Original Article

Association between reproductive lifespan and lung function among postmenopausal women

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Background: Both age of menarche and menopause are associated with impaired lung function. However, there is limited data on the association between reproductive lifespan (RL) and lung function. This study aims to evaluate the association between RL and lung function among postmenopausal women.

Methods: In the Korean National Health and Nutrition Examination Survey (2010–2015), an annual cross-sectional survey of a national representative sample of non-institutionalized Korean population, the postmenopausal women aged 40–64 years who underwent spirometry were included. Spirometry was performed according to the recommendations of the American Thoracic Society and European Respiratory Society, and RL (years) was calculated by subtracting the age at menarche from age at menopause.

Results: Among 3,410 postmenopausal women, the mean RL were 34.91 (standard error 0.07). In spline regression models, shorter RL was associated with reduced predicted forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV_1), and the associations were linear. In multivariable-adjusted models, the prevalence ratios (95% confidence interval) for abnormal lung function (restrictive or obstructive ventilatory disorder) comparing women with RL ≤30 years and >30 to <39 years to women with RL ≥39 years were 1.83 (1.15, 2.50) and 1.42 (1.01, 1.84), respectively. Women with RL ≤30 years showed a 2.13 (1.28, 3.54) times higher prevalence of restrictive ventilatory disorder than women with RL ≥39 years.

Conclusions: In postmenopausal women, a shorter RL was associated with abnormal lung function, particularly with a restrictive ventilatory disorder.

Keywords: Sex hormones; menopause; menarche; respiratory function tests

Introduction

With the increase in life expectancy, women spend a greater proportion of their lifetime in the postmenopausal state (1,2). Menopause is a physiological phase characterized by a decrease in hormone production due to the depletion of ovarian function and cessation of menstruation (3). With menopause, women experience various health problems such as hot flashes, night sweats, vaginal dryness, headache, insomnia, and osteoporosis. Postmenopausal women are often considered as a risk population for chronic diseases such as cardiovascular disease and metabolic diseases including diabetes mellitus and obesity (4-6). Likewise, menopause was associated with impaired lung function along with respiratory symptoms (7-12). In addition, menopause is associated with accelerated lung function decline, especially for forced vital capacity (FVC) beyond the expected age change. The population-based longitudinal European Community Respiratory Health Survey (ECRHS) showed that FVC declined more rapidly among transitional (–10.2 mL/year) and post-menopausal women (–12.5 mL/year) compared with women menstruating regularly (8).

Low levels of estradiol are associated with increased systemic inflammation and lung inflammation, which accelerates lung function decline (13). Studies found that early onset menopause was associated with abnormal lung function (7,14). In a recent study conducted with data from UK Biobank, lower lung function, particularly lower FVC having higher risk of spirometric restriction was associated with cessation of menstruation, especially if it occurs early in life (7). Meanwhile, studies found that early age of menarche was also associated with abnormal lung function (15-17). Among participants in the ECRHS II, women with early menarche (age 10 years or less) had lower FEV_1 (adjusted difference, –113 mL) and FVC (adjusted difference, –126 mL) (15). Earlier initiation of menstruation may lead to premature completion of lung development and lower maximally attained lung function (17).

Considering that both age of menarche and menopause were associated with abnormal lung function, reproductive lifespan (RL), a potential marker for the lifetime exposure of female sex hormones, may be associated with lung function. Yet, there is limited data about the association between RL and lung function. This study aims to evaluate the association between RL and lung function among postmenopausal women using the Korea National Health and Nutrition Examination Survey (KNHANES). Main hypothesis is that a shorter RL is associated with abnormal lung function.

Methods

Participants

KNHANES from 2010 to 2015 was used in this study. KNHANES is a cross-sectional survey of a nationally representative noninstitutionalized sample using a stratified, multistage, clustered probability sampling design (18).

The 2010–2015 KNHANES study protocols were approved by the Institutional Review Boards of the Korea Centers for Disease Control and Prevention. Written informed consent was obtained from all participants.

