Preventive Medicine Reports 4 (2016) 277–282

Contents lists available at ScienceDirect

Preventive Medicine Reports

journal homepage: http://ees.elsevier.com/pmedr

Influence of cardiorespiratory fitness and physical activity levels on cardiometabolic risk factors during menopause transition: A MONET study

Joseph Abdulnour [a,b,c], Sahar Razmjou [a,b,c], Éric Doucet [a,c], Pierre Boulay [d,e], Martin Brochu [d,e], Rémi Rabasa-Lhoret [f,g,h], Jean-Marc Lavoie [i], Denis Prud'homme [a,b,*]

[a] School of Human Kinetics, Faculty of Health Sciences, University of Ottawa, Ottawa, ON, Canada
[b] Institut de recherche de l'Hôpital Montfort, Ottawa, ON, Canada
[c] Behavioral and Metabolic Research Unit, University of Ottawa, Ottawa, ON, Canada
[d] Université de Sherbrooke, Faculté des sciences de l'activité physique, Sherbrooke, QC, Canada
[e] Research Centre on Aging, Social Services and Health Centre-University Institute of Geriatrics of Sherbrooke, PQ, Canada
[f] Department of Nutrition, Université de Montréal, Montreal, PQ, Canada
[g] Montréal Diabetes Research Centre, Montréal, PQ, Canada
[h] Institut de Recherche Cliniques de Montréal, Montreal, PQ, Canada
[i] Department of Kinesiology, Université de Montréal, Montréal, PQ, Canada

ARTICLE INFO

Article history:
Received 22 February 2016
Received in revised form 1 June 2016
Accepted 27 June 2016
Available online 29 June 2016

Keywords:
Cardiorespiratory fitness
Fitness
Physical activity
Cardiometabolic risk factors
Menopause

ABSTRACT

To determine the influence of cardiorespiratory fitness (hereafter "fitness") and physical activity levels on cardiometabolic risk factors in premenopausal women going through the menopause transition. An ancillary study including 66 premenopausal women who participated to a 5-year observational, longitudinal study (2004 to 2009 in Ottawa) on the effects of menopause transition on body composition and cardiometabolic risk factors. Women underwent a graded exercise test on treadmill to measure peak oxygen uptake (VO_2 peak) at year 1 and 5 and physical activity levels were measured using accelerometers. Cardiometabolic risk factors included: waist circumference, fasting plasma lipids, glucose and insulin levels, HOMA-IR score, c-reactive protein, apolipoprotein B (apoB) and resting systolic and diastolic blood pressure. Change in fitness was not associated with changes in cardiometabolic risk factors. The changes in total physical activity levels on the other hand showed a significant negative association with apoB levels. Three-way linear mixed model repeated measures, showed lower values of waist circumference, fasting triglycerides, insulin levels, HOMA-IR score, apoB and diastolic blood pressure in women with a fitness ≥30.0 $mlO_2\ kg^{-1}\ min^{-1}$ compared to women with a fitness <30.0 $mlO_2\ kg^{-1}\ min^{-1}$ ($P < 0.05$). However, only fasting triglycerides was lower in women with physical activity levels ≥770.0 Kcal/day ($P < 0.05$). Between fitness and physical activity levels, fitness was associated with more favorable values of cardiometabolic risk factors in women followed for 5 years during the menopause transition.

1. Introduction

Cardiovascular disease (CVD) is the leading cause of mortality among women in developed countries (Bittner, 2002). Many CVD risk factors have been identified such as abdominal obesity, physical inactivity, diabetes, hypertension and dyslipidemia (Bittner, 2002; Pearson, 1999). Cardiorespiratory fitness (hereafter "fitness") as well as physical activity levels are important and independent predictors of CVD, cardiac events and death among symptomatic and asymptomatic women (Blair & Jackson, 2001; Gulati et al., 2005; Berlin & Colditz, 1990; Hu et al., 2005).

Fitness is a physiological attribute, defined by maximal oxygen uptake (VO_2 max) measured using a maximal exercise test (Lee et al., 2011). A high fitness level estimated in metabolic equivalents (METs) has been defined as the 2 highest quintiles, which represents ≥8.5 METs for women between the ages of 50–59 years according to the Aerobics Center Longitudinal study (Sui et al., 2007). Furthermore, a low fitness value (<8.5 METs) was shown to be associated with a higher incidence of CVD events in men and women (Sui et al., 2007). Conversely, high fitness has been found to be inversely associated with the levels of visceral fat, insulin resistance, blood lipids and blood pressure as well as with the prevalence of the metabolic syndrome (Abdulnour et al., 2010; Arsenault et al., 2007; LaMonte et al., 2005; LaMonte & Blair, 2006) collectively reducing the risk of CVD.

