

## Correlation between lower gastrointestinal tract symptoms and quality of life in patients with stable chronic obstructive pulmonary disease

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### Abstract

**OBJECTIVE:** To explore correlations between the symptoms of constipation and abdominal distention and severity of chronic obstructive pulmonary disease (COPD) in patients with stable disease.

**METHODS:** We studied 191 patients with stable COPD (according to defined criteria) in this cross-sectional study from four three-level class A Chinese medicine hospitals in China. We built an Epidata 3.0 database and performed statistical analysis with SPSS, version 17.0. We analyzed correlations between the frequency of lower gastrointestinal tract symptoms (constipation and abdominal distention) and scores for major pulmonary symptoms (cough, sputum and wheezing) based on the St. George's Respiratory Questionnaire (SGRQ), 6-minute walking distance (6MWD) and frequency of acute exacerbations of COPD (AECOPD).

**RESULTS:** In addition to their pulmonary symptoms, 39.79% and 40.31% of study patients with

stable COPD reported constipation and abdominal distention, respectively. Scores for major pulmonary symptoms (cough, sputum and wheezing), AECOPD and SGRQ values in patients with constipation and abdominal distention were significantly greater, and the 6MWD markedly shorter, than in those without them. According to Pearson's correlation analysis, there were strong correlations between these lower gastrointestinal tract symptoms and scores for pulmonary symptoms, SGRQ, 6MWD and AECOPD.

**CONCLUSION:** Lower gastrointestinal tract symptoms such as constipation and abdominal distention can adversely affect pulmonary symptoms, frequency of acute exacerbations and quality of life in patients with stable COPD.

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**Key words:** Chronic obstructive pulmonary disease; Constipation; Flatulence; Quality of life; Questionnaires

### INTRODUCTION

Chronic obstructive pulmonary disease (COPD), a common chronic respiratory disease, which prevalence was 8.2%, making it the third leading cause of death in China.<sup>1</sup> Dyspnea and limitation of mobility are its main clinical symptoms; these tend to worsen as the disease progresses. COPD has recently been recognized not only as an inflammatory respiratory disorder, but also as a chronic systemic inflammatory syndrome. The systemic inflammation causes a variety of abnormali-

ties. Systemic comorbidities involving the cardiovascular, endocrine, and gastrointestinal systems and psychological disorders are prevalent in patients with advanced COPD. These disorders together with related pulmonary complications have a great impact on patients' quality of life (QOL) and mortality.<sup>2</sup> Some researchers have found that upper gastrointestinal diseases such as gastroesophageal reflux correlate closely with acute exacerbations of COPD and QOL in patients with stable COPD.<sup>3,5</sup> Constipation and diarrhea are disorders of the lower portion of the gastrointestinal tract that manifest as changes in frequency of defecation and consistency of stools.<sup>6,7</sup> Ludvigsson *et al*<sup>8</sup> reported that patients with celiac disease have higher COPD-associated morbidity, which could affect the course of their disease; however, there is no published research on correlations between constipation and abdominal distention and COPD.

We performed cross-sectional questionnaire surveys in four three-level class A Chinese medicine (CM) hospitals in China and identified 191 patients with stable COPD according to defined diagnostic and inclusion criteria. We assessed the frequency of constipation and abdominal distention in these patients and investigated correlations between these symptoms and scores for major pulmonary symptoms (cough, sputum and wheezing), the St. George's respiratory questionnaire (SGRQ), 6-min walking distance (6MWD) and frequency of acute exacerbation of COPD (AECOPD). We analyzed our findings to develop guidelines for clinical prevention and treatment of COPD morbidity.

## MATERIALS AND METHODS

### Patients

One hundred and ninety-one outpatients and inpa-

tients with stable COPD were recruited from November 2009 to February 2013 from four three-level class A CM hospitals in China. These comprised 58 patients from Dongzhimen Hospital affiliated with Beijing University of Chinese Medicine (30.4%), 74 from Hebei Provincial Hospital of Traditional Chinese Medicine (38.7%), 39 from the Hospital Affiliated with Gansu College of Traditional Chinese Medicine (20.4%), and 20 from the Hospital of Traditional Chinese Medicine affiliated with Liaoning University of Traditional Chinese Medicine (10.5%). All the patients signed informed consents.

