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ORIGINAL STUDY

The role of cardiorespiratory fitness and body composition in the association between physical activity and menopausal symptoms

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Abstract

Objective: The aim of the study was to conduct exploratory analyses on the role of cardiorespiratory fitness (CRF) and body composition in the association between physical activity and menopausal symptoms.

Methods: This was a cross-sectional (N = 298) study of women aged 51–59 years including a subsample of 82 women followed for 4 years. The severity of menopausal symptoms was assessed with the Menopause Rating Scale in total symptoms as well as using the somato-vegetative, psychological, and urogenital subscales. Physical activity was assessed with accelerometers and self-reports, body composition with dual-energy x-ray absorptiometry, and CRF with a custom-made prediction model based on the six-minute walking distance and spiroergometry. The associations of interest were studied using unstandardized regression coefficients derived from multiple linear regression models with the severity of menopausal symptoms as the outcome.

Results: Higher total body and fat mass (kg) were associated with more severe total symptoms (B = 0.06 [95% CI, 0.01 to 0.12] and 0.07 [0.01 to 0.14], respectively) as well as somato-vegetative (0.03 [0.01 to 0.05]; 0.04 [0.01 to 0.06]) and psychological symptoms (0.03 [0.00 to 0.05]; 0.03 [0.00 to 0.06]) in cross-sectional design. Total and lean body mass interacted with physical activity in total and psychological symptoms with stronger indirect associations being observed in participants with lower total and lean body mass. CRF was not associated with menopausal symptoms and did not interact with physical activity.

Conclusions: Maintaining a healthy weight is associated with less severe menopausal symptoms in middle-aged women. The association between physical activity and the severity of menopausal symptoms varied based on the differences in total and lean body mass.

Key Words: Exercise – Hot flashes – Menopause – Night sweats – Obesity – Women's health.

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Menopausal symptoms are caused by hormonal changes that arise from the menopause-related gradual cessation of ovarian function. They include but are not limited to vasomotor symptoms (VMS; eg, hot flashes and night sweats), sleep disturbances, mood instability, and sexual dysfunction.[1,2] The majority of middle-aged women experience these symptoms that significantly impair the quality of life during the time when women have important roles in society and within the family.[2]

The role of physical activity in the alleviation of menopausal symptoms has been studied in several observational studies as well as in randomized controlled trials, but the results of these studies have been contradictory, and the overall evidence is still inconclusive.[3-5] Physical activity is known to affect cardiorespiratory fitness (CRF) and body composition,[6-8] which both have also been associated with menopausal symptoms.[9-11] Furthermore, previous studies have shown that the aging related decline in CRF and accumulation of adipose tissue accelerates in midlife women.[12,13] However, the role of CRF and body composition has rarely been investigated in the studies focusing on the associations of physical activity and menopausal symptoms. Notably, exercise interventions that have also included CRF measurement have reported intervention to alleviate menopausal symptoms more in women with better CRF at baseline[14] and in women who improved their CRF more during the intervention.[15] Nonetheless, it has also been observed that the changes in CRF and body composition do not modify the exercise intervention effect on menopausal symptoms.[16]

Therefore, the role of CRF and body composition in the association between physical activity and menopausal symptoms is still unclear, and further insight on this topic could provide tools for promotion of health and quality of life in middle-aged and elderly women. Thus, this exploratory study aimed to investigate the associations of CRF, body composition, and physical activity with menopausal symptoms.

METHODS

Study design and population

This study was conducted using Estrogenic Regulation of Muscle Apoptosis (ERMA) cohort data (dataset: doi.10.17011/jyx/dataset/83491).[17] The used data sets includes data from the ERMA and the Estrogen, MicroRNAs and the risk of Metabolic Dysfunction (EsmiRs) studies. The ERMA measurements were conducted in 2015–2016 and the EsmiRs measurements in 2019–2020. The EsmiRs measurements were discontinued due to coronavirus disease 2019 (COVID-19) restrictions on March 16, 2020.

The primary cross-sectional analyses of this study were carried out using the data from the EsmiRs study, which is a 4-year follow-up study for the ERMA study.[18] The EsmiRs study included questionnaires for severity of the menopausal symptoms, range of physiological measurements, and EsmiRs metabolism substudy[19] including detailed CRF assessment. For the auxiliary longitudinal analyses for participants with no symptoms at ERMA baseline, we utilized the data from the ERMA measurements and the data from the EsmiRs measurements conducted 4 years after ERMA baseline. The studies were performed in accordance with the Declaration of Helsinki, and they were approved by the ethical committee of the Central Finland Health Care District. All participants provided written informed consent.

