学 位 論 文 の 要 旨

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論 文 内 容 の 要 旨

INTRODUCTION

Early detection of chronic obstructive pulmonary disease (COPD) is vital because COPD is associated with an increased risk of lung cancer. However, respiratory function tests, which are essential for the diagnosis of COPD in the primary care setting, have not been widely used, and a system for early COPD detection has not yet been established. A simple questionnaire was suggested as a useful noninvasive method for predicting high-risk groups for COPD. Price et al. proposed a questionnaire for identifying COPD (IPAG questionnaire) using data from the UK and USA. However, Kawayama et al. reported that the specificity of the IPAG questionnaire was very low for the Japanese population. Therefore, since the optimal cutoff value of the questionnaire differs in each country, an optimal questionnaire for the Japanese population is required. For lung cancer diagnosis, low-dose computed tomography (CT) screening has been used. The Division of Medical Oncology & Respiratory Medicine, Shimane University Faculty of Medicine and Japan Agricultural Cooperatives Shimane Koseiren have been conducting voluntary low-dose CT screening for the early detection of lung cancer and COPD since 2009. This study aims to retrospectively evaluate the validity of the IPAG questionnaire for the Japanese and to propose a useful COPD-screening questionnaire using the CT screening data in Shimane, Japan.

MATERIALS AND METHODS

Participants over 40 years of age completed a medical questionnaire and underwent low-dose CT examination. The original questionnaire was based on the IPAG questionnaire with eight additional items prepared by our department members. Participants with emphysema, smoking history, and respiratory symptoms were instructed to undergo a respiratory function test. The participants with the forced expiratory volume in one second (FEV1)/forced vital capacity (FVC) <0.7 on the respiratory function test, were diagnosed with COPD. 11,458 participants underwent CT screening from 2013 to 2016 and were enrolled and filtered using <22.5 pack-years. Data from 3,252 participants were selected for the final analysis. The receiver operating characteristic (ROC) curve determined the best cutoff points for discriminating patients with COPD. The efficacy of the questionnaire items was determined using logistic regression analysis. The present study was a database-based retrospective study, and the study protocol was approved by the Research Ethics Committee of Shimane University.

RESULTS AND DISCUSSIONS

The ROC curve analysis for IPAG score determined the cutoff value of 23, with a sensitivity and specificity of 60.4% and 63.8%, respectively. Therefore, the best cutoff point of the IPAG questionnaire for the Japanese population was considered as 23. The logistic regression analysis revealed significant differences in the question items of "age", "pack-year", "cough", "phlegm", and "feeling of dyspnea". We named the novel COPD screening questionnaire based on CT screening data, including these five items, "COPD-CT." Furthermore, we used the logistic regression model to determine the COPD predicted value. For example, when the patients' responses to the questions "Do you often develop cough?", "Do you often produce sputum?", and "Do you often have a feeling of dyspnea?" were all "yes", and the target age was 80 years old and the pack-years was 60, the COPD predictive value was 44.2%.

The results of this study revealed that for Japanese, the IPAG questionnaire may be too sensitive for screening, because the distribution of points for age and BMI is too large. Therefore, our study also highlighted the desirability of using a questionnaire that is appropriate for the target population. We successfully obtained the COPD predicted value based on the questionnaire items, age, and pack-years. Because the prevalence of COPD in this study (n = 3252) was 6.77%, COPD predicted values more than 6.77% were considered higher than average. Therefore, we believe that the possibility of COPD was high when the COPD predicted value exceeded 6.77%. Furthermore, a combination of the items, which have high predictive values, could be chosen from the tables to match the purpose of each screening.

The study has a few limitations. First, the CT screening indicates emphysema as "present" or "absent", which is a subjective binary assessment and may cause problems with variability in

assessment between different observers. In future studies, it will be necessary to consider not only subjective visual evaluation but also quantitative evaluation of LAA using automated analysis software. Second, COPD is generally classified into "emphysema type" and "bronchial type". In our study, respiratory function tests were performed only on patients with emphysema on CT. Therefore, the bronchial type of COPD may not have been diagnosed. However, since the emphysema type COPD is more common than bronchial type COPD in Japan, if the screening for the emphysema type COPD was feasible, the number of final COPD diagnosed cases was not significantly affected. Third, since respiratory function tests were performed at the discretion of the respiratory physicians at each facility, participants without prior use of bronchodilators were included. Therefore, participants with bronchial asthma may be included among the participants diagnosed with COPD in this study. However, it has been reported that among smokers who underwent respiratory function tests, only a few cases of obstructive disorders disappeared after the use of bronchodilators, so the results of this study will not have a significant impact.

The COPD-CT and the COPD predicted value developed in our study can be used widely by respiratory specialists and general internists as a screening method for COPD. Even without a spirometer, suspected COPD cases can be easily detected in clinics at an early stage, and the suspected patients can be referred to a hospital. The COPD-CT and the COPD predicted value can also be useful for smoking cessation in clinics. Future studies will involve conducting research to further enhance the model by comparing the COPD predicted value and the actual result of CT screening.

CONCLUSION

The IPAG questionnaire had low specificity as a COPD screening questionnaire for Japanese participants. A novel COPD-CT questionnaire and the COPD predicted value was proposed, which is based on the logistic regression analysis of CT screening data in Shimane, Japan.