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STUDY OF CLINICAL AND FUNCTIONAL CHARACTERISTICS OF CHRONIC NON-SPECIFIC LUNG DISEASES PREVALENCE IN YOUNG PEOPLE

***Кодиров Д.**, к.м.н. доцент кафедра ВОП-1*
***Ахмедов А.К.**, магистр, Андижанский государственный медицинский институт*

Annotation: Early identification of chronic obstructive pulmonary disease (COPD) in young individuals could be beneficial to attempt preventive interventions. The objective of this study was to investigate clinical features and outcomes of young individuals with COPD from the general population cohort.

Key words: prevalence, morbidity, and mortality, symptoms, clinical information, spirometry results.

Chronic obstructive pulmonary disease (COPD) is a common progressive disease that is characterized by persistent respiratory symptoms and airflow limitation due to airway and/or alveolar abnormalities. It is usually caused by significant exposure to noxious particles or gases. Although COPD is not a fully reversible disease, it is regarded as a preventable and treatable disease. To date, COPD has been considered a disease of the elderly. However, growing evidence has shown that COPD can begin in early life and develop over many years. Thus, the concept of early COPD has gained interest. Furthermore, taking account for the prevalence, morbidity, and mortality of COPD with a high burden on clinical and healthcare resources, early detection and preventive interventions are needed to delay progression of COPD.

Half of COPD cases are developed from those with under-growth and maturation of lung during early adulthood. Another half of COPD cases are attributed to accelerated decline of lung function [8]. It has been recognized that COPD can start early in life. Thus, many efforts have been made to define those patients. Some studies have used the term of “mild” airflow limitation as a surrogate for “early COPD”. However, mild airflow limitation can occur at any age. This term does not mean early disease. It rather refers to the severity of the disease. Definitions for early COPD have not been standardized yet. Recently, Martinez et al. have redefined “young individuals with COPD” as an age-dependent term for patients with COPD (FEV1/FVC < 0.7) at age of 20–50 years independent of the severity of airflow limitation. This simple definition is anticipated to be helpful for screening young patients with early stage of COPD.

Both pharmacologic and non-pharmacologic preventive interventions may lead to better outcomes for young patients with COPD than for old aged clinically diagnosed

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COPD patients, resultantly slowing down the progression of disease and reducing healthcare expenditures. However, it is extremely difficult to enroll young patients with COPD because they rarely exhibit COPD related symptoms and visit hospitals. Thus, there is a lack of clinical information about such subjects. Moreover, approximately two-thirds of patients at risk of COPD in many individuals of primary clinics based studies are underdiagnosed and untreated appropriately. However, we have the opportunity to evaluate this group of patients through our unique national insurance system. Thus, the objective of the present study was to determine the prevalence of young patients with COPD and assess their clinical features and outcomes with focused on COPD exacerbation risk and healthcare expenses.

For this study, cross-sectional data from the Korean National Health and Nutrition Examination Survey (KNHANES) were used. The KNHANES provides nationwide statistical data on the Korean population's health and diet conducted annually. We included participants from January 2008 to December 2009 as index cases. We then merged the Korean National Health Insurance (NHI) database from 2007 to 2012 to investigate clinical information for a year prior to enrollment with follow-up period of 3 years. South Korea implements a compulsory health insurance system for people. The NHI database provides nationwide data with regard to illness and healthcare utilization patterns.

The KNHANES provides a variety of clinical information including demographic data (age, sex, body-mass index [BMI], education level, marital status, and self-perceived income status) and spirometry results. The Korean version of the EuroQoL-5 dimensions questionnaire (EQ-5D), a simple health-related quality of life instrument consisting of five health dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression), was used to measure quality of life (QoL) status. Comorbid conditions were identified by searching for the International Classification of Disease, tenth Revision (ICD-10) codes in the Health Insurance Review and Assessment (HIRA) Service database.

Outcome measurement

For this study, the primary outcome measure was moderate-to-severe exacerbation. A moderate exacerbation was defined as an outpatient clinic visit with an ICD-10 code for COPD (J43.x-J44.x, except J430) and a prescription of systemic steroids and/or antibiotics. Severe exacerbation was defined as an exacerbation necessitating hospitalization or an emergency department visit and prescription of systemic steroids and/or antibiotics. Another outcome measure was medical cost. We analyzed COPD associated medical costs extracted from the NHI database. All expenses are presented in US dollar (USD) with an exchange rate of 1 USD = 1211 Korean won.

Statistical analysis

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Clinical features among the four groups based on smoking and COPD status were compared using the Chi-square test for categorical variables and an analysis of variance for continuous variables. Exacerbation risk was compared by univariate and stepwise multivariate logistic regression analyses. Multivariable analyses were adjusted for covariates including age, sex, FEV1 of %predicted value, and prior exacerbation history. All analyses were two-sided and conducted at a significance level of 0.05 unless otherwise noted.

