain in people with COPD.<sup>10</sup> Secondly, the hyper-expanded and relatively rigid chest wall<sup>11</sup> could position thoracic articulations in a hyper extended position and decrease their range of motion. Abnormal joint position and limited range of motion contribute to pain in several joint pathologies<sup>12</sup> and similarly, may contribute to thoracic pain experienced by people with COPD. Lastly, inactivity may aggravate common age-related comorbidities such as osteoarthritis,<sup>13</sup> low back pain,<sup>12</sup> and osteoporosis.<sup>14</sup>

Reductions across multiple dimensions in health related quality of life (HRQoL), including depression, anxiety, and mental health, and activity limitation have been reported in nonmalignant pain patients.<sup>15</sup> Therefore, it is highly probable that people with COPD who experience substantial pain will demonstrate similar consequences. To date, the severity of pain in people with COPD and its association with physical activity and quality of life have not been studied extensively. The purpose of this study was to determine if pain severity and interference with activities are more common in COPD patients than in healthy people and if pain is related to self-reported physical activity and health related quality of life (HRQoL). Another aim was to determine independent correlates of pain in COPD patients.

## Methods and materials

Approval for the study was obtained from the Clinical Research Ethics Board of the University of British Columbia.

## Subjects

Sedentary healthy people, and people with moderate to severe COPD ( $FEV_1 < 80\%$  predicted,  $FEV_1/FVC < 0.7$ ),<sup>2</sup> over 50 years of age, matched for age and gender participated in a cross-sectional survey study. Exclusion criteria were: (1) comorbidities that interfered with independent ambulation; (2) lack of English fluency or cognitive impairment that interfered with the ability to provide informed consent or to complete the questionnaires. People with COPD were also excluded if they had an acute exacerbation within the last three months. Sedentary healthy people were excluded if they had self-reported respiratory conditions, such as bronchitis, emphysema, moderate to severe asthma or if they met exclusion criteria (1) or (2) stated above. COPD patients were recruited from the caseload of respirologists and pulmonary rehabilitation programs at local hospitals. Healthy people were recruited from the posters at local community centers and newspaper advertisements.

## Outcomes and measurements

Participants were initially screened using a standardized questionnaire via telephone. Chart reviews were performed on all COPD participants in order to confirm the diagnosis of COPD. After obtaining informed consent, standard survey methods were employed by mailing a package of forms and questionnaires to participants.<sup>16</sup> The package included: instructions, a form to record medications and comorbidities, the Medical Outcomes Study Short Form-36 (SF-36), the short form of the McGill Pain Questionnaire (MPQ), the short form of the Brief Pain Inventory (BPI), the Community Health Activities Model Program for Seniors (CHAMPS), and the modified Tampa Scale for Kinesiophobia (TSK). One week later, all subjects were contacted by telephone to address any questions. Subjects were asked to return packages in a self-addressed stamped envelope by mail.

## Pain characteristics

The MPQ questions pain characteristics over the past week and consists of: 1) 15 *sensory* related items; 2) 4 *affective* related items; 3) the visual analog scale to provide the intensity pain score. A fourth component, evaluates Present Pain Intensity (PPI).<sup>17</sup>

The BPI measures the *intensity* of pain (sensory dimension), uses body diagrams to indicate *pain location*, and evaluates *interference* of pain in the patient's life (including general activity, mood, sleep, enjoyment of life, and relationship with others). It also asks the patient about pain relief, pain quality, and pain medications. Because of these different attributes, the BPI and MPQ were used to provide a more comprehensive description of the pain experienced by individuals.<sup>18</sup> Both MPQ<sup>19,20</sup> and BPI<sup>21,22</sup> have been established as valid and reliable tools for assessing pain severity and interference.

The TSK evaluates the *pain-related fear of (re)injury* due to movement and activities. The TSK consists of 17 questions which identify fear of injury/re-injury due to activities with item scores ranging from 1 (strongly disagree) to 4 (strongly agree) which are tallied to

a potential total score ranging between 17 to 68. The modified version of TSK was used (without reversed key items) as it has been found to improve the internal consistency.<sup>23</sup>

## Physical activity

The Community Health Activities Model Program for Seniors (CHAMPS) questionnaire includes 41 questions that ask the participants to rate the length of time spent on a variety of activities in a typical week during the past month. It includes physical and leisure activities that vary in intensity including household chores and several non-physical activities (such as reading, card games, and social participation). This provides a broad selection of activities such that respondents tend to minimize overestimation of physical activities. The CHAMPS questionnaire provides measures for frequencies and estimated energy expenditure for moderate and high intensity activities.<sup>24</sup>

## Health related quality of life

The SF-36 contains 36 items distributed across eight domains (physical-functioning, role-physical, bodily pain, general health, vitality, social-functioning, role-emotional, and general health perception), and has two component scales (physical and mental).<sup>25</sup>

The data related to medications and comorbidities were obtained using self-report questionnaires. In addition, patients' medical charts and hospital databases were reviewed to verify the medications and comorbidities. Medications were coded according to the Canadian Medical Association.<sup>26</sup>

## Statistical analysis

Precise sample size calculation was not possible as similar studies have not been performed. However, comparing a group of healthy subjects with a patient group, we expected to have a medium effect size (0.5). Therefore, a sample size of  $\geq 65$  in each group would provide a power for a *t*-test with an  $\alpha_2 < 0.05$  to be more than 0.8.<sup>27</sup> However, sampling was stopped after statistically significant differences were achieved.

