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ORIGINAL RESEARCH

# The outcome and the influencing factors of the age of onset in post-mortem of chronic bronchitis patients: a retrospective study

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Linyun Zhu[1]
Zhenhua Ni[2]
Xuming Luo[1]
Zhuhua Zhang[1]
Shiqiang Wang[1]
Ziyu Meng[1]
Xiandong Gu[1]
Xiongbiao Wang[1]

[1]Department of Respiratory Medicine, Putuo Hospital, Shanghai University of Traditional Chinese Medicine, Shanghai, [2]Central Laboratory, Putuo Hospital, Shanghai University of Traditional Chinese Medicine, Shanghai, China

**Purpose:** Chronic bronchitis is thought to occur in elderly patients, and smoking seems to be an important risk factor. The outcomes related to the age of onset in patients with chronic bronchitis are still unclear.

**Patients and methods:** A retrospective study was conducted on deceased patients whose diagnosis included bronchitis from 2010 to 2016. Patients were separated into two groups according to the age of onset (Group I, age ≤50 years old; Group II, age >50 years old). Information regarding disease course, smoking history, death age, number of admissions per year, Hugh Jones Index, and self-reported comorbidities of the patients was recorded.

**Results:** The courses of chronic cough and sputum were 33.38±7.73 years and 14.44±8.60 years in Group I and Group II, respectively ($p<0.05$). The death ages of Group I and Group II were 77.65±7.87 years and 84.69±6.67 years, respectively ($p<0.05$). There was a significant negative correlation between the number of hospital admissions per year and the age of onset. The age of onset was negatively associated with daily smoking count ($r=-0.210$) and total smoking count ($r=-0.146$). In Group I, there were fewer cases of coronary heart disease (OR =0.41 [0.24–0.71]), neurological diseases (OR =0.48 [0.24–0.97]), and total comorbidities (OR =0.67 [0.54–0.85]) than in Group II.

**Conclusion:** Patients with early onset chronic bronchitis had a longer history, younger death age, poorer health status, and lower incidence of comorbidities.

**Keywords:** chronic airway disease, comorbidity, Hugh Jones Index, smoking, hospital admission, disease course

## Introduction

Chronic bronchitis is often thought to be an age-related disease that occurs after years of cigarette smoking. It is characterized by chronic coughing, chest tightness, and dyspnea. Chronic bronchitis occurs not only in older individuals but also in younger people. The age of onset is determined by the interaction of gene polymorphisms and environmental factors. Smoking status,[1] location, occupational dust exposure, type of house,[2] radiation,[3] allergic history, childhood asthma, parental bronchitis symptoms,[4] and biomass fuels[5] are all related to the incidence of chronic bronchitis. Chronic bronchitis also shows a moderate familial aggregation, particularly in women.[6] The T5-TG12 haplotype of the cystic fibrosis transmembrane receptor (*CFTR*) gene,[7] *CFTR* dysfunction due to smoking,[8] and aberrant expression of epigenetic markers may cause a higher incidence of chronic bronchitis.[9] Although chronic bronchitis is associated with impaired quality of life, hospital admissions, and increased mortality,[10] it has not garnered much attention since the introduction of the term chronic obstructive

Correspondence: Xiongbiao Wang
Department of Respiratory Medicine, Putuo Hospital, Shanghai University of Traditional Chinese Medicine, Shanghai, China
Tel +86 021 2223 3222 ext 58073
Fax +86 021 6254 1705
Email xiongbiao6@yahoo.com

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pulmonary disease. Previous studies have shown that chronic bronchitis notably increases the risk of continuous airflow limitation and all-cause mortality in subjects <50 years old, but not among subjects ≥50 years old.[11] Few studies have focused on the clinical features, related factors, and outcomes according to the age of onset in chronic bronchitis. Our study aims to determine the relationship between the age of onset and severity of chronic bronchitis, the influencing factors of the age of onset on comorbidities, and the cause of death in patients with chronic bronchitis.

