

Impact of premature natural menopause on body composition and physical function in elderly women

A Korean frailty and aging cohort study

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Abstract

Induced premature menopause accelerates the rate of body composition changes (decrease in skeletal muscle mass and increase in fat mass) and deteriorating physical function. However, few studies have focused on the impact of premature natural menopause. This study aimed to investigate the impact of age at natural menopause (ANM) on body composition and physical function in elderly women.

Using data from the Korean Frailty and Aging Cohort Study, 765 community-dwelling elderly women aged 70 to 85 years who experienced natural menopause were recruited in this study. Body composition was measured using dual-energy X-ray absorptiometry. Physical function was evaluated by grip strength, the timed up and go test (TUG), and the short physical performance battery (SPPB). Participants were categorized into 4 groups according to their ANM: <40 (premature natural menopause, PNM), 40 to 44 (early natural menopause, ENM), 45 to 54 (normal menopause, NM), and ≥55 (late menopause, LM) years.

There were no significant differences in the body composition parameters, such as the appendicular skeletal muscle mass index (PNM: 5.90 ± 0.90 vs ENM: 5.91 ± 0.70 vs NM: 5.85 ± 0.73 vs LM: 5.90 ± 0.75 , kg/m², P = .75) and trunk fat mass index (PNM: 19.4 ± 3.9 vs ENM: 19.9 ± 4.4 vs NM: 19.9 ± 3.9 vs LM: 20.0 ± 3.8 , %, P = .87) between the groups. In the physical function evaluation, there was no significant difference between the groups in grip strength (PNM: 19.8 ± 0.6 vs ENM: 20.3 ± 0.4 vs NM: 20.6 ± 0.2 vs LM: 20.6 ± 0.4 , kg, P = .53). However, in the TUG (PNM: 11.8 ± 0.4 vs ENM: 10.3 ± 0.3 vs NM: 10.6 ± 0.1 vs LM: 10.2 ± 0.3 , seconds, P < .01) and SPPB (PNM: 10.0 ± 0.2 vs ENM: 10.5 ± 0.2 vs NM: 10.6 ± 0.1 vs LM: 10.8 ± 0.2 , points, P < .05), the PNM group showed significantly lower values than the other groups did. There was no difference in physical function between the groups except the PNM.

Premature natural menopause did not affect the body composition in elderly women but was associated with physical function deterioration. Therefore, more attention should be paid to the prevention of the physical function deterioration caused by premature natural menopause in elderly women.

Abbreviations: AFM = appendicular fat mass, ANCOVA = analysis of covariance, ANM = age at natural menopause, ASM = appendicular skeletal mass, ASMI = appendicular skeletal muscle mass index, BMI = body mass index, DXA = dual-energy X-ray absorptiometry, ENM = early natural menopause, KFACS = Korean Frailty and Aging Cohort Study, LM = late menopause, NM = normal menopause, PNM = premature natural menopause, SPPB = short physical performance battery, TrFM = trunk fat mass, TUG = timed up and go test.

Keywords: body composition, elderly, physical function, premature menopause, skeletal muscle

Editor: Sinan Kardes.

CWW and HHK have contributed equally to this work.

Received: 28 January 2021 / Received in final form: 27 May 2021 / Accepted: 31 May 2021 http://dx.doi.org/10.1097/MD.00000000026353

This research was supported by a grant of the Korea Health Technology R&D Project through the Korean Health Industry Development Institute (KHIDI), funded by the Ministry of Health and Welfare, Republic of Korea (grant number: HI15C3153).

The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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How to cite this article: Cho H, Gu MS, Won CW, Kong HH. Impact of premature natural menopause on body composition and physical function in elderly women: a Korean frailty and aging cohort study. Medicine 2021;100:25(e26353).