Normal distribution of the data was confirmed by inspecting the histograms and normality plots. Frequencies were determined for the total number of pain locations, comorbidities and medications in addition to the number of participants that had at least one pain location, one comorbidity or one medication. MPQ, BPI, and TSK scores were calculated as the percentage of the maximum score that could be obtained on each questionnaire. Two-tailed *t*-tests were performed to examine for differences in pain severity (MPQ and BPI), pain interference (BPI), physical activity, pain-related fear of movement/re-injury (TSK), number of pain locations, HRQoL, number of comorbidities, and number of medications between healthy people and those with COPD. The chi-square test was performed to detect between group differences in the number of subjects who reported pain for different body locations,

the number of subjects who had at least one comorbidity, and the number who reported at least one medication. Means and standard errors are reported unless otherwise specified. A *p* value  $< 0.01$  was set to indicate significant differences.

Correlations were performed amongst pain measures in order to determine their convergent and discriminant validity. Independent correlates that might be predictive of pain were determined by performing correlation analysis followed by linear regression. Correlations between pain measures (severity—by MPQ and BPI and interference by BPI severity) and potential predictors of pain (TSK, CHAMPS, comorbidities, medications) were examined using two-tailed Pearson product moment correlations. Variables that were moderately to highly correlated to pain severity and interference scores ( $p < 0.01$  and  $r > 0.40$ ) were entered into the linear regression model. The model was not controlled for age and gender as the groups were initially matched for these factors. The outcomes were checked for multicollinearity; if two measures were highly correlated, one was removed (e.g. medications removed because of high correlation with comorbidities).

## Results

Forty-seven COPD patients and 47 healthy people completed all questionnaires. The groups were  $70 \pm 6.7$  (SD) and  $68.2 \pm 8.8$  (SD) years, respectively. Both groups had female:male ratios of 20:27 and the COPD group had an FEV<sub>1</sub> of  $44.7 \pm 19.2$  (SD) percent predicted. Originally 87 healthy people and 92 people with COPD were recruited for the study; sixty-three healthy (72%) and 65 people (70%) with COPD completed the study. To match groups for age and gender, people younger than 55 and older than 86 were excluded from the study, which resulted in 47 (female/male = 20/27) participants in each group. Considering a medium effect size of 0.5 in order to have a power of more than 0.8 using a *t*-test at  $\alpha_2 < 0.05$ ,<sup>27</sup> we originally aimed for 75 people in each group. However, we stopped the recruitment when we reached the significance level of ( $p < 0.000$ ) for primary outcomes.

Severity of pain (measured by the MPQ and BPI), bodily pain (lower score indicates more pain for SF-36) and pain interference (measured by BPI) was greater in COPD patients than in healthy people (Table 1;  $p < 0.000$ ). The number of COPD patients with moderate to very severe pain was 7.5 and 2.2 times greater than for healthy people evaluated by the MPQ and BPI, respectively (Fig. 1;  $p < 0.002$ ). The number of COPD patients who had moderate to very high pain interference with activities was 5.4 fold greater than for healthy people (Fig. 1;  $p < 0.002$ ). The number of pain locations was greater in COPD patients compared to healthy people with the most common occurrence in the neck and trunk region (Fig. 2;  $p < 0.005$ ). COPD patients also had a greater pain-related fear of movement/re-injury (TSK – Table 1;  $p < 0.001$ ) than healthy people.

Significant correlations amongst pain measures are shown in Table 2. Pain severity and interference measured by the MPQ and BPI showed strong correlations<sup>27</sup> amongst the three measures in each of the participant groups and in

**Table 1** Measures of pain, physical activity, health related quality of life, medication and comorbidities in healthy people and COPD patients.