Measurement

KNHANES is composed of three component surveys: health examination, health interview, and nutrition survey. For this study, data from the health examination and health interview was used. Health interview was conducted using a standardized questionnaire by a trained interviewer and detailed physical examination was performed at a mobile examination center (18). All methods were carried out in accordance with the approved guidelines and regulations.

Spirometry was part of the health examination and it was performed according to the recommendations of the American Thoracic Society and European Respiratory Society (19). Absolute values of forced expiratory volume in 1 second (FEV_1) and FVC were obtained, and the percentage of predicted values (% predicted) for FEV_1 and FVC were calculated using the reference equation obtained on analysis of the representative Korean sample (20). Spirometry-defined lung function was classified as normal (FEV_1/FVC ≥0.7 and FVC ≥80% predicted), restrictive ventilatory disorder (FEV_1/FVC ≥0.7 and FVC <80% predicted), and obstructive ventilatory disorder (FEV_1/FVC <0.7) (21). Restrictive or obstructive ventilatory disorder was considered as having abnormal lung function. Because there could be age related over-diagnosis of obstructive lung disease with fixed ratio, we also conducted a sensitivity analysis using the lower limits of the normal range (LLN) criterion to define abnormal lung function. LLN criterion -defined lung function was classified as normal (FEV_1/FVC ≥ LLN and FVC ≥ LLN), restrictive ventilatory disorder (FEV_1/FVC ≥ LLN and FVC < LLN), and obstructive ventilatory disorder (FEV_1/FVC < LLN) using the reference equations from the KNHANES II (22). Height,

weight, and waist circumference were measured by trained nurses. Body mass index (BMI) was calculated by dividing the weight (kg) by the height squared (m) and classified as underweight (<18 kg/m^2), normal (18–22.9 kg/m^2), overweight (23–24.9 kg/m^2), and obese (≥25 kg/m^2), according to the World Health Organization guidelines for Asian populations (23). Number of parity was classified into two groups (<4 and ≥4). Comorbid condition included arterial hypertension, dyslipidemia, diabetes mellitus, which were based on laboratory data and self-reports of physician diagnosis from questionnaire conducted by the KNHANES (24,25). All clinical analyses were performed by the Neodin Medical Institute, a laboratory certified by the Korea Ministry of Health and Welfare.

For RL and endogenous hormone-related factors including number of parity, or use of oral contraceptive, the data was obtained from the health interview. RL (years) was calculated by subtracting the age at menarche from age at menopause. Since there was no cut-off for RL, we categorized it into 3 groups according to the sample distribution: 10th percentile (≤30 years), 11th–89th percentiles (>30 to <39 years), and 90th percentile (≥39 years). Age at menarche and age at menopause were categorized into 3 groups: 10th percentile (≤13 years), 11th–89th percentile (>13 to <18 years), and 90th percentile (≥18 years); 10th percentile (≤46 years), 11th–89th percentile (>46 to <54 years), and 90th percentile (≥54 years), respectively. Smoking history was divided into 3 categories: current or former smoker (those who had smoked 100 or more cigarettes over their lifetimes and did or did not smoke currently respectively) and never smoker (those who had smoked 100 or less cigarettes over their lifetimes). In addition, information on scholarly level, monthly family income, marital status, smoking status, medical history, and comorbidities were obtained from the health interview. Comorbid conditions also included tuberculosis, asthma, stroke, myocardial infarction, cancer, osteoarthritis, and rheumatoid arthritis.

Statistical methods

The KNHANES sampling weights accounting for the complex survey design, survey non-response and post-stratification were used (18). Descriptive statistics were used to summarize the characteristics of participants by the presence of abnormal lung function. Continuous and categorical variables were compared among the two categories of group using linear regression and χ^2 tests,

respectively. Nominal variables were presented as a number and percentage, and continuous variables were presented as a mean ± standard error of the mean.