1. Introduction

During the normal ageing process, women usually experience natural menopause at an approximate age of 49 to 52 years.^[1] Decrease in sex hormones after menopause are associated with several health problems, including cardiovascular disease^[2] and osteoporosis.^[3] Moreover, menopause results in body composition changes, such as an accelerated decrease in the skeletal muscle mass, an increase in the central fat mass,^[4] and declining physical function.^[5]

Menopause occurring before 40 years of age is termed premature menopause and can be divided into premature natural menopause (PNM) and induced premature menopause; the latter is caused by surgery such as bilateral oophorectomy or chemoradiation therapy.^[6] Women with premature menopause have a higher risk of long-term health problems such as osteoporosis, stroke, and cardiovascular disease than women with normal menopause.^[7] In addition, women with induced premature menopause after chemotherapy showed increased body composition changes, such as decreased truncal lean mass and increased truncal fat mass, than did women who received chemotherapy but had preserved ovarian function.^[8] Women with surgical premature menopause also tend to exhibit poorer physical function than do those with normal menopause.^[9]

Although the effects of induced premature menopause on body composition and physical function are known through previous studies,^[8,9] no study has investigated the effect of PNM on body composition parameters such as skeletal muscle and fat tissue in elderly women. Furthermore, previous studies on the effects of PNM on physical functions in elderly women showed different results by regions. Age at natural menopause (ANM) was associated with both gait speed and grip strength in Albania, and only with grip strength in Latin America.^[10] No association was found in Canada.^[10] Furthermore, previous studies have failed to investigate the effect of PNM on the various aspect of physical functions by measuring only grip strength and gait speed.^[10,11]

We hypothesized that a woman's body composition and physical function in old age may differ according to the ANM, because women with PNM may experience long-term sex hormone deficiency compared with those with normal menopause. Therefore, we investigated the effect of PNM on body composition and physical function in elderly women using a large-scale cohort data of elderly women aged \geq 70 years, by various physical function methods.

2. Methods

2.1. Study population

The study participants consisted of community-dwelling elderly women aged 70 to 84 years who were enrolled in the Korean Frailty and Aging Cohort Study (KFACS) in 2016 to 2017. The KFACS is a longitudinal multicenter cohort study established for the identification of the factors that cause frailty and prevention of frailty in a total of 3014 elderly people living in communities across 10 cities and rural areas in Korea.

Among the elderly women registered in the KFACS, we included women with information on body composition, as measured using dual-energy X-ray absorptiometry (DXA), anthropometric data and information on physical function, information on menstrual history such as age at menarche and menopause, and information on comorbid diseases (cardiac disease, cerebrovascular diseases, diabetes mellitus, asthma, chronic obstructive pulmonary disease, arthritis, etc) that may affect physical function. However, women from 2 centers in which body composition was measured using bioelectrical impedance analysis, those who underwent chemoradiation therapy that can cause induced menopause, women who underwent hysterectomy or ovarian resection, and those who received postmenopausal hormone therapy were excluded. Of 1582 elderly women included in the baseline study, 765 were finally included in this study (Fig. 1). The Institutional Review Board of the Clinical Trial Review Committee at Kyung Hee University Medical Center approved the study. All participants provided a written informed consent (IRB number: 2015–12–103).