## Patients and methods

### Participants

We conducted a retrospective study by reviewing the medical records of deceased patients admitted to the Shanghai Putuo District Central Hospital and whose diagnosis included chronic bronchitis (ICD-10: J42) from 2010 to 2016. Data were acquired from the hospital database. This study enrolled 558 patients whose baseline characteristics, disease history, and self-reported comorbidities were recorded.

Patients with chronic bronchitis were defined as having a sputum-producing cough daily for at least 3 months per year for two consecutive years. Smoking patients are defined as having a smoking history, including current and former smokers. Smoking history included smoking duration, daily smoking count, and total smoking count. The number of hospital admissions per year was considered to be an average admission of the past year.

The age of onset was defined as the first occurrence of recurrent cough and sputum, which was reported by the patients in their medical records as a retrospective indicator. Patients were separated into two groups according to the age of onset. The age of Group I was ≤50 years, while the participants in Group II were >50 years old. The course of disease was detailed through retrospective data and defined as the occurrence of this disease until the patients' death. The clinical dyspnea index was evaluated using the Hugh Jones Index. The self-reported comorbidities included coronary heart disease (ischemic heart disease, myocardial infarction, and coronary artery disease), diabetes, heart failure, hypertension, malignant tumor, mental disease (depression, mania, dementia), neurological disease, and renal failure (renal function lower than chronic kidney disease [CKD] stage III), all of which were referred from the Charlson Comorbidity Index.

### Statistical analysis

All data are expressed as the mean ± SD for continuous variables and as frequencies and percentages for categorical variables. Continuous data were compared using the Student's *t*-test or the Wilcoxon's test, while categorical data were compared using the chi-squared and Fisher's exact tests. Spearman's rank correlation techniques were used to analyze the relationships between several continuous variables. The survival analysis used the Cox proportional hazard model. A $p$-value <0.05 was considered statistically significant for single comparisons. All the reported $p$-values were two sided. Data were analyzed using the SPSS 22.00 software package (SPSS Inc, Chicago, IL, USA).

### Ethics approval and consent to participate

The study protocol was approved by the institutional review board of Putuo Hospital, Shanghai University of Traditional Chinese Medicine. The patients' approval or informed consent was not required for a retrospective review of their records. The patient data used in our study did not include any identifying information.

## Results

Five hundred fifty-eight deceased patients who met all of the criteria were included in this study. There were 405 males (72.6%) and 153 females (27.4%). Patients were divided into two groups according to the age of onset. Group I (the age of onset was ≤50 years) included 63 patients, whereas Group II (the age of onset was >50 years) included 495 patients.

### Longer course of disease, earlier age of death, and poorer dyspnea status in early onset chronic bronchitis patients

The average course of chronic cough and sputum was 16.71±10.66 years. The age of onset was 67.32±12.35 years, and the age of death was 83.89 years. The course of chronic cough and sputum was notably longer in Group I than in Group II. The Hugh Jones Index showed significant differences between these two groups. The age of onset was significantly negatively correlated with the number of hospital admissions per year (Table 1).

### The correlation between smoking history and the age of onset

There were 233 patients with a history of smoking, of which only 35 patients had not quit smoking. There were more patients with a smoking history in Group I than in Group II (Table 2). There were no differences between Group I and Group II in terms of daily smoking counts, smoking duration, and total smoking counts. Furthermore, the age of

**Table 1** The relationship between patient history and the age of onset

| | Group I, mean ± SD | Group II, mean ± SD | *p*-value |
|---|---|---|---|
| Course of chronic cough and sputum (years) | 33.38±7.73 | 14.44±8.60 | 0.000 |
| Age of death (years) | 77.65±7.87 | 84.69±6.67 | 0.000 |
| Hugh Jones Index | 3.84±0.87 | 3.55±0.69 | 0.002 |
| The correlation between the number of hospital admissions per year and the age of onset | $r^2$=–0.146 | | 0.000 |

onset was negatively associated with daily smoking counts ($r$=–0.210, $p$=0.001) and total smoking counts ($r$=–0.146, $p$=0.027), but there was no correlation between the duration of smoking and the age of onset ($r$=–0.116, $p$=0.078, Figure 1).