Multinomial logistic regression to evaluate the association between RL and abnormal lung function was used, and participants with normal lung function were used as the reference group. For the main analyses, the multivariable-adjusted prevalence ratios (PR) and 95% confidence intervals (CI) of abnormal lung function prevalence comparing RLs were calculated. The same analyses were performed for age at menarche and menopause. Age, BMI categories, smoking status, cardiovascular disease, diabetes mellitus, musculoskeletal disease, asthma, tuberculosis, oral contraceptive use, and number of high parity were adjusted to control potential confounders.

In addition to categorical analysis, RL was modeled as continuous variables using restricted cubic splines with knots at the 5th, 35th, 65th, and 95th percentiles of the sample distribution to provide a flexible estimate of the dose-response relationship between RL and predictive FVC and FEV$_1$. Stratified analyses were also performed to evaluate the association of RL and abnormal lung function in pre-specified subgroups defined by obesity (no and yes) and smoking status (never and ever).

P value <0.05 was considered as statistically significant. All analyses were performed using the STATA version 14 (StataCorp LP, College Station, TX, USA) and R 3.2.1 (Vienna, Austria; http://www.R-project.org/).

Results

Postmenopausal women aged 40 to 64 years old who underwent spirometry (N=4,466) were included. Women who experienced premature menopause (<40 years; N=191), artificial menopause (N=1,000), or history of lung cancer (N=11) were excluded. In addition, 17 participants who had missing information regarding age at menarche or menopause onset were excluded. The final sample size was 3,410 (*Figure 1*).

Among 3,410 postmenopausal women, the mean (standard error) age at survey was 56.53 (0.10). The mean menarche age, menopause age, and RL was 15.33 (0.04), 50.24 (0.07), 34.91 (0.07), respectively (*Table 1*).

The prevalence of abnormal lung function was 15.0% (*Table 1*). Women with abnormal lung function were older (57.42 *vs.* 56.38 years, P<0.01), and more likely to have higher BMI (24.66 *vs.* 24.02, P<0.01), asthma (10.59% *vs.* 2.5%, P<0.01), tuberculosis (10.41% *vs.*
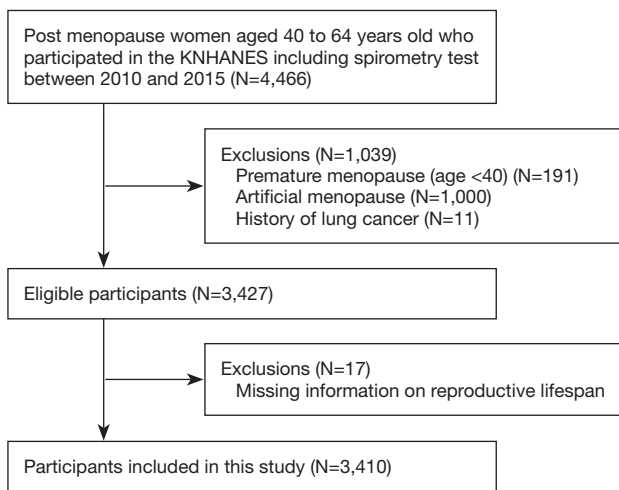
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Post menopause women aged 40 to 64 years old who participated in the KNHANES including spirometry test between 2010 and 2015 (N=4,466)

Exclusions (N=1,039)
Premature menopause (age <40) (N=191)
Artificial menopause (N=1,000)
History of lung cancer (N=11)

Eligible participants (N=3,427)

Exclusions (N=17)
Missing information on reproductive lifespan

Participants included in this study (N=3,410)

Figure 1 Flow chart.

3.12%, P<0.01), arterial hypertension (41.80% *vs.* 32.91%, P<0.01), myocardial infarction (1.07% *vs.* 0.41%, P=0.11), and diabetes mellitus (15.88% *vs.* 9.24%, P<0.01) than those with normal function. Women with abnormal lung functions reported later menarche (15.66 *vs.* 15.27 years, P<0.01) and shorter RL (34.54 *vs.* 34.97 years, P=0.049) than women with normal lung function.