2.2. Measurement of anthropometry and body composition

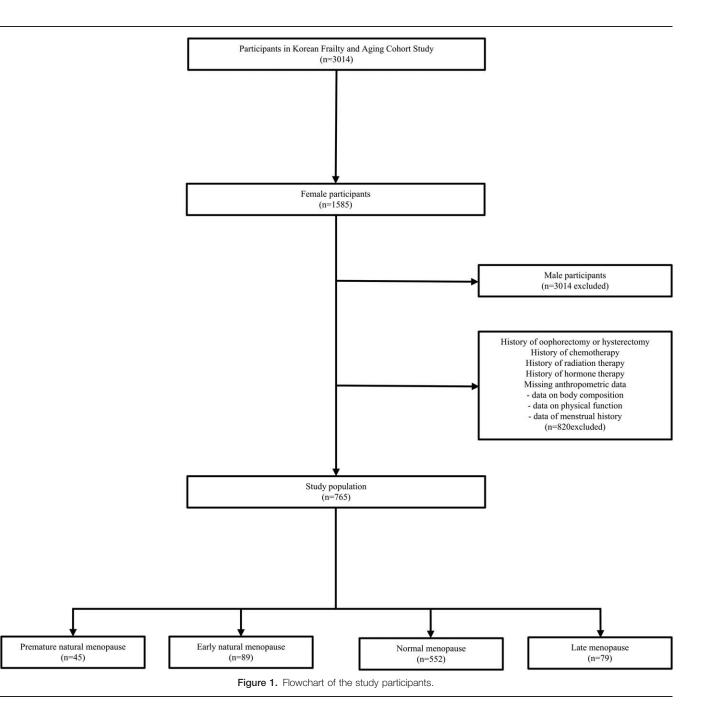
Waist circumference was measured in the exhalation state by a trained examiner using inelastic tape at the midpoint between the lower end of the last rib and iliac crest. Body composition was measured using a hologic scanner (Hologic Inc., Bedford, MA) at 4 centers and a lunar scanner (GE Healthcare, Madison, WI) at 4 other centers. Appendicular skeletal muscle mass (ASM, kg) was defined as the sum of the skeletal muscle mass of the extremities, as measured using DXA. The appendicular skeletal muscle mass index (ASMI) was defined as follows: ASM divided by height squared, ^[12] ASM/ht² (kg/m²), ASM divided by weight, ^[13] ASM/wt (%), and ASM divided by body mass index (BMI),^[14] ASM/BMI (m²). Appendicular fat mass (AFM, kg) was defined as the sum of the fat mass of the extremities, and trunk fat mass (TrFM, kg) was defined as the sum of the fat mass in the trunk. The fat mass index was calculated as AFM divided by body weight, AFM/wt (%) and TrFM divided by body weight, TrFM/wt (%).^[15]

2.3. Measurement of physical function and physical activity level

Grip strength was measured twice in both hands at 3-minute intervals using a digital grip dynamometer (Takei TKK 5401, Takei Scientific Instruments, Tokyo, Japan). The highest value was defined as the grip strength. The timed up and go test (TUG) was measured as the time taken in seconds for the woman to stand up from a chair without an armrest, walk 3 m, turn, walk back to the chair, and sit down. The short physical performance battery (SPPB) comprises 3 subtests: balance tests (side-by-side stand, semi-tandem stand, and tandem stand), gait speed test, and 5-times chair stand tests (single chair stand and repeated chair stand). Each category was scored from 0 to 4, with the total score ranging from 0 to 12 points. Each SPPB item was tested following established guidelines. Walking speed was defined as the time taken for a participant to walk the middle 4 m of a total distance of 7 m with acceleration and deceleration phases of 1.5 m each in their usual speed.^[16] The 5times chair stand test measures the time taken to stand 5 times from a sitting position from a straight-backed armchair without using the arms. The physical activity level of the participants was measured using the Korean version of the International Physical Activity Questionnaire short form and classified into 3 groups: high, moderate, and minimal physical activity level.^[17]

2.4. Assessment of age at natural menopause and age at menarche

Information on age at menopause (age at a time-point at which menstruation had stopped for at least 1 year and had not



restarted) and age at menarche was obtained through a selfreported questionnaire. The reproductive period was defined as the period between menarche and menopause, and the postmenstrual period was defined as the period between menopause and the time of our investigation. Age at menopause was categorized into 4 groups: <40 (PNM), 40 to 44 (early natural menopause, ENM), 45 to 54 (normal menopause, NM), and \geq 55 (late menopause, LM) years.^[18]

2.5. Statistical analysis

All data are described as mean ± standard deviation or number (proportion). One-way analysis of variance was used to compare continuous variables between groups divided according to ANM.

Chi-squared tests were used for comparison of categorical variables. Analysis of covariance (ANCOVA) was performed after adjustment for age, which can have a confounding effect on differences in the body composition and physical function parameters between groups. Statistical analysis was conducted using SPSS version 23.0 (IBM corp., Chicago, IL). A *P*-value of <.05 was considered statistically significant.

3. Results

3.1. Baseline characteristics

Of the 765 enrolled women, 45 (5.9%) had PNM, 89 (11.6%) ENM, 552 (72.2%) NM, and 79 (10.3%) LM. The mean ages in

Table 1

Baseline characteristics of participants by age at natural menopause.