* Corresponding author at: Montfort Hospital, Scientific Director, Institut de recherche de l'Hôpital Montfort, 745-A ch. Montréal Rd, suite 202, 2e étage/Floor, Ottawa, ON K1K 0T1, Canada.
E-mail address: denisprudhomme@montfort.on.ca (D. Prud'homme).

http://dx.doi.org/10.1016/j.pmedr.2016.06.024

Physical activity is defined as any body movement that increases energy expenditure, including both leisure time and non-leisure time activities (American College of Sports Medicine et al., 2006). The 2011 Canadian Physical Activity Guidelines for adults recommends at least 150 min of moderate-to-vigorous intensity of aerobic physical activity per week (Tremblay et al., 2011 Feb). It has also been recommended to expend a minimum of 150 kcal/day or 1000 kcal/week of moderate-to-vigorous physical activity energy expenditure (Anon., 1996). Such physical activity levels recommendations have been demonstrated to be associated with increased health benefits, by reducing the risk of cardiometabolic risk factors and CVD in men and women (Hu et al., 2005; Tremblay et al., 2011; Warburton et al., 2010; Dvorak et al., 2000; Owens et al., 1990).

Despite the fact that several studies having simultaneously investigated the association between fitness and physical activity levels and body composition, body fat distribution and cardiometabolic risk factors (Lee et al., 2011; Dvorak et al., 2000; Eriksen et al., 2013; Minder et al., 2014; Yu et al., 2013), controversy remains. While the majority reported that fitness is more strongly associated than physical activity levels with CVD and cardiometabolic risk factors (Lee et al., 2011; Dvorak et al., 2000; Minder et al., 2014; Yu et al., 2013), one study suggested that physical activity level is as good as fitness to predict individual health (Eriksen et al., 2013). However, the majority of the studies used self-reported questionnaire for the assessment of physical activity levels (Lee et al., 2011; Eriksen et al., 2013; Minder et al., 2014; Yu et al., 2013). Although, self-reported physical activity may be useful for ranking physical activity levels in large epidemiological studies, it lacks precision and validity (Dvorak et al., 2000) for longitudinal and prospective studies compared to the measurement of total volume of physical activity by accelerometry (Bassett et al., 2015). Furthermore, accelerometer-derived physical activity measurements are more closely associated to cardiometabolic risk factors than that obtained from self-reported questionnaire (Bassett et al., 2015).

The evidence supporting a relationship between fitness and/or physical activity levels and CVD risk factors has been well documented in the general population. Still, it is questionable if these relationships are the same in women going through the menopause transition. First, this is a period in a woman's life that results in a progressive decrease in estrogen (Lovejoy et al., 2008 Jun), which is associated with an increase incidence and prevalence of cardiometabolic risk factors (Lovejoy et al., 2008) and CVD (Rosano et al., 2007). Second, we have previously reported, in the same cohort, that the time spent performing light physical activity have a greater effect on adiposity during menopause transition than moderate and/or vigorous physical activity (Riou et al., 2014). Third, the intensity of non-leisure time activities is lower than the relative intensity necessary to improve fitness (American College of Sports Medicine et al., 2006).

Thus, the aim of the present study was to determine the influence of fitness and physical activity levels on cardiometabolic risk factors in non-obese women going through the menopause transition. We tested the following hypothesis: fitness and physical activity levels would be related with a favorable cardiometabolic risk factors in women followed through the menopause transition.

2. Methods

2.1. Subjects

The study includes data from healthy premenopausal women aged between 47 and 55 years who participated in a 5-year longitudinal study from 2004 to 2009 (MONET Study: Montreal Ottawa New Emerging Team) (Abdulnour et al., 2012). For the purpose of this secondary analysis, 66 out of the 91 participants who completed the original study were included, based on peak oxygen uptake (VO_2 peak) and physical activity levels value availability at years 1 and 5. However, no differences were observed for baseline characteristics (data not shown) between those who completed the study and the sub-sample of participant used in the present analysis. Premenopausal women were included if they met the following criteria: (1) premenopausal status (two menstruations in the last three months, no increase in cycle irregularity in the 12 months preceding testing, and a plasma follicular-stimulating hormone level < 30 IU/l as a mean of verification); (2) aged between 47 and 55 years; (3) no surgically-induced menopause; (4) non-smoker; (5) BMI between 20 and 29 kg/m^2; and (6) reported weight stability (±2 kg) for ≥6 months before enrolment in the study. Exclusion criteria were: (1) pregnant women or planned to become pregnant; (2) had medical problems that could have interfered with outcome variables including cardiovascular and/or metabolic diseases; (3) were taking oral contraceptives or hormone replacement therapy; (4) had high risk for hysterectomy; and (5) had a history of drug and/or alcohol abuse. Prior to inclusion in the study, written informed consent was obtained from each participant. This study was conducted according to the guidelines of the Declaration of Helsinki, and received the approval from the University of Ottawa and the Montfort Hospital Ethics committees.