In adjusted multivariable models, the PRs for abnormal lung function in women with RL ≤30 years and >30 to <39 years compared to that in women with ≥39 years of RL were 1.83 and 1.42, respectively (*Table 2*). In spline regression models, the association between RL (years) and the predicted FVC and FEV_1 was linear, with reduced function across shorter RL (*Figure 2*). Women who experienced menarche ≥18 years had 1.72 times higher prevalence of abnormal lung function than woman who experienced menarche ≤13 years. Women with menopausal age ≤46 years had 1.32 times higher prevalence of abnormal lung function than women with menopausal age ≥54 years (*Table 2*).

In the fully adjusted model, women with ≤30 years of RL showed a 2.13- and 1.54-time higher prevalence of restrictive and obstructive ventilatory disorder, respectively, than women with ≥39 years of RL. Women who experienced menarche ≥18 years were more likely to have an obstructive ventilatory disorder than women who experienced menarche ≤13 years. Women with menopausal age ≤46 years were more likely to have a restrictive ventilatory disorder than women with menopausal age ≥54 years (*Table 2*). In the sensitivity analysis using LLN

criterion, the results were similar (*Table S1*).

The positive association between shorter RL and higher prevalence of abnormal lung function was stronger in women without obesity and non-smoking status, but the interactions were not statistically significant (all P values for interactions >0.05; *Table 3*).

Discussion

With nationally representative sampled data, shorter RL was associated with abnormal lung function, in particular, restrictive ventilatory disorder. The relationship seemed more robust among non-obese and non-smoking women, but the interactions were not statistically significant. Late onset of menarche was associated with abnormal lung function, particularly with an obstructive ventilatory disorder, and early menopause was associated with restrictive ventilatory disorder suggesting that there would be several mechanisms through which female hormones affect lung function.

In this study, shorter RL was associated with restrictive ventilatory disorder. While there have been many studies evaluating the association either between age of menopause or menarche and lung function, there was no study regarding the association between RL and lung function. Women who had a RL ≤30 years had about 1.8 times higher risk of having restrictive ventilatory disorder compared to women who had ≥39 years of RL. Women with ≤30 years of RL would have reduced exposure to estradiol compared to women with ≥39 years of RL. The restrictive ventilatory disorder may be due to similar mechanisms of abnormal lung function in postmenopausal women. Estradiol has been demonstrated to have an anti-inflammatory effect (13). In line, the hypoestrogenism associated with changes in the hypothalamo-pituitary-gonadal axis in menopause is associated with increased systemic inflammation and lung inflammation, which may contribute to deteriorating lung function (13,26). Further, the decrease in estradiol increases the risk of osteoporosis, which causes compression of the vertebra. This interferes with the lung expansion, resulting in a decrease in lung function, particularly FVC (27). Moreover, postmenopausal women become more insulin resistant (5,28), which is associated with lower lung function and increased respiratory symptoms (29-31). Women with shorter RLs may be more likely to be insulin resistant, resulting in lower lung function. However, the mechanisms underlying associations between RL and lung function impairment need to be further investigated.