Total 191 patients with stable COPD in the study: 132 men (69.11%) and 59 women (30.89%). The average age was 66.87 years (range, 45-80 years). Seventy-seven patients (40.31%) reported constipation, 76 (39.79%) abdominal distention and 85 (44.52%) neither of these two symptoms. The three groups were similar in sex, age, lung function, smoking habit, and body mass index (Table 1).

### Selection criteria

Diagnostic criteria for stable COPD: The diagnostic criteria for stable COPD were the Global Initiative for Chronic Obstructive Lung Disease (2007)<sup>9</sup> and Chronic Obstructive Pulmonary Disease Diagnostic guides<sup>10</sup> (COPDGroup, Chinese Society of Respiratory Diseases).

### Inclusion criteria

Patients meeting the following criteria were included in the study: (a) diagnostic criteria for COPD; (b) stable stage of COPD; (c) age between 18 and 80 years at inclusion; (d) voluntary participation and signed informed consent.

Table 1 Relevant patient variables

Variables	AD (+) (n=76)	Constipation (+) (n=77)	LGTS (-) (n=85)	t/ $\chi^2$ /Z	P
Mean age (year)	64.0±10.2	65.7±9.8	63.4±9.4	2.496	0.085
Gender					
Male	57	59	56	2.74	0.2539
Female	19	18	29		
Tobacco status					
Current	8	8	14	2.44	0.6556
Past	36	37	42		
Never	32	32	29		
BMI (kg/m <sup>2</sup> )	23.1±2.5	22.6±2.5	23.1±2.4	0.677	0.509
Lung function					
FEV1%	54.2±15.3	56.4±17.4	59.0±13.8	1.836	0.162
FEV1/FVC	63.6±13.8	64.2±13.1	61.6±6.4	0.941	0.392

Notes: data are presented as mean±SD or % (No.). AD (+): patients with abdominal distention; Constipation (+): patients with constipation; LGTS (-): patients without lower gastrointestinal tract symptoms (including abdominal distention and constipation). BMI: body mass index; FVC: forced vital capacity; FEV1: forced expiratory volume in 1 second.

**Exclusion criteria**

Patients meeting any of the following criteria were excluded from the study: (a) airflow limitation due to bronchiectasis, cystic fibrosis, active tuberculosis, lung cancer or other disorders; (b) concurrent other severe, potentially fatal diseases such as mechanical intestinal obstruction, peritonitis, hernia, intestinal stenosis, severe hemorrhoids, post-colorectal surgery, anal mucosal inflammatory edema, aneurysm, major intestinal bleeding or perforation, colorectal cancer, anal fistula, severe anemia including aplastic anemia, acute left heart failure, and acute cerebral hemorrhage; (c) pregnant or breast-feeding; (d) psychiatric disorders or any type of neural impairment (aphasia or cognitive impairment) that rendered them unable to understand the nature, scope and possible consequences of the study; and (e) serious hepatic and renal diseases.

**Questionnaire development**

A questionnaire was developed based on previous national research (973 projects) titled Symptom Standardization in Traditional Chinese Medicine, research of published reports,<sup>11</sup> a pilot survey and expert opinions. It comprised measurement of relevant patient variables including lung function, frequency of acute exacerbations of COPD, 6MWD, scoring according to the SGRQ, pulmonary symptom scoring (cough, sputum and wheezing) and scoring of lower gastrointestinal tract symptoms. The details are as follows:

**Symptom scores**

According to the Likert response scale<sup>12</sup> and symptom quantification and classification method in the Guide to New Traditional Chinese Medicines Research,<sup>13</sup> the values of 0, 2, 4 and 6 were designated as denoting No, Mild, Moderate and Severe, respectively; the higher the score, the more serious the symptoms. Major pulmonary symptoms (cough, sputum, wheezing) and lower gastrointestinal tract symptoms (constipation and abdominal distention) were evaluated and reported by patients accordingly.