2.2. Menopausal status

Menopausal status was determined yearly by self-reported questionnaire about menstrual bleeding and its regularity and follicle-stimulating hormone (FSH) levels were measured annually during the early follicular phase to verify the menopausal status. Women were classified as premenopausal if they reported no change in menstrual cycle frequency and perimenopausal if they reported changes in menstrual frequency and/or amenorrhea for 3–11 months. Finally women were classified as postmenopausal based on their final menstrual period (FMP) and confirmed by 12 month of amenorrhea (Soules et al., 2001).

2.3. Anthropometric assessment

Body weight and height were measured with a BWB-800AS digital scale and a Tanita HR-100 height rod, respectively (Tanita Corporation of America, Inc. Arlington Heights, IL). Body mass index (BMI) was then calculated [body weight kg/height (m^2)]. Waist circumference (mean of two measures) was determined using a Gulick tape at the mid-distance between the lowest rib and the iliac crest (Canadian Society for Exercise Physiology, 2003). Body composition (fat mass and lean body mass) and % body fat were measured using dual-energy X-ray absorptiometry (DEXA) (GE-LUNAR Prodigy module, GE Medical Systems, Madison, Wi, USA) as previously described (Abdulnour et al., 2012).

2.4. Cardiorespiratory fitness

A graded progressive exercise test on the treadmill was performed to measure VO_2 peak by indirect calorimetry. The progressive test consisted of 3-minute stages starting with a speed of 3.4 mph and a slope of 0% with an increasing workload to the point of participant exhaustion (speed increased to 4.0 mph by stage 6, 5.2 mph by stage 8 and 6.0 mph by stage 10; slope increased by 4% at every stage). Heart rate, blood pressure and the rate of perceived exertion (Borg scale) (Borg, 1982) were taken at rest and at the end of each stage during the test. Breath-by-breath samples of expired air were collected through a mouthpiece during the test, and measurements of VO_2 and VCO_2 were obtained using a Vmax 229 series metabolic cart (SensorMedics Corporation, Yorba Linda, CA). The indirect calorimetry unit was calibrated before each test according to the manufacturer's specifications.

After a brief warm up on the treadmill, women performed the exercise test. The test was terminated when at least 2 of the following criteria were achieved (Gulati et al., 2005): 1) predicted maximal

heart rate reached, 2) respiratory quotient >1.1, 3) VO_2 remained stable or decreased with an increase in workload, or 4) rate of Borg-type scale reached ≥19. VO_2 peak was considered as the highest 30 s average VO_2 reached during the test.

2.5. Physical activity levels

An accelerometer (Actical; Mini Mitter Co, Inc., Bend, OR) was used to measure physical activity levels in kcal/day and time spent in physical activity of various intensities (sedentary, light, moderate and vigorous) per week. Once a year, participants wore the accelerometer upon waking up and took it off just before going to bed for 7 consecutive days, as previously described (Abdulnour et al., 2012). 24 h of continuous recording was performed by the accelerometers and time spent performing sedentary exercise was also considered when participants were not wearing the device (sleep time). Daily activity levels measured via accelerometry were found to be a good predictor of energy expenditure (r = 0.92–0.97) (Bouten et al., 1997). The accelerometers used to measure physical activity energy expenditure in this study were also validated with the use of doubly labeled water measurements (Goris et al., 2001).

2.6. Resting blood pressure

Qualified research assistants measured supine resting blood pressure manually from the left arm after participants had been resting quietly for 5 min using a standard stethoscope and a mercury sphygmomanometer. For this measurement, an appropriate cuff size was selected for each participant based on arm circumference. Assessment of resting blood pressure was standardized according to the (American College of Sports Medicine et al., 2000) SBP was considered as the first detectable Korotkoff sound (phase 1) and DBP was considered as the last detectable Korotkoff sound (phase 5) (Chobanian et al., 2003).

2.7. Blood sampling

Blood samples were taken after a 12-h overnight fast. Plasma insulin concentrations were measured in duplicate by radioimmunoassay using ^{125}I-labeled human insulin and a human insulin antiserum (Millipore, St. Charles, MO, USA). Plasma glucose levels were determined using spectrophotometric analysis after conversion of glucose to glucose-6-phosphate by hexokinase (Sigma-Aldrich Canada Ltd., Oakville, ON, CAN; Fisher Scientific Limited, Nepean, ON, CAN). Insulin resistance was estimated using the homeostasis model assessment [HOMA-IR = (fasting glucose × fasting insulin)/22.5]. Total cholesterol (TC), high-density-lipoproteins cholesterol (HDL-C), and triglycerides (TG) were analyzed using the Vitros 950 immunoassay analyzer (Ortho Clinical Diagnostics, Johnson & Johnson Company, Markham, ON, CAN) at a wavelength of 540 nm. TC, HDL-C, and TG were used in the Friedewald (Friedewald et al., 1972) formula to calculate low-density-lipoproteins cholesterol (LDL-C) concentration. Serum c-reactive protein (CRP), was assessed by immunonephelometry on an Image analyzer (Beckman-Coulter, Villepinte, France) with detection limits of 0.20 mg/l. Apolipoprotein B (apoB) was assessed by immunoturbidimetry (Architect, Abbott, Rungis, France) with detection limits of 0.03 g/l. All measures of blood profile presented a coefficient of variation of <15%.