Table 1 Characteristics of study participants

Characteristics	Overall (N=3,410)	Abnormal lung function		
		No (N=2,902, 85%)	Yes (N=508, 15%)	P value
Age (years)	56.53 (0.10)	56.38 (0.11)	57.42 (0.24)	<0.01
Body mass index (kg/m^2)	24.12 (0.06)	24.02 (0.07)	24.66 (0.18)	<0.01
Scholarly level (%)				<0.01
Less than middle school	34.14 (1.07)	32.56 (1.15)	43.39 (2.54)	
Middle school	22.30 (0.90)	22.79 (0.99)	19.42 (2.08)	
High school	31.47 (1.00)	32.06 (1.08)	28.02 (2.23)	
College or more	12.10 (0.72)	12.59 (0.79)	9.18 (1.52)	
Income level (%)				0.17
Low	23.61 (0.92)	23.04 (0.97)	26.93 (2.53)	
Low to middle	25.55 (0.89)	26.25 (0.97)	21.48 (2.19)	
Middle to high	25.55 (0.86)	25.70 (0.94)	24.66 (2.28)	
High	25.29 (0.96)	25.01 (1.01)	26.93 (2.42)	
Occupation, yes (%)	54.20 (1.11)	55.23 (1.20)	48.17 (2.71)	0.02
Marital status, yes (%)	99.14 (0.20)	99.07 (0.23)	99.56 (0.27)	0.25
Smoking (%)				0.44
Current	4.16 (0.43)	3.95 (0.45)	5.35 (1.18)	
Former	2.59 (0.31)	2.53 (0.33)	2.92 (0.97)	
Never	93.26 (0.52)	93.52 (0.54)	91.73 (1.46)	
Age at menarche (years)	15.33 (0.04)	15.27 (0.04)	15.66 (0.11)	<0.01
Reproductive lifespan (years)	34.91 (0.07)	34.97 (0.08)	34.54 (0.20)	0.049
Oral contraceptives, yes (%)	19.38 (0.81)	19.07 (0.89)	21.15 (2.22)	0.20
Number of parity (%)				0.07
<4	92.71 (0.54)	93.08 (0.57)	90.53 (1.47)	
≥4	7.29 (0.54)	6.92 (0.57)	9.47 (1.47)	
Age at menopause (years)	50.24 (0.07)	50.25 (0.08)	50.20 (0.17)	0.81
Asthma, yes (%)	3.68 (0.37)	2.50 (0.32)	10.59 (1.66)	<0.01
Tuberculosis, yes (%)	4.19 (0.39)	3.12 (0.37)	10.41 (1.53)	<0.01
Cardiovascular disease (%)				
Arterial hypertension, yes	34.20 (0.98)	32.91 (1.05)	41.80 (2.55)	<0.01
Dyslipidemia, yes	41.70 (1.07)	40.63 (1.14)	47.96 (2.59)	<0.01
Stroke, yes	1.08 (0.21)	0.99 (0.23)	1.64 (0.62)	0.25
Myocardial infarction, yes	0.51 (0.15)	0.41 (0.16)	1.07 (0.53)	0.11
Diabetes mellitus, yes (%)	10.21 (0.65)	9.24 (0.65)	15.88 (2.09)	<0.01
Musculoskeletal disease (%)				
Osteoarthritis, yes	21.4 (0.84)	21.5 (0.91)	20.85 (2.29)	0.79
Rheumatoid arthritis, yes	3.33 (0.35)	3.25 (0.38)	3.85 (1.00)	0.55
Osteoporosis*, yes	16.63 (1.80)	16.71 (1.93)	16.15 (5.65)	0.93

*, osteoporosis was measured only year 2015.

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Table 2 Prevalence ratio and 95% confidence interval of prevalence of spirometry-defined restrictive and obstructive ventilator disorder by reproductive life span (N=3,410)

Variables	Abnormal lung function		Type of ventilatory disorder			
			Restrictive		Obstructive	
	PR (95% CI)	P value	PR (95% CI)	P value	PR (95% CI)	P value
Reproductive lifespan						
≤30 years	1.83 (1.15, 2.50)	0.002	2.13 (1.28, 3.54)	0.003	1.77 (0.87, 3.61)	0.114
>30 to <39 years	1.42 (1.01, 1.84)	0.017	1.54 (1.03, 2.28)	0.034	1.40 (0.84, 2.33)	0.197
≥39 years	Reference		Reference		Reference	
Menarche age						
≥18 years	1.72 (1.13, 2.31)	0.002	1.51 (0.92, 2.47)	0.099	3.22 (1.62, 6.41)	0.001
>13 to <18 years	1.09 (0.79, 1.40)	0.528	0.87 (0.60, 1.26)	0.455	1.93 (1.10, 3.39)	0.022
≤13 years	Reference		Reference		Reference	
Menopause age						
≤46 years	1.32 (0.80, 1.83)	0.167	1.73 (1.03, 2.90)	0.040	0.86 (0.41, 1.82)	0.702
>46 to <54 years	1.30 (0.93, 1.67)	0.071	1.56 (1.04, 2.32)	0.030	1.06 (0.64, 1.73)	0.827
≥54 years	Reference		Reference		Reference	

