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Physical performance in relation to menopause status and physical activity

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Abstract

Objective: The aim of this study was to examine differences in physical performance (muscle power, muscle strength, aerobic capacity, and walking speed) across menopausal stages and potential of leisure physical activity (PA) to modify the impact of menopause on physical performance.

Methods: In this cross-sectional study, women aged 47 to 55 were randomly selected from the Finnish National Registry and categorized as premenopausal ($n = 233$), perimenopausal ($n = 381$), or postmenopausal ($n = 299$) based on serum concentrations of follicle-stimulating hormone and bleeding diary. Physical performance was measured by knee extension force, handgrip force, vertical jumping height, maximal walking speed, and 6-minute walking distance. PA level was assessed by self-report and categorized as low, moderate, or high. Multivariate linear regression modeling was used for data analysis.

Results: After including fat mass, height, PA, and education in the model, the postmenopausal women showed 12.0 N weaker ($P < 0.001$) handgrip force and 1.1 cm lower ($P < 0.001$) vertical jumping height than the premenopausal women. There was no significant interaction between menopausal stage and PA on physical performance. The peri- and postmenopausal women with a high PA, however, showed better performance in the maximal knee extension strength and 6-minute walking test, and showed greater lower body muscle power than those with a low PA.

Conclusions: Menopause status is associated with muscle strength and power, whereas the association between menopause status and mobility/walking is clearly weaker. A high leisure PA level provides more capacity to counteract the potential negative influence of menopausal factors on muscle function.

Key Words: Aerobic capacity – Menopause status – Muscle power – Muscle strength – Physical activity – Walking.

Physical performance declines with aging. Low muscle strength and decline in the ability to produce force quickly (power) are associated with low walking speed and, further, with mobility limitations, disabilities,[1,2] and falls among older populations.[3,4] The pattern of decline in physical performance differs by sex, women showing more rapid decline than men during middle age.[5,6] This sex difference may be due to the hormonal changes that occur during the menopausal years.[7,8]

The mean menopausal age varies between 46 and 52.[9] During the menopausal transition, dramatic changes occur in the secretion of pituitary gonadotropins (follicle-stimulating hormone [FSH] and luteinizing hormone [LH]), ovarian steroids (estradiol and estrone), and inhibin B peptide. Based on data published by Rannevik et al,[10] 7 to 12 months after the final menstrual cycle, serum FSH concentration rises on average by 68%, with a concomitant decline of 60% and 32%, respectively, in estradiol and estrone concentrations, compared with the period 1 to 6 months before the final menstrual cycle. Owing to increased life expectancy, women spend one-third of their lives in a sex hormone-deficient state.

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Cross-sectional studies investigating differences in muscle strength across menopause status in middle-aged women have shown that postmenopausal women have lower strength and lower body muscle power than premenopausal women.[11-13] A 5-year follow-up study by Sowers et al[14] also showed that the decline in muscle strength is greater among middle-aged women characterized as postmenopausal compared with either pre- or perimenopausal women. Contradictory results, however, have also been published.[15-17] For example, the few studies that have investigated differences or changes in walking speed during the menopausal transition have reported mixed results. A cross-sectional study with 389 participants aged 40 to 65 reported no significant difference between pre-, peri-, and postmenopausal women in habitual walking speed,[13] whereas a follow-up study by Sowers et al[14] showed significantly greater decline in walking speed among middle-aged postmenopausal compared with either pre- or perimenopausal women.

Previous studies have predominantly defined menopause status according to self-reported bleeding data along with various criteria for menopause groups. This may blur the precise identification of menopause status and hence the association of menopausal factors with physical performance. In addition, earlier studies have used only a limited number of physical performance tests and thus not been able to capture a comprehensive range of physical performance dimensions, such as muscle power, muscle strength, aerobic capacity, and walking speed.

Physical activity (PA) is an important determinant of physical performance. In postmenopausal women, for example, it has been shown to be related to greater muscle strength.[8,17] Sex hormone deficiency during menopause may have an indirect effect on skeletal muscle through decreased spontaneous daily PA; in rodents, this has been shown to be reversed by estradiol replacement.[18] Moreover, earlier studies have shown a reduction in daily energy expenditure and a shift toward a more sedentary lifestyle during the menopausal transition.[19,20] Thus, the observed decline in physical performance during menopause may partially be an outcome of estrogen deficiency as well as the decline in the level of PA.

The purpose of this study was to investigate the association between physical performance and menopause status among middle-aged women and to test if this association varies with the level of PA. This study utilizes a comprehensive battery of physical performance tests, and categorization of menopausal groups was based on current guidelines, including serum hormonal analysis and bleeding diaries.