2.8. Statistical analysis

Data are presented as means ± standard deviation. Variables were first checked for normality. Consequently, only TG and CRP were log-transformed to normalize the distribution. ANOVA was performed to compare fitness and physical activity levels between menopause status (premenopause, perimenopause and postmenopause), for the purpose of this analysis the database was transformed into cases as previously described (Abdulnour et al., 2012). Pearsons' correlations were performed to document the associations between the changes (year 5 - baseline) in fitness, physical activity levels and the changes observed in variables of interest. Participants were divided into groups based on their VO_2 peak (<30.0 vs. ≥30.0 $mlO_2\ kg^{-1}\ min^{-1}$) according to the high fitness (8.5 METs) classification for age and sex-specific estimated metabolic equivalent levels of fitness (Sui et al., 2007). Furthermore, we elected to use daily total volume of physical activity levels expressed in kcal/day. The latter has shown to be a better metric than time spent in various physical activity intensities because it incorporates the full continuum of physical activity intensities (Bassett et al., 2015). Participants were therefore divided in two sub-group based on physical activity levels (<770.0 vs. ≥770.0 kcal/day). Three-way linear mixed model repeated measures analyses were used for determination of main effects on cardiometabolic risk factors (waist circumference, fasting plasma lipids, glucose and insulin levels, HOMA-IR score, CRP, apoB and resting systolic and diastolic blood pressure). Time (baseline and year 5) was considered as a *within-subject* factor; VO_2 peak (low < 30.0 vs. high ≥ 30.0 $mlO_2\ kg^{-1}\ min^{-1}$) and physical activity levels (<770.0 vs. ≥770.0 kcal/day) were considered as *between-subject* factor. Results are expressed as the mean ± standard deviation. A P value ≤0.05 was considered as significant. SPSS 17.0 for windows (SPSS Inc. Chicago, IL, USA) was used to perform statistical analyses.

3. Results

Participants' characteristics are presented in Table 1. At baseline, mean age of the participants was 49.8 ± 1.9 years (range: 47 to 54 years), and % body fat was 31.1 ± 7.0 (range: 18.2 to 41.7%). The mean VO_2 peak was 33.6 ± 6.5 (range: 20.9 to 52.0 $mlO_2\ kg^{-1}\ min^{-1}$) and daily physical activity levels was 829.9 ± 266.4 (range: 326.3 to 1904.7 kcal/day). All 66 women were premenopausal at year 1. By the end of year 5, 4 were still premenopausal (FSH: 26.5 ± 24.7 IU/l), 17 were perimenopausal (FSH: 48.6 ± 38.9 IU/l) and 46 had become postmenopausal (FSH: 85.2 ± 29.5 IU/l).

To analyze the effect of menopause transition on fitness and physical activity levels, the database was transformed into cases based on menopausal status (Abdulnour et al., 2012). As a result, no significant differences were observed between menopause group (premenopause vs. perimenopause vs. postmenopause) for VO_2 peak, and for physical activity levels (Table 2).

Table 1
Anthropometric and cardiometabolic characteristics of premenopausal women (n = 66) at baseline (MONET study 2004–2009, Ottawa).

Variables	Mean ± SD	Minimum	Maximum
Age (yrs)	49.8 ± 1.9	47	54
Body mass index (kg/m^2)	23.2 ± 2.4	19.3	28.7
% Body fat	31.1 ± 7.0	18.2	41.7
Fat mass (kg)	19.0 ± 5.6	9.6	29.9
Lean body mass (kg)	38.9 ± 3.9	31.1	47.3
Waist circumference (cm)	78.1 ± 7.1	62.2	93.7
Triglycerides (mmol/l)	0.84 ± 0.31	0.41	1.98
Total cholesterol (mmol/l)	4.39 ± 0.69	3.05	6.23
HDL-C (mmol/l)	1.53 ± 0.33	0.81	2.29
LDL-C (mmol/l)	2.47 ± 0.65	1.33	4.25
TC/HDL-C	3.01 ± 0.79	1.78	5.40
Fasting Glucose (mmol/l)	4.79 ± 0.38	3.80	5.70
Fasting Insulin (uU/ml)	11.45 ± 4.02	5.03	32.07
HOMA-IR	2.45 ± 0.90	1.14	6.98
CRP (mg/l)	1.70 ± 1.90	0.20	10.40
apoB (g/l)	0.74	0.47	1.20
VO_2 peak ($mlO_2\ kg^{-1}\ min^{-1}$)	33.6 ± 6.5	20.9	52.0
Physical activity (kcal/day)	829.9 ± 266.4	326.3	1904.7

n: number of subjects (number differ because of missing data); SD: standard deviation; HDL-C: high-density lipoproteins cholesterol; LDL-C: low-density lipoproteins cholesterol; TC: total cholesterol; HOMA-IR: homeostasis model assessment; CRP: C-reactive protein; apoB: apolipoprotein B.

