Prevalence and risk factors for reduced pulmonary function in diabetic patients: The Korea National Health and Nutrition Examination Survey

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Background/Aims: An association between reduced pulmonary function and diabetes has been observed. Our aim was to evaluate the prevalence and risk factors associated with reduced pulmonary function in diabetic patients.

Methods: We analyzed data from the Korea National Health and Nutrition Examination Survey 2011 to 2013. The study population included data from 8,784 participants (including 1,431 diabetics) aged ≥ 40 years. Reduced pulmonary function was defined as patients with restrictive (forced expiratory volume in 1 second/forced vital capacity [FEV_1/FVC] ≥ 0.7 and FVC < 80% of predicted value) or obstructive (FEV_1/FVC < 0.7) patterns.

Results: Subjects with diabetes had a higher prevalence of restrictive (18.4% vs. 9.4%, p < 0.001) and obstructive impairments (20% vs. 12.6%, p < 0.001) than those without diabetes. The adjusted odds ratios (aORs) (95% confidence interval [CI]) for obstructive and restrictive pulmonary impairment were 0.91 (0.75 to 1.11) and 1.57 (1.30 to 1.89), respectively. In the diabetes population, age (aOR, 1.04; 95% CI, 1.02 to 1.06), male sex (aOR, 1.40; 95% CI, 1.04 to 1.88), and body mass index (aOR, 1.15; 95% CI, 1.10 to 1.21) were independently associated with restrictive pulmonary impairment. Age (aOR, 1.12; 95% CI, 1.09 to 1.14), male sex (aOR, 4.24; 95% CI, 2.42 to 7.44), and smoking at any point (ever-smoker: aOR, 1.96; 95% CI, 1.16 to 3.33) were independent risk factors for obstructive pulmonary impairment in diabetics. Diabetes duration or glycated hemoglobin had no association with pulmonary impairment in diabetes.

Conclusions: Subjects with diabetes had a higher risk of restrictive pulmonary impairment than those without diabetes after adjusting for confounding factors. Older age, male sex, body mass index, and smoking were associated with reduced lung function in diabetes.

Keywords: Diabetes; Prevalence; Respiratory function tests; Risk factors

INTRODUCTION

The rise of a Westernized lifestyle and an increasing prevalence of obesity in Korea has contributed to the growing prevalence of diabetes (12.4% of adults over 30 years old) and prediabetes (38.3%) [1]. In subjects with diabetes, only 45.6% of diabetics reach glycemic control (glycated hemoglobin [HbA1c] < 7%) [2], whereas half of

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the subjects with diabetes are consistently hyperglycemic, leading to an increased risk of developing complications and ultimately elevated morbidity and mortality [3,4]. Reduced pulmonary function in patients with diabetes has been observed in both cross-sectional and prospective studies [3-6]. Systematic review and meta-analysis of pulmonary function in diabetics supports the observation that diabetes is associated with a modest reduction in the forced expiratory volume in 1 second (FEV_1) as well as in the forced vital capacity (FVC) [7,8]. Therefore, decreased pulmonary function has been suggested as a potential complication of diabetes. Microangiopathy, systemic low-grade inflammation, autonomic neuropathy, and diminished respiratory muscle function have been proposed as possible causes of decreased pulmonary function in diabetics [7].

In addition to the rise in diabetes cases, the prevalence of chronic obstructive pulmonary disease (COPD) in Korea has increased from 7.8% to 12.9% in the past 10 years; most subjects with COPD were undiagnosed and untreated [9,10]. A recent general population-based study reported that 11.3% of subjects aged ≥ 40 years had spirometrically-defined restrictive ventilator defects [11]. However, the prevalence of obstructive or restrictive pulmonary dysfunctions in diabetics has not yet been reported. Moreover, the risk factors associated with lung impairments in diabetes remain elusive.

In the present study, we investigated the prevalence of reduced pulmonary function and evaluated its associated risk factors in subjects with diabetes from a nationwide representative Korean population aged ≥ 40 years.

METHODS

Study population

The Korea National Health and Nutrition Examination Survey (KNHANES) is a cross-sectional and nationally representative survey of the health and nutritional status of the Korean population by the Korean Centers for Disease Control and Prevention. A stratified multistage clustered probability sampling design was used to select a representative sample of civilian, non-institutionalized Korean adults at least 18 years of age. This survey consisted of a questionnaire about medical history and health-related lifestyle choices, anthropometric measurements, a physical examination, and biochemical laboratory measurements. For biochemical measurements, participants underwent blood sampling after 8 hours of overnight fasting. Pulmonary function test (PFT) was performed in subjects older than 40 years. For this study, we used data obtained during the 2011 to 2013 KNHANES. We excluded participants among the 24,594 sample individuals as follow: age < 40 years (n = 11,273), no available PFT data (n = 3,985), unacceptable spirometry performance (n = 379), or a history of malignancy (n = 173). Finally, a total of 8,784 participants (including 1,431 diabetics) were included in the analysis of the reduced pulmonary function in diabetes. This survey protocol was approved by the Institutional Review Board of the Korean Centers for Disease Control and Prevention.