METHODS

Study design and participants

The study data were drawn from the Estrogenic Regulation of Muscle Apoptosis (ERMA) study.[21] Women aged 47 to 55 years living in the city of Jyväskylä or neighboring municipalities were randomly selected from the Finnish National Registry kept by the Population Register Centre

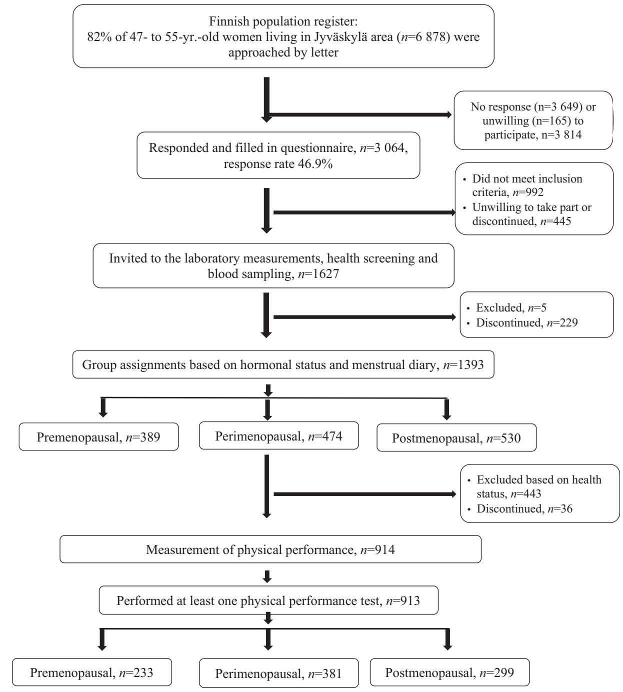

FIG. 1. Enrollment of the study participants.

(Fig. 1). Exclusion criteria were a self-reported body mass index (BMI) $>35\,kg/m^2$, being currently pregnant or lactating, conditions affecting ovarian function, including bilateral ovariectomy, estrogen-containing hormonal preparations (given orally or transdermally), or other medications affecting ovarian function, and chronic diseases or medications seriously affecting muscle function. A written invitation was sent to 6,878 potential participants. The response rate was 46.9%. Eligible participants ($n = 1{,}627$) were invited to the laboratory for a structural interview on their health status and to give fasting blood samples. Participants who had reported serious or unclear health problems were examined by a physician to ensure their safe participation in the physical performance measures. In total, 443 participants were excluded from the physical performance measurements for health and safety reasons. The present analysis only included women who performed at least one of the physical performance tests acceptably ($n = 913$).

All study participants provided written informed consent. The study was conducted in accordance with the guidelines for good clinical and scientific practice laid down by the Declaration of Helsinki and was approved by the ethics committee of the Central Finland Health Care District (K-SSHP Dnro 8U/2014).

Demographics, anthropometry, and body composition

Level of education was assessed by a single question and categorized as basic (primary and secondary school), college (applied science degree, bachelor, or nurse training) or university (master's degree or PhD) levels. *Marital status* comprised three categories: single, married or living with a partner, and divorced, separated, or widowed.

Body mass was measured with a digital scale and *height* with a stadiometer. *BMI* was calculated as body mass (kg) divided by height squared (m^2).

Fat mass was measured with an eight-point tactile electrode multifrequency bioelectrical impedance analyzer [InBody (720), Biospace, Seoul, Korea].

Physical activity

Current level of leisure PA was determined by a 7-point scale.[22] A similar seven-level scale has been validated with good outcomes against accelerometer-based PA and mobility variables.[23] The response categories were: (1) inactive, (2) light activity 1 to 2 times per week, (3) light activity several times per week, (4) moderate activity 1 to 2 times per week, (5) moderate activity several times per week, (6) high activity several times per week, and (7) competitive sports and related training several times per week. For the analysis, categories 1 and 2 were combined to indicate a low level of PA; 3 and 4 were combined to indicate a moderate level of activity; and 5 to 7 were combined to indicate a high level of PA.

Menopause status and health

Hormone assessments were performed from fasting serum samples taken between 8:00 and 10:00 AM, and in the women with a menstrual cycle, during cycle days 1 to 5. Serum was separated by centrifugation for 10 minutes at 2,200 × *g*. Systemic FSH and 17β-estradiol levels were immunoassayed using IMMULITE 2000 XPi (Siemens Healthcare Diagnostics, UK).

Participants' menopause status was determined based on systemic FSH and self-reported menstrual cycle (assessed by menstrual diary) after the Stages of Reproductive Aging Workshop (STRAW) criteria.[24] A detailed description of the categorization has been reported earlier by Kovanen et al.[21] In brief, the categories were premenopausal if regular menstrual cycle and FSH < 17 IU/L, perimenopausal if irregular menstrual cycle and FSH 9.5 to 30 IU/L, or if occasional menstrual bleeding occurred during past 3 months even if FSH >30 IU/L, and postmenopausal if no menstrual bleeding during the past 6 months and FSH >30 IU/L or no menstrual bleeding had occurred during past 3 months and FSH >39 IU/L. A few women who had very high FSH (>130 IU/L), but reported occasional bleeding, were also considered postmenopausal. For women with incomplete menstrual cycle information (eg, users of progestogen-containing medications), the categorization was based solely on FSH level and stricter cutoff values were applied (premenopausal: FSH < 15 IU/L, perimenopausal: FSH 15-39 IU/L, and postmenopausal: FSH >39 IU/L) to avoid potential errors due to gaps in the data. Participants self-reported their health problems, gynecologic status, and use of medications. Data related to parity, use of progestogen-releasing intrauterine coil, or other progestogen preparation for contraception, progestogen products (to treat gynecological bleeding disorders), as well as current and past smoking, presence of musculoskeletal diseases or conditions, hypertension, hypo- and hyperthyroidism were self-reported with a standard questionnaire.