## The incidence of self-reported comorbidities according to the age of onset in patients with chronic bronchitis

There were eight comorbidities considered, including coronary heart disease (ischemic heart disease, myocardial infarction, and coronary artery disease), diabetes, heart failure, hypertension, malignant tumor, mental disease (depression, mania, dementia), neurological disease, and renal failure (renal function lower than CKD stage III). In Group I (early onset chronic bronchitis patients), there were fewer cases of coronary heart diseases (OR =0.41 [0.24–0.71]), neurological diseases (OR =0.48 [0.24–0.97]), and total complications (OR =0.67 [0.54–0.85]) than in Group II (late-onset chronic bronchitis patients). However, the incidences of diabetes, heart failure, hypertension, malignant tumor, mental disease (including depression, mania, and dementia), and renal failure (renal function lower than CKD stage III) were similar in the two groups (Figure 2).

## The relationship between cause of death and the age of onset

There was no difference in the cause of death in the two groups. Most patients died from chronic respiratory disease (37.6%) and cardiovascular disease (28.9%). Other cause of death included neurological disease, digestion disease, malignant tumor, and so on (Figure 3).

## The relationship between the survival curves of the two groups and the age of onset

The mean ages of death were 77.65±7.87 years and 84.69±6.67 years ($p<0.05$) in Group I and Group II, respectively (Figure 4).

# Discussion

Chronic bronchitis often occurs in elderly individuals. An investigation of community-dwelling individuals aged 40–80 years found that the incidence of chronic bronchitis was 12.7%,[12] and other studies observed similar results.[13,14] Though smoking is the most important risk factor, low socioeconomic class and urban living,[10,15] gender, asthma history,[16] changes in living habits,[14] odor or the musty smell of mildew/mold in the house, exposure to 1,1,1-trichloro-2,2-bis(4-chlorophenyl)ethane (DDT),[49] body mass index,[17] and air pollution[18] play roles in the development of chronic bronchitis. Studies have demonstrated that aging (especially >50 years old) is also a high risk factor for chronic bronchitis.[14,19] As a result of persistent mucus hypersecretion, longer courses of productive cough are related to quicker reductions in the lung function.[20] Early onset chronic bronchitis has a higher risk to develop into irreversible airflow limitation and all-cause mortality.[11]

Though chronic bronchitis is related to aging, our study found that the early onset patients had longer productive cough courses, in which the age of death was much lower than the other patients. Lindberg et al showed that productive cough has a significantly higher risk for death even after adjustment for common risk factors.[21] With the progress of disease, chronic bronchitis has an increased risk for frequent exacerbation.[22,23] Not only did patients with chronic

**Table 2** Smoking history according to the age of onset

| | Group I | Group II | *p*-value |
|---|---|---|---|
| Smoking patients (total patients) n (N) | 35 (63) | 198 (495) | 0.018 |
| Daily smoking count[a] | 23.71±11.84 | 22.18±10.41 | 0.431 |
| Duration of smoking[a] | 39.86±13.09 | 39.51±12.22 | 0.880 |
| Total smoking count (cigarettes×years)[a] | 982.35±617.16 | 862.89±467.05 | 0.288 |

**Notes:** [a]Accessed for smoking patients. Data presented as mean ± SD unless otherwise indicated. N is a total number of patients.

