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Kaiqin Tian 



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# The Gender Difference on Acute Exacerbation of Chronic Obstructive Pulmonary Disease Combined with Osteoporosis

Kaiqin Tian<sup>1, a)</sup>

<sup>1</sup>*Department of pharmacy, The First Affiliated Hospital of Zhengzhou University, Zhengzhou City, 450000, Henan Province, China.*

<sup>a)</sup>Corresponding author email: yanpingss6@163.com

**Abstract.** Background: with the gradually profound study on chronic obstructive pulmonary disease (COPD) in recent years, the clinical manifestation of COPD were found a great deal of heterogeneity. Simple “airflow obstructive level” did not fully reflect the heterogeneity, the increasingly attention were paid to the research on COPD clinical phenotype, especially the COPD gender difference. Chinese medicine put that gender and disease were correlation and differentiation, while, there was no correlation between gender differences and COPD traditional Chinese Medicine (TCM) syndromes in the literature. This study adopted the cross-sectional survey research method to summarize the gender distribution difference of TCM in AECOPD, in order to provide a new view for TCM prevention and diagnosis and treatment of COPD. Objective: to explore the characteristics of COPD in gender difference, and to summarize the differences in the distribution of common symptoms and syndromes in different gender. Method: A cross-sectional study was conducted to select AECOPD patients from The First Affiliated Hospital of Zhengzhou University from July 2014 to March 2016, and conducted epidemiological investigation and bone density examination. This study summarized the gender differences in epidemiology, clinical manifestations, test indexes, and complications of AECOPD patients; through syndrome investigation, this study analyzed the gender difference of TCM symptom and syndrome on AECOPD patients. Results: There were 289 cases in this study, including 183 cases of male, 106 cases of female, gender ratio was 1.73:1. Compared to male, it was more common on female with AECOPD combined with osteoporosis ( $P=0.0354$ ). Conclusion: The results of this study showed that there were gender difference in TCM syndromes, age, complications, clinical symptoms and indicators of AECOPE patients. However, the samples quantity of this project was small and the selected patient’s scope was relatively limited. It may be insufficient in the distribution of different gender syndromes, which required further study. This paper discussed the distribution of different gender in AECOPD TCM syndrome and expected could provide new solutions for TCM prevention and diagnosis and treatment of COPD.

**Key words:** Chronic Obstructive Pulmonary Disease; Consolidation of Osteoporosis; Gender Difference; TCM Syndrome.

## INTRODUCTION

COPD was one of the major public health problem in the world. COPD was the vital chronic respiratory diseases that impair human health (Rothberg et al., 2010). In recent years, with the gradual-in-depth research on COPD, a great heterogeneity was found in COPD clinical manifestations, simple “airflow obstructive

Level” did not fully reflect the heterogeneity (Han et al., 2010), so that the research on COPD clinical phenotype became more and more attention, among which COPD gender differences became one of research hot spots. So far, many foreign studies had found that COPD had gender differences in epidemiology, pathophysiology, genetics, diagnostics, clinical manifestations, treatment and prognosis.

Traditional Chinese medicine had detailed interpretation on gender and the correlation of diseases, considering there was a great differences on men and women in congenital aspect, Qi and Blood physiological and pathological aspects, such as the deficiency syndrome on women, susceptible to mental disorder, women is Qi and Blood deficiency.

The treatment of women' disease shall pay more attention on liver, while, men' disease shall pay more attention on kidney. Even if women and men suffered from the same disease, there were still differences in syndrome differentiation and treatment.

COPD belonged to "lung expansion", "asthma" in traditional Chinese medicine aspect. The TCM pathogenesis of COPD was asthenia in origin and asthenia in superficiality. Acute aggravating period of pathogenesis was phlegm obstruction or phlegm and blood stasis resistance, the pathogenesis in stability period was Qi deficiency and Yin deficiency, combined with phlegm and blood stasis. From the collected literature, there was no gender differences and the correlation of COPD in TCM syndrome. This study used cross-sectional survey research methods, explored the distribution of different gender patients with AECOPD syndromes differences, so as to provide new ideas for TCM prevention and treatment on COPD.