Physical performance

Maximal isometric knee extension strength was measured in Newtons (N) from the side of the dominant hand in a sitting position on a custom-made dynamometer chair (Good Strength; Metitur Oy, Palokka, Finland) at a knee angle of 60° from full extension. The ankle was attached via a belt to a strain-gauge system. A belt around the pelvis was used to hold a participant to the chair. Participants were encouraged to extend the knee to produce maximal force.

Handgrip strength was measured in Newtons (N) on the dominant side by fixing the arm to the armrest of the chair with the elbow flexed at 90°. Participants were instructed to squeeze the handle as forcefully as possible. The contraction was maintained for 2 to 3 seconds and peak value was taken for analysis.

Lower body muscle power, that is, the ability of the neuromuscular system to produce the greatest possible force as fast as possible, was assessed as the height that the participant was able to elevate her body's center of gravity during a vertical countermovement jump (vertical jumping height) on a contact mat. Flight time (*t*) was measured, and vertical jumping height was calculated: $(g \times t^2) \div 8 \times 100$.[25]

In all tests, three to five maximal efforts were conducted and the best performance with the highest value was accepted as a result. In our laboratory, the coefficient of variation (CV) between two consecutive measurements with the same procedures has been 6% for knee extension force and handgrip force and 5% for vertical jumping height.[26]

Maximal walking speed was assessed for 10 m in a laboratory corridor. Five meters were allowed for acceleration, and the time was measured with photocells. Participants were advised to ''walk as fast as possible, without compromising your safety''. The fastest performance of two maximal walking tests was accepted as the result. In our laboratory, the CV for maximal walking speed has been 5%.[27]

Six-minute walking test was used to assess aerobic capacity. The test was performed on a 20-m indoor track, and participants were instructed to complete as many laps as possible within 6 minutes. The distance covered was used in the analysis.

Data analysis

To test differences in physical performance between the three menopausal stages, analysis of variance (ANOVA, *P* for trend shown in tables) was used with post hoc Tukey test (significant *P* values are shown in the text). For categorical variables, differences were tested with a Chi-square test.

The associations between menopause status and physical performance and the interaction effect of menopause status and PA on physical performance were analyzed using multivariate linear regression modeling.

Multiple regression analyses were conducted to examine the associations between menopause status and physical performance and the interaction effect of menopause status and PA on physical performance. A fully specified model for each performance variable, including main effects and an interaction term of menopause status with PA, was run.[28]

For the interaction analysis, a cross product of the three-level menopause status variable and the three-level PA variable was entered to the regression model as a categorical variable, resulting in four interaction terms for the model.

After performing fully specified multiple linear regression models, we observed that the interactions were nonsignificant in all the models predicting physical performance (the smallest *P*-value for knee extension force was 0.100, for handgrip force was 0.055, for vertical jumping height 0.445, for walking speed 0.474, for 6-min walking distance 0.261). Therefore, we excluded the interaction term from further analyses. The final tables include the models without the interaction terms.

The regression analyses were adjusted for body height and fat mass to take into account the size and composition of the total body[16,29] and also adjusted for PA and education. Body height and fat mass were entered into the models as mean-centered.[30] In addition, we repeated the analysis with the inclusion of chronological age (as mean-centered) and checked if this would meaningfully change the relationship between menopause status, PA, and the physical performance variables (see Table, Supplemental Digital Content 1, http://links.lww.com/MENO/A318 which illustrates age-adjusted regression models for knee extension, handgrip and vertical jumping height and Table, Supplemental Digital Content 2, http://links.lww.com/MENO/A319 which illustrates age-adjusted regression models for walking speed and distance). Standardized (β) and unstandardized (B) coefficients are provided for all models.

Despite the nonsignificant interaction effects of menopause status and PA on physical performance, we continued the analysis with the marginal means differences tests. Here, marginal means represent the means across the menopause status categories (pre-, peri-, and postmenopausal) and across the PA levels (low, moderate, and high) adjusted for height, fat mass, and education. Analysis of marginal means differences gives additional information not yielded by the full model with an interaction term,[31] especially in the case of an independent variable containing more than two categories.[32] Furthermore, this allowed us to test more specifically, whether the difference in physical performance of women with a low versus those with a high PA level increases when the menopause status progresses from pre- to postmenopause. The ANOVA and Chi-square analyses were performed using IBM SPSS Statistics 22.0 (SPSS, Chicago, IL). The regression and marginal means differences analyses were performed with R (www.r-project.org), version 3.3.3.

RESULTS

Demographics, anthropometry, body composition, and the level of PA of the sample across the three menopausal stages are presented in Table 1. As expected, the postmenopausal women were significantly older than the perimenopausal women (Tukey test $P < 0.001$), whereas the premenopausal women were the youngest (Tukey test $P < 0.001$). The mean difference in age between the pre- and postmenopausal groups was, however, less than 2 years. The postmenopausal group contained proportionally fewer women with a university degree and more women with a basic education than the premenopausal ($P = 0.005$) or perimenopausal ($P = 0.006$) groups. There was no difference between the groups in the level of PA.