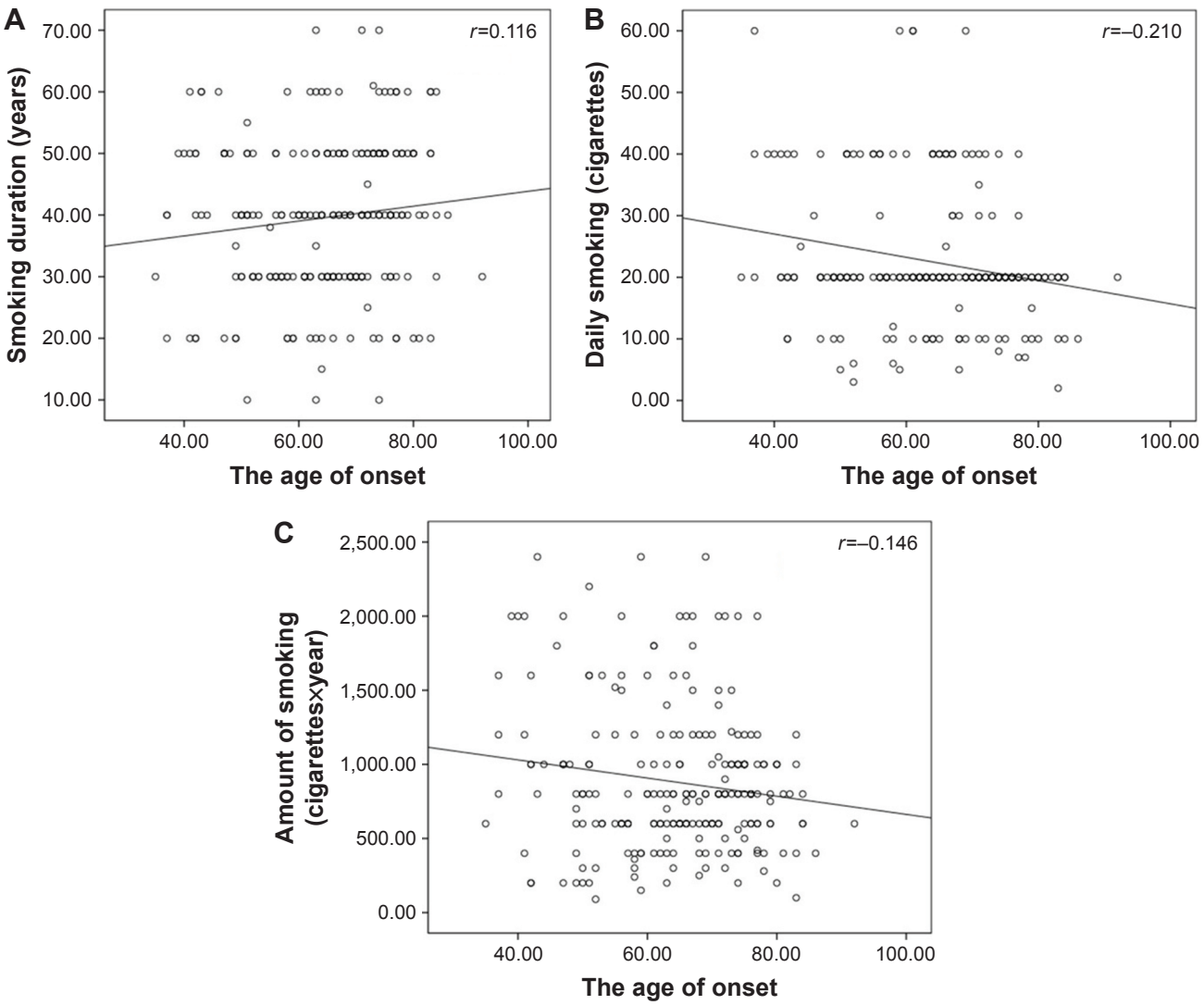


**Figure 1** The correlation between smoking history and the age of onset.
**Notes:** (**A**) The age of onset showed no relationship with smoking duration, $p>0.05$; (**B**) the age of onset and daily smoking count were negatively correlated, $r=-0.210$ ($p<0.05$); (**C**) the age of onset and total smoking counts were negatively correlated, $r=-0.146$ ($p<0.05$).