**Pulmonary function**

Forced vital capacity (FVC), forced expiratory volume in 1 second (FEV1), and percentage of the predicted FEV1 (FEV1%) were assessed.

**Frequency of AECOPD**

AECOPD refers to sudden worsening of COPD symptoms (cough, phlegm and wheezing) that typically lasts for several days and requires a change in medication.<sup>14</sup> The frequency of AECOPD in 1 year was noted.

**Six-minute walking distance**

Standardized 6-minute walking tests (6MWTs) as specified by the American Thoracic Society<sup>15</sup> were used to measure the 6MWD, the distance walked on a flat surface in 6 min. This patient-reported outcome measure

has been widely used for integrated assessment of patients with pulmonary and cardiac disease, both by clinicians to monitor functional status and by affected individuals, who are thus able to monitor changes in their functional capacity and self-manage.<sup>16</sup>

**SGRQ**

Health-related quality of life was evaluated using the SGRQ,<sup>17</sup> which contains 50 items in three domains, namely symptoms, activity, and disease impact.

**Data entry and statistical analysis**

Data were entered by two independent researchers using EpiData 3.0 software ("The EpiData Association" Odense, Denmark) to build the clinical database; SPSS, version 17.0 (SPSS, Inc., Chicago, IL, USA) was used to perform the statistical analyses. All statistical tests were two-sided and  $P < 0.05$  was considered the threshold for statistical significance. The  $\chi^2$  test was used for enumeration data. Data are presented as mean  $\pm$  standard deviation (*SD*) ( $\bar{x} \pm s$ ). Multiple samples were processed by the homogeneity of variance test and comparison between groups by single factor analysis of variance. Relationships between lower gastrointestinal tract symptoms (constipation and abdominal distention) and major pulmonary symptoms (cough, sputum and wheezing), SGRQ, 6MWD and frequency of AECOPD were assessed by Pearson correlation analysis.

**RESULTS****Pulmonary symptom scores**

As shown in Table 2, scores for pulmonary symptoms (cough, sputum and wheezing) in patients with constipation were  $3.7 \pm 1.1$ ,  $3.5 \pm 1.2$ , and  $3.4 \pm 1.4$ , respectively. In patients with abdominal distention, these scores were  $3.6 \pm 1.4$ ,  $3.2 \pm 1.5$ , and  $3.4 \pm 1.7$ , respectively. Pulmonary symptom scores were significantly higher for patients with constipation and abdominal distention than for patients without these symptoms ( $2.2 \pm 1.6$ ,  $2.3 \pm 1.4$ ,  $1.7 \pm 1.6$  for cough, sputum and wheezing, respectively) ( $P < 0.01$  for each comparison).

**Frequency of acute exacerbations of COPD**

As shown in Table 3, the frequency of AECOPD in patients with constipation was  $2.6 \pm 1.4$ , and in patients with abdominal distention  $2.6 \pm 1.6$ . These frequencies were significantly higher than those in patients without constipation and abdominal distention ( $1.6 \pm 1.2$ ) ( $P < 0.01$ ).

**Six-minute walking distance**

As shown in Table 3, the 6MWD was ( $379.8 \pm 72.7$ ) m in COPD patients with constipation and ( $356.0 \pm 53.8$ ) m in those with abdominal distention. These dis-

tances were significantly shorter than those in patients without constipation and abdominal distention ( $408.5 \pm 61.6$  m) ( $P < 0.01$ ).

### Scores for SGRQ

As shown in Table 4, scores on SGRQ for symptoms, activities, effects and total in stable COPD patients with constipation were  $64 \pm 18$ ,  $58 \pm 18$ ,  $52 \pm 20$ , and  $56 \pm 17$ , respectively. These scores were  $63 \pm 17$ ,  $52 \pm 21$ ,  $48 \pm 22$ , and  $54 \pm 18$ , respectively, in stable COPD patients with abdominal distention. These scores were significantly higher than those in patients without constipation and abdominal distention ( $49 \pm 23$ ,  $40 \pm 19$ ,  $28 \pm 16$ ,  $35 \pm 16$ ) ( $P < 0.01$ ).