The recruitment and participant selection procedures for the ERMA,[17] EsmiRs,[18] and EsmiRs metabolism studies[19] have been described elsewhere. Briefly, a random sample of 6,878 women aged 47–55 years living in the Central Finland drawn from the Population Information System were invited to participate in the ERMA baseline measurements. Of those women, 1,393 consented and were not excluded. Exclusion criteria of the study were conditions affecting ovarian function, systemic hormone levels, or inflammatory status, such as bilateral oophorectomy, pregnancy, lactation, and severe obesity (self-reported body mass index [BMI] ≥ 35 kg/m^2).[17] Of the 1,393 participants in the ERMA measurements in 2015-2016, 298 participated in the EsmiRs measurements after the 4-year follow-up in 2019–2020.[18] The loss of participants from ERMA baseline to EsmiRs is illustrated in Figure 1.

For the EsmiRs metabolism substudy, participants who were either pre- or perimenopausal, postmenopausal, or postmenopausal hormone therapy users were recruited. Furthermore, the aim was to recruit an even number of participants with normal weight and overweight (BMI threshold 25 kg/m^2) with similar physical activity levels based on the single question for leisure time physical activity.[19,20] The other exclusion criteria of the EsmiRs metabolism substudy are illustrated in Figure 1, and more detailed participant characteristics are shown in Table 1. EsmiRs metabolism substudy measurements were conducted after the EsmiRs measurements, the median (interquartile range) time between the measurements being 9 (7-19) weeks.

Menopausal symptoms

Menopausal symptoms were assessed using structured questionnaires in ERMA and EsmiRs measurements. The questionnaire used in the EsmiRs was the Menopause Rating Scale (MRS), a standardized and validated measure of health-related quality of life and severity of menopausal symptoms.[21,22] The MRS includes 11 symptoms for which the respondent reports one of the five categories of the perceived symptom severity (none, mild, moderate, severe, very severe). The individual score of each symptom varies from 0 (none) to 4 (very severe), and the total symptom score (ranging from 0 to 44) is the sum of all symptom scores. The three subscales of the MRS (with their respective symptoms) are somato-vegetative (hot flashes/sweating, heart discomfort, sleep problems, and joint/muscular discomfort), psychological (depressive mood, irritability, anxiety, and physical/mental exhaustion), and urogenital (sexual problems, bladder problems, vaginal dryness).[21]

In the ERMA questionnaire, participants were asked to report dichotomously if they had menopausal symptoms from the list of 10 common symptoms.[17,23] The questionnaire also included the option to describe a maximum of three additional symptoms. There were 82 participants who did not report any symptoms at baseline ERMA measurements.

Physical activity

Accelerometer-measured physical activity (ACC-PA) was assessed with mean amplitude deviations of hip-worn accelerometer data.

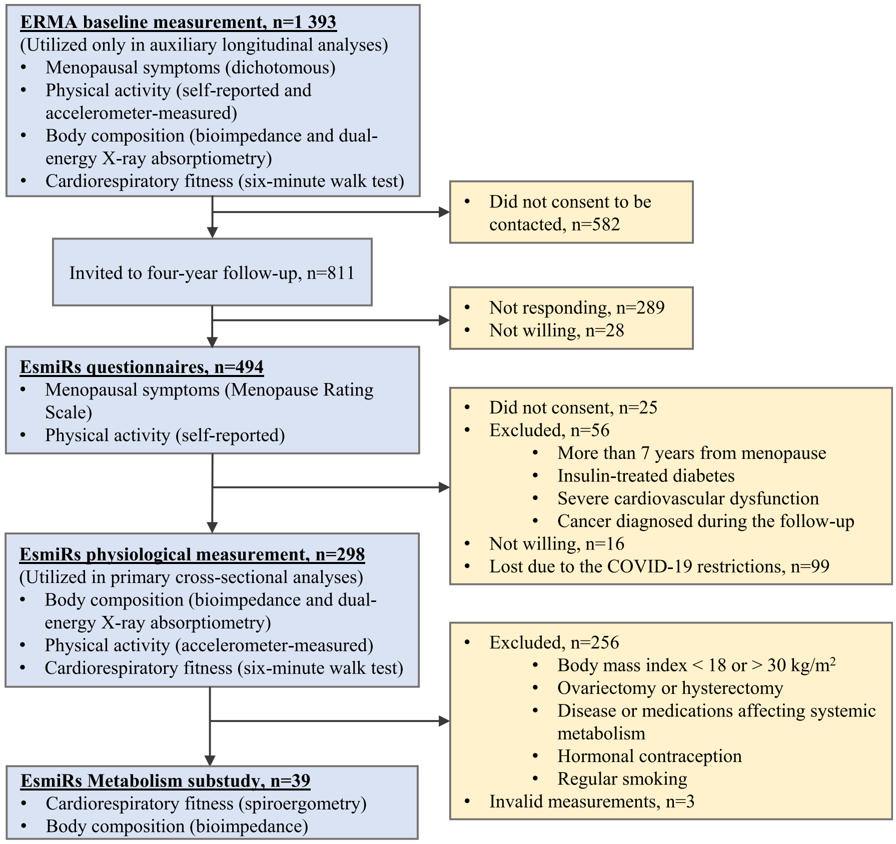

FIG. 1. Flow chart of the study.