Outcomes	Healthy mean $\pm$ SE	COPD mean $\pm$ SE	Absolute mean difference	Fold difference	P value
<b>Pain measures</b>					
Severity – MPQ	3.8 $\pm$ 0.7	10.0 $\pm$ 1.4	6.3	2.63	0.000
Severity – BPI	12.4 $\pm$ 1.9	28.5 $\pm$ 3.5	16.1	2.30	0.000
Bodily pain SF-36	76.7 $\pm$ 3.2	49.1 $\pm$ 4.2	27.60	0.64	0.000
Interference – BPI	9.7 $\pm$ 1.8	35.5 $\pm$ 4.1	25.8	3.66	0.000
Fear of movement – TSK	22.2 $\pm$ 0.8	27.0 $\pm$ 1.0	4.7	0.21	0.001
Number of pain locations	1.3 $\pm$ 0.2	3.1 $\pm$ 0.4	1.8	2.38	0.000
<b>Physical activity – CHAMPS</b>					
All activities – EE	4184 $\pm$ 309	1748 $\pm$ 221	2435	–0.42	0.000
Moderate EE (MET $\geq$ 3.0)	2560 $\pm$ 239	710 $\pm$ 135	1849	–0.28	0.000
Number of comorbidities	1.77 $\pm$ 0.23	3.85 $\pm$ 0.30	2.08	2.18	0.000
Number of medications	2.21 $\pm$ 0.34	6.64 $\pm$ 0.54	4.43	3.00	0.000
<b>Health related quality of life</b>					
Physical component score	52.0 $\pm$ 1.3	35.2 $\pm$ 1.7	16.9	–0.68	0.000
Mental component score	54.7 $\pm$ 1.30	42.0 $\pm$ 1.8	12.8	–0.78	0.000

MPQ, McGill Pain Questionnaire-short form; BPI, Brief Pain Inventory-short form; TSK, Modified Tampa Scale of Kinesiophobia; CHAMPS, Community Health Activities Model Program for Seniors; SE: standard error of difference.

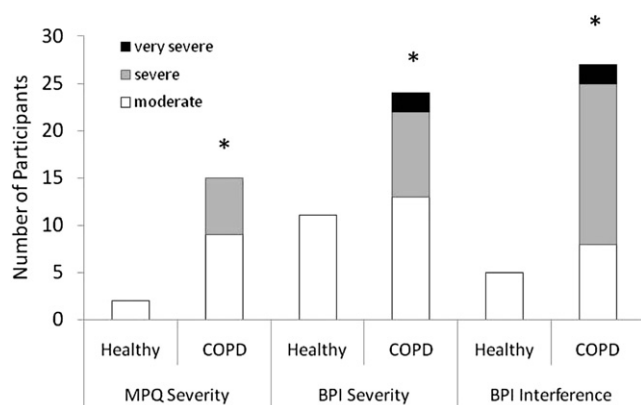
both groups combined. These pain measures also showed moderate to strong correlations<sup>27</sup> with analgesic medications and the number of pain locations in the COPD patients and both groups. Pain-related fear of movement/re-injury (TSK) was correlated to a lesser degree to MPQ and BPI pain measures in the COPD patients and both groups; only pain interference (BPI) was correlated to pain-related fear of movement (TSK) in COPD patients.

Self-reported physical activity (CHAMPS) was lower in COPD patients compared to healthy people (Table 1;  $p < 0.000$ ), and the total energy expenditure estimated from CHAMPS demonstrated a moderate inverse correlation<sup>27</sup> to pain interference (BPI) ( $r = -0.294$ ,  $p = 0.004$ ) for both groups. Physical and Mental Component Scores of the SF-36 were lower in COPD patients than in healthy people (Table 1;  $p < 0.000$ ). Pain severity (measured by the

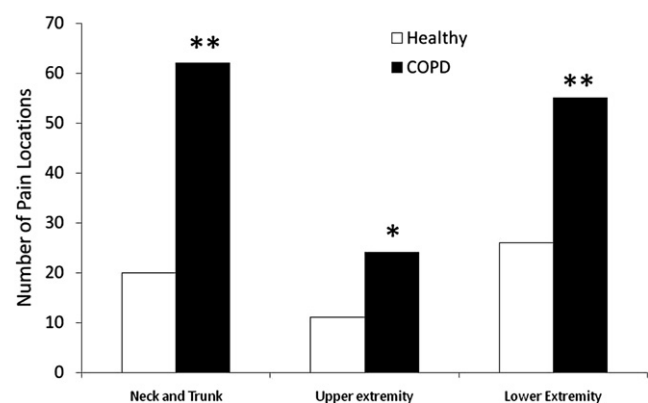
MPQ and BPI) and pain interference showed moderate to strong negative correlations<sup>27</sup> to the Physical Component Score of the SF-36 ( $-0.45$ ,  $-0.61$ ,  $-0.70$ , respectively;  $p = 0.000$ ).