No statistically significant differences were observed in body height or body mass between the groups. Body mass index was, however, lower in the postmenopausal than perimenopausal women ($P = 0.037$). No significant differences between the groups were observed in fat mass.

Table 2 shows the differences in gynecological and health status across the menopausal stages. Although all the

TABLE 1. *Demographics, anthropometry, and body composition across menopausal stages*

Variables	Premenopausal ($n = 233$)	Perimenopausal ($n = 381$)	Postmenopausal ($n = 299$)	*P*
Age, y	50.6 (1.63)	51.2 (1.92)	52.5 (1.89)	<0.001
Education	($n = 230$)	($n = 373$)	($n = 295$)	0.014
Basic	127 (55)	205 (55)	191 (64)	
College	26 (12)	49 (14)	42 (15)	
University	77 (33)	119 (31)	62 (21)	
Marital status	($n = 231$)	($n = 377$)	($n = 297$)	0.505
Single	19 (8)	32 (9)	28 (9)	
Married or registered partnership	181 (79)	290 (77)	215 (73)	
Divorced, separated or widowed	31 (13)	55 (14)	54 (18)	
Physical activity	($n = 232$)	($n = 378$)	($n = 298$)	0.227
Low level	36 (16)	64 (17)	59 (20)	
Moderate level	140 (60)	248 (65)	181 (61)	
High level	56 (24)	66 (18)	58 (19)	
Height, m	1.66 (0.05)	1.65 (0.06)	1.65 (0.06)	0.126
Body mass, kg	70.2 (10.02)	70.3 (11.12)	68.4 (11.17)	0.056
Body mass index, kg/m^2	25.4 (3.28)	25.8 (3.86)	25.1 (3.79)	0.048
Fat mass, %	21.2 (7.6)	22.5 (8.33)	21.5 (8.14)	0.137

Values given are *n* (%) for variables without units and mean (SD) for variables with units.

TABLE 2. *Gynecological status and health across menopausal stages*

Variables	Premenopausal (*n* = 233)	Perimenopausal (*n* = 381)	Postmenopausal (*n* = 299)	*P*
Parity: number of children born				0.952
Nulliparous	28 (13)	43 (12)	39 (13)	
One or two	133 (57)	216 (57)	163 (55)	
Three and more	71 (30)	118 (31)	95 (32)	
Use of hormonal contraception	(*n* = 232)	(*n* = 379)	(*n* = 298)	<0.001
No user	88 (38)	209 (55)	166 (56)	
Former user	35 (15)	54 (15)	57 (19)	
Current user[a]	109 (47)	116 (30)	75 (25)	
Using progestogens	(*n* = 230)	(*n* = 375)	(*n* = 294)	0.101
No	176 (76)	276 (74)	198 (68)	
Former	30 (14)	64 (17)	54 (18)	
Current	24 (10)	35 (9)	42 (14)	
Smoking	(*n* = 231)	(*n* = 376)	(*n* = 297)	0.691
Never	153 (66)	249 (66)	202 (68)	
Former	64 (28)	94 (25)	75 (25)	
Current	14 (6)	33 (9)	20 (7)	
Musculoskeletal problems	75 (32)	137 (36)	94 (31)	0.352
	(*n* = 232)	(*n* = 375)	(*n* = 297)	
Hypertension	27 (11)	57 (15)	39 (13)	0.474
	(*n* = 231)	(*n* = 378)	(*n* = 298)	
Hypothyroidism	22 (9)	28 (7)	32 (10)	0.449
	(*n* = 232)	(*n* = 378)	(*n* = 298)	
Hyperthyroidism	1 (1)	5 (1)	3 (1)	0.357
	(*n* = 232)	(*n* = 378)	(*n* = 298)	
17β-Estradiol, nmol/L	0.62 (0.66)	0.32 (0.26)	0.14 (0.29)	<0.001
Follicle-stimulating hormone, IU/L	7.91 (3.54)	31.68 (20.73)	82.97 (28.66)	<0.001

Values given are *n* (%) for variables without units and mean (SD) for variables with units.
[a]Current users of estrogen-containing medication (given orally or transdermally) were excluded from this study, therefore the category ''Current user'' only includes users of progestogen-containing medications.

estrogen-containing hormonal contraceptive/therapy users were initially excluded, there were users of progestogen-containing hormonal contraceptive medications with a decreasing trend from the pre- to peri- and postmenopausal groups. The premenopausal group contained proportionally more current users of progestogen-containing contraception than the perimenopausal ($P < 0.001$) or postmenopausal ($P < 0.001$) groups.

No intergroup differences were observed in the proportions of users of progestogens, current smokers, musculoskeletal diseases or conditions, hypertension, hypothyroidism, and hyperthyroidism. As expected, the level of 17β-estradiol was significantly lower in the post- than perimenopausal women ($P < 0.001$) followed by premenopausal women ($P < 0.001$), whereas the level of FSH showed the expected reversed pattern ($P < 0.001$ for all comparisons).

