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Association Between Childhood Asthma and Chronic Obstructive Pulmonary Disease in Later Life

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Abstract

Persistent chronic inflammation and impaired lung growth due to asthma in childhood may have long-term impact on pulmonary function and increase susceptibility to chronic obstructive pulmonary disease (COPD) in later life. To investigate whether childhood asthma is associated with adult lung function and the risk of developing COPD among Japanese older adults, a case–control study was conducted in central Japan. A total of 300 patients with COPD aged 50 to 75 years were referred by respiratory physicians, while 400 controls were recruited from the community. All participants underwent spirometric measurements of lung function. Information on childhood asthma, demographic characteristics, and lifestyle characteristics was obtained by face-to-face interview using a structured questionnaire. The prevalence of childhood asthma was higher ($P = .015$) among the cases (6.3%) than among the control group (2.4%). Childhood asthma was significantly associated with the risk of COPD (adjusted odds ratio 3.32, 95% confidence interval 1.05-10.45). Participants with childhood asthma had lower ($P = .010$) forced expiratory volume in 1 second (mean 1.63 L, standard deviation [SD] 0.64 L) than those without (mean 2.04 L, SD 0.75 L). However, the adjusted lung function difference did not attain statistical significance after controlling for confounding variables such as age and cumulative smoking exposure. The epidemiological evidence suggested a positive association between childhood asthma and COPD in later life. Further study of the effect of adequate childhood asthma treatment on future risk of COPD should be undertaken.

Keywords

case–control studies, lung function, retrospective recall, risk factors, smoking

Introduction

Chronic obstructive pulmonary disease (COPD) is a leading cause of mortality and disability worldwide.[1] It is characterized by a progressive irreversible air flow limitation with common

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symptoms that include chronic cough, sputum production, and dyspnea on exertion.[2] Although tobacco smoking is established as the principal risk factor, 25% to 45% of patients with COPD have never smoked.[3] Therefore, environment exposures and other host factors may contribute to the development of this disease.[2-4]

There has been an increasing focus on the early life origins of COPD. Epidemiological evidence has suggested that host characteristics such as asthma, atopy, and bronchial hyperresponsiveness can impair lung growth during childhood, which in turn increases susceptibility to COPD in adult life.[5] A multicenter European study of more than 13 000 adults aged 20 to 56 years found that childhood asthma was significantly associated with reduced adult forced expiratory volume in 1 second (FEV_1) and the prevalence of COPD for both men and women.[6] Another cross-sectional study of 749 New Zealanders also showed that those with childhood asthma conferred an increased risk of COPD relative to those without.[7] The effect of childhood asthma remained significant even after adjustment for established confounding variables including smoking exposure.[6,7]

The present study aimed to ascertain the strength of association between childhood asthma, adult lung function and the prevalence of COPD among Japanese older adults, which has not been reported in the literature. Findings of the study have important implications on the prevention of the COPD epidemic by appropriate intervention and treatment of asthma in early life.

Methods

Study Design and Subjects

A case–control study was conducted in central Japan in 2006. Three hundred COPD patients referred by respiratory physicians were recruited from the outpatient departments of 6 hospitals in Aichi, Gifu, and Kyoto. Following standard protocol[2] and the Japanese Respiratory Society's guidelines,[8] diagnosis of COPD was confirmed by spirometry after bronchodilation with $FEV_1/FVC < 0.7$, where FEV_1 = forced expiratory volume in 1 second and FVC = forced vital capacity. Inclusion criteria for cases were (*a*) age between 50 and 75 years and (*b*) had COPD as the primary functionally limiting illness, which was diagnosed within the past 4 years. Subjects were excluded if they had a recent stroke, dementia, or other health conditions that prohibited them from being interviewed. Twenty-two eligible patients were subsequently excluded because of missing or incomplete demographic and lifestyle details. The remaining 278 patients (244 men and 34 women) were available for analysis. No statistically significant differences were found between the included and excluded cases in terms of mean age and gender distribution ($P > .05$). Permission to recruit patients and access to medical records were granted by the participating hospitals in Japan.

During the same period, 400 adults residing in the same catchment areas as the cases were recruited. These controls were approached and interviewed at shopping malls, community centers, or when they attended health checks at hospitals. They were selected to be frequency matched to the prevalent cases by age (within 5 years). A higher ratio of controls to cases was intended to improve the sample size. All participants underwent spirometric measurements of respiratory function to avoid misclassification of case-control status. The same exclusion criteria as cases were applied, resulting in 340 eligible controls (272 men and 68 women). Sixty potential controls were excluded mainly on the basis of health conditions rather than spirometry. Approval of the study protocol was obtained from the Human Research Ethics Committee of Curtin University (approval number HR 90/2005) and the 6 hospitals in Japan.