Participants were instructed to wear accelerometers (ActiGraph GT3X and wGT3X, Actigraph, Pensacola, FL) for seven consecutive days during waking hours, except for water-based activities. The data were collected at 60 Hz, and the Euclidian norm of the resultant acceleration was computed for each timepoint. Mean amplitude deviation values were computed for nonoverlapping 5-second epochs, and ACC-PA was computed as their mean value.[18]

Additionally, self-reported physical activity (SR-PA) was assessed with a structured questionnaire that included questions about the average frequency, intensity, and duration of leisure time physical activity as well as the average duration of commuting activity. Finally, leisure time physical activity in metabolic equivalent (MET) hours per day was computed based on the responses to these four questions.[24]

Anthropometrics and body composition

Body composition was measured with dual-energy x-ray absorptiometry (DXA; LUNAR Prodigy, GE Healthcare, Chicago, IL) and bioelectrical impedance analysis (BIA; InBody720, Biospace, Seoul, Korea) after overnight fasting. BMI was calculated using total body mass and height measured with standard procedures. DXA, BIA, and BMI measurements were conducted in both timepoints. Furthermore, BIA was carried out in the EsmiRs metabolism substudy.

Cardiorespiratory fitness

In the EsmiRs metabolism substudy (n = 39), CRF was determined as maximal oxygen consumption (VO_{2max}) measured with metabolic cart (Vmax Encore 92, Sensormedics, Yorba Linda, CA) during maximal incremental bicycle ergometer (Ergoselect 200, Ergoline, Bitz, Germany) test. A more detailed description of the protocol has been reported previously.[19] All participants (n = 298) performed a 6-minute walk test on a 20-meter indoor track at baseline ERMA measurements and after the 4-year follow-up in EsmiRs measurements. Participants were instructed to complete as many laps as possible, and distance walked during the test (6-minute walking distance, 6MWD) was measured.[25] Sitting heart rate was assessed before the test and heart rate as well as the rating of perceived exertion (RPE) were assessed after the test.[17]

A custom-made prediction model for VO_{2max} based on the 6MWD and body composition measurements was constructed to estimate VO_{2max} for participants without spiroergometry. The VO_{2max} estimate derived from the constructed model was used to assess CRF at ERMA baseline measurements and after the 4-year follow-up in EsmiRs. The constructed model is described in more detail in the statistical analyses and results section.

Confounding factors

The serum concentrations of estradiol and follicle-stimulating hormone (FSH) were determined (IMMULITE 2000 XPi,