### Correlation of scores for constipation and abdominal distention with QOL

According to Pearson's correlation analysis, there were

significant positive correlations between constipation and pulmonary symptoms (cough, sputum and wheezing), frequency of acute exacerbations of COPD and scores on SGRQ for total, symptoms, activity, and impact, the correlation coefficients being 0.355, 0.436, 0.337, 0.26, 0.187, 0.372, 0.411, and 0.437, respectively. There was a significant negative correlation between constipation and 6MWT, the correlation coefficient being  $-0.517$ .

There were significantly positive correlations between abdominal distention and pulmonary symptoms (cough, sputum and wheezing), frequency of acute exacerbation of COPD and scores on SGRQ for total, symptoms, activity, and impact, the correlation coefficients being 0.410, 0.420, 0.508, 0.226, 0.298, 0.295, 0.512, and 0.462, respectively. There was a significantly negative correlation between abdominal distention

Table 2 Comparison of symptom scores ( $\bar{x} \pm s$ )

Group	n	Cough	Sputum	Dyspnea
AD (+)	76	$3.6 \pm 1.4^a$	$3.2 \pm 1.5^a$	$3.4 \pm 1.7^a$
Constipation (+)	77	$3.7 \pm 1.1^a$	$3.5 \pm 1.2^a$	$3.4 \pm 1.4^a$
LGTS (-)	85	$2.2 \pm 1.6$	$2.3 \pm 1.4$	$1.7 \pm 1.6$
F	-	34.983	21.047	34.414
P	-	0.000	0.000	0.000

Notes: AD (+): patients with abdominal distension; constipation (+): patients with constipation; LGTS (-): patients without lower gastrointestinal tract symptoms (including abdominal distension and constipation). <sup>a</sup> $P < 0.01$ , compared with patients without lower gastrointestinal tract symptoms (including abdominal distension and constipation).

Table 3 Frequency of acute exacerbation of COPD and 6MWD ( $\bar{x} \pm s$ )

Group	n	Frequency of acute exacerbation (No.)	6MWD (m)
AD (+)	76	$2.6 \pm 1.6^a$	$356.0 \pm 53.8^a$
Constipation (+)	77	$2.6 \pm 1.4^a$	$379.8 \pm 72.7^b$
LGTS (-)	85	$1.6 \pm 1.2$	$408.5 \pm 61.6$
F	-	14.641	11.979
P	-	0.000	0.000

Notes: AD (+): patients with abdominal distension; constipation (+): patients with constipation; LGTS (-): patients without lower gastrointestinal tract symptoms (including abdominal distension and constipation). COPD: chronic obstructive pulmonary disease; 6MWD: 6-minute walking distance. <sup>a</sup> $P < 0.01$ , <sup>b</sup> $P < 0.05$ , compared with the patients without lower gastrointestinal tract symptoms (including abdominal distension and constipation).

Table 4 SGRQ among groups ( $\bar{x} \pm s$ )

Group	n	Symptom	Activity	Impact	Total
AD (+)	76	$63 \pm 17^a$	$52 \pm 21^a$	$48 \pm 22^a$	$54 \pm 18^a$
Constipation (+)	77	$64 \pm 18^a$	$58 \pm 18^a$	$52 \pm 20^a$	$56 \pm 17^a$
LGTS (-)	85	$49 \pm 23$	$40 \pm 19$	$28 \pm 16$	$35 \pm 16$
F	-	15.375	20.325	36.279	35.510
P	-	0.000	0.000	0.000	0.000

Notes: AD (+): patients with abdominal distension; constipation (+): patients with constipation; LGTS (-): patients without lower gastrointestinal tract symptoms (including abdominal distension and constipation). SGRQ: St. George's respiratory questionnaire. <sup>a</sup> $P < 0.01$ , compared with patients without lower gastrointestinal tract symptoms (including abdominal distension and constipation).

and 6MWT, the correlation coefficient being  $-0.501$  (Table 5).