Table 2
Comparison of fitness and physical activity levels between menopausal status (MONET study 2004–2009, Ottawa).

	Menopause status			*P* Value
	Premenopause	Perimenopause	Postmenopause	
n	66	17	45	
Fitness ($mlO_2\ kg^{-1}\ min^{-1}$)	33.9 ± 6.3	33.9 ± 6.1	32.7 ± 6.6	=0.56
n	66	15	41	
Physical activity levels (kcal/day)	825.6 ± 266.7	849.0 ± 244.2	803.9 ± 256.6	=0.81

n: number of subjects. Results are expressed as mean ± standard deviation.

Pearsons' correlations between the changes (year 5 - baseline) in fitness, physical activity levels and the changes observed in cardiometabolic risk factors were preformed. As a result, only the change in physical activity levels showed significant negative association with apoB ($P < 0.05$). No significant correlations were observed between changes in fitness and cardiometabolic risk factors (Table 3).

Three-way linear mixed model repeated measures (Table 4) were performed to document the main effect of time (baseline and year 5), fitness, and physical activity levels on cardiometabolic risk factors, in women going through the menopause transition. A significant effect of time was observed for various indices of cardiometabolic risk factors, indicating an overall increase over time, with the exception of fasting plasma glucose and CRP, which showed a decrease in time. Significant effect of fitness was also observed for waist circumference, fasting TG, insulin, HOMA-IR score, apoB and diastolic blood pressure. These variables were significantly lower in women with a VO_2 peak ≥30.0 $mlO_2\ kg^{-1}\ min^{-1}$ compared to women with a VO_2 peak <30.0 $mlO_2\ kg^{-1}\ min^{-1}$. Despite significant effect of physical activity level was observed for waist circumference and TG (<0.05) only the TG was lower in women with physical activity levels ≥770.0 Kcal/day. Finally, no fitness × physical activity levels interaction was observed for any variables of interest.

4. Discussion

The present study determined the influence of objective measures of fitness and physical activity levels on cardiometabolic risk factors in non-obese premenopausal women going through menopause transition. According to the mixed model repeated measures, we found that fitness had independent effects on measures of waist circumference, fasting TG, insulin, HOMA-IR score, apoB and diastolic blood pressure. The results showed overall lower values in women with a high fitness. Physical activity levels, on the other hand, was negatively associated with apoB, however this observation no longer remained in the repeated measures analysis. In fact, physical activity did not have an independent impact on more favorable values of cardiometabolic risk factors compared to fitness. This suggests that fitness may have greater cardioprotective effects than physical activity levels in women transitioning to menopause. These findings further support existing studies (Lee et al., 2011; Dvorak et al., 2000; Minder et al., 2014; Yu et al., 2013) that reported fitness as a stronger correlate of cardiometabolic risk factors, despite the use of accelerometers in this study for the measurement of physical activity levels compared to self-reported questionnaire. One study reported, in a sample of Chinese women aged 55 to 69, that both physical activity (self-reported questionnaire) and fitness were associated with the prevalence of the metabolic syndrome, adjusted for confounding variables (Yu et al., 2013). However, when physical activity was further adjusted for fitness, the association with metabolic syndrome was eliminated; when fitness was adjusted for physical activity, the association remained (Yu et al., 2013). Another study reported, in 53 men (68 ± 9 years) and 63 women (67 ± 7 years) that high fitness, independent of physical activity (measured by doubly labeled water and accelerometer), showed lower levels of fasting triglycerides, total cholesterol, TC/HDL-C, insulin and waist circumference ($0.01 > P < 0.05$) (Dvorak et al., 2000).

Overall, the results are in line with the classical knowledge that fit individuals have better CVD risk factors profile than unfit subjects (Haddock et al., 1998; Lee et al., 2005; Vainionpaˆaˆ et al., 2007; Wong et al., 2004). However, even if higher values of cardiometabolic risk factors were observed in our women with lower fitness, the absolute values were still within normal ranges. This can be explained by the fact that this cohort is composed of healthy non-obese women with no major cardiometabolic complications. Also the participants' mean waist circumference value is lower than the reported thresholds of 88.0 cm; which has been associated with an increased risk of cardiometabolic disturbance in women (Klein et al., 2007).

Even though physical activity levels was not a better correlate of cardiometabolic risk factors, it is known to be an important determinant of fitness (LaMonte & Blair, 2006). However, in the present study, we did not find a significant correlation between physical activity levels and fitness (data not shown). This supports the idea that these two phenotypes may act in an independent manner on various CVD risk factors (Dvorak et al., 2000) and could explain why we did not observe a fitness x physical activity levels interactions in the present study.