TABLE 1. *Characteristics of the study population*

	Cross-sectional study		Longitudinal study[a]	
	EsmiRs[b] (n = 298)	*EsmiRs metabolism[b] (n = 39)*	*Baseline, ERMA[c] (n = 82)*	*Follow-up, EsmiRs[b] (n = 82)*
Age (year)	55.1 ± 1.8	55.4 ± 1.6[d]	50.9 ± 1.7	54.7 ± 1.7
Body height (m)	1.66 ± 0.06	1.66 ± 0.05	1.66 ± 0.05	1.66 ± 0.05
Total body mass (kg)	70.9 ± 11.5	68.3 ± 8.2	67.0 ± 11.1	70.4 ± 11.7
Body mass index (kg/m^2)	25.8 ± 4.1	24.8 ± 2.7	24.9 ± 3.7	25.4 ± 3.9
Menopausal status[e]				
Pre	5 (15)	3 (1)	59 (48)	7 (6)
Peri	14 (42)	15 (6)	34 (28)	22 (18)
Post	81 (241)	82 (32)	7 (6)	71 (58)
Menopause rating scale score (n)	298	39	82	82
Total	8.60 ± 5.00	7.87 ± 4.74		7.19 ± 4.26
Somato-vegetative	3.90 ± 2.18	3.72 ± 2.03	No	3.45 ± 2.06
Psychological	2.53 ± 2.40	2.18 ± 2.15	Symptoms	1.85 ± 1.83
Urogenital	2.15 ± 1.89	1.97 ± 1.71		1.88 ± 1.70
Cardiorespiratory fitness (n)	–	39	–	–
VO_{2max} (l/min)	–	2.15 ± 0.34[d]	–	–
VO_{2max} (ml/kg/min)	–	31.7 ± 5.1[d]	–	–
Dual-energy x-ray absorptiometry (n)	293	39	72	81
Body fat mass (kg)	25.9 ± 9.0	24.3 ± 6.2	23.4 ± 9.0	25.0 ± 9.3
Lean body mass (kg)	42.2 ± 4.2	41.3 ± 3.8	42.9 ± 3.9	42.6 ± 4.0
Fat percentage (%)	37.1 ± 7.7	36.6 ± 5.7	34.2 ± 8.3	35.9 ± 7.9
Bioelectrical impedance analysis (n)	292	39	75	79
Fat mass (kg)	23.6 ± 8.9	21.7 ± 5.4[d]	20.3 ± 8.5	22.7 ± 9.1
Fat free mass (kg)	47.5 ± 4.9	46.5 ± 4.6[d]	48.6 ± 4.7	47.8 ± 4.7
Skeletal muscle mass (kg)	26.2 ± 2.9	25.6 ± 2.8[d]	26.9 ± 2.8	26.4 ± 2.8
Accelerometer-measured PA (n)	283	36	69	77
ACC-PA (mg)	28.3 ± 8.6	29.8 ± 9.2	30.3 ± 11.3	29.0 ± 8.9
Self-reported leisure time PA (n)	298	39	82	82
SR-PA (MET-h/d)	4.91 ± 3.93	5.20 ± 3.63	5.26 ± 5.41	5.14 ± 3.93
6-minute walk test (n)	259	38	69	76
Sitting heart rate (bpm)	71.1 ± 9.5	69.8 ± 9.7	78.5 ± 12.4	71.1 ± 9.0
6-minute heart rate (bpm)	152 ± 17	156 ± 17	156 ± 15	154 ± 18
6-minute RPE	14.4 ± 2.0	14.4 ± 2.1	14.4 ± 1.8	14.5 ± 2.2
Distance walked (m)	672 ± 61	683 ± 49	686 ± 60	678 ± 68
Lifestyle habits (n)	298	39	82	82
Alcohol consumption (portions/wk)	3.24 ± 3.43	2.79 ± 2.86	3.50 ± 2.80	3.01 ± 2.65
Smoking[e]				
Nonsmoker	94 (280)	95 (37)	96 (79)	94 (77)
Smoker	6 (18)	5 (2)	4 (3)	6 (5)
Education[e]				
Primary or secondary	55 (165)	51 (20)	63 (52)	63 (52)
Tertiary	45 (133)	49 (19)	37 (30)	37 (30)
Use of hormonal preparations[e]				
Nonuser	60 (180)	82 (32)	59 (48)	57 (47)
Progestogen	19 (56)	0 (0)	42 (34)	31 (25)
Estrogen	3 (10)	0 (0)	0 (0)	2 (2)
Progestogen + estrogen	18 (52)	18 (7)	0 (0)	10 (8)

ACC-PA, accelerometer-measured physical activity mean amplitude deviation; CRF, cardiorespiratory fitness; ERMA, Estrogenic Regulation of Muscle Apoptosis; Estrogen, MicroRNAs and the risk of Metabolic Dysfunction; mg, milligravity (0.00981 m/s^2); PA, physical activity; RPE, rating of perceived exertion; SR-PA, self-reported physical activity; VO_{2max}, maximal oxygen consumption.

Data are mean ± standard deviation unless otherwise specified.

[a]Participants who did not report any menopausal symptoms at baseline ERMA measurement were included in the longitudinal study.

[b]Measurements were conducted in 2019-2020.

[c]Measurements were conducted in 2015-2016.

[d]Measured on the EsmiRs metabolism day.

[e]Data are % (n).

Siemens Healthineers, Erlangen, Germany) from the fasting blood samples. For participants with predictable menstrual cycles, the blood samples were taken during the first 5 days of the menstrual cycle. Furthermore, the participants provided a diary that included information about the menstrual bleedings during the 6-month period prior to the ERMA measurements. Participants were categorized as pre-, peri-, or postmenopausal based on their serum FSH concentrations and menstrual bleeding diaries using the adapted Stages of Reproductive Aging Workshop (STRAW +10) guidelines.[1]

Education level (primary/secondary or tertiary), smoking status (nonsmoker or smoker), and alcohol consumption in portions per week were assessed using structured questionnaires. Furthermore, participants reported their current use of hormonal preparations for contraception or menopausal hormone therapy, and they were classified as nonuser, only progestogen, only estrogen, and combined estrogen and progestogen users. All exogenous sex hormone preparations for contraceptive and hormone therapy use were included, except for the intravaginal local estrogen therapy.