Regarding the number of comorbidities and medications, COPD patients had a greater frequency of self-reported circulatory (47 versus 22;  $p = 0.002$ ), musculoskeletal (33 versus 14;  $p = 0.005$ ), digestive (15 versus 3;  $p = 0.001$ ), and renal diseases (11 versus 3;  $p = 0.02$ ) compared to healthy people. In accordance, COPD patients had a greater numbers of respiratory ( $p = 0.000$ ), cardiovascular ( $p = 0.030$ ), immune (0.008), and analgesic medications ( $p = 0.030$ ) than the healthy group.

From the regression analysis, only the number of comorbidities was a significant independent correlate of pain severity (MPQ and BPI) in people with COPD (Fig. 3;  $r = 0.61$  and  $0.56$ , respectively;  $p = 0.000$ ).



**Figure 1** Number of healthy people and COPD patients that self-reported moderate, severe or very severe for pain severity (McGill Pain Questionnaire [MPQ] and Brief Pain Inventory [BPI]) and pain interference (BPI). \* indicates significant difference from healthy people at  $p < 0.002$ .



**Figure 2** Number of pain locations in healthy people and COPD patients. \*\* indicates significant difference at  $p < 0.005$  and \* indicates a tendency to be different from healthy people at  $p < 0.04$ .

**Table 2** Significant correlations amongst pain measures in healthy people and COPD patients at  $p < 0.01$ .  $r$  ( $p$  value) are shown.

	FEV <sub>1</sub>	Pain severity – MPQ	Pain severity – BPI	TSK – pain-related fear of movement	Analgesic meds	Number of pain locations
Pain severity – MPQ						
Healthy	—	—	—	—	—	0.39 (0.007)
COPD	—	—	—	—	0.38 (0.009)	0.68 (0.000)
Both groups	—	—	—	0.362 (0.000)	0.42 (0.000)	0.67 (0.000)
Pain severity – BPI						
Healthy	—	0.77 (0.000)	—	—	0.36 (0.013)	0.44 (0.002)
COPD	0.46 (0.003)	0.82 (0.000)	—	—	0.54 (0.000)	0.683 (0.000)
Both groups	—	0.76 (0.000)	0.36 (0.000)	—	0.54 (0.000)	0.681 (0.000)
Pain interference – BPI						
Healthy	—	0.72 (0.000)	0.82, (0.000)	—	0.38 (0.008)	0.46 (0.001)
COPD	0.56 (0.000)	0.66 (0.000)	0.74, (0.000)	0.49 (0.001)	0.36 (0.012)	0.58 (0.000)
Both groups	—	0.73 (0.000)	0.79, (0.000)	0.52 (0.000)	0.42 (0.000)	0.63 (0.000)

MPQ, McGill Pain Questionnaire-short form; BPI, Brief Pain Inventory-short form; TSK, Modified Tampa Scale of Kinesiophobia; FEV<sub>1</sub>, forced expiratory volume in 1 s.

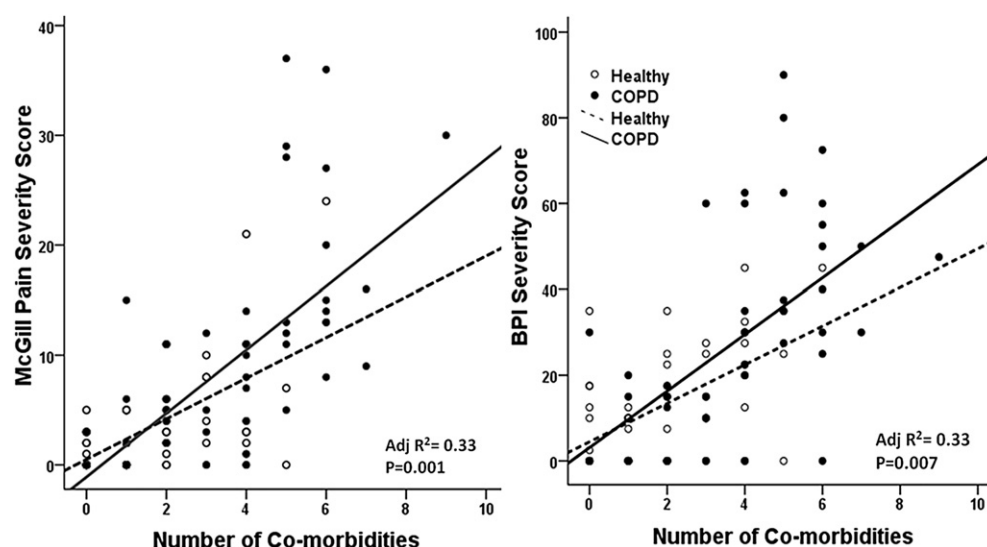
## Discussion

Our study demonstrated that people with COPD report almost 2.5 times greater pain compared to healthy adults. In addition, pain interferes with daily activities 3.7 times more often in people with COPD than in healthy people. Furthermore, not only is pain more severe, but it is also more common in people with COPD. Moderate to severe pain was self-reported 2.2 and 7.5 times more often in COPD patients than matched healthy people as measured by the BPI and MPQ, respectively. Moderate to severe pain affected half of our COPD sample of participants, a rate which falls between the 25–70% found in end-of-life COPD patients reporting pain<sup>5</sup> and a rate much higher than the