## DISCUSSION

A complex disease, COPD is characterized by a variety of pulmonary and extrapulmonary manifestations that have impacts upon various aspects of affected patients' lives. The most characteristic respiratory symptoms are shortness of breath and limitation of mobility.<sup>18</sup> In addition, patients with COPD may present with systemic symptoms, including weight loss, reduced appetite, skeletal muscle atrophy and dysfunction, depression and/or anxiety. These systemic symptoms may be experienced by patients with different degrees of airway limitation and have a wide range of deleterious effects on acute exacerbations, clinical outcomes, hospitalization and death; therefore, they should be managed appropriately.<sup>19-21</sup> Although lung function testing is essential for COPD diagnosis and evaluation of efficacy of treatment, it is far from being an appropriate marker for quality of life and some aspects of improvement in response to interventions. A more comprehensive approach that consers symptoms, body mass index, exercise tolerance, exacerbations, impaired health-related quality of life, and so on is commonly used for evaluation of COPD.<sup>22</sup>

Because epidemiological data have shown that 50% of deaths of patients with COPD are closely related to cardiovascular complications,<sup>23</sup> there have been numerous studies on correlations between COPD and cardiovascular disease. Constipation, one of the commonest lower gastrointestinal tract symptoms, is defined as defeca-

tion once per 3 or more days.<sup>24</sup> Constipation can cause abdominal pain and discomfort, gas, headaches, nausea, and anorexia.<sup>25</sup> Mostafa *et al.*<sup>26</sup> found that constipation occurs in 83% of ICU patients and that 42% of constipated patients fail to be weaned from mechanical ventilation. Selective decontamination of the digestive tract by oral administration of antibiotics or methyl cellulose can reduce the morbidity of ventilator-associated pneumonia, decrease the incidence of secondary respiratory tract infection and shorten the length of ICU stay.<sup>27</sup>

Patients with COPD are usually senile and limited in mobility by their dyspnea. Because of their medications<sup>28</sup> and mechanical ventilation,<sup>29</sup> they tend to suffer from lower gastrointestinal tract symptoms such as constipation and abdominal distention. Wei *et al.*<sup>30</sup> found that patients with COPD and heart disease had gastrointestinal dynamic and hormonal disorders and that these correlated closely with ventilatory dysfunction. Powell *et al.*<sup>31</sup> reported that patients with allergic rhinitis and asthma more commonly present with lower gastrointestinal tract symptoms than do patients with diabetes, osteoarthritis and rheumatoid arthritis. Although some reports about constipation and abdominal distention in COPD patients have been published, they focused on acute exacerbations of COPD and there are few reports about the effects of such symptoms on COPD.<sup>32</sup> In addition, there has been no research on any correlations between these symptoms and quality of life, symptoms or progression of COPD in COPD patients.

The present study used a cross-sectional questionnaire survey to assess the percentage of COPD patients with

Table 5 Correlation between lower gastrointestinal tract symptoms (including abdominal distension and constipation) and HRQL

	AD	Constipation	Cough	Sputum	Dyspnea	F AE	6MWD	SGRQ Total	SGRQ Symptom	SGRQ Activity	SGRQ Impact
AD	1	-	-	-	-	-	-	-	-	-	-
Constipation	0.387 <sup>a</sup>	1	-	-	-	-	-	-	-	-	-
Cough	0.410 <sup>a</sup>	0.355 <sup>a</sup>	1	-	-	-	-	-	-	-	-
Sputum	0.420 <sup>a</sup>	0.436 <sup>a</sup>	0.600 <sup>a</sup>	1	-	-	-	-	-	-	-
Dyspnea	0.508 <sup>a</sup>	0.337 <sup>a</sup>	0.379 <sup>a</sup>	0.303 <sup>a</sup>	1	-	-	-	-	-	-
F AE	0.226 <sup>a</sup>	0.260 <sup>a</sup>	0.312 <sup>a</sup>	0.269 <sup>a</sup>	0.205 <sup>a</sup>	1	-	-	-	-	-
6MWD	$-0.501^a$	$-0.517^a$	$-0.194^b$	$-0.116$	$-0.394^a$	$-0.171^b$	1	-	-	-	-
SGRQ total	0.462 <sup>a</sup>	-0.137	0.264 <sup>a</sup>	0.337 <sup>a</sup>	0.478 <sup>a</sup>	0.032	$-0.416^a$	1	-	-	-
SGRQ symptom	0.298 <sup>a</sup>	0.187 <sup>b</sup>	0.353 <sup>a</sup>	0.246 <sup>a</sup>	0.321 <sup>a</sup>	0.038	$-0.339^a$	0.691 <sup>a</sup>	1	-	-
SGRQ activity	0.295 <sup>a</sup>	0.372 <sup>a</sup>	0.115	0.205 <sup>a</sup>	0.401 <sup>a</sup>	0.058	$-0.283^a$	0.880 <sup>a</sup>	0.491 <sup>a</sup>	1	-
SGRQ impact	0.512 <sup>a</sup>	0.411 <sup>a</sup>	0.269 <sup>a</sup>	0.376 <sup>a</sup>	0.472 <sup>a</sup>	0.014	$-0.440^a$	0.960 <sup>a</sup>	0.571 <sup>a</sup>	0.759 <sup>a</sup>	1