Adjusted for age, body mass index categories, smoking status, cardiovascular disease, diabetes mellitus, musculoskeletal disease, asthma, tuberculosis, oral contraceptive use and number of high parity. PR, prevalence ratio; CI, confidence interval.
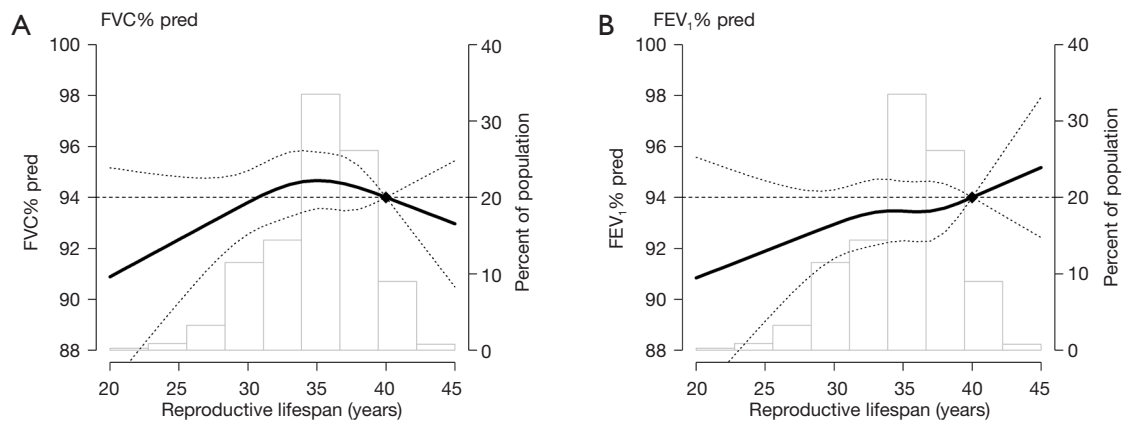

Figure 2 Coefficient (95% CI) for (A) forced vital capacity (FVC) % predicted (% pred) and (B) forced expiratory volume in one second (FEV$_1$; % pred) by reproductive lifespan (years). The curves represent the coefficient (solid line) and their 95% confidence intervals (dashed lines) for lung function based on restricted cubic splines for reproductive lifespan (years). With knots at the 5th, 35th, 65th, and 95th percentiles of their sample distributions. The reference value (diamond dot) was set at the 90th percentile.

While the interactions were not statistically significant, we found that non-obese and non-smoking women with shorter RLs were at a bit higher risk of restrictive ventilator disorder. Hormonal status might not be a very strong predictor of abnormal lung function among postmenopausal women when other important comorbidities such as obesity and smoking are also present. In fact, previous studies showed that a restrictive ventilator disorder, represented by a low FVC, was not only associated with cardiovascular diseases (32), but also with a multitude of

Table 3 Prevalence ratio and 95% confidence interval of prevalence of spirometry-defined restrictive and obstructive ventilator disorder by reproductive lifespan by subgroup