20% who reported more than low intensity chronic pain in a large survey ( $n = 3605$ ) of general practice patients.<sup>28</sup>

Greater pain in people with COPD might be due to more prolonged induction of painful stimuli or possibly to lower thresholds for pain compared to healthy people. Possible etiologies could be systemic inflammation, central adaptations related to pain and dyspnea, and musculoskeletal disorders including mechanical limitation of chest wall movement due to hyperinflation.

Systemic inflammation in COPD may provide one explanation for increased pain severity in these patients. The macrophage and neutrophilic response central to the etiology of the lung disease<sup>29</sup> results in the release of large amounts of proinflammatory cytokines that perpetuate



**Figure 3** Scatter plots depicting relationship between McGill and brief pain inventory pain severity scores and the number of comorbidities. Adjusted  $R^2$  and  $p$  values are shown for both groups. Data for the COPD group is provided in the text.



a local inflammatory response and can also impact distant tissues via the circulation.<sup>30,31</sup> TNF- $\alpha$  has been shown to increase mechanical allodynia and thermal hyperalgesia<sup>32</sup> and decrease the mechanical activation threshold in C fibers.<sup>33</sup> It is involved in the generation and the maintenance of neuropathic pain.<sup>34</sup> Moreover, IL-1 $\beta$  is considered to be a key cytokine associated with increased pain and hyperalgesia, especially in neuropathies and inflammatory diseases.<sup>9,35</sup> Marked increase in cytokine IL-6 is associated with increased pain and hyperalgesia.<sup>36</sup> Thus, proinflammatory cytokines can induce or increase inflammatory pain. Given that COPD is associated with marked and prolonged systemic elevation of inflammatory cytokines due to lung pathology, it is tenable that this systemic inflammation may contribute to the generation of pain or lower the threshold to painful stimuli.

COPD patients may have an altered sensation to pain due to protracted central processing of dyspnea and pain. In addition to their common unpleasant, alarming character, recurrence of chronic experiences of dyspnea or pain are prominent and threatening symptoms in several pulmonary diseases such as asthma<sup>37</sup> and COPD.<sup>2</sup> Both pain and dyspnea have been mapped to activation of common brain areas including the anterior/mid insula, dorsal anterior cingulate cortex, sensorimotor and somatosensory cortex II, supplementary motor area, amygdale and medial thalamus.<sup>37,38</sup> Due to similar sensory and affective-related brain networks, the protracted experience of dyspnea in COPD patients and associated prolonged activation of brain centers may induce permanent changes in the perception of pain, especially after sensitization. Whether or not the reduced sensitivity to discriminate between different noxious and non-noxious stimuli, such as pain and dyspnea at cortical level, is affected by sensitization and is impaired in people with COPD requires further investigation.

The pain severity and interference scores are somewhat similar to those previously reported. The pain severity score of BPI in our study is lower to that of Borge et al.<sup>7</sup> (28.5/100 versus 3.7/10), whereas the pain interference scores in our study are similar (35.5/100 versus 3.9/10). These results are similar to those of previous studies, which reported marked pain in COPD patients.<sup>5–7,39</sup> Regarding SF-36 data, Hajiro et al.<sup>8</sup> found higher scores in the pain domain (indicated better HQoL) compared to our pain domain scores of the SF-36. However, these authors also suggested that this domain had a small number of items, which may “bring less discriminatory power to the SF-36 when evaluating the HRQOL of patients with stable COPD.”

Of interest, pain in the neck and trunk was more common than in other body locations, which is consistent with previous studies.<sup>7,39</sup> This finding might be attributable in part, to the location of the primary and accessory muscles of respiration. For example, the diaphragm and intercostal muscles might be overused during the abnormal breathing pattern in COPD<sup>7,39</sup> accentuated by their mechanical disadvantage due to hyperexpansion of the chest wall. Chest wall hyperinflation in COPD consequent to alveolar destruction and airway inflammation results in the resting position of the chest wall being shifted to the left on the pressure–volume curve causing higher volumes with a decreased available range of motion during ventilation, i.e. decreased thoracic excursion. This hyperinflation is

accentuated by exertion even during such functional tests as the 6 min walk test.<sup>40</sup> The limited range of motion due to hyperinflation may result in reactive muscle spasm similar to what occurs in other conditions with limited range of motion of joints and reduced operating lengths of muscle, such as osteoarthritis.<sup>12</sup> In addition to joint pain and muscle spasm, the mechanical disadvantage of the inspiratory muscles in the hyperinflated state, compounded by increased levels of tidal ventilation, may make these muscles more prone to overuse injury and subsequent delayed onset muscle soreness (DOMS) as evidenced by microscopic muscle injury in COPD patients.<sup>41</sup> DOMS of the inspiratory muscles has been reported in healthy people.<sup>42</sup> In summary, the mechanical abnormalities of the thorax due to hyperinflation and increased levels of ventilation may contribute to joint pain, muscle spasm and delayed onset muscle soreness in people with COPD.