Notes: <sup>a</sup>Correlation is significant at the 0.01 level (2-tailed). <sup>b</sup>Correlation is significant at the 0.05 level (2-tailed). AD: abdominal distention; FAE: frequency of acute exacerbations; HRQL: health-related quality of life; 6MWD: 6-minute walking distance; SGRQ: St. George's respiratory questionnaire.

constipation and abdominal distention and identify relationships between lower gastrointestinal tract symptoms (constipation and abdominal distention) and scores for major pulmonary symptoms (cough, sputum and wheezing), 6MWD, SGRQ, and frequency of AE-COPD to develop guidelines for prevention and treatment of COPD symptoms. The 191 patients with stable COPD were recruited from four three-level class A CM hospitals in China and, in addition to pulmonary symptoms (cough, sputum and wheezing), 39.79% and 40.31% of them were found to have constipation and abdominal distention, respectively. In patients with constipation and abdominal distention, pulmonary symptoms (cough, sputum and wheezing) were significantly more severe, the frequency of acute exacerbations of COPD significantly higher, scores for SGRQ greater, and 6MWT shorter than in patients without these lower abdominal symptoms. Pearson correlation analysis showed a significant positive correlation between constipation and abdominal distention and scores for pulmonary symptoms (cough, sputum and wheezing) and SGRQ and for frequency of acute exacerbations of COPD. There was also a significant negative correlation between constipation and abdominal distention and 6MWT. These findings suggest that there is a close relationship between the condition of stable COPD patients and lower gastrointestinal tract symptoms such as constipation and abdominal distention. Our findings suggest that alleviation or prevention of these lower abdominal symptoms and maintenance of regular bowel movement by use of laxatives, adjustment to dietary patterns and ventral massage may improve COPD patients' respiratory symptoms and QOL.

This study has three limitations. First, because it was a cross-sectional study, our findings of statistically significant correlations between constipation and abdominal distention and scores for pulmonary symptoms (cough, sputum and wheezing) and SGRQ, frequency of acute exacerbations of COPD, and 6MWT do not imply that this relationship is causal. However, we consider it undeniable that constipation and abdominal distention affect the condition of COPD patients. Professor Nanshan Zhong, a well-known respiratory specialist and academic in China, once stated that constipation does affect COPD patients' breathing and conversely, good digestion and bowel habits improve their breathing.<sup>33</sup> While anecdotal, this statement stemmed from extensive clinical experience and is therefore likely accurate. Second, there was recall bias in this study because the patients themselves primarily reported and assessed their symptoms. In recent decades, however, patient-reported outcomes have become more widely used<sup>34</sup> for assessing subjective symptoms such as cough, sputum and wheezing, QOL and health-related QOL. Third, this was a relatively small study compared with other large-scale COPD studies. Nonetheless, we ob-

tained sufficient data to confirm our hypothesis.

The lower gastrointestinal tract symptoms such as constipation and abdominal distention can affect pulmonary symptoms of patients with COPD, incidence of acute exacerbations of COPD and QOL. Thus, it is important to focus on managing lower gastrointestinal tract symptoms and keeping the intestinal tract clear to improve COPD patients' general condition and QOL.

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