Pulmonary function test

Spirometry was conducted by specially trained technicians using a dry rolling seal spirometer (2130 Spirometer, Sensor Medics, Yorba Linda, CA, USA). Measurement of FEV_1 and FVC were conducted in accordance with guidelines from the American Thoracic Society [12]. Spirometry was repeated at least three times to ensure reproducibility and validity. Values used in the study were FEV_1, FVC, and FEV_1 to FVC ratio (FEV_1/FVC). Predicted spirometry values were calculated from the Korean reference equations, based on representative samples of the Korean population [13].

Definitions

Obstructive impairment was defined as FEV_1/FVC < 0.70. Restrictive impairment was defined as FEV_1/FVC ≥ 0.70 and FVC < 80% predicted. Normal lung function was defined as FEV_1/FVC ≥ 0.70 and FVC ≥ 80% [14,15]. Diabetes was defined as fasting plasma glucose levels ≥ 126 mg/dL (≥ 7.0 mmol/L), HbA1c ≥ 6.5% or treatment with antidiabetes medications or previous diagnosis of diabetes by a doctor.

Statistical analyses

Data are expressed as means or percentages with standard errors. Clinical characteristics were compared according to presence of diabetes using the Student *t* test for continuous variables and the chi-square test for categorical variables. Differences among groups based on spirometry were compared by analysis of variance for

Table 1. Clinical characteristics of the study population

Characteristic	Diabetics (n = 1,431)	Non-diabetics (n = 7,353)	p value
Age, yr	59.1 ± 0.3	53.3 ± 0.2	< 0.001
Male sex, %	56.9 (1.6)	48.9 (0.6)	< 0.001
Body mass index, kg/m²	25.4 ± 0.1	24.2 ± 0	< 0.001
Waist circumference, cm	87.5 ± 0.3	82.4 ± 0.2	< 0.001
Smoker, %			0.026
Non-smoker	17 (0.6)	65.2 (0.8)	
Ex-smoker	60.1 (1.8)	17.8 (0.7)	
Current-smoker	20 (1.4)	19.9 (1.5)	
Heavy drinker, %	20.1 (1.3)	19 (0.6)	0.426
Regular exercise, %	15.9 (1.2)	19.2 (0.6)	0.021
Hypertension, %	55.6 (1.7)	32.5 (0.7)	< 0.001
Antidyslipidemia drug, %	18.4 (1.1)	5.5 (0.3)	< 0.001
Diabetes duration, yr	4.7 ± 0.22	0.003 ± 0.002	< 0.001
Fasting plasma glucose, mg/dL	135.8 ± 1.2	95 ± 0.2	< 0.001
HbA1c, %	7.3 ± 0.004	5.6 ± 0.01	< 0.001
Total cholesterol, mg/dL	190.1 ± 1.5	195.8 ± 0.5	< 0.001
Triglyceride, mg/dL	156.7 (150.2–163.5)	119.6 (117.5–121.8)	< 0.001
HDL-C, mg/dL	46.5 ± 0.3	51.7 ± 0.2	< 0.001
LDL-C, mg/dL	108.1 ± 1.3	116.8 ± 0.4	< 0.001
FEV_1 % predicted	89.3 ± 0.4	92.4 ± 0.2	< 0.001
FVC % predicted	89.2 ± 0.4	93.9 ± 0.2	< 0.001
FEV_1/FVC	0.8 ± 0.002	0.8 ± 0.001	< 0.001
Spirometry, %			
Restrictive	18.4 (1.4)	9.4 (0.5)	< 0.001
Obstructive	20 (1.4)	12.6 (0.5)	< 0.001
Restrictive or obstructive	32.2 (1.5)	19.8 (0.6)	< 0.001

Values are presented as mean ± SE, percentage (SE), or geometric mean (95% confidence interval).
HbA1c, glycated hemoglobin; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity.

continuous variables and the chi-square test for categorical variables. The odds ratio (OR) and 95% confidence interval (95% CI) for factors associated with obstructive or restrictive pulmonary impairment were analyzed using multivariate logistic regression analysis. p values < 0.05 were considered statistically significant. SAS version 9.3 software (SAS Inc., Cary, NC, USA) for Windows was used for our analyses.