Our data indicates that the frequency and number of COPD patients with self-reported musculoskeletal disease is about double that found in healthy adults; this difference likely contributes to the two- to three-fold greater number of pain locations in the upper and lower extremities compared to healthy people. We did not explore the types of musculoskeletal comorbidities that might contribute to pain in our study samples. However, osteoporosis is commonly reported (60–70%) in COPD<sup>14</sup> and age-related prevalence of osteoarthritis ranges from 14 to 58%<sup>13</sup> in the 50–86 year age-range of our study participants. Along with joint specific pathologies, systemic influences of inflammatory cytokines and central processing of altered sensations may also increase pain experienced in the extremities by COPD patients compared to healthy people.

The number of comorbidities was found to be an independent correlate of pain severity in people with COPD, as measured by MPQ and BPI. This result is not surprising given that many comorbidities manifest with pain symptoms.<sup>43</sup> During a week-long general practice survey, 22% of approximately 3,000 patients presented with pain as a primary complaint with the most common underlying cause being musculoskeletal (50%) followed by visceral including cardiovascular (20%), infectious (15%) and headaches (8%). From a mail survey of general practice patients, the subsample of those who were 55 yrs or older, attributed pain most often to musculoskeletal causes (~40%) and angina (6.3%) [55–64 yr] to 11.1% [ $\geq 75$  yr].<sup>28</sup> In comparison, just over 50% of COPD patients complained of pain and self-reported cardiovascular conditions (67%) and musculoskeletal conditions (51%), which may be primary sources of pain in our survey sample. Further investigation is required to determine the contributing factors to the etiology of pain in COPD patients.

The significance of pain in people with COPD was reflected in greater pain-related interference in activities (BPI) that may partly explain the lower Physical Component Scores in HRQoL (SF-36) and the lower physical activity scores (CHAMPS questionnaire) in people with COPD compared to healthy adults. Patients with COPD also experience greater pain-related fear as indicated by the scores on the modified TSK, a finding which is similar to chronic pain patients compared to healthy people.<sup>43</sup> Pain sufferers can worry about how increasing pain may lead to progressive disability and this can be heightened if they

perceive themselves as being beyond help by care givers and health care providers. Fear and anxiety are also associated with pain-exacerbating activities, such as avoidance of physical activity, that can further reduce muscle flexibility, strength, and endurance leading to a downward spiral of increased disability.<sup>43</sup> Indeed, fear of movement and injury are better predictors of functional limitations than biomedical parameters or even pain severity and duration.<sup>44</sup> Treating symptoms of fear and anxiety, and also establishing pain coping strategies is essential for optimizing pain management.

To date, pain does not appear to be strongly associated with the severity of airflow limitation. We did not find a significant relationship between FEV<sub>1</sub> and pain severity score of MPQ, similar findings to those of previous studies that examined the severity of pain measures with spirometry.<sup>7,45,46</sup> That being said, these results do contrast the moderate correlation that we found between BPI severity and interference scores and FEV<sub>1</sub>. One plausible explanation might be that in our sample, people with minor disease severity may be more active and expose themselves to more extraneous activities that can induce pain. Given these disparate findings, further research is required to clarify the relationship between pain and disease severity.

## Limitations

The primary limitation of this study is the use of self-report questionnaires. However, the participant's perception is essential to evaluate subjective sensations such as pain. Other constructs evaluated, such as activities, comorbidities and medications can be underestimated or overestimated using this method of inquiry.<sup>16</sup> In addition, the study sample was a convenience sample and relatively small; thus, it is difficult to determine if the two sample groups were affected unequally by self-selection and recruitment, although given the high response rate of participants in both groups, these effects might be minimal. The study sample also came from a small geographical location. The experience and underlying causes of pain may vary in different cultures because of associated variations in the prevalence of disorders causing pain and pain perceptions. Furthermore, this study did not examine the effects of dyspnea, a major symptom of people with COPD. Future studies need to investigate the relationship between dyspnea and pain (commonalities and differences), as the perception of dyspnea shares many characteristics with the perception of pain, and both sensations might be linked to affective states.