Finally, in healthy women, menopause *per se* was found to be associated with decrease in fitness through cardiopulmonary alterations affected by estrogen deficiency and a reduced level of nitric oxide (Mercuro et al., 2006). These alterations account partially for the impairment of endothelium-dependent vasodilation, preventing O_2 flow to match the increase O_2 requirement during exercise (Mercuro et al., 2006). Despite what has been reported in the previous study, no effect of the menopausal status was observed for fitness in the present sub-group as well as reported by our group for the whole MONET cohort (Abdulnour et al., 2012). This is partly due to the fact that the participant remained fairly active, based on the absence of a significant change in physical activity levels between menopausal status, in this study, and during the 5 years follow-up, as reported elsewhere (Duval et al., 2013).

Our study presents some limitations. First, the population studied consisted of healthy women with a BMI < 30 kg/m^2. Therefore, our findings cannot be generalized to the whole population with a wide range of BMIs. Nonetheless, it is important to mention that 45% of the women aged between 40 and 59 years in the Canadian population present a normal BMI and 76% have a BMI < 30 kg/m^2. Second, we

Table 3
Relationships between 5-year changes of fitness, physical activity levels and changes in cardiometabolic risk profile in women transitioning from pre to post-menopausal (MONET study 2004–2009, Ottawa).

	Fitness	Physical activity levels
n	65	56
Waist circumference	−0.16	−0.06
n	61	55
Triglycerides	−0.14	−0.03
Total cholesterol	−0.13	−0.06
HDL-C	0.09	0.16
LDL-C	−0.18	−0.26
TC/HDL-C ratio	−0.19	−0.26
Fasting glucose	−0.06	−0.01
Fasting insulin	−0.18	−0.07
HOMA-IR	−0.19	−0.06
CRP	−0.02	−0.24
apoB	0.01	−0.38**
n	59	53
Blood pressure		
Systolic	−0.05	0.25
Diastolic	−0.004	0.19

n: Number of subjects; HDL-C: high-density lipoproteins cholesterol; LDL-C: low-density lipoproteins cholesterol; TC: total cholesterol; HOMA-IR: homeostasis model assessment; CRP: c-reactive protein; apoB: apolipoprotein B. Triglycerides and CRP were log-converted for analysis.
** $P < 0.01$.

Table 4
Cardiometabolic risk factors characteristics of women by time point, fitness ($mlO_2\ kg^{-1}\ min^{-1}$) and physical activity levels (kcal/day) (MONET study 2004–2009, Ottawa).

	Fitness < 30.0 Mean ± SD		Fitness ≥ 30.0 Mean ± SD		Physical activity levels < 770.0 Mean ± SD		Physical activity levels ≥ 770.0 Mean ± SD		Independent effects (*P* value)		
	Baseline	Year 5	Baseline	Year 5	Baseline	Year 5	Baseline	Year 5	Time	Fitness	PAEE
n	24	28	42	37	32	23	34	33			
Waist circumference (cm)	81.7 ± 6.6	82.5 ± 7.4	76.1 ± 6.5	74.3 ± 4.8	75.6 ± 6.9	76.4 ± 6.7	80.5 ± 6.5	79.1 ± 7.7	NS	<0.001	<0.05
n	24	27	42	34	32	24	34	30			
Triglycerides (mmol/l)	0.96 ± 0.38[a]	0.94 ± 0.38[b]	0.76 ± 0.24	0.85 ± 0.36	0.89 ± 0.39	1.01 ± 0.41	0.78 ± 0.20[c]	0.77 ± 0.28[d]	NS	<0.05	<0.05
Total cholesterol (mmol/l)	4.52 ± 0.69	5.02 ± 0.79	4.31 ± 0.69	4.87 ± 0.72	4.24 ± 0.60	4.90 ± 0.77	4.53 ± 0.76	5.98 ± 0.74	<0.001	NS	NS
HDL-C (mmol/l)	1.52 ± 0.40	1.68 ± 0.33	1.53 ± 0.29	1.73 ± 0.36	1.47 ± 0.32	1.68 ± 0.37	1.58 ± 0.34	1.74 ± 0.33	<0.001	NS	NS
LDL-C (mmol/l)	2.53 ± 0.73	2.87 ± 0.69	2.44 ± 0.61	2.75 ± 0.60	2.37 ± 0.53	2.75 ± 0.62	2.57 ± 0.74	2.85 ± 0.67	<0.001	NS	NS
TC/HDL-C	3.19 ± 1.02	3.11 ± 0.84	2.90 ± 0.60	2.90 ± 0.60	3.01 ± 0.72	3.01 ± 0.68	3.00 ± 0.85	2.97 ± 0.77	NS	NS	NS
Fasting glucose (mmol/l)	4.86 ± 0.49	4.63 ± 0.44	4.75 ± 0.31	4.55 ± 0.36	4.76 ± 0.35	4.57 ± 0.35	4.82 ± 0.42	4.60 ± 0.44	<0.001	NS	NS
Fasting insulin (uU/ml)	13.2 ± 5.0	11.8 ± 2.9	10.5 ± 2.9	10.2 ± 2.8[e]	11.6 ± 5.1	10.7 ± 2.7	11.2 ± 2.7	11.0 ± 3.1[f]	NS	<0.01	NS
HOMA-IR	2.86 ± 1.11	2.46 ± 0.66	2.21 ± 0.66	2.12 ± 0.55[g]	2.48 ± 1.12	2.20 ± 0.47	2.42 ± 0.64	2.34 ± 0.75[d]	NS	<0.01	NS
CRP (mg/l)	2.02 ± 2.01	1.47 ± 1.52[h]	1.51 ± 1.83[i]	0.99 ± 1.63[j]	1.71 ± 1.97	1.35 ± 1.98	1.69 ± 1.86[k]	1.05 ± 1.08[k]	<0.01	NS	NS
apoB (g/l)	0.78 ± 0.18	0.80 ± 0.19[h]	0.72 ± 0.12[i]	0.71 ± 0.18[j]	0.74 ± 0.13	0.73 ± 0.17	0.75 ± 0.16[k]	0.76 ± 0.21[k]	NS	<0.05	NS
n	24	27	42	33	32	22	34	32			
Resting blood pressure											
Systolic (mmHg)	114.4 ± 9.6	119.9 ± 12.3	116.2 ± 11.6	119.1 ± 11.5	115.3 ± 11.6	121.5 ± 12.1	115.8 ± 10.3	117.5 ± 11.3	NS	NS	NS
Diastolic (mmHg)	75.4 ± 6.2	75.3 ± 7.4	71.6 ± 7.6	73.3 ± 7.4	71.9 ± 7.8	75.6 ± 8.5	73.9 ± 6.8	73.9 ± 6.3	NS	<0.05	NS