	Age at natural menopause				
Characteristics	<40 (n=45)	40-44 (n=89)	45–54 (n=552)	≥55 (n=79)	P value
Age, y	77.2±4.2 [*]	$76.8 \pm 3.7^{*}$	75.6±3.9	75.9 ± 3.4	<.01
Height, cm	149.9 ± 5.4	151.3 ± 4.7	151.8±5.0	151.4±5.6	.08
BMI, kg/m ²	25.0 ± 3.5	25.1 ± 3.7	24.7 ± 3.0	25.0 ± 3.0	.72
Waist circumference, cm	88.1 ± 10.0	87.5±9.7	86.7 ± 8.3	88.5 ± 8.0	.25
Menstrual history, y					
Age at menarche	16.8 ± 2.3	$17.0 \pm 2.2^{*}$	16.4±1.9	16.7 ± 2.4	<.05
Age at menopause	$38.2 \pm 3.5^{*,**,***}$	$43.8 \pm 1.4^{*,**}$	50.7±2.4	$58.2 \pm 2.4^*$	<.001
Reproductive period	$21.4 \pm 4.3^{*,**,***}$	$26.8 \pm 2.7^{*,**}$	34.3 ± 3.0	$41.6 \pm 3.0^{*}$	<.001
Postmenopausal period	$39.0 \pm 5.3^{*,**,***}$	$33.0 \pm 3.8^{*,**}$	24.9±4.7	$17.6 \pm 3.9^{*}$	<.001
Physical activity level					
High	12 (26.7%)	26 (29.2%)	140 (25.4%)	25 (31.6%)	.30
Moderate	20 (44.4%)	49 (55.1%)	298 (54.0%)	45 (57.0%)	
Low	13 (28.9%)	14 (15.7%)	114 (20.7%)	9 (11.4%)	
Smoking					
Never smoker	44 (97.8%)	88 (98.9%)	540 (97.8%)	76 (96.2%)	.97
Ex-smoker	0 (0%)	0 (0%)	9 (3.8%)	3 (3.8%)	
Current smoker	1 (2.2%)	1 (1.1%)	3 (0.5%)	0 (0%)	
Alcohol drinker	23 (51.1%)	45 (50.6%)	276 (50.2%)	45 (57.0%)	.59
Number of comorbidities	0.84 (0.81)	0.69 (0.77)	0.65 (0.74)	0.57 (0.71)	.28

Values are presented as the mean \pm standard deviation or numbers (percent).

BMI = body mass index.

Significantly different from 45 to 54 year group (P < .05).

** Significantly different from >55 year group (P < .05).

**** Significantly different between 40 and 40–44 year groups (P<.05).</p>

the PNM and ENM groups were significantly higher than those in the NM group (77.2 ±4.2 vs 76.8 ±3.7 vs 75.6 ±3.9 vs 75.9 ± 3.4, years, P < .01). The reproductive period was shorter (P < .001) and the postmenopausal period was longer (P < .001) in association with a lower ANM. There were no differences in height, BMI, waist circumference, physical activity level, smoking and alcohol intake history, and the number of comorbid diseases between-group (Table 1).

3.2. Difference in body composition and physical function between groups

In terms of the skeletal muscle, the ASM/ht² (5.90 ± 0.90 vs 5.91 ± 0.70 vs 5.85 ± 0.73 vs 5.90 ± 0.75 , kg/m²), ASM/wt (23.7 ± 3.2 vs 23.8 ± 2.9 vs 23.8 ± 3.0 vs 23.8 ± 3.1 , %), and ASM/BMI (0.53 ± 0.08 vs 0.55 ± 0.07 vs 0.55 ± 0.08 vs 0.55 ± 0.08 , m²) were not significantly different between the groups. For fat tissue, the AFM/ wt (35.8 ± 6.4 vs 37.1 ± 6.5 vs 36.9 ± 5.7 vs 37.0 ± 5.1 , %) and TrFM/wt (19.4 ± 3.9 vs 19.9 ± 4.4 vs 19.9 ± 3.9 vs 20.0 ± 3.8 , %) values were also not significantly different between the groups.