Missing data

The number of missing data values was 989 out of 13,112 (7.5%), where 13,112 is the number of potential data values (44 variables in the full wide format data set multiplied by 298 participants). The percentage of missing values varied from 0 to 23% across the variables. Missing data occurred because of invalid or missing measurements and unclear and incomplete questionnaire responses. Missing data were assumed to occur at random.[26] Multiple imputation with 50 imputed data sets and 50 iterations for chained equations was used to deal with the missing data. Variables measured at the same timepoint and the target variable measurement from the other timepoint were used for the imputation of each variable. Derived variables, which were imputed with passive imputation, were not used for imputation of their originals. Model parameters were estimated separately for each data set. Multiple imputation and pooling of the model estimates were carried out in R using the standard settings of the "mice" package.[27,28] We also performed the complete case analysis, and the results were not notably different from the ones acquired using multiple imputation.

Statistical analyses

The selection of the model for the prediction of absolute VO_{2max} was carried out using the lasso regression in the EsmiRs metabolism subsample using the "glmnet" package in R.[29] The 14 candidate predictors for the model included age, height, weight, BMI, DXA fat mass, DXA lean mass, DXA appendicular lean mass, BIA fat mass, BIA skeletal muscle mass, BIA fat-free mass, heart rate before and after the 6MWT, RPE after the 6MWT, and 6MWD. Both DXA and BIA measures were included as candidate predictors because BIA was conducted on the same day with spiroergometry in EsmiRs metabolism substudy, while DXA was conducted earlier during the EsmiRs measurements. To avoid overfitting to our subsample of 39 participants, the number of predictors was limited to three.[30] We studied the predictive performance of our model against measured VO_{2max} with Pearson correlation, model errors, and Bland-Altman plot using leave-one-out cross-validation. Furthermore, we calculated intraclass correlation (ICC) estimates in R using the "irr" package based on the single measurement, absolute agreement, and two-way mixed-effect model.[31] For sensitivity analyses, we also compared the performance of our model with another model with 6MWD as a predictor published by Mänttäri et al.[32]

The primary cross-sectional analyses were conducted with multiple linear regression models using the follow-up measurements from the EsmiRs study. MRS total symptoms, and its subscales were used separately as the outcome variable, while physical activity (ACC-PA and SR-PA), CRF (VO_{2max}), and body composition (total body mass, DXA body fat mass, and DXA lean body mass) were included in the model as predictors one at a time. CRF and body composition were used as the predictors with physical activity measures, and their interaction was also included in the model. Additionally, simple linear regression models with physical activity as predictor were fitted for participants in each tertile based on the total body mass, body fat mass, and lean body mass separately. The regression lines of each tertile were plotted on the same figure to further illustrate the interactions between physical activity and body composition measures. In the auxiliary analyses for participants that did not report any symptoms at baseline, multiple linear regression models with baseline physical activity, CRF, body composition measures as predictors, and the follow-up MRS scores as outcome were used. For sensitivity analyses, we ran the same analyses after excluding the premenopausal women. The models were adjusted with menopausal status, age, smoking, alcohol consumption, education, and the use of hormonal preparations. Additionally, VO_{2max} models were adjusted with lean body mass and body composition models were adjusted with body height. Residual plots, Q–Q plots, and correlation analysis between the covariates were used for assessing the model assumptions.

RESULTS

Characteristics of the study population

In the full EsmiRs sample (n = 298), participants reported a total mean MRS score of 8.6 ± SD 5.0 with only two participants being fully asymptomatic (total MRS score = 0). Most severe symptoms were reported in the somato-vegetative subscale (Table 1). On average, participants tended to be slightly overweight with mean BMI being 25.8 ± 4.1. Participants who did not report any symptoms at baseline ERMA measurements and in the EsmiRs metabolism subsample tended to have lower fat mass and BMI, as well as higher physical activity, CRF levels, and less severe symptoms compared to full EsmiRs sample. The mean time between the ERMA and EsmiRs measurements was 3.8 ± 0.1 years.

Model for predicting VO_{2max}

The estimated prediction model for VO_{2max} was:

$$VO_{2\,max} = 2.6897 - 0.0292 \times height + 0.1059 \times SMM + 0.0023 \times 6MWD$$

where VO_{2max} is absolute maximal oxygen consumption (l/min), height is body height (cm), SMM is BIA skeletal muscle mass (kg), and 6MWD is the 6-minute walking distance (m).