## STUDY CONTENT AND METHOD

### Diagnostic Criteria for COPD

The diagnostic criteria for COPD referred to the guidelines for diagnosis and treatment of chronic obstructive pulmonary disease developed by the Chinese medical association respiratory branch in December 2007. Clinical manifestations were chronic cough, expectoration, a short breath or difficulty in breathing, wheezing and chest tightness, systemic symptoms in patients in serious period. The systemic symptoms may occur, such as weight loss, loss of appetite, peripheral muscle atrophy and dysfunction, depression and/or anxiety, blood coughing and/or haemoptysis when combined with infection; Disease history: smoking history, history of occupational or environmental exposures, such as long-term exposure to dust, smoke, harmful particles or harmful gases, family history, the seasonal onset was autumn and winter cold weather, and the age onset was after middle age, chronic pulmonary primary heart history. Physical signs: abnormal thoracic morphology from visual diagnosis and palpation, shallow breathing with increased rapidly frequency, the auxiliary respiratory muscle participates in the respiratory movement, the severe visual chest abdominal contradiction movement, patients uses lip breathing to increase the volume of exhalation. The leaning forward when breathing difficulty became severe, hypoxemia patients could appear mucosa and skin violet, lower limb edema and liver enlargement when patients combined with right heart failure. Percussion: the reduced heart dullness and declined boundary of lung and liver due to lung hyperinflation, the lung percussion could be overvoiced. From the auscultation, the two lungs breathing voice could be reduced, the exhalation can be prolonged, the dry rale voice could be heard when in calm breath, the wet rale could be heard in the lung bottom area and other lung area, the heart sound is a little further, the heart sound near xiphoid area was clear and aloud. Experimental basis: pulmonary function examination was an objective indicator for judging airflow constraints, which was determined by the reduction of FEV<sub>1</sub>% and FEV<sub>1</sub>/FVC%. The FEV<sub>1</sub> /FVC% < 70% of inhalation of bronchial diastolic agent could be determined to be airflow incomplete reversible limitation, as seen in Table 1. There was no obvious changes in the X-ray chest film of COPD in early stage. Gradually, the subsequent non-characteristic changes happened in pulmonary texture and disorder. Main X-ray sign for lung excessive air included increased lung volume, the chest diameter growth, flattened ribs, increased lung field transparency, low diaphragmatic position, heart volume becoming long and narrow, lung blood vessel's residual roots shaped texture, lung field perivascular texture thin sparsely populated vessels, sometimes visible pulmonary bulla formation. HRCT was with high sensitivity and specification to determine the size and quantity of lobular center type or full-lobular emphysema and the determination of pulmonary bullae. Blood-air examination shall be conducted when FEV<sub>1</sub>% was less than 40% expected level or with respiratory failure or right heart failure on COPD patients. Hemoglobin, red blood cell count and sputum cultivation could also be the experimental evidence.

**TABLE 1.** Pulmonary functional classification of COPD (after inhalation of bronchial diastolic agent).

Classification	Feature
I stage (mild)	FEV <sub>1</sub> /FVC% <70%, FEV <sub>1</sub> occupied not less than 80% of expected level
II stage (medium)	FEV <sub>1</sub> /FVC% <70%, 50% ≤ FEV <sub>1</sub> , occupied expected level was less than 80%.
III stage (severe)	FEV <sub>1</sub> /FVC% <70%, 30% ≤ FEV <sub>1</sub> , occupied expected level was less than 50%.
IV stage (extremely severe)	FEV <sub>1</sub> /FVC% <70%, FEV <sub>1</sub> occupied less than 30% of expected level or FEV <sub>1</sub> occupied less than 50%, or combined with chronic breath failure.