PAEE: physical activity energy expenditure; N: number of subjects; HDL-C: high-density lipoproteins cholesterol; LDL-C: low-density lipoproteins cholesterol; TC: total cholesterol; HOMA-IR: homeostasis model assessment.
Linear mixed models repeated measures; Independent effect of time (within subject factor); Independent effect of fitness (between subject factor); Independent effect of PAEE (between subject factor).
Triglyceride and CRP were log-converted for statistical analysis and reconverted for presentation in table format.
[a] n = 23.
[b] n = 26.
[c] n = 33.
[d] n = 29.
[e] n = 35.
[f] n = 31.
[g] n = 33.
[h] n = 28.
[i] n = 40.
[j] n = 36.
[k] n = 32.

used data taken from year 1 and year 5, based on fitness and physical activity levels availability. Therefore we could not account for fitness and physical activity levels at every year and between the yearly testing sessions during the 5-year follow-up. Finally, because we worked with healthy premenopausal women at low risk for CVD, the duration of the follow-up might be insufficient to capture the magnitude of the effect of menopause transition on cardiometabolic risk factors. Despite these limitations, the well-characterized cohort of healthy non-obese (BMI < 30 kg/m^2) physically active women followed for 5 years strengthens the present study. We used indirect calorimetry and accelerometry, for the measurement of VO_2 peak and physical activity levels respectively, which are valid and highly reproducible measure of these phenotype (Bassett et al., 2015; Goris et al., 2001; Vanhees et al., 2005).

5. Conclusion

The results of this study suggest that menopause does not have an impact on fitness and physical activity levels expressed in kcal/day. Furthermore, fitness was associated with more favorable values of cardiometabolic risk factors compared to physical activity levels in active non-obese premenopausal women transitioning to menopause.

Conflict of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

Acknowledgment

This research was supported by the Canadian Institutes of Health Research (T 0602145.02). Rémi Rabasa-Lhoret holds a scholarship from FRSQ (Fonds de Recherche en Santé du Québec) and is the recipient of the J-A DeSève chair in clinical research. The authors thank Mrs. Ann Beninato, Dr. Geneviève Leroux, Miss Véronique Bertrand, Miss Isabelle Giguère, and Miss Karine Duval for their assistance and excellent technical support throughout the study.