Prevalence of young patients with COPD

Among 7005 adults with spirometry data, those aged over 50 years regardless of smoking status data were excluded. A total of 2236 subjects were then classified into non-COPD with FEV1/FVC ratio ≥ 0.70 ($n = 2141$, 95.8%) and young patients with COPD and FEV1/FVC ratio < 0.70 ($n = 95$, 4.2%). Both group of subjects were further classified depending on their smoking status into never-smoker and ever-smoker. Resultantly, four groups depending on COPD and smoking status were included in our final analyses: (1) never-smoker, non-COPD ($n = 1294$), (2) ever-smoker, non-COPD ($n = 847$), (3) never-smoker, COPD ($n = 36$), and (4) ever-smoker, COPD ($n = 59$) (Fig. 1).

Clinical characteristics of young patients with COPD

Baseline characteristics are presented in Table 1. Comparison of baseline characteristics revealed that individuals with COPD had more past history of pulmonary tuberculosis and depression than individuals without COPD. Ever-smokers regardless of COPD had more males. Young individuals with COPD had lower FEV1%predicted value and lower FEV1/FVC ratio than young individuals without COPD. Although smoking pack-year was negatively correlated with FEV1 and FEV1/FVC ratio (correlation coefficient: − 0.12 and − 0.18, respectively; both $p < 0.001$), smoking status did not differ.

Disease related medical expenses

There was no significant difference in the cost of disease-related hospitalization or outpatient visits between non-COPD and COPD in young patients. Total cost per person-year was 1085.21 ± 954.61 USD vs. 1259.96 ± 1362.40 vs. 1005.52 ± 1189.53 USD for non-COPD vs. never-smoker COPD vs. ever-smoker COPD groups; $p = 0.984$). Detailed medical costs related to smoking and COPD are presented in Table 3. Compared to the non-COPD group, admission-related medical expenses were higher in the ever-smoker COPD group. However, overall medical expenses were similar between groups.

Using a Korean population-based cohort with 2236 randomly selected individuals aged 40–50 years with spirometry and smoking data, the prevalence of young patients with COPD was 4.2% according to the definition by FEV1/FVC less than 0.7. Risk of exacerbation during a 3-year follow up in ever smokers without COPD and young

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patients with COPD regardless of smoking status tended to be higher compared to that for the non-smoker without COPD group. However, the risk was not significantly higher because the occurrence of an exacerbation event itself was very rare. Moreover, disease-related medical expenses were not significantly different according to smoking or COPD status.

The prevalence of COPD in young individuals aged between 40 and 50 years old in our study was 4.2% (95 of 2236 participants). In a nationally representative sample cohort of China, age-standardized prevalence of COPD in young individuals was 1.4% for age group of 20–29 years, 3% for age group of 30–39 years, 5.1% for age group of 40–49 years. Both general population cohorts in China and Korea showed similar prevalence of spirometry-defined COPD in young participants.

Studies of mild or asymptomatic COPD with mild to moderate airflow limitation are rare, especially in young individuals because such patients generally do not have sufficient respiratory symptoms that would lead to a voluntary hospital visit. Therefore, it has been difficult to find and enroll these patients into trials or observational cohorts. However, we are able to assess those individuals through the KNHANES database which represents the general population in Korea. In our study, EQ-5D scores of COPD in young patients were almost normal. Most patients did not know their COPD status and were not given maintenance inhaler treatment from a clinician. They were found incidentally via spirometry screening. An extremely low prescription rate of inhaler therapy and normal ranged EQ-5D score indicated that these patients truly comprised of asymptomatic, mild COPD patients who had little motivation to visit clinics and follow up regularly.

Respiratory symptoms including chronic bronchitis (such as cough and phlegm) and shortness of breath are associated with increased risk of having airflow obstruction. They are also associated with accelerated decline in lung function with − 2.71 ml/year excess decline in FEV1 and − 2.18 in FVC ($p < 0.001$ for both) as well as greater odds of incident airflow obstruction (odds ratio [OR]: 1.40; 95% confidence interval. This suggests that respiratory symptoms are among predictors for early identification of individuals who are at risk for developing COPD. Moreover, Woodruff et al. [25] showed that although subjects who do not meet diagnostic criteria for COPD, ever smokers with respiratory symptoms can experience exacerbations and activity limitation. Among 825 subjects of preserved pulmonary function, 18.9% had chronic bronchitis symptoms and 26.4% reported that they have diagnosed as COPD previously. As our study is not a multicenter observational cohort study, but general population based study, comprehensive, in-depth survey for respiratory symptoms might be limited. There is no available information on respiratory symptom of COPD in young patients in the KNHANES survey, but quality of life status was near normal and most subjects did not have history of previous COPD diagnosis in young COPD

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group. This suggestive of most young COPD subjects in this study might be asymptomatic and rarely visit hospital. Data of asymptomatic young COPD are rare, but we can approach those group of individuals through the KNHANES database.

It has become more evident that COPD can begin early in life and develop over many years . Individuals we encounter in the clinic are mainly older patients with a severe disease. Therefore, most researchers on COPD have focused on these patients. Identifying individuals who are likely to develop COPD at an early age could allow us to implement preventive interventions and resultantly delay progression, thereby reducing clinical and social burden. To date, the lack of a standardized definition for these group of COPD patients is regarded as one of main problems that hinder clinicians to focus on these patients.

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