However, physical function-related differences were observed between the groups. Although not statistically significant, the grip strength in the PNM group was the lowest (19.4 ± 4.4 vs 20.1 ± 4.0 vs 20.7 ± 4.1 vs 20.6 ± 3.9 , kg, P = .15). The time to perform the TUG in the PNM group was significantly longer than that in the other groups (12.1 ± 3.5 vs 10.5 ± 2.5 vs 10.5 ± 2.6 vs 10.2 ± 2.3 , second, P < .01). In the SPPB, the gait speed test (3.6 ± 0.9 vs 3.8 ± 0.5 vs 3.9 ± 0.4 vs 3.8 ± 0.5 , point, P < .01), chair stand test (2.7 ± 1.2 vs 3.1 ± 1.0 vs 3.1 ± 1.0 vs 3.3 ± 0.8 , point, P < .05), and total SPPB (9.9 ± 1.9 vs 10.4 ± 1.5 vs 10.6 ± 1.5 vs 10.8 ± 1.4 , point, P < .01) values were significantly lower in the PNM group than in the NM or LM group. There were no significant differences between the ENM, NM, and LM groups in all the physical function tests (Table 2).

3.3. Difference in body composition and physical function between groups after adjustment for covariates

After adjustment for age, which showed significant differences between the groups in the baseline characteristics using ANCOVA, there were no significant differences in the ASM/ ht² (P=.75), ASM/wt (P=.99), and ASM/BMI (P=.83) between the groups according to ANM. Additionally, there were no significant differences in the AFM/wt (P=.70) and TrFM/wt (P=.87) between the groups.

In the physical function evaluation, there was no significant difference in the grip strength between the groups according to the ANM after adjustment (P=.53). However, even after adjustment, the PNM group still had significantly lower physical function values in the TUG (P<.01), gait speed test (P<.05) and chair stand test (P<.05), and lower total SPPB score (P<.05). There remained no significant difference between the ENM, NM, and LM groups (Table 3).

4. Discussion

In this study, contrary to our hypothesis, there were no significant differences in the body composition parameters, such as skeletal muscle and fat tissue, according to the ANM. However, in the TUG and SPPB, women with PNM had poorer physical function than did those in the other groups; no differences in physical function were observed between the ENM, NM, and LM groups. Our findings indicate the need for close monitoring of physical function in elderly women with PNM. Table 2

	Age at natural menopause				
	<40 (n=45)	40–44 (n=89)	45–54 (n=552)	≥55 (n=79)	P value
Body composition					
ASM/ht ² , kg/m ²	5.90 ± 0.90	5.91 ± 0.70	5.85 ± 0.73	5.90 ± 0.75	.84
ASM/wt (%)	23.7 ± 3.2	23.8 ± 2.9	23.8 ± 3.0	23.8 ± 3.1	.99
ASM/BMI, m ²	0.53 ± 0.08	0.55 ± 0.07	0.55 ± 0.08	0.55 ± 0.08	.64
AFM/wt (%)	35.8 ± 6.4	37.1 ± 6.5	36.9 ± 5.7	37.0±5.1	.67
TrFM/wt (%)	19.4±3.9	19.9 ± 4.4	19.9 ± 3.9	20.0 ± 3.8	.84
Physical function					
Grip strength, kg	19.4 ± 4.4	20.1 ± 4.0	20.7±4.1	20.6 ± 3.9	.15
TUG (s)	12.1 ± 3.5 ^{*,**,***}	10.5 ± 2.5	10.5 ± 2.6	10.2±2.3	<.01
SPPB (point)					
Balance test	3.6 ± 0.7	3.5 ± 0.7	3.6 ± 0.6	3.6 ± 0.6	.49
Gait speed test	$3.6 \pm 0.9^{*}$	3.8 ± 0.5	3.9 ± 0.4	3.8 ± 0.5	<.01
Chair stand test	$2.7 \pm 1.2^{*,**}$	3.1 ± 1.0	3.1 ± 1.0	3.3 ± 0.8	<.05
Total SPPB score	$9.9 \pm 1.9^{*,**}$	10.4 ± 1.5	10.6 ± 1.5	10.8 ± 1.4	<.01

Body composition	and physical function	on by age at natura	al menopause.