RESULTS

Clinical characteristics of the study population

The characteristics of the 8,784 eligible subjects stratified by the presence of diabetes are summarized in Table 1. Age, body mass index (BMI), waist circumference, the proportion of subjects who are currently or are ex-smokers (ever-smokers), had hypertension, or were taking antidyslipidemia medications were higher in those with diabetes than in those without diabetes. Subjects with diabetes had a higher prevalence of restrictive

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Table 2. Clinical characteristics of the diabetic study population according to pulmonary function

Characteristic	Normal (n = 941)	Restrictive (n = 235)	Obstructive (n = 255)	p value
Age, yr	57.1 ± 0.4	60.6 ± 0.7[a]	65.6 ± 0.7[a]	< 0.001
Male sex, %	53 (2)	52.5 (3.9)	76.5 (3.1)[a]	< 0.001
Body mass index, kg/m^2	25.3 ± 0.1	26.6 ± 0.3[a]	24.5 ± 0.2[a]	< 0.001
Waist circumference, cm	86.9 ± 0.3	90 ± 0.7[a]	87.7 ± 0.7	< 0.001
Smoker, %				< 0.001
Non-smoker	64.9 (2.2)	60.8 (4.2)	37.7 (4.2)[a]	
Ex-smoker	16.4 (1.7)	18.5 (3.4)	37.5 (4.4)	
Current-smoker	18.7 (1.9)	20.7 (4.1)	24.8 (4.1)	
Heavy drinker, %	19.6 (1.7)	20.6 (3.7)	21.7 (3.1)	0.845
Regular exercise, %	16.7 (1.5)	18.3 (3)	10.7 (2)	0.070
Hypertension, %	52.5 (2.1)	60.7 (3.9)	63 (3.7)[a]	0.019
Antidyslipidemia drug, %	17.9 (1.4)	23.7 (2.9)	16 (2.6)	0.110
Diabetes duration, yr	4.5 ± 0.3	4.6 ± 0.5	5.9 ± 0.5	0.060
Fasting plasma glucose, mg/dL	138 ± 1.6	133.9 ± 2.8	129.1 ± 2.2[a]	0.009
HbA1c, %	7.3 ± 0.1	7.3 ± 0.1	7.1 ± 0.1[a]	0.028
Total cholesterol, mg/dL	192 ± 1.9	187.6 ± 3.3	184.7 ± 3.4	0.134
Triglyceride, mg/dL	156.1 (148.1–164.5)	159.3 (143.8–176.5)	156.7 (141.9–173)	0.943
HDL-C, mg/dL	46.8 ± 0.4	46.1 ± 0.7	45.9 ± 0.9	0.544
LDL-C, mg/dL	110.3 ± 1.6	104.3 ± 3	102.2 ± 2.7[a]	0.017
FEV$_1$ % predicted	95.1± 0.4	78.1 ± 0.6[a]	76.1 ± 1.2[a]	< 0.001
FVC % predicted	93.2 ± 0.3	74.0 ± 0.4[a]	86.9 ± 1.0[a]	< 0.001
FEV$_1$/FVC	0.8 ± 0.002	0.8 ± 0.004	0.6 ± 0.005[a]	< 0.001

Values are presented as mean ± SE, percentage (SE), or geometric mean (95% confidence interval).
HbA1c, glycated hemoglobin; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; FEV$_1$, forced expiratory volume in 1 second; FVC, forced vital capacity.
[a]$p < 0.05$ compared to subjects with normal lung function.

(18.4% vs. 9.4%, $p < 0.001$) and obstructive impairments (20% vs. 12.6%, $p < 0.001$) than those without diabetes. However, subjects with diabetes were older, predominantly male, with higher BMI and a greater waist circumference, and ever-smokers compared to subjects without diabetes. The ORs (95% CI) adjusted for age, sex, BMI, waist circumference, and ever-smoker of diabetes for obstructive and restrictive pulmonary impairment were 0.91 (0.75 to 1.11) and 1.57 (1.30 to 1.89), respectively.

Clinical characteristics of the diabetes population according to pulmonary function

Among subjects with diabetes (n = 1,431), those with restrictive pulmonary impairment were more likely to be of older age with higher BMI and a greater waist circumference compared to subjects with normal pulmonary function (Table 2). Subjects with obstructive pulmonary impairment were more likely to be older, with lower BMI, ever-smokers, and have lower fasting plasma glucose levels, lower HbA1c, and lower low density lipoprotein cholesterol levels compared to subjects with normal pulmonary function.