## Conclusion

Compared to their healthy counterparts, pain is more common and of a greater magnitude in people with COPD. The relationship between pain interference and daily physical activities requires further exploration to determine whether or not pain is a major contributor to decreased physical activity and HRQoL in COPD patients. The assessment and treatment of pain is often overlooked in the plan of care for COPD patients. A greater appreciation of factors involved in pain perception will be beneficial

for designing COPD-specific pain management programs aimed at improving physical, psychological, and social well-being in people with COPD.

## Conflict of interest

None.

## Funding

This study was supported by the Canadian Respiratory Health Professionals of the Lung Association and B HajGhanbari was supported by the British Columbia Lung Association. L. Holsti was supported by a Canadian Institutes of Health Research Canada Research Chair.

## Acknowledgments

The authors would like to acknowledge Dr. Cristiane Yamabayashi for her role in data entry.

## References

1. *Global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease*. Global Initiative for Chronic obstructive Lung Disease (GOLD), [www.goldcopd.com](http://www.goldcopd.com); 2009.
2. O'Donnell DE, Hernandez P, Kaplan A, et al. Canadian thoracic society recommendations for management of chronic obstructive pulmonary disease – 2008 update – highlights for primary care. *Can Respir J*(Suppl. A: 1A–8A), [http://www.pulsus.com/Respir/11\\_SB/contents.pdf](http://www.pulsus.com/Respir/11_SB/contents.pdf), 2008;15.
3. Killian KJ, Leblanc P, Martin DH, et al. Exercise capacity and ventilatory, circulatory, and symptom limitation in patients with chronic air flow limitation. *Am Rev Respir Dis* 1992; **146**(4):935–40.
4. Miller JD, Reid WD, Miller PA. Construct validity of health utility index in persons with emphysema. American thoracic society meeting. Toronto. May 16–21, 2008. the ATS website Available from: [http://www.abstracts2view.com/ats08/view.php?nu=ATS08L\\_683](http://www.abstracts2view.com/ats08/view.php?nu=ATS08L_683).
5. Lynn J, Ely EW, Zhong Z, et al. Living and dying with chronic obstructive pulmonary disease. *J Am Geriatr Soc* 2000; **48**(Suppl. 5):S91–100.
6. Lohne V, Heer HCD, Andersen M, et al. Qualitative study of pain of patients with chronic obstructive pulmonary disease. *Heart Lung* 2010; **39**(3):226–33.
7. Borge CR, Wahl AK, Moum T. Pain and quality of life with chronic obstructive pulmonary disease. *Heart Lung* 2011 May–Jun; **40**(3):e90–101.
8. Hajiro T, Nishimura K, Tsukino M, et al. A comparison of the level of dyspnea vs disease severity in indicating the health related quality of life of patients with COPD. *Chest* 1999; **116**:1632–7.
9. Watkins LR, Maier SF. Implications of immune-to-brain communication for sickness and pain. *Proc Natl Acad Sci U S A* 1999; **96**:7710–3.
10. Ozge A, Atis S, Sevim S. Subclinical peripheral neuropathy associated pulmonary disease. *Electromyogr Clin Neurophysiol* 2001; **41**:185–91.
11. Laghi F, Tobin MJ. Disorders of the respiratory muscles. *Am J Respir Crit Care Med* 2003; **168**:10–48.