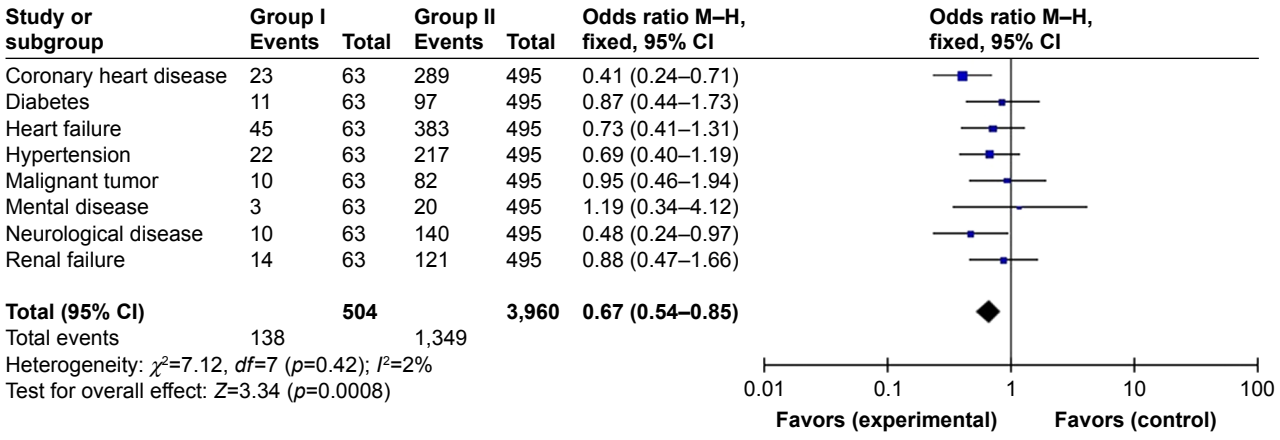


**Figure 2** The relationship between the incidence of self-comorbidities and the age of onset.
**Abbreviation:** M–H, Mantel–Haenszel.

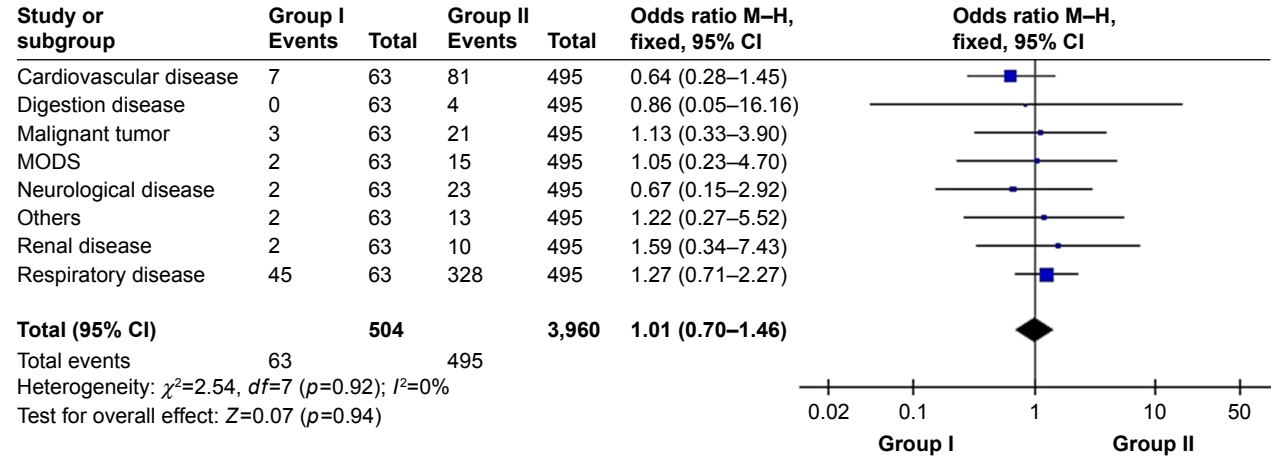


**Figure 3** The relationship between cause of death and the age of onset.
**Abbreviations:** M–H, Mantel–Haenszel; MODS, imultiple organ dysfunction syndrome.

bronchitis have a higher frequency of exacerbation, but also had longer stays in the hospital.[23] We found that the age of onset is negatively correlated with the number of hospital admissions, which was similar to these results. The earlier the onset, the more frequently these patients presented with exacerbation.