## **Diagnostic Criteria for AECOPD**

Referred to GOLD in 2011 (GOLD, 2010), the acute changes appeared in the basic level of respiratory difficulties, coughs and/or expectorant sputum in the course of disease development, which were beyond the daily variation of patients, whom required a change in the treatment regimen. According to AECOPD definitions from Anthonisen (Rothberg et al., 2010), the AECOPD shall have one of the following main symptom, namely, difficulty breathing, increased sputum volume and purulent sputum, or accompanied by one or more of the following minor symptoms, fever without reason in the past 5 days, heavier breathing, aggravated coughing, breathing and heart rate increased by more than 20% than usual.

## **Research Content and Methods**

This study had adopted cross-sectional investigation method selected the patients from respiratory department of The Affiliated Hospital of Zhengzhou University from July 2014 to March 2016. The selected patients were up to the AECOPD diagnostic criteria. The TCM syndrome survey referred to Clinical Terminology of Traditional Chinese Medical Diagnosis and Treatment-Syndromes, and combined with high frequency evidence from literature related to COPD and listed the TCM syndrome and related symptoms, and discriminated classification to each case of patients. This research performed TCM syndromes and other indicators in AECOPD patients with different gender.

## **Observation Item**

Firstly, observation items included the patients' basic information, such as gender, age, weight, personal history, previous history, history of COPD, etc. Secondly, Physical and chemical indicators contained lung function test which was adopted JAEGER instrument master screen diffusion model and evaluation of COPD classification, bone density, blood gas analysis, chest film and CT; Clinical research questionnaire included physical examination, clinical symptoms of western medicine and TCM diagnosis, and TCM syndrome questionnaire, and Hospital anxiety and depression scale (HAD) survey.

## **COLLECTION OF CLINICAL MATERIAL AND STATISTICAL METHOD**

### **Case Collection**

Case collection was strictly according to the plan, and eliminated the patients hindered the TCM syndrome analysis.

### **Statistical Processing of Material**

The date of this study were recorded in Excel, and the statistical analysis of date was carried out by SPSS19.0 software, and the statistical description,  $t$  test and  $\chi^2$  test. The differences were compared with  $\chi^2$  analysis. The correlation was based on Spearman rank correlation, and 0.05 as the criterion of judgement,  $P < 0.05$  was considered statistically significant, whereas the other results was not statistically significant.

## **CLINICAL SURVEY RESULTS**

### **Basic Clinical Material**

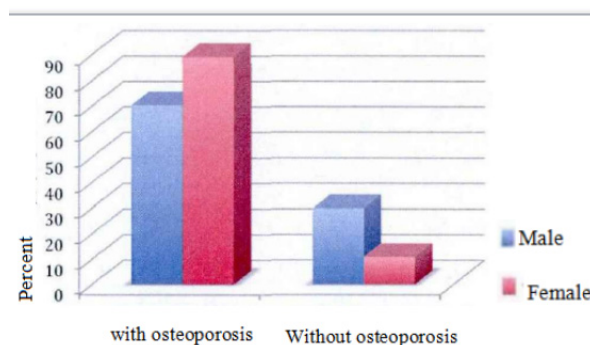
This study selected COPD patients 368 cases from July 2014 to March 2016, including 38 cases were unwilling to participate in this study, 15 cases had difficulty in language, mind consciousness, and could not cooperate to complete the survey of syndromes, and 26 cases were the patients with COPD in stable stage. Actually, 289 cases of patients including 17 cases of hospitalized patients and could not line for lung function test, but had diagnosed with COPD, and the disease condition was acute exacerbated.

## Gender Composition of Patients in AECOPD

There were a total of 289 cases selected in this study, including 183 cases of male with gender ratio 63.32%, 106 cases of female with gender ratio 36.68%. There were 84 cases of patients performed bone mineral density, including 66 cases combined with osteoporosis (bone mineral density  $T \leq -2.0$ ), and in which there were 33 cases of male and 33 cases of female, accounting for 78.57%; there were 18 cases of patients who were not combined with osteoporosis (14 cases of male and 4 cases of female) accounting for 21.43%. According to SPSS19.0 statistical software card test,  $\chi^2=4.43$ ,  $P=0.0354$ , which was less than 0.05. Female patients with AECOPD combined with osteoporosis were more common than male patients, as seen in Table 2 and Fig. 1.