Values are presented as mean ± standard deviation.

AFM/wt = appendicular fat mass divided by weight, ASM/BMI = appendicular skeletal mass divided by body mass index, ASM/ht² = appendicular skeletal mass divided by height squared, ASM/wt = appendicular skeletal mass divided by weight, SPPB=short physical performance battery, TrFM/wt=truncal fat mass divided by weight, TUG=timed up and go test.

Significantly different from 45 to 54 year group (P < .05).

Significantly different from >55 year group (P < .05).

Significantly different between 40 and 40–44 year groups (P < .05).

Previous studies have reported that women experience a decrease in their skeletal muscle mass and an increase in their total and central fat mass in association with a decrease in sex hormone levels during the normal menopausal transition.^[4] In addition, women with chemotherapy-induced premature menopause also experience a greater degree of body composition changes, such as increases in the truncal fat mass and decreases in the truncal lean mass than women who received chemotherapy but had preserved ovarian function.^[8] According to the results of previous studies, since elderly women with PNM experience sex hormone deficiency for longer durations than NM women, it is expected that there will be differences in the body composition

parameters such as skeletal muscle and fat; however, we were unable to identify relevant results. In a longitudinal study conducted by Greendale et al,^[19] body composition changes due to menopause occurred predominantly during the menopausal transition period and the change in the fat and lean mass after 2 years of menopause was insignificant. Accordingly, it is presumed that the presence of PNM did not affect body composition in the elderly because even though the longer postmenopausal period has been experienced due to PNM, the major change in body composition occurs during the menopause transition period.

In terms of physical function, the results of the TUG and SPPB (excluding the balance test), which reflect the whole-body

Table 3

	Age at natural menopause				
	<40 (n=45)	40–44 (n=89)	45–54 (n=552)	≥55 (n=79)	P value
Body composition					
ASM/ht ² , kg/m ²	5.91 ±0.11	5.92 ± 0.08	5.85 ± 0.03	5.90 ± 0.08	.75
ASM/wt (%)	23.7 ± 0.5	23.8 ± 0.3	23.8 ± 0.1	23.8 ± 0.3	.99
ASM/BMI, m ²	0.54 ± 0.01	0.55 ± 0.01	0.55 ± 0.01	0.55 ± 0.01	.83
AFM/wt (%)	35.9 ± 0.9	37.1 ± 0.6	36.9 ± 0.3	37.0 ± 0.7	.70
TrFM/wt (%)	19.4 ± 0.6	19.9 ± 0.4	19.9 ± 0.2	20.0 ± 0.4	.87
Physical function					
Grip strength, kg	19.8 ± 0.6	20.3 ± 0.4	20.6 ± 0.2	20.6 ± 0.4	.53
TUG (s)	$11.8 \pm 0.4^{*,**,***}$	10.3 ± 0.3	10.6 ± 0.1	10.2 ± 0.3	<.01
SPPB (point)					
Balance test	3.6 ± 0.1	3.6 ± 0.1	3.6 ± 0.0	3.6 ± 0.1	.88
Gait speed test	$3.6 \pm 0.1^*$	3.8 ± 0.1	3.8 ± 0.0	3.8 ± 0.1	<.05
Chair stand test	2.8±0.1 ^{**}	3.1 ± 0.1	3.1 ± 0.0	3.3 ± 0.1	<.05
Total SPPB score	$10.0 \pm 0.2^{**}$	10.5 ± 0.2	10.6 ± 0.1	10.8±0.2	<.05

Values are presented as mean + standard deviation.

AFM/wt = appendicular fat mass divided by weight, ASM/BMI = appendicular skeletal mass divided by body mass index, ASM/ht² = appendicular skeletal mass divided by height squared, ASM/wt = appendicular skeletal mass divided by weight, SPPB=short physical performance battery, TrFM/wt=truncal fat mass divided by weight, TUG=timed up and go test.