With leave-one-out cross-validation, the mean absolute error between the measured and predicted values in the EsmiRs metabolism subsample was 0.19 ± 0.15 l/min for absolute VO_{2max} and 2.75 ± 2.38 ml/min/kg for VO_{2max} relative to body weight. Pearson correlations and ICCs with 95% confidence intervals were 0.71 (0.50 to 0.84) and 0.69 (0.48 to 0.83), respectively (Supplemental Fig. 1A, http://links.lww.com/MENO/B275). Applying the previously published prediction model for VO_{2max} relative to body weight[32] to our study population resulted in a mean absolute error of 3.88 ± 2.67 ml/kg/min as well as Pearson correlations and ICCs of 0.69 (0.48 to 0.83) and 0.46 (−0.09 to 0.76), respectively (Supplemental Fig. 1B, http://links.lww.com/MENO/B275).

Associations between physical activity, CRF, body composition, and menopausal symptoms

In the primary analyses, higher total body and fat mass were associated with more severe total symptoms, somato-vegetative symptoms, and psychological symptoms with 1 kg higher mass predicting 0.03 to 0.07 higher symptoms score (Table 2).

TABLE 2. *Associations of physical activity, cardiorespiratory fitness, and body composition with menopausal symptoms in the cross-sectional study (n = 298)*

	Total symptoms		Somato-vegetative symptoms		Psychological symptoms		Urogenital symptoms	
	B	95% CI	B	95% CI	B	95% CI	B	95% CI
ACC-PA (10 mg)	−0.16	−0.86 to 0.55	−0.23	−0.53 to 0.08	−0.05	−0.39 to 0.28	0.12	−0.15 to 0.39
SR-PA (MET-h/d)	−0.13	−0.27 to 0.02	−0.07[c]	−0.13 to −0.00	−0.03	−0.10 to 0.04	−0.02	−0.08 to 0.04
Predicted VO_{2max} (l/min)[a]	1.08	−1.80 to 3.95	0.35	−0.90 to 1.60	0.27	−1.08 to 1.63	0.45	−0.64 to 1.54
Total body mass (kg)[b]	0.06[c]	0.01 to 0.12	0.03[d]	0.01 to 0.05	0.03[c]	0.00 to 0.05	0.01	−0.01 to 0.03
Body fat mass (kg)[b]	0.07[c]	0.01 to 0.14	0.04[c]	0.01 to 0.06	0.03[c]	0.00 to 0.06	0.01	−0.02 to 0.03
Lean body mass (kg)[b]	0.13	−0.03 to 0.30	0.05	−0.02 to 0.12	0.07	−0.01 to 0.15	0.02	−0.05 to 0.08

Multiple imputation was applied in the analyses. All models are adjusted with menopausal status, age, use of hormonal preparations, smoking, education, and alcohol consumption.
ACC-PA, accelerometer-measured physical activity mean amplitude deviation; mg, milligravity (0.00981 m/s^2); SR-PA, self-reported physical activity; VO_{2max}, maximal oxygen consumption.
[a]Model is additionally adjusted with lean body mass.
[b]Model is additionally adjusted with body height.
[c]$P < 0.05$
[d]$P < 0.01$

Physical activity and CRF were not associated with the severity of menopausal symptoms, except for the higher SR-PA being associated with less severe somato-vegetative symptoms. In the auxiliary analyses of the 82 participants that did not report any symptoms at baseline, ERMA baseline physical activity, VO_{2max}, and body composition were not associated with the severity of menopausal symptoms assessed 4 years later (Table 3). The results did not change significantly after excluding the premenopausal women from the analyses (data not shown).

In separate models with interaction between VO_{2max} and physical activity as well as body composition measures and physical activity, all body composition measures showed positive interactions with ACC-PA or SR-PA (Supplemental Tables 1–2, http://links.lww.com/MENO/B275). Notably, interactions of total body and fat mass with physical activity measures were strongest with urogenital symptoms. Total body mass and especially lean body mass interacted with physical activity measures in total and psychological symptoms. VO_{2max} showed no interaction with physical activity measures.

Figure 2 and Supplemental Tables 3–4 (http://links.lww.com/MENO/B275) illustrate that ACC-PA and SR-PA were inversely associated with total, somato-vegetative, and psychological symptoms in participants with the lowest lean body mass. In the lowest lean body mass tertile, 10 mg higher ACC-PA predicted decrease of 1.43 (0.26 to 2.60) in total symptom score. With participants in lowest total body and fat mass tertiles, inverse associations of physical activity and menopausal symptoms were not as distinct as with participants in lowest lean body mass tertile. However, in participants with highest body fat mass ACC-PA associated directly with psychological and urogenital symptoms.