12. Hunter DJ. Imaging insights on the epidemiology and pathophysiology of osteoarthritis. *Rheum Dis Clin North Am* 2009; **35**(3):447–63.
13. Kopec JA, Rahman MM, Berthelot JM, et al. Descriptive epidemiology of osteoarthritis in British Columbia, Canada. *J Rheumatol* 2007; **34**:386–93.
14. Ferguson GT, Claverley PM, Anderson JA, et al. Prevalence and progression of osteoporosis in patients with COPD: results from the towards a revolution in COPD health study. *Chest* 2009; **136**:1456–65.
15. Niels B, Annemarie BT, Alf K. Pain epidemiology and health related quality of life in chronic non-malignant pain patients referred to a Danish multidisciplinary pain center. *Pain* 1997; **73**:393–400.
16. Dillman DA. *Mail and internet surveys, the tailored design method*. 2nd ed. John Wiley & Sons, Inc; 2000.
17. Melzack R. The short-form McGill pain questionnaire. *Pain* 1987; **30**(2):191–7.
18. Sawyer J, Haslam L, Robinson S, et al. Pain prevalence study in a large Canadian teaching hospital. *Pain Manag Nurs* 2008; **9**(3): 104–12.
19. Love A, Leboeuf DC, Crisp TC. Chiropractic chronic low back pain sufferers and self-report assessment methods: a reliability study of the visual analogue scale, the pain drawing, and the McGill pain questionnaire. *J Manipulative Physiol Ther* 1989; **12**(pt1):21–5.
20. Reading AE, Everitt BS, Sledmere CM. The McGill pain questionnaire: a replication of its construction. *Br J Clin Psychol* 1982; **21**:339–49.
21. Keller S, Bann CM, Dodd SL, et al. Validity of the brief pain inventory for use in documenting the outcomes of patients with noncancer pain. *Clin J Pain* 2004; **20**(5):309–18.
22. Tan G, Jensen MP, Thornby J, et al. Validation of the brief pain inventory for chronic nonmalignant pain. *J Pain* 2004; **5**: 133–7.
23. Roelofs J, Goubert L, Peters ML, et al. The Tampa scale for kinesiophobia: further examination of psychometric properties in patients with chronic low back pain and fibromyalgia. *Eur J Pain* 2004; **8**(5):495–502.
24. Stewart AL, Mills KM, King AC, et al. CHAMPS physical activity questionnaire for older adults: outcomes for interventions. *Med Sci Sports Exerc* 2001; **33**(7):1126–41.
25. Ware Jr JE, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992; **30**(6):473–83.
26. Canadian Medical Association. *Prescription & over the counter drugs for Canadians*. Toronto, Canada: Reader's Digest; 2002.
27. Cohen J. *Statistical power for the behavioral sciences*. 2nd ed. New Jersey: Lawrence Erlbaum; 1988.
28. Elliot AM, Smith BH, Penny KI, Smith WC, Chambers WA. The epidemiology of chronic pain in the community. *Lancet* 1999; **354**:1248–52.
29. Linden M, Rasmussen JB, Piitulainen E. Airway inflammation in smokers with nonobstructive and obstructive chronic bronchitis. *Am Rev Respir Dis* 1993; **148**:1226–32.
30. Culpitt SV, Rogers DF, Shah P. Impaired inhibition by dexamethasone of cytokine release by alveolar macrophages from patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2003; **167**:24–31.
31. Mio T, Romberger DJ, Thompson AB. Cigarette smoke induces interleukin-8 release from human bronchial epithelial cells. *Am J Respir Crit Care Med* 1997; **155**:1770–6.
32. Junger H, Sorkin LS. Nociceptive and inflammatory effects of subcutaneous TNF alpha. *Pain* 2000; **85**:145–51.
33. Wagner R, Myers RR. Schwann cells produce tumor necrosis factor alpha: expression in injured and non-injured nerves. *Neuroscience* 1996; **73**:625–9.
34. Sommer C, Schmidt C, George A. Hyperalgesia in experimental neuropathy is dependent on the TNF receptor 1. *Exp Neurol* 1998; **151**:138–42.
35. Lindenlaub T, Sommer C. Cytokines in sural nerve biopsies from inflammatory and non-inflammatory neuropathies. *Acta Neuropathol* 2003; **105**:593–602.
36. Banzett RB, Mulnier HE, Murphy K, et al. Breathlessness in humans activates insular cortex. *Brain Imaging* 2000; **11**(10): 2117–20.
37. von Leupoldt A, Sommer T, Kegat S, et al. Down regulation of insular cortex responses to dyspnea and pain in asthma. *Am J Respir Crit Care Med* 2009b; **180**(3):232–8.
38. Casey KL. Forebrain mechanisms of nociception and pain: analysis through imaging. *Proc Natl Acad Sci U S A* 1999; **96**:7668–74.
39. Bentsen SB, Rustøen T, Miasowski C. Prevalence and characteristics of pain in patients with chronic obstructive pulmonary disease compared to the Norwegian general population. *J Pain* 2011 May; **12**(5):539–45.
40. Callens E, Graba S, Gillet-Juvin K, et al. Measurement of dynamic hyperinflation after 6-minute walk test in patients with COPD. *Chest* 2009; **139**:1466–72.
41. Orozco-Levi M, Lloreta J, Minguella J, et al. Injury of the human diaphragm associated with exertion and chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2001; **164**:1734–9.
42. Mathur S, Sheel AW, Road JD, Reid WD. Delayed onset muscle soreness after inspiratory threshold loading in healthy adults. *Cardiopulm Phys Ther J* 2010; **21**(1):5–12.
43. Boersma K, Linton SJ. Psychological processes underlying the development of a chronic pain problem: a prospective study of the relationship between profiles of psychological variables in the fear avoidance model in disability. *Clin J Pain* 2006; **22**: 160–6.
44. Crombez G, Vlaeyen JW, Heuts PH. Pain-related fear is more disabling than pain itself: evidence on the role of pain-related fear in chronic back pain disability. *Pain* 1999; **80**:329–39.
45. Tsukino M, Nishimura K, Ikeda A, et al. Physiologic factors that determine the health-related quality of life in patients with COPD. *Chest* 1996; **110**:896–903.
46. Boueri FM, Bucher-Bartelson BL, Glenn KA, et al. Quality of life measured with a generic instrument (short form-36) improves following pulmonary rehabilitation in patients with COPD. *Chest* 2001; **119**:77–84.