Significantly different from 45 to 54 year group (P < .05).

*** Significantly different from >55 year group (P<.05).

Significantly different between 40 and 40–44 year groups (P < .05).

function related to locomotion, were significantly lower in the PNM group. In previous studies, elderly women with PNM had a gait speed that was 0.054 m/s lower than that among women with an ANM of 50 to 54 years,^[11] and those with ANM > 55 years had a gait speed that was 0.05 m/s faster than that among women with ANM < 45 years.^[9] In this study, through the TUG and SPPB subtests, we confirmed that women with PNM had poorer function in terms of not only gait speed but also other physical function parameters than did women with NM. In addition, since there was no significant difference in physical function between the ENM, NM, and LM groups, we confirmed that ANM < 40 years was a risk factor for lower physical function. As women with PNM experience menopause at a younger age, the duration of exposure to sex hormones, such as estrogen and progesterone decreases, which directly or indirectly affects the degree of decrease in the muscle performance through complex mechanisms.^[20] In particular, given that there was no difference in body composition such as skeletal muscle mass, but there was difference in physical function according to ANM groups, it is considered that PNM had a stronger influence on the reduction of muscle quality (muscle function delivered per unit of muscle mass)^[21] than on the muscle quantity (skeletal muscle mass). Further research is needed to elucidate how PNM changes the muscle physiology and affects muscle quality in elderly women.

In this study, the grip strength did not significantly differ according to the ANM. In a multinational cohort study of elderly women aged >65 years, PNM was associated with a low grip strength and slow walking speed. However, in the subgroup analysis, by country, while gait speed was related to the ANM in all countries, in terms of grip strength, the association differed by country.^[10] While grip strength is generally known to be associated with age, sex, and skeletal muscle mass,^[22,23] the TUG and SPPB are reported to be correlated with the aerobic capacity of elderly people.^[24-26] Reductions in the levels of sex hormones after menopause can reduce aerobic capacity through changes in the cardiovascular and respiratory system as well as musculoskeletal system.^[24] In this study, while there was no difference in the skeletal muscle mass or grip strength according to the ANM, there was a significant difference in the TUG and SPPB results, suggesting that the impact of PNM on aerobic capacity in elderly women may act through the cardiovascular or respiratory system and not skeletal muscle mass. A decreased peripheral vasodilator reserve after natural menopause may increase the rate of local vascular resistance and thus reduce the peripheral arterial flow rate,^[25] and estrogen deficiency itself may play an important role in the degree of left ventricular diastolic dysfunction through several mechanisms.^[26]

This study has some limitations. First, since it had a crosssectional design, causal relationships cannot be confirmed. Second, since the cohort enrolled in this study comprised elderly women from a single Asian country, there are limitations associated with the generalizability of our results to different races and population groups across various countries. However, the major strength of this study is its enrollment of a large sample representative of community-dwelling elderly women living in Korea. Additionally, physical function was evaluated by trained investigators through various tests including the TUG and SPPB and not using self-reported questionnaires. Also we identified that there was no significant association between PNM and body composition in elderly women.

5. Conclusions

In this study, we confirmed that despite the lack of differences in body composition parameters, such as skeletal muscle and fat tissue, according to the ANM, PNM is associated with decreased physical function in elderly women. Since physical function deterioration in elderly people is associated with increased mortality and disability^[27,28] and poor life quality,^[29] our finding supports the early monitoring of women with PNM and for preventive interventions against physical function deterioration such as exercise^[30,31] and nutritional supplement.^[32,33]

Author contributions

Conceptualization: Hangyeol Cho, Chang Won Won, Hyun Ho Kong.

Data curation: Chang Won Won.

- Formal analysis: Hyung Ho Kong, Min Su Gu.
- Funding acquisition: Chang Won Won.
- Supervision: Chang Won Won, Hyun Ho Kong.
- Writing original draft: Hangyeol Cho, Hyun Ho Kong.
- Writing review & editing: Hangyeol Cho, Chang Won Won, Hyun Ho Kong.

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