Maximal knee extension strength decreased significantly across the three menopausal groups (Table 3). Specifically, the postmenopausal women were weaker than the perimenopausal ($P = 0.019$) or premenopausal ($P = 0.023$) women. The postmenopausal women had significantly lower handgrip strength compared with the perimenopausal ($P < 0.001$) and premenopausal ($P < 0.001$) women. Both the post- ($P < 0.001$) and perimenopausal ($P = 0.022$) women had a significantly lower jumping height than the premenopausal women. The postmenopausal women had a significantly slower maximal walking speed than the premenopausal women ($P = 0.024$). In the 6-minute walking test, the differences between the groups were not statistically significant.

The final adjusted models showed that menopause status was significantly associated with handgrip strength and vertical jumping height. The postmenopausal women were

TABLE 3. *Physical performance across menopausal stages*

Variables	Premenopausal	Perimenopausal	Postmenopausal	*P*
Knee extension strength, *n*	470 (100.9)	468 (93.6)	447 (90.4)	0.008
	(*n* = 199)	(*n* = 328)	(*n* = 262)	
Hand grip strength, *n*	323 (60.5)	317 (61.6)	298 (54.2)	0.001
	(*n* = 233)	(*n* = 377)	(*n* = 297)	
Vertical jumping height, m	0.20 (0.04)	0.19 (0.04)	0.18 (0.04)	0.001
	(*n* = 210)	(*n* = 322)	(*n* = 285)	
Maximal walking speed, ms^{-1}	2.70 (0.49)	2.63 (0.48)	2.59 (0.39)	0.032
	(*n*=232)	(*n* = 375)	(*n* = 297)	
Six-minute walking distance, m	676 (58.8)	664 (64.2)	668 (58.5)	0.089
	(*n* = 214)	(*n* = 345)	(*n* = 280)	

Values given are mean (SD).

TABLE 4. *Regression models and marginal means differences in isometric muscle strength and power, menopause status, and physical activity*

	Knee extension strength, N				Hand grip strength, N				Vertical jumping height, cm			
Model	Coefficients (SE)	*t*	*P*	*β*	Coefficients (SE)	*t*	*P*	*β*	Coefficients (SE)	t-value	*P*-value	β
Intercept	449.1 (11.8)				324.1 (6.7)				18.5 (0.4)			
Menopause status[a]												
Perimenopause	4.9 (8.3)	0.595	0.551	0.03	−2.5 (4.8)	−0.517	0.605	−0.02	−0.5 (0.3)	−1.578	0.114	−0.06
Postmenopause	−16.6 (8.7)	−1.906	0.057	−0.08	−12.0 (5.0)	−4.335	<0.001	−0.17	−1.1 (0.3)	−3.461	<0.001	−0.13
Physical activity[b]												
Moderate	7.0 (9.1)	0.768	0.443	0.04	1.6 (5.2)	0.305	0.761	0.01	0.2 (0.3)	0.691	0.490	0.03
High	53.7 (11.2)	4.784	<0.001	0.23	2.2 (6.4)	0.337	0.736	0.01	1.8 (0.4)	4.510	<0.001	0.18
Marginal means differences												
Premenopausal women												
Low PA (reference)	470.5 (18.6)				332.8 (10.2)				18.8 (0.6)			
Moderate PA	−15.0 (19.5)	−0.771	0.441	−0.06	−7.0 (10.8)	−0.647	0.517	−0.04	−0.2 (0.7)	−0.294	0.768	−0.01
High PA	22.9 (21.6)	1.060	0.289	0.06	−12.5 (12.3)	−1.015	0.310	−0.06	1.7 (0.8)	2.156	0.031	0.11
Perimenopausal women												
Low PA (reference)	442.2 (14.1)				313.0 (8.1)				17.8 (0.5)			
Moderate PA	21.0 (14.2)	1.480	0.139	0.10	8.9 (8.0)	1.101	0.2271	0.07	0.5 (0.5)	0.867	0.386	0.05
High PA	68.9 (17.9)	3.862	<0.001	0.19	23.0 (10.2)	2.244	0.025	0.10	2.1 (0.6)	3.180	<0.001	0.14
Postmenopausal women												
Low PA (reference)	433.4 (14.3)				305.4 (8.1)				17.4 (0.5)			
Moderate PA	4.0 (15.1)	0.267	0.789	0.02	−0.6 (8.6)	−0.062	0.946	−0.01	0.3 (0.5)	0.494	0.621	0.04
High PA	58.7 (18.4)	3.184	<0.001	0.15	−9.0 (10.7)	−0.843	0.398	−0.04	1.6 (0.6)	2.442	0.014	0.11

Coefficients, unstandardized coefficients (represent differences between reference and respective categories); SE, standard errors; *β*, standardized coefficient; PA, physical activity.
Regression models and marginal means differences analysis are adjusted for fat mass, body height, and education.
[a]Reference category is premenopausal group.
[b]Reference category is low physical activity level.

12.0 N weaker in handgrip strength than the premenopausal women. They also had 1.1 cm lower jumping height than the premenopausal group. In knee extension strength, the postmenopausal women were 16.6 N weaker than the premenopausal women, but the result did not reach statistical significance ($P = 0.057$). The 6-minute walking and maximal walking speed test results did not differ by menopause status after accounting for confounders (Tables 4 and 5).