In the early onset group, patients showed higher Hugh Jones Index values indicating a poorer health status in our study. Respiratory symptoms are common in chronic bronchitis or COPD. Previous studies have shown that cough is associated with the health-related quality of life,[24] that is, poor quality of life, and breathing problems of chronic bronchitis that limit daily activities.[25] Patients with chronic bronchitis had a greater incidence of chronic dyspnea and activity restriction,[26]

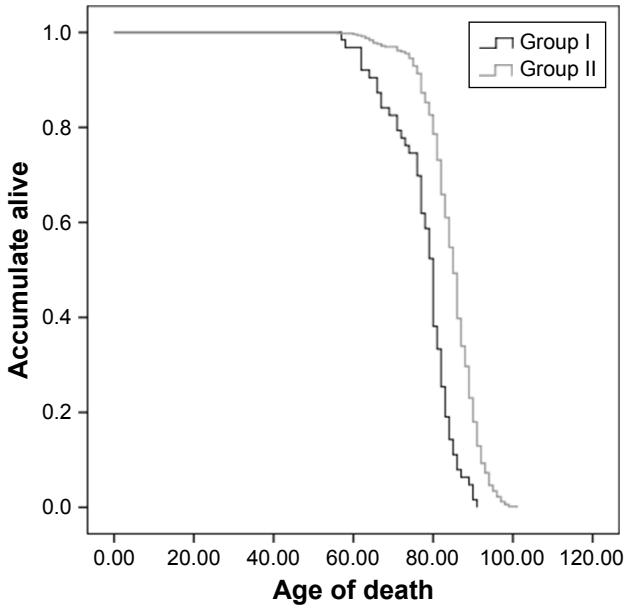


**Figure 4** The mortality between the two groups as a function of the age of onset.

and chronic bronchitis significantly lowered exercise capacity in COPD patients.[27] There may be a reasonable explanation for the occurrence of early onset chronic bronchitis with longer courses of disease and higher activity restrictions. On the other hand, Riesco et al discovered that active smoking was significantly associated with higher grades of dyspnea.[28] Long-term smoking negatively affects the health of patients.[29] The early onset subjects showed higher rates of smoking, which may lead to increase levels of dyspnea shown as higher Hugh Jones Index scores.

Smoking has been proven to be a definitive risk factor for the incidence of chronic bronchitis. Liu et al conducted a prospective study to assess the duration of smoking and airway symptoms. They found that smoking duration showed a linear relationship with symptoms including frequent productive cough, frequent shortness of breath, and shortness of breath affecting physical activity.[29] In our study, though duration of smoking was not related to the age of onset, daily smoking count and total smoking count are negatively associated with the age of onset. Using the time to first cigarette (TTFC) after waking parameter as an indicator of nicotine dependence, current smokers who were found to have shorter TTFC times had an increased risk of chronic bronchitis.[30] While quitting or reducing smoking might lead to fewer chronic productive cough symptoms,[31] other studies have shown that the smokers who quit because of illness had a significantly higher prevalence of chronic respiratory disease.[32] Smoking-related chronic mucus hypersecretion usually resolves following smoking cessation, but the duration of smoking correlated with poorer airway disease activity that reflected the underlying course.[20] There were strong associations between smoking history (including current smokers and ex-smokers) and high incidence of

chronic respiratory diseases.[32] In our study, the daily smoking count and total smoking count were greater with earlier onset, which could perhaps explain why these subjects had a younger age of onset. We found that early onset patients had more active smoking histories and a higher smoking rate than the other group. Not only did smoking history has an impact on the incidence of chronic bronchitis, but also the amount of cigarettes smoked contributed to this disease.