| Variables | Abnormal lung function | | Type of ventilatory disorder | | | |
| | | | Restrictive | | Obstructive | |
	PR (95% CI)	P value	PR (95% CI)	P value	PR (95% CI)	P value
Obesity						
Without obesity (N=2,250)						
≤30 years	1.87 (1.07, 2.68)	0.016	2.43 (1.18, 5.01)	0.016	1.78 (0.76, 4.16)	0.181
>30 to <39 years	1.45 (0.96, 1.93)	0.058	1.68 (0.98, 2.88)	0.058	1.44 (0.77, 2.68)	0.248
≥39 years	Reference		Reference		Reference	
With obesity (N=1,160)						
≤30 years	1.79 (1.05, 2.53)	0.060	1.93 (0.89, 4.17)	0.094	1.77 (0.52, 6.09)	0.362
>30 to <39 years	1.41 (0.94, 1.87)	0.149	1.44 (0.82, 2.54)	0.205	1.30 (0.52, 3.26)	0.577
≥39 years	Reference		Reference		Reference	
P for interaction	0.98		0.99			
Smoking						
Never-smoker (N=3,194)						
≤30 years	1.98 (1.21, 2.75)	0.001	2.21 (1.29, 3.78)	0.004	2.22 (1.03, 4.76)	0.041
>30 to <39 years	1.52 (1.06, 1.98)	0.004	1.55 (1.03, 2.33)	0.034	1.77 (1.02, 3.08)	0.044
≥39 years	Reference		Reference		Reference	
Ever-smoker (N=208)						
≤30 years	1.19 (0.33, 2.05)	0.819	1.25 (0.23, 6.94)	0.797	0.60 (0.09, 3.95)	0.596
>30 to <39 years	0.97 (0.35, 1.59)	0.551	1.27 (0.31, 5.11)	0.739	0.34 (0.08, 1.49)	0.150
≥39 years	Reference		Reference		Reference	
P for interaction	0.33		0.35			

Adjusted for age, body mass index categories, smoking status, cardiovascular disease, diabetes mellitus, musculoskeletal disease, asthma, tuberculosis, oral contraceptive use and number of high parity. PR, prevalence ratio; CI, confidence interval.

clinical conditions, such as aging (33), smoking (34), obesity, metabolic syndrome, and diabetes mellitus (35,36). In line with low FVC under systemic influence, the relationship of RL with cardiovascular diseases has been previously suggested. Risk of coronary heart disease and cardiovascular mortality were lower among women with a higher age at menopause (37-39) and one study observed a reduction in cardiovascular mortality among women with longer exposure to endogenous estrogen (39). Another study showed that shorter RL was associated with an increased risk of noncardioembolic stroke (40). Further studies are necessary to elucidate the relationships among RL, lung function, and cardiovascular disease risk. Yet, considering

the burden of pulmonary and cardiovascular diseases in middle- and older-aged women, health professionals need to consider screening and monitoring lung and cardiac function in postmenopausal women irrespective of obesity and smoking status.

In this study, late onset of menarche was associated with abnormal lung function, particularly an obstructive ventilatory disorder. The subjects with late age of menarche (≥18 years) were significantly older than other groups. Considering that half of them were born during the Korean war, there may be birth cohort effects, such as malnutrition during the war, on abnormal lung growth and development (41). This submaximal lung growth and development could be

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one possible explanation for the relationship between late onset of menarche and obstructive ventilatory disorder (42). Nevertheless, results in this study are different from those of previous studies. Early onset of menarche has been considered one of the clinical factors associated with increased risk of asthma or abnormal lung function, particularly low FVC (15-17,43-45). The multinational ECRHS also showed that lower lung function measured by FEV_1 and FVC was more common in women with early menarche, and abnormal lung health mainly appeared to be related to menarche before the age of 11 years (15). However, in this study, there were only a few subjects who had menarche before the age of 11 years, and it was not possible to evaluate the association.

We also found that restrictive ventilatory disorder was associated with the early onset of menopause. This is consistent with the results from a previous large multicenter population-based study which used the UK Biobank data. The study reported that women with early menopause had lower FVC and higher risk of spirometric restriction among postmenopausal women, but early onset of menopause was not associated with airflow obstruction (7). Given that change of FVC was more pronounced than the change of FEV_1 among transitional and postmenopausal women in the previous study (8), restrictive ventilatory disorder determined by FVC may be more associated with early onset of menopause than obstructive ventilatory disorder determined by FEV_1.