Factors influencing restrictive and obstructive pulmonary impairment among the diabetes population

A multivariable logistic regression model for factors associated with restrictive and obstructive pulmonary impairment is shown in Table 3. Subjects who were older (adjusted OR, 1.04; 95% CI, 1.02 to 1.06), male (adjusted OR, 1.40; 95% CI, 1.04 to 1.88) and who had higher BMI (adjusted OR, 1.15; 95% CI, 1.10 to 1.20) had increased ORs for restrictive pulmonary impairment, whereas

Table 3. Logistic regression analysis of restrictive and the obstructive pulmonary impairment among diabetic subjects

Variable	Restrictive pulmonary impairment				Obstructive pulmonary impairment			
	Model 1[a]		Model 2[b]		Model 1[a]		Model 2[c]	
	OR (95% CI)	p value	OR (95% CI)	p value	OR (95% CI)	p value	OR (95% CI)	p value
Age	1.04 (1.02–1.05)	< 0.001	1.04 (1.02–1.06)	< 0.001	1.12 (1.10–1.14)	< 0.001	1.12 (1.09–1.14)	< 0.001
Sex								
Female	Reference		Reference		Reference		Reference	
Male	1.40 (1.04–1.88)	0.025	1.40 (1.04–1.88)	< 0.001	2.85 (2.24–3.63)	< 0.001	4.24 (2.42–7.44)	< 0.001
Body mass index	1.15 (1.10–1.20)	< 0.001	1.15 (1.10–1.20)	< 0.001	0.98 (0.93–1.03)	0.424		
WC	1.05 (1.03–1.06)	< 0.001			1.01 (1.00–1.03)	0.156		
Ever-smoker								
No	Reference				Reference		Reference	
Yes	1.06 (0.64–1.74)	0.823			1.98 (1.19–3.31)	0.009	1.96 (1.16–3.33)	0.013
Heavy drinker								
No	Reference				Reference			
Yes	0.99 (0.63–1.55)	0.956			1.14 (0.76–1.73)	0.528		
Regular exercise								
No	Reference				Reference		Reference	
Yes	1.11 (0.76–1.64)	0.586			0.61 (0.38–0.98)	0.041	0.71 (0.41–1.21)	0.208
Hypertension								
No	Reference				Reference			
Yes	1.28 (0.94–1.76)	0.119			0.94 (0.67–1.31)	0.701		
Antidyslipidemia Drug								
No	Reference				Reference		Reference	
Yes	1.24 (0.89–1.73)	0.211			0.72 (0.47–1.08)	0.111	0.62 (0.38–0.99)	0.047
Diabetes duration	0.99 (0.97–1.01)	0.261			0.98 (0.96–1.00)	0.091	0.99 (0.97–1.01)	0.429
FBS	1.00 (1.00–1.00)	0.505			1.00 (0.99–1.00)	0.162		
HbA1c	1.02 (0.92–1.13)	0.773			0.92 (0.81–1.05)	0.227		
Total cholesterol	1.00 (1.00–1.00)	0.747			1.00 (1.00–1.01)	0.176		
Log (triglyceride)	1.09 (0.85–1.41)	0.485			1.28 (0.96–1.71)	0.090	1.29 (0.91–1.83)	0.148
HDL-C	0.99 (0.98–1.01)	0.351			1.00 (0.98–1.02)	0.902		
LDL-C	1.00 (0.99–1.00)	0.293			1.00 (1.00–1.01)	0.830		

Reference category: subjects with normal lung function.

OR, odds ratio; CI, confidence interval; WC, waist circumference; FBS, fasting blood sugar; HbA1c, glycated hemoglobin; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol.

[a]Model 1: adjusted for age and sex.

[b]Model 2: adjusted for age, sex, body mass index, waist circumference, regular exercise, antidyslipidemia drug, diabetes duration, and log (triglyceride).

[c]Model 2: adjusted for age, sex, ever-smoker, regular exercise, antidyslipidemia drug, diabetes duration, and log (triglyceride).

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older age (adjusted OR, 1.12; 95% CI, 1.09 to 1.14), male sex (adjusted OR, 4.24; 95% CI, 2.42 to 7.44), and ever-smokers (adjusted OR, 1.96; 95% CI, 1.16 to 3.33) were independently associated with obstructive pulmonary impairment. There was no association between diabetes duration or HbA1c and pulmonary impairment in participants with diabetes.