Due to the significant interrelationship between age and menopause status ($r = 0.39$, $P < 0.001$), chronological age was not included in the final models as a confounding factor. The potential effect of age was, however, tested and found not to notably change the results. Briefly, in handgrip strength the postmenopausal women were 18.5 N weaker ($P < 0.001$) and in vertical jumping height the postmenopausal women had 1 cm lower jumping height ($P = 0.040$)

TABLE 5. *Regression models and marginal means differences in walking, menopause status, and physical activity*

	Maximal walking speed (ms^{-1})				Six-min walking distance, m			
Model	Coefficients (SE)	*t*	*P*	*β*	Coefficients (SE)	*t*	*P*	*β*
Intercept	2.45 (0.05)				642.3 (6.4)			
Menopause status[a]								
Perimenopausal	−0.02 (0.03)	−0.796	0.425	−0.03	−2.1 (4.5)	−0.463	0.643	−0.02
Postmenopausal	−0.05 (0.03)	−1.509	0.132	−0.06	−0.6 (4.7)	−0.135	0.892	−0.01
Physical activity[b]								
Moderate	0.04 (0.03)	1.082	0.280	0.05	11.4 (4.9)	2.286	0.022	0.09
High	0.05 (0.04)	1.141	0.254	0.05	23.3 (6.1)	3.800	<0.001	0.15
Marginal means differences								
Premenopausal women								
Low PA (reference)	2.44 (0.07)				648.4 (9.7)			
Moderate PA	0.07 (0.08)	0.912	0.362	0.08	4.3 (10.3)	0.425	0.671	0.04
High PA	0.02 (0.09)	0.315	0.753	0.04	16.0 (11.5)	1.380	0.168	0.08
Perimenopausal women								
Low PA (reference)	2.42 (0.06)				640.0 (7.8)			
Moderate PA	0.02 (0.06)	0.460	0.646	0.04	9.1 (7.8)	1.167	0.208	0.07
High PA	0.11 (0.07)	1.477	0.140	0.08	32.3 (9.8)	3.280	0.001	0.15
Postmenopausal women								
Low PA (reference)	2.40 (0.06)				637.6 (7.8)			
Moderate PA	0.04 (0.06)	0.638	0.523	0.05	19.1 (8.2)	2.329	0.020	0.13
High PA	0.02 (0.08)	0.327	0.743	0.03	19.4 (10.0)	1.930	0.053	0.09

Coefficients, unstandardized coefficients (represent differences between reference and respective categories); SE, standard errors; *β*, standardized coefficient; PA, physical activity.
Regression models and marginal means differences analysis are adjusted for fat mass, body height, and education.
[a]Reference category is premenopausal group.
[b]Reference category is low physical activity level.

than the premenopausal women (see Table, Supplemental Digital Content 1, http://links.lww.com/MENO/A318). No significant associations of knee extension strength, 6-minute walking distance and maximal walking speed with menopause status were observed (see Table, Supplemental Digital Content 1, http://links.lww.com/MENO/A318 and Table, Supplemental Digital Content 2, http://links.lww.com/MENO/A319).

After adjusting for body height, fat mass, education and PA, marginal means difference analysis (Tables 4 and 5) revealed that although the women with high PA, in general, performed better than those with low PA, the difference varied by menopause status. In all three menopausal groups, vertical jumping height was greater among the women with high compared with low PA. Among the perimenopausal women, higher PA was significantly associated with better performance in all the physical performance measures except for maximal walking speed. In addition to greater vertical jumping height, the postmenopausal women with high PA had greater maximal knee extension strength than those with low PA. In the 6-minute walking test, the postmenopausal women with moderate PA walked a significantly longer distance than those with low PA.

DISCUSSION

This study examined the difference in physical performance between menopausal stages and whether this difference varies with level of PA among 47- to 55-year-old women. After controlling for PA, education, body height and fat mass, the postmenopausal women had significantly lower handgrip strength and lower body muscle power production when compared to the premenopausal women. In all three menopausal groups, the women with a high PA level had greater muscle power production than those with a low PA level. Furthermore, in the peri- and postmenopausal groups, maximal knee extension strength was greater, and distance traveled in 6 minutes longer, in the women with a high compared with low leisure PA level.

Our results are in line with those of previous studies showing that postmenopausal women have lower handgrip strength than premenopausal women.[12,13] In this study, absolute handgrip strength showed a significant declining trend of 25 N. Moreover, after controlling for confounders, the postmenopausal women remained significantly weaker (by 12 N) than the premenopausal women. Earlier cross-sectional studies[15,16] reported no difference in handgrip strength across menopause status groups. The discrepancy between these studies and ours may be due to differences in the study design. Cooper et al[16] assessed menopause status when women were 53 years of age, leaving out other age groups. Bassey et al,[15] in turn, used self-reported bleeding regularity to assess menopause status, a criterion that could lead to misclassification. A longitudinal study,[17] however, reported a nonsignificant decline in grip strength of 0.93 kg (less than 10 N) in late perimenopause and of 1.04 kg (10 N) in postmenopause. The reason for the absence of significant changes in grip strength in this longitudinal study could be the relatively low proportion of women who become postmenopausal (around 12%) during the short 3-year follow-up.