There were several limitations in this study. First, this study was a cross-section design, which limits the assessment of causal inference between abnormal lung function and reproductive life span. As reverse causality for the impact of abnormal lung function on early onset of menarche or menopause could be possible, further studies with longitudinal follow-up analyses need to be conducted. Secondly, data on age of menarche and menopause onset were based on questionnaires, so there was a possibility of measurement errors. However, as age of menarche and menopause onset mark important points to women, this measurement error would be small. Thirdly, the RL acquired from questionnaires may also have measurement errors despite adjustment for the number of high parity and the use of oral contraceptive or hormone replacement therapy. Fourth, measurement of total lung capacity (TLC) to determine accurate restrictive ventilatory disorder was not available in the KNHANES data and some women with obstructive ventilatory disorder might be classified as having restrictive ventilatory disorder. Further studies

with comprehensive lung function tests including TLC are needed to validate our study findings. In addition, information for hazardous substances at the workplace, which might affect lung function, was lacking. However, there were more participants with abnormal lung function among women who did not have a job at the time of survey. Finally, this study used a nationwide representative sample of Koreans, which might not be generalizable to subjects in different countries or of other ethnicities. Despite these limitations, the national representative nature of the patient sample considered in conjunction with the strict quality control procedures of the Korea NHANES is a major strength of this study, adding plausibility to findings.

Conclusions

In conclusion, we demonstrated that shorter RL in postmenopausal women is associated with a decrease in lung function, particularly with a restrictive ventilatory disorder. Clinicians should pay attention to respiratory impairment as well in postmenopausal women, especially with short female hormonal exposure.

Acknowledgments

Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/jtd-19-3726). HYP serves as an unpaid editorial board member of The *Journal of Thoracic Disease* from Feb, 2019 to Jan, 2021. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The 2007–2015 KNHANES study protocols were approved by the Institutional Review Boards of the Korea Centers for Disease Control and Prevention (No. 2007-02CON-04-P, 2008-04EXP-01-C, 2009-01CON-03-2C, 2010-02CON-21-C, 2011-02CON-06-C, 2012-01EXP-01-2C, 2013-07CON-03-4C, 2013-12EXP-03-5C, and 2015-01-02-6C). All patients

enrolled completed the informed consent form.

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Table S1 Prevalence ratio (PR) and 95% CI of prevalence of spirometry-defined restrictive and obstructive ventilatory disorder using LLN criterion by reproductive lifespan

Variables	Abnormal lung function, PR (95% CI)	Type of ventilatory disorder	
		Restrictive ventilatory disorder, PR (95% CI)	Obstructive ventilatory disorder, PR (95% CI)
Reproductive lifespan			
≤30 years	1.52 (0.98, 2.06)	2.01 (1.21, 3.34)	1.20 (0.61, 2.38)
>30 to <39 years	1.22 (0.89, 1.55)	1.36 (0.92, 2.01)	1.13 (0.71, 1.79)
≥39 years	Reference	Reference	Reference
Menarche age			
≥18 years	1.53 (1.01, 2.05)	1.44 (0.86, 2.42)	1.65 (0.98, 2.77)
>13 to <18 years	1.15 (0.85, 1.45)	1.03 (0.72, 1.49)	1.10 (0.73, 1.67)
≤13 years	Reference	Reference	Reference
Menopause age			
≤46 years	1.30 (0.90, 1.70)	1.81 (1.09, 3.01)	0.84 (0.42, 1.68)
>46 to <54 years	1.20 (0.91, 1.48)	1.49 (1.01, 2.22)	0.99 (0.62, 1.59)
≥54 years	Reference	Reference	Reference

Adjusted for age, body mass index categories, smoking status, cardiovascular disease, diabetes mellitus, musculoskeletal disease, asthma, tuberculosis, oral contraceptive use and number of high parity. CI, confidence interval; LLN, lower limits of the normal; PR, prevalence ratio.