Interview and Questionnaire

A structured questionnaire was administered face-to-face by the first author to collect information from each participant. Demographic and lifestyle characteristics solicited included age, gender, weight (kg) at 5 years before interview, current height (m), education level (high school or below, college or university), marital status (single or divorced, married), residential location (urban, rural), cigarette smoking (pack-years), and alcohol drinking status (nondrinker, drinker). The presence of "childhood asthma" was defined as ever asthma with onset at or before the age of 10 years,[6] which included individuals who had a doctor-diagnosed asthma or a history of asthma treatment in their childhood. A further question on lifelong physical fitness (inactive, active) was added to the questionnaire, defined as "doing active sports or vigorous exercise long enough to get sweaty, at least twice a week," over the entire life course.[9]

For the prevalent cases, each interview was conducted after making appointment with their respiratory physician. The purpose of the study was explained to each participant before obtaining their formal written consent. Confidentiality of the information provided and the right to withdraw without prejudice were ensured and maintained throughout the study. All interviews, averaging 30 minutes in duration, took place in the hospital outpatient departments for patients with COPD and their place of recruitment for controls.

Statistical Analysis

Descriptive statistics were first applied to summarize participant characteristics and lung function measures. After comparing the case and control groups using χ^2 and t tests, unconditional logistic regression analyses were performed to assess the effects of childhood asthma on the COPD risk, whereas multiple linear regression models were used to examine the association between childhood asthma and lung function measures. Besides childhood asthma, independent variables included in the regression models were age, gender, body mass index (BMI = weight [kg]/height $[m]^2$) of 5 years ago, education level, lifelong physical fitness, marital status, residential location, cumulative smoking exposure, and alcohol drinking status. These variables were considered potential confounders from the literature. All statistical analyses were undertaken using the SPSS for Windows package version 20.

Results

Table 1 presents the demographic and lifestyle characteristics of the participants. The majority of them were male (83%), married (84%), with mean age about 66 years. Most participants had high school or below education and resided in rural areas. For the case group, 220 patients (80%) had their COPD diagnosed within the past 2 years. The mean BMI (5 years ago) of patients with COPD was lower than that of control subjects. As expected, the patients with COPD had more cumulative smoking exposure and consequently a weaker lung function than their counterparts without the disease. They also appeared to be less educated when compared with the controls.

The relation between childhood asthma and COPD was next investigated, and the results are presented in Table 2. The prevalence of childhood asthma was significantly higher among the cases (6.3%) than the control group (2.4%) according to χ^2 test ($P = .015$). Logistic regression analysis further confirmed that childhood asthma was significantly associated with at least a 3-fold increase in risk of COPD. Table 3 shows the strength of the association between childhood asthma and adult lung function measures. A substantial decrease in mean FEV_1 was found after

Table 1. Characteristics of Participants by Case–Control Status.

	COPD (n = 278)	Control (n = 340)	*P*
Gender; n (%)			.010
Male	244 (87.8)	272 (80.0)	
Female	34 (12.2)	68 (20.0)	
Education; n (%)			<.001
High school or lower	221 (80.1)	213 (63.6)	
College or university	55 (19.9)	122 (36.4)	
Marital status; n (%)			.881
Single or divorced	43 (15.6)	54 (16.0)	
Married	233 (84.4)	283 (84.0)	
Residential location; n (%)			.014
Urban	48 (17.6)	87 (26.0)	
Rural	224 (82.4)	248 (74.0)	
Alcohol drinking; n (%)			.023
Drinker	158 (56.8)	223 (65.8)	
Nondrinker	120 (43.2)	116 (34.2)	
Lifelong physical fitness; n (%)			.097
Inactive	214 (77.0)	238 (71.0)	
Active	64 (23.0)	97 (29.0)	
Age in years; mean (SD)	66.46 (6.73)	65.35 (5.49)	.028
BMI in kg/m^2; mean (SD)	21.93 (3.09)	23.54 (2.94)	<.001
Smoking in pack-years; mean (SD)	62.43 (26.71)	25.08 (28.55)	<.001
FEV_1 in liters; mean (SD)	1.58 (0.69)	2.39 (0.58)	<.001
FVC in liters; mean (SD)	2.96 (0.87)	3.06 (0.73)	.104
FEV_1/FVC; mean (SD)	0.54 (0.18)	0.78 (0.07)	<.001

Abbreviations: COPD, chronic obstructive pulmonary disease; SD, standard deviation; BMI, body mass index; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity.

Table 2. Childhood Asthma and Risk of COPD for Japanese Older Adults.

	Frequency (%)		Risk of COPD		
Childhood Asthma	Case	Control	Crude OR (95% CI)	Adjusted OR[a] (95% CI)	*P*[a]
No	251 (93.7)	328 (97.6)	1	1	
Yes	17 (6.3)	8 (2.4)	2.78 (1.18, 6.54)	3.32 (1.05, 10.45)	.040

Abbreviations: COPD, chronic obstructive pulmonary disease; OR, odds ratio; 95% CI, 95% confidence interval.
[a]Adjusted for age, gender, cumulative smoking exposure, education level, body mass index, alcohol drinking status, lifelong physical fitness, residential location, and marital status.

sustaining asthma in early life ($P = .01$), even though the corresponding adjusted difference did not reach statistical significance based on the multiple regression model. On the other hand, little association was evident between childhood asthma and adult FVC.