DISCUSSION

We observed that the association between physical activity and menopausal symptoms varied based on the differences in body composition. The association of physical activity with total symptoms and psychological symptoms varied based on the differences in total and lean body mass with stronger indirect associations being observed in participants with lower total and lean body mass. The association between physical activity and urogenital symptoms was affected by the differences in total body and fat mass with direct associations being observed in participants with increased total body and fat mass. Furthermore, higher total body and fat mass were associated with more severe menopausal symptoms in the cross-sectional study, but CRF was not observed to associate with menopausal symptoms or to interact with physical activity.

TABLE 3. *Associations of baseline physical activity, cardiorespiratory fitness, and body composition with follow-up menopausal symptoms in the longitudinal study (n = 82)*

	Total symptoms		Somato-vegetative symptoms		Psychological symptoms		Urogenital symptoms	
	B	95% CI	B	95% CI	B	95% CI	B	95% CI
ACC-PA (10 mg)	−0.18	−1.08 to 0.72	−0.13	−0.55 to 0.29	0.03	−0.38 to 0.44	−0.08	−0.43 to 0.27
SR-PA (MET-h/d)	−0.01	−0.19 to 0.18	0.01	−0.08 to 0.10	0.00	−0.08 to 0.08	−0.01	−0.09 to 0.06
Predicted VO_{2max} (l/min)[a]	−2.06	−7.23 to 3.12	−1.12	−3.63 to 1.39	−0.56	−2.84 to 1.71	−0.37	−2.40 to 1.67
Total body mass (kg)[b]	−0.03	−0.13 to 0.06	−0.03	−0.07 to 0.02	0.01	−0.03 to 0.05	−0.02	−0.05 to 0.02
Body fat mass (kg)[b]	−0.04	−0.39 to 0.31	0.01	−0.16 to 0.17	−0.05	−0.20 to 0.10	0.01	−0.13 to 0.14
Lean body mass (kg)[b]	0.04	−0.29 to 0.37	0.00	−0.16 to 0.16	0.06	−0.09 to 0.20	−0.02	−0.15 to 0.11

Multiple imputation was applied in the analyses. All models are adjusted with baseline menopausal status, age, use of hormonal preparations, smoking, education, and alcohol consumption.
ACC-PA, accelerometer-measured physical activity mean amplitude deviation; mg, milligravity (0.00981 m/s^2); SR-PA, self-reported physical activity; VO_{2max}, maximal oxygen consumption.
[a]Model is additionally adjusted with baseline lean body mass.
[b]Model is additionally adjusted with baseline body height.