References

Abdulnour, J., Boulay, P., Brochu, M., Rabasa-Lhoret, R., Yasari, S., Prud'homme, D., 2010 Augg. Relationship between the percentage of predicted cardiorespiratory fitness and cardiovascular disease risk factors in premenopausal women: a MONET study. Climacteric 13 (4), 347–354.
Abdulnour, J., Doucet, E., Brochu, M., et al., 2012 Jull. The effect of the menopausal transition on body composition and cardiometabolic risk factors: a Montreal-Ottawa New Emerging Team group study. Menopause 19 (7), 760–767.
American College of Sports Medicine, Franklin, B.A., Whaley, M.H., Howley, E.T., Balady, G.J., 2000. ACSM's guidelines for exercise testing and prescription. sixth ed. Lippincott Williams & Wilkins, Philadelphia.
American College of Sports Medicine, Whaley, M.H., Brubaker, P.H., Otto, R.M., Armstrong, L.E., 2006. ACSM's Guidelines for Exercise Testing and Prescription. seventh ed. Lippincott Williams & Wilkins, Baltimore.
Anon., 1996 Aug 21. Surgeon General's report on physical activity and health. JAMA 276 (7), 522.
Arsenault, B.J., Lachance, D., Lemieux, I., et al., 2007. Visceral adipose tissue accumulation, cardiorespiratory fitness, and features of the metabolic syndrome. Arch. Intern. Med. 167 (14), 1518–1525.
Bassett, D.R., Troiano, R.P., McClain, J.J., Wolff, D.L., 2015 Aprr. Accelerometer-based physical activity: total volume per day and standardized measures. Med. Sci. Sports Exerc. 47 (4), 833–838.
Berlin, J.A., Colditz, G.A., 1990. A meta-analysis of physical activity in the prevention of coronary heart disease. Am. J. Epidemiol. 132 (4), 612–628.

Bittner, V., 2002. Women and coronary heart disease risk factors. J. Cardiovasc. Risk 9 (6), 315–322.
Blair, S.N., Jackson, A.S., 2001. Physical fitness and activity as separate heart disease risk factors: a meta-analysis. Med. Sci. Sports Exerc. 33 (5), 762–764.
Borg, G.A.V., 1982. Psychophysical bases of perceived exertion. Med. Sci. Sports Exerc. 14 (5), 377–381.
Bouten, C.V., Sauren, A.A., Verduin, M., Janssen, J.D., 1997 Jann. Effects of placement and orientation of body-fixed accelerometers on the assessment of energy expenditure during walking. Med Biol Eng Comput. 35 (1), 50–56.
Canadian Society for Exercise Physiology, 2003. The Canadian Physical Activity, Fitness & Lifestyle Approach. third ed. (Ottawa).
Chobanian, A.V., Bakris, G.L., Black, H.R., et al., 2003 Decc. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension 42 (6), 1206–1252.
Duval, K., Prud'homme, D., Rabasa-Lhoret, R., et al., 2013 Aprr. Effects of the menopausal transition on energy expenditure: a MONET group study. Eur. J. Clin. Nutr. 67 (4), 407–411.
Dvorak, R.V., Tchernof, A., Starling, R.D., Ades, P.A., DiPietro, L., Poehlman, E.T., 2000. Respiratory fitness, free living physical activity, and cardiovascular disease risk in older individuals: a doubly labeled water study. J. Clin. Endocrinol. Metab. 85 (3), 957–963.
Eriksen, L., Curtis, T., Gronbaek, M., Helge, J.W., Tolstrup, J.S., 2013 Decc. The association between physical activity, cardiorespiratory fitness and self-rated health. Prev. Med. 57 (6), 900–902.
Friedewald, W.T., Levy, R.I., Fredrickson, D.S., 1972. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin. Chem. 18 (6), 499–502.
Goris, A.H., Meijer, E.P., Kester, A., Westerterp, K.R., 2001 Marr. Use of a triaxial accelerometer to validate reported food intakes. Am. J. Clin. Nutr. 73 (3), 549–553.
Gulati, M., Black, H.R., Shaw, L.J., et al., 2005. The prognostic value of a nomogram for exercise capacity in women. N. Engl. J. Med. 353 (5), 468–475.
Haddock, B.L., Hopp, H.P., Mason, J.J., Blix, G., Blair, S.N., 1998. Cardiorespiratory fitness and cardiovascular disease risk factors in postmenopausal women. Med. Sci. Sports Exerc. 30 (6), 893–898.
Hu, G., Tuomilehto, J., Silventoinen, K., Barengo, N.C., Peltonen, M., Jousilahti, P., 2005. The effects of physical activity and body mass index on cardiovascular, cancer and all-cause mortality among 47 212 middle-aged Finnish men and women. Int. J. Obes. 29 (8), 894–902.
Klein, S., Allison, D.B., Heymsfield, S.B., et al., 2007 Mayy. Waist circumference and cardiometabolic risk: a consensus statement from shaping America's health: Association for Weight Management and Obesity Prevention; NAASO, the Obesity Society; the American Society for Nutrition; and the American Diabetes Association. Obesity (Silver Spring) 15 (5), 1061–1067.
LaMonte, M.J., Blair, S.N., 2006. Physical activity, cardiorespiratory fitness, and adiposity: contributions to disease risk. Curr. Opin. Clin. Nutr. Metab. Care 9 (5), 540–546.
LaMonte, M.J., Barlow, C.E., Jurca, R., Kampert, J.B., Church, T.S., Blair, S.N