Discussion

The present study provided the first report on the association between childhood asthma and COPD for Japanese adults. Although tobacco smoking is a major determinant of COPD, wide

Table 3. Childhood Asthma and Lung Functions for Japanese Older Adults.

	FVC			
Childhood Asthma	Mean (SD); Liters	Crude Coefficient (95% CI)	Adjusted Coefficient[a] (95% CI)	P^a
No	3.02 (0.80)	—	—	
Yes	2.92 (0.87)	−0.10 (−0.43, 0.23)	0.08 (−0.20, 0.35)	.589
	FEV_1			
Childhood Asthma	Mean (SD); Liters	Crude Coefficient (95% CI)	Adjusted Coefficient[a] (95% CI)	P^a
No	2.04 (0.75)	—	—	
Yes	1.63 (0.64)	−0.41 (−0.71, −0.10)	−0.20 (−0.46, 0.06)	.138

Abbreviations: FVC, forced vital capacity; FEV_1, forced expiratory volume in 1 second; SD, standard deviation; 95% CI, 95% confidence interval.

[a]Adjusted for age, gender, cumulative smoking exposure, education level, BMI, alcohol drinking status, lifelong physical fitness, residential location and marital status.

variations in adult lung function not explained by smoking alone may be related to early life factors.[6] Our study found that childhood asthma was associated with an increased risk of subsequent COPD among Japanese adults. In support of the finding, a longitudinal study reported that patients with active asthma had significantly higher hazard ratios for acquiring COPD than inactive patients or nonasthmatics.[10] A recent cross-sectional study in New Zealand also identified childhood asthma as the strongest predictor of COPD,[7] while a large cohort study of European young adults concluded that airway hyperresponsiveness, childhood respiratory infections, and a family history of asthma were major determinants of COPD.[11] The emerging epidemiological evidence concurs with another editorial comment that chronic asthma carries a greater risk of developing COPD than that caused by smoking.[12] Moreover, Japanese adults with childhood asthma tended to have a lower adult FEV_1. It has been documented that mild to moderate asthma can affect lung growth in children and adolescents.[13] The persistent chronic inflammation and lung growth impairment may then lead to a larger decline in lung functon and increased susceptibility to COPD in later life.[5,6] More research is needed to untangle the complex relationship between asthma and COPD.

In this study, the sample size of 618 subjects allowed sufficient power for the multivariable analysis. Another strength of the study was that spirometric measurements of lung function were taken to ensure correct classification of the case–control status. All interviews and assessments were performed by the same investigator (first author) to eliminate inter-interviewer bias. However, a significant difference in male to female ratio between the case and control groups was observed, which could be avoided by matching the controls with cases by gender.

The main limitation of the present study concerned the retrospective recall of childhood asthma. It was not possible to verify asthma status with medical records of the elderly participants as these were mostly nonexistent or lost during World War II. The prevalence of childhood asthma might thus be underestimated based on the self-report information. Recall bias between COPD patients and controls was also possible, but a previous study revealed that adults could recall important childhood events with high consistency regardless of symptom status.[14] Nevertheless, caution should be taken in drawing conclusions, though the low rates of asthma were consistent with expectation over 3 decades ago.[15]

Another problem was the lack of data on the severity, duration and treatment of childhood asthma that affected on pulmonary function to different extents.[16] Other confounding variables

not accounted for in the multivariable analyses, such as parental smoking, premature birth, and hospitalization for lower respiratory tract infection in early childhood,[5] might also attenuate the observed associations. To avoid misclassification of asthma status and to determine the casual effect of host factors, a prospective cohort study design using clinical records and collecting accurate baseline information is preferred. However, a long-term follow up (over 40 years) of asthmatic and symptoms-free children is difficult to implement in practice. Indeed, all previous reports in the literature had relied on the retrospective recall of childhood characteristics by the adult participants.

In this study, the community-dwelling controls were recruited during the same period and from the same catchment area as the cases. They should be representative of the elderly Japanese population, but the inherent selection bias could not be ruled out because of their voluntary participation. Finally, the detrimental effect of asthma during childhood was not established for COPD and all participants were blinded to the study hypothesis, so that information bias was unlikely.

Conclusions

Chronic respiratory diseases have resulted in considerable burden of morbidity and mortality across the Asia-Pacific region.[17] This case–control study suggested that Japanese who experienced asthma during childhood are susceptible to a weaker adult lung function and COPD in later life. In addition to tobacco abstinence, more focus and awareness on early life environment particularly further study of the effect of adequate childhood asthma treatment on future risk of COPD should be undertaken.

Declaration of Conflicting Interests

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