In the present study, the postmenopausal women performed significantly worse in isometric knee extension strength; however, after adjustment for confounders, this result did not reach statistical significance ($P = 0.057$). To date, only a few studies have investigated low limb strength in women across menopausal stages. An earlier study showed no difference in isokinetic knee extension force between 45- and 50- to 59-year-old women.[11] Although these age groups correspond to the menopausal transition phase, an analysis based solely on age may inaccurately represent menopause status. In another cross-sectional study, no menopause status differences in isometric knee extension strength were observed.[15] Lower limb strength reflects daily PA level due to frequent loading of limb muscles during daily activities. It is thus possible that the moderating effect of PA weakens the association between menopause status and lower limb strength.

The present results found stronger evidence for a negative impact of the menopausal transition on handgrip strength than on isometric lower limb strength. This finding is supported by the longitudinal study of Sowers et al,[14] who followed pre- to perimenopausal women over a period of 5 years. They observed no significant changes in quadriceps isometric strength, but noted a significant decline in handgrip strength. In contrast to lower limb strength, which is more affected by environmental factors (eg, PA), handgrip strength may better reflect intrinsic vitality[2] and be less influenced by leisure PA. The earlier reported association between handgrip and disability[2] may be driven by a subclinical condition which later develops into disability and which may be exacerbated by menopausal factors.

Lower body muscle power is an important determinant of functional independence and has shown a stronger association than muscle strength with performance in daily tasks such as stair climbing, standing up from a chair and walking speed.[33] Our study showed that postmenopausal women have diminished muscle power in comparison to premenopausal women. Other studies that have measured performance in the chair rise test, which is a crude surrogate of muscle power, have reported no difference in performance across menopause status.[13,14,16] Bassey et al[15] measured leg extension muscle power in a rig but found no variation across the menopausal transition stages. The discrepancy between our results and those reported by Bassey et al[15] can be explained by differences in the menopause status classification and strength tests employed. Vertical jumping height, used in our study, is a weight-bearing test based on ballistic movements that also involves activity of the plantar flexor muscles, and hence better relates to everyday activities such as stair climbing. The present results suggest that menopausal factors such as estrogen deficiency may affect the mechanisms that earlier drive muscle power and later affect muscle strength. This finding is indirectly supported by studies of postmenopausal women on hormone therapy (HT) that have shown exogenous estrogen to have a greater influence on muscle power than on muscle force.[34]

Estrogens have an effect on multiple sites along the neuromuscular system, all of which contribute to the muscle strength and power output. These sites express estrogen receptors and therefore are most likely targets for estrogens regulation. We know that sex steroids activate the IGF-1 pathway[35] which controls the net balance of muscle protein turnover by activating protein synthesis and inhibiting protein degradation. It has been shown that postmenopausal women have significantly lower expression of IGF-1 compared with premenopausal women[36] which can predispose postmenopausal women to decrements in muscle function and quality.

Despite the differences observed across the three menopause status groups in muscle strength and power, no difference was observed in 6-minute walking distance. This may indicate that early menopausal changes affect the musculoskeletal system more than they affect the cardiovascular and respiratory system. A 5-year observational study[37] showed no decline in maximal oxygen consumption during the menopausal transition. In another study menopause-related estrogen deficiency was, however, associated with reduced exercise tolerance and impairment in maximal aerobic function.[38] Nevertheless, for our participants the walking test performed in our study is a more typical everyday activity than the incremental workload until exhaustion performed on a cycle ergometer used in that study.[38] Therefore, the aerobic capacity required to walk for 6 minutes either does not seem to be compromised by menopause, or if so, longer time is needed for the effect to become evident. This can be supported by a longitudinal study with women aged 45 to 57 (median follow-up time is 9.7 y) showed that postmenopausal women more likely self-reported functional limitations in performing daily living activities, such as carrying groceries, climbing stairs or walking; performance which mainly relies on the musculoskeletal system.[39]

Although the pre- and postmenopausal groups differed significantly in maximal walking speed, this difference was attenuated after adjusting for confounders. Studies with postmenopausal women on HT have shown higher maximal walking speed in HT users than nonusers,[34,40] suggesting that sex hormones play a role in the physiological systems governing performance during maximal walking. The age-associated reduction in walking speed accelerates after middle age, at around 60 years.[41] The fact that the oldest participants in the present study were early postmenopausal and younger than those in the above-mentioned studies may explain the inconsistency in maximal walking speed outcome between the women in the present study and those on HT in other studies.

Previous studies have shown that PA is a significant determinant of physical performance in postmenopausal woman.[8,17,42] In those studies PA has, however, been viewed as a controlling variable rather than a moderator. Our study, in turn, showed that irrespective of menopause status physical performance was considerably lower in women with a low than high level of leisure PA. Interestingly, we observed that the expected difference in physical performance between the low and high PA groups widened across the menopausal transition. For example, the difference between the low and high PA groups increased from 22.9 to 58.7 N in knee extension strength, and from 16 to 19.4 m in the 6-minute walking distance. These results suggest that PA may counteract the possible negative effect of menopausal factors on muscle strength and power: a higher level of PA may mean greater physical performance at the menopausal transition.