DISCUSSION

In this study, we examined the prevalence and risk factors for obstructive and restrictive pulmonary impairments in diabetics using a nationally representative sample of the Korea population. Weighted prevalence of obstructive and restrictive pulmonary impairment were 20% and 18.4%, respectively, in diabetic subjects aged ≥ 40 years. Older age, male sex, and increasing BMI were independently associated with restrictive pulmonary impairment. Older age, male sex, and ever-smoking were statistically significant variables for obstructive pulmonary impairment.

Previous epidemiologic studies have reported a prevalence of restrictive pulmonary impairment in 7% to 13% of adults [16,17]. The prevalence of restrictive lung disease was 11.3% in a recent general population-based study using the KNHANES [11]. In our analysis, restrictive pulmonary impairments were present in subjects with or without diabetes at 18.4% and 9.4%, respectively. Diabetes was independently associated with restrictive pulmonary impairment adjusted for age, sex, BMI, waist circumference, and ever-smoker (adjusted OR, 1.57; 95% CI, 1.30 to 1.89). Previous studies suggesting an association between diabetes and restrictive pulmonary dysfunction [4,18-20] support a high prevalence of restrictive pulmonary impairment among the diabetic population. The prevalence of obstructive lung disease was reported to be 12.9% in Korea [10]. Although less consistent association of diabetes with reduction in FEV_1 than FVC, adults with diabetes have lower FEV_1 compared to non-diabetic subjects [7]. In our analysis, obstructive pulmonary impairment was present in 20% and 12.6% in subjects with or without diabetes, respectively. However, subjects with diabetes were older, predominantly male, with higher BMI and a greater waist circumference, and ever-smokers compared to subjects

without diabetes in our KNHANES data. Diabetes was not a significant risk factor for obstructive pulmonary impairment after adjusting for age, sex, BMI, waist circumference, and ever-smoker (adjusted OR, 0.91; 95% CI, 0.75 to 1.11). Further analysis is needed to determine diabetes is an independent risk factor for obstructive pulmonary impairment.

To our knowledge, few studies have investigated the risk factors for reduced pulmonary function in diabetics. Our study showed that aging was independently associated with reduced pulmonary function in diabetics. FEV_1 and FVC gradually decrease with age. Due to the greater decline in FEV_1, the FEV_1/FVC ratio also decreases with age [21]. We also determined that male sex was associated with reduced pulmonary function. This may be partly explained by the greater fat deposits in the abdominal region of men in contrast with the greater gynoid fat presence in women. The excess adiposity encasing the thorax and the abdomen disturbs the respiratory muscles, especially in men [22]. Our study also showed that BMI was significantly related to restrictive pulmonary impairment. This result was in line with previous studies reporting an association between restrictive pulmonary impairment and obesity [23,24]. The accumulation of fat may affect lung and chest wall compliance, causing a stiffening of the total respiratory system [23]. Cigarette smoking was a risk factor for obstructive pulmonary impairment in this study. The effect of cigarette smoking on FEV_1 decline has been documented previously [25,26].

It has been suggested that the reduced pulmonary function in diabetics is associated with diabetes duration as well as HbA1c [3,4]. However, neither diabetes duration nor HbA1c was a significant factor for reduced pulmonary function in this study; this may be partly explained by the relatively short duration of diabetes (4.7 ± 0.22 years) and good glycemic control (HbA1c, 7.3% ± 0.004%). Moreover, the HbA1c level at one particular time does not reflect lifetime glycemic control.

This study had several limitations. First, due to the cross-sectional design, a causal relationship between decreased lung function and risk factors in diabetes could not be determined. Second, due to the lack of data on the measurement of total lung capacity, restrictive pulmonary impairment was defined by a low FVC along with a normal or high FEV_1/FVC ratio. However, any

misclassification of pulmonary impairment may have biased toward no association, and underestimating the effect. Despite these limitations, this study makes some important contributions. The risk factors for reduced pulmonary function in diabetes pose great implications. Although the decreased lung function caused by diabetes has minimal effects on the pulmonary reserve capacity, overlapping conditions such as age, obesity, male sex, or smoking, may have synergistic effects on the loss of lung function.

In summary, subjects with diabetes had a higher risk of restrictive pulmonary impairment than those without diabetes after adjusting for confounding factors. Older age, male sex, BMI, and smoking were all independently associated with reduced lung function in diabetics.

KEY MESSAGE

1. Older age, male sex, and higher body mass index were independent risk factors for restrictive pulmonary impairment.
2. Older age, male sex, and ever-smokers were independently associated with obstructive pulmonary impairment.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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