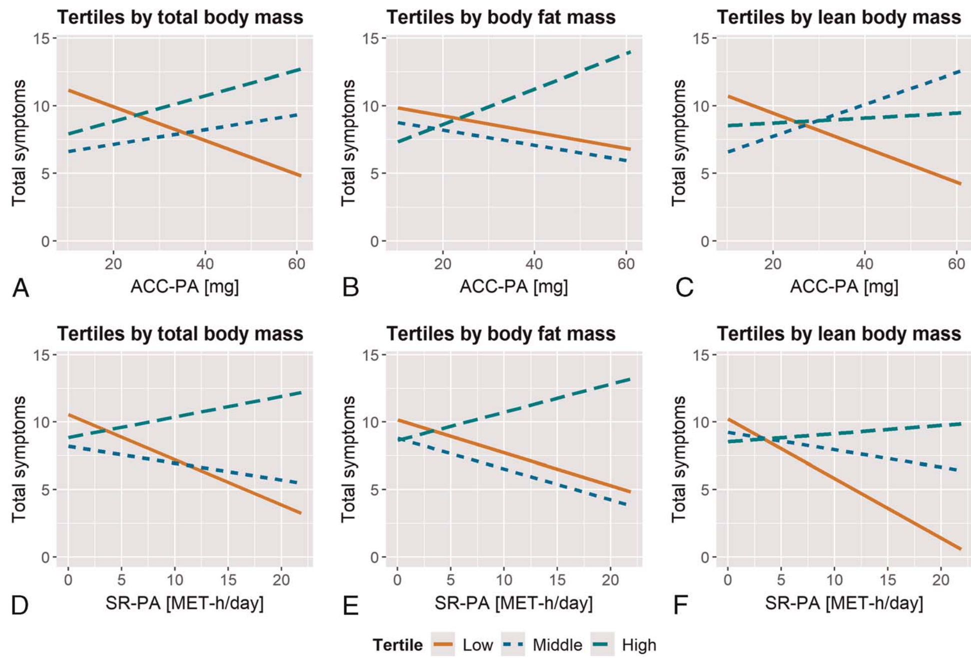

FIG. 2. Simple linear regression lines for total menopausal symptoms with ACC-PA and SR-PA as predictors by total body mass, body fat mass, and lean body mass tertiles. (**A**) ACC-PA and tertiles by body mass (n = 298), (**B**) ACC-PA tertiles by body fat mass (n = 293), (**C**) ACC-PA and tertiles by lean body mass (n = 293), (**D**) SR-PA and tertiles by body mass (n = 298), (**E**) SR-PA tertiles by body fat mass (n = 293), (**F**) SR-PA and tertiles by lean body mass (n = 293). Tertile mean values in kg from lowest to highest are 59.0, 69.6, and 84.3 for total body mass, 16.8, 24.7, and 36.3 for body fat mass, and 37.6, 42.3, and 46.8 for lean body mass. Multiple imputation was applied in the analyses. ACC-PA, accelerometer-measured physical activity; SR-PA, self-reported physical activity.

In the cross-sectional analyses, physical activity and CRF were not associated with menopausal symptoms. Our results are in line with the previous literature proposing very weak or negligible indirect associations between physical activity and menopausal symptoms.[3–5] Contradictory to our results, the few previous observational studies focusing on the role of CRF in this context have reported inverse associations between CRF and menopausal symptoms.[9,33] Similarly, an inverse association between CRF and menopause-related quality of life has also been reported in one randomized controlled trial with exercise intervention in middle-aged women.[15] However, another exercise intervention study did not observe an association between CRF and menopausal symptoms in postmenopausal women.[16]

Our results from the cross-sectional analyses with interactions included in the models suggested that the association between physical activity and the severity of menopausal symptoms fluctuates based on body composition. Notably, the association between physical activity and urogenital symptoms varied based on the differences in total body mass and especially body fat mass with the strongest direct associations between physical activity and urogenital symptoms being observed in participants with highest total body and fat mass. This may be accounted for by the fact that more active women are more likely to engage in activities with higher intensity; however, women with higher total body and fat mass may be less accustomed to high-intensity exercise, predisposing them to pelvic floor disorders such as urinary incontinence.[34]

Furthermore, body weight and especially lean body mass explained the differences in association of physical activity with menopausal symptoms. Participants with the lowest lean body mass had strong direct associations between physical activity and the severity of somato-vegetative, psychological, and total symptoms. This observation may be due to the differences in physical activity type among participants with different lean body mass. However, with the physical activity assessment methods used in this study, we were not able to identify the type of physical activity participants are engaging. Nonetheless, the exercise that does not significantly increase muscle mass (eg, aerobic training) may be more beneficial for alleviating symptoms compared to exercise that builds muscle mass (eg, resistance training). This hypothesis is supported by the results of the study with the aerobic and resistance training interventions in which the severity of menopausal symptoms decreased in both intervention groups, but the decrease was more significant in the group with aerobic training intervention.[35] Moreover, the exercise intervention studies for menopausal symptoms have mainly focused on aerobic training and yoga rather than resistance training,[3–5] and therefore the difference between aerobic and resistance training for menopausal symptoms is not well known.

Overall, the association between physical activity and menopausal symptoms varied significantly between the different body composition tertiles as well as between the different body composition measures. Consequently, because of this significant variation and relatively small sample size in this study, the results of this study should be considered as preliminary findings on this topic that should be verified in future studies.

When studying the associations between body composition and menopausal symptoms, we observed that participants with higher total body and fat mass had more severe total symptoms, somato-vegetative symptoms, and psychological symptoms in the cross-sectional analyses. However, in the auxiliary analyses with a smaller sample size, baseline body composition measures were not associated with menopausal symptoms assessed after the four-year follow-up. The direct association between BMI and body adiposity with menopausal symptoms has also been reported previously in cross-sectional and longitudinal studies, especially with vasomotor symptoms.[10,36] Direct association between obesity and the severity of urogenital symptoms has also been reported.[37,38] Therefore, in agreement with previous studies, our results indicate that obesity may be a risk factors for a variety of menopausal symptoms.

The strengths of the study are the assessment of menopausal symptoms with a validated questionnaire that accounts for the severity of the symptoms and the assessment of CRF with spiroergometry. Furthermore, body composition measured accurately with DXA, the use of accelerometer-measured physical activity, a comprehensive set of measured confounders including the use of hormonal preparations. The limitation of the study is the homogeneous sample of White women with exclusion of women with severe obesity and severe medical disorders, thus limiting the generalizability of the results. Furthermore, the statistically significant findings should be interpreted with caution due to the multiple statistical comparisons conducted in the study.

CONCLUSIONS

Maintaining healthy weight is associated with less severe menopausal symptoms in middle-aged women. Furthermore, the results of this study provide preliminary evidence that the association between physical activity and menopausal symptoms varies based on the differences in total and lean body mass highlighting the need for further research on this topic.

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