**TABLE 2.** The distribution of AECOPD combined with osteoporosis in different gender n (%)

osteoporosis	Gender		Total	Statistics
	Male	Female		
With osteoporosis (BMD $T \leq -2.0$ )	33(70.21)	33(89.19)	66(78.57)	
Without osteoporosis(BMD $T \geq -2.0$ )	14(29.79)	4(10.81)	18(21.43)	
Total	47	37	84	$\chi^2=4.43$ $P=0.0354$



**FIG 1.** The distribution of AECOPD combined with osteoporosis in different gender

## Conclusion

Female AECOPD patients combined with osteoporosis ( $P=0.0354$ ) and anxiety depression status ( $P<0.001$ ) were more common than male patients.

## DISCUSSION

### The AECOPD Gender Difference in Epidemiology

The proportion of male was larger than the proportion of female in this study. The incidence of AECOPD were higher than female which was coordinate with the study at home and abroad (Han et al., 2002). The reason may be that male population with smoking history were larger than female population, and male had more possibility to expose to occupation that was harmful to the respiratory tract. From the age distribution, there was no statistical significance between make patients and female patients, whom were mainly in 70-89 years old (Houston, 2003). There may be some limitations, and the patients selected were all from hospitalized patients. There were still difference that whether choose medical treatment or not when patients in COPD acute exacerbation between male patients and female patients (Mannino et al., 2002). In terms of age, the incidence of male COPD patients in the lower age group was higher than that of women COPD patients, suggesting that the onset of COPD was earlier than that of women.

## Gender Difference of AECOPD Combined with Osteoporosis

The etiology of osteoporosis was very complicated, and the pathogenesis was not completely clear. After menopause, the estrogen levels dropped in women, and the lack of estrogen caused bone absorption and redevelopment balance disorder was recognized as an important cause of osteoporosis (Lozo et al., 2004). The study found that women with AECOPD had a much higher prevalence of osteoporosis than man. For women with COPD were mainly after postmenopausal period. The main pathogenesis of postmenopausal osteoporosis were the imbalance of higher nervous activity, autonomic nervous function disorders, endocrine (high prolactin). Liver disorder was the mian pathogenesis of TCM (Yang, 2011). And blood stasis was major component of osteoporosis TCM syndrome (Varkey, 2004). The above could explain that gender had highly correlation with osteoporosis, and women with AECOPD were more vulnerable to osteoporosis.

## CONCLUSION

Study of correlation between gender phenotype with COPD had attracted more and more attention in the world. The Global Initiative for Chronic Obstructive Lung Disease (GOLD) had mentioned the influence of different gender in COPD occurrence. The research had been carried out extensively on the impact of clinical phenotype on disease development. Chinese medicine believed that men and women were endowed with different biological bases, different physiological bases and different types of emotions, which would directly affect the diseases. Through the clinical observation and records, it could judge whether the gender difference had relation with disease, or inherent correlation, or whether one gender were more vulnerable to COPD, or more tend to certain symptom. These could provide evidence, assist to carry out clinical diagnosis and treatment and prevention of the disease, so as to have a positive impact in the whole course of the disease among patients with COPD.

This paper showed that there were gender differences in the age of onset, the degree of respiratory difficulty, complications, imaging examination and TCM syndromes of AECOPD patents. The AECOPD was based on empirical evidence, and men were more likely to have clinical evidence than women. From the specific classification, Qi and blood stasis and liver depression usually happen on women, while, the lung and kidney Yin deficiency syndrome usually happen men. These provided certain guiding significance for future clinical diagnosis and treatment. It could be continuously repeated follow-up and verify the differences of clinical cases, then judge it with COPD clinical onset, development, treatment and prognosis of relationships, and provided a new method for the prevention and treatment of traditional Chinese medicine COPD. This paper had small sample size, the selected patients group were all hospitalized patients, relatively limited, might had inadequate in TCM syndrome distribution of different gender, and remained to be further research in the future.

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