Subjects with physician-diagnosed COPD were more likely have coexisting arthritis, depression, osteoporosis, cancer, coronary heart disease, congestive heart failure, and stroke.[33] Our study found that heart failure, coronary heart disease, and hypertension are the most common complications. Furthermore, in the early onset group, the incidences of coronary heart disease and neurological disease were lower than in the other group. We speculate that as patients grow older, these age-related diseases become more common.

Renal failure is an often neglected problem with regard to chronic bronchitis. A previously conducted meta-analysis demonstrated that COPD was found to be associated with a significantly increased prevalence of CKD (OR =2.20).[34] We found that the incidence of chronic renal failure was similar in both groups, so this disease may not be associated with the age of onset.

Chronic bronchitis increased the risk of ischemic events in all age groups. This observation reached significance for patients >60 years of age, especially over the previous 2 months.[35] The early onset age group presented with a lower incidence of neurological disease likely because these diseases are associated with aging.

Diabetes mellitus (DM) is becoming more common. Previous research has shown that the incidence of diabetes is associated with accumulated smoking exposure, impaired spirometry pattern pulmonary function, reduced 6-minute walking distance without the influence of body mass index, high blood pressure, and high cholesterol.[36] Patients with chronic bronchitis have an increased risk of type 2 diabetes, which is independent of smoking. In addition, chronic bronchitis has a genetic correlation to diabetes.[37] However, there is a decreased incidence of inflammatory diseases such as chronic bronchitis in diabetic patients; thus, type 2 diabetes might reduce the risk of these diseases.[38] We found that there is no difference between the two groups in terms of the incidence of diabetes. Both aging and chronic inflammation might interact in diabetes as a comorbidity of chronic bronchitis. Although DM was not associated with reduced quality of life and poorer pulmonary function, untreated DM was related to reduced quality of life and worse pulmonary function.[39]

Lung cancers are more common in chronic bronchitis. Several studies have found that COPD increases the risk of lung cancer,[40] and that these lung cancers might be more aggressive.[41] Other malignant tumors were found in our study, including colorectal cancer or leukemia. Some are associated with a history of smoking,[42] while some are not well known.

In our study, there were no differences in the incidence of mental illness between the two groups, but it is worth noting that both groups of chronic bronchitis patients presented with mental illness. Mental illnesses, especially depression, gradually increase[43] and become a threat to health in elderly individuals. Both depression and chronic respiratory disease lead to cognitive impairments at the early stages of chronic airway damage and progress with worsening conditions.[44] Individuals with mental illness have a significantly increased incidence of chronic physical health disorders compared with people without mental illness.[45] Patients with chronic bronchitis presented with worse mental well-being than those without chronic bronchitis.[46] Therefore, clinicians and researchers should pay more attention to the mental state of patients with chronic bronchitis.

We found that most patients died from chronic respiratory diseases, which was similar to other studies.[47] There was no difference between the two groups and no differences in all-cause of death in the patients. Instant airway inflammation and longer durations of smoking may account for the earlier death of patients. Mekov et al discovered that the risk factors for increased mortality were age, $FEV_1$ values, severe exacerbation in the previous year, and reduced quality of life.[48] Chronic bronchitis increased all-cause mortality and mortality from respiratory causes, cardiovascular diseases, and cancer.[23] In our study, early onset patients had more frequent exacerbation and poorer health status, which could cause death at younger ages.

Our retrospective study on chronic bronchitis focused on the case histories of deceased patients. Many of these subjects were in critical condition with a long course of disease, which may have introduced some bias into the dataset. Until now, little research focusing on the patient's history prior to death has been conducted, and as a result, this study could lay the foundation for future investigations that center on early onset patients.

## Conclusion

We found that patients with early onset chronic bronchitis had a longer history, younger death age, more smokers, poorer health status, and lower incidence of comorbidities. Further, we need a large, prospective cohort study focusing on the age of onset in chronic bronchitis.

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## Disclosure

The authors report no conflicts of interest in this work.

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