Earlier studies have shown that higher intensity and greater frequency of PA is associated with better physical performance in middle-aged women.[42-44] Consistent with these results, our study showed that in the peri- and postmenopausal groups, the women with high PA performed better in knee extension force and in lower body power production than those whose PA level was moderate or low. In the 6-minute walking test, moderate PA was, however, already sufficient to counteract the negative impact of menopause on muscle performance. These results prompt the question of whether interventions for promoting functional independence should primarily focus on habitual free-living PA or on more structured and intensive exercise programs.

The absence of a significant difference in maximal walking speed between the women with low and those with high PA across the menopause status groups shows that although women with low PA can walk at the same maximal speed as women with high PA, they are not able to maintain that speed over a longer time. Performance in maximal walking speed resembles usual walking and differences in PA level do not seem to significantly affect this in a middle-aged women population. The observation that PA modifies the effect of menopause status on physical performance needs to be studied further, as this may reveal a possible underlying mechanism that has consequences for functional independence in later life.

Strength and limitations

Unique to this study is the careful characterization of the menopause status of our participants following the STRAW criteria. Previous studies investigating the association of menopause status and muscle function have predominantly employed a self-reported menstruation questionnaire. Several studies have shown that although menopausal age can be fairly accurately measured by questionnaires,[45,46] some caution is warranted when menopause status is assessed retrospectively by self-report. Women who use hormonal contraception may, if they report regular menses, be misclassified as premenopausal or, if they do not bleed or bleeding is very minimal, be misclassified as postmenopausal. At the same time, some women with an irregular cycle but still premenopausal may be misclassified as peri- or postmenopausal.[47] The STRAW guidelines recommend applying the criterion of 12 months of amenorrhea when defining the postmenopausal state. Given our aim in this study of ascertaining menopause status for more than 900 participants within a reasonable period of time, and as we also assessed FSH concentrations, we decided to apply 6 months amenorrhea as the minimum requirement for categorizing a participant as postmenopausal. This may have led to some misclassification in the postmenopausal group. If so, our results may underestimate the differences between the postmenopausal and other groups.

Use of progestogen as well as thyroid dysfunction may influence bleeding patterns and ovarian function[48,49] and thereby these may interfere with the categorization by menopause status. In our study progestogen use and thyroid dysfunction was self-reported. Unfortunately, we do not have information on the dose and the length of use of progestogen medications. To avoid potential misclassification, for users with incomplete menstrual cycle information (eg, users of progestogen-containing medications) the more stringent cutoff criteria for the FSH level to categorize participants by menopause status was used in the present study. We also assumed that each participant who reported hypo- or hyperthyroidism receives treatment and thus have euthyroid range of serum thyroid hormone. In our sample, the distribution of those who reported use of progestogen and having hypo- or hyperthyroidism was equal across the menopause status groups. Therefore, it is unlikely that these conditions would influence the main results.

As expected, the pre-, peri-, and postmenopausal women differed in age, and hence it is reasonable to assume that, despite the narrow age range of the sample, the observed differences in physical performance between the groups were partly explained by aging. This is, however, impossible to test conclusively the aging effect separately from that of the menopause as aging and menopause are, by definition, intertwined. The inclusion of chronological age as a confounder in the multiple regression models attenuated the levels of significance of the associations between menopause status and the physical performance variables, but did not otherwise substantially change the results.

It should also be noted that self-reported PA may introduce some bias by underestimating the number of low and overestimating the number of high physically active individuals.[50] In our study, we used a questionnaire developed into a seven-level scale to enable the inclusion of physical activities performed for fitness and sports and household activities such as gardening, cleaning and housework.[22] An earlier validity assessment of the scale has shown it to be fairly accurate and to correlate significantly with accelerometer-based PA measurements.[23]

Our study is limited to nonsevere obese (BMI $<35\,kg/m^2$) individuals. Obesity and menopausal factors can act synergistically, which may worsen muscle functioning of obese middle-aged women.[51] Even though, we controlled the regression analysis for fat mass, we cannot generalize our results for obese individuals.

Furthermore, we used a reliable structured protocol to comprehensively measure physical performance. Our sample represents a large homogeneous cohort of relatively healthy Finnish women. This reduces the possibility for the analysis to be contaminated by unobservable potential confounders (eg, ethnicity, income or early-life stressors). On the contrary, this restricts the generalizability of the results to other more heterogeneous populations, particularly those in non-Western countries.

Although our discussion assumes that PA drives the difference in physical performance across menopause status, the possibility of a reverse relationship also exists. It is possible that better physical fitness enables women to be more physically active. To investigate this issue, longitudinal studies on premenopausal women followed up through the peri- and postmenopausal years with carefully characterized menopause status and a comprehensive battery of physical performance measures are needed.

CONCLUSIONS

This study showed that postmenopausal women had lower handgrip strength and lower body power production in comparison with premenopausal women after controlling for confounders. It seems that menopausal factors influence the mechanisms that govern general isometric strength and muscle power more strongly than performance in functional tests such as maximal walking speed and 6-minute walking. Importantly, leisure PA attenuates the menopausal-related declining pattern in physical performance: peri- and postmenopausal women with a high PA level had higher maximal knee extension strength and muscle power and they performed better in the six-min walking test than those with a low PA level. This suggests that leisure PA counteracts the possible negative effect of menopausal factors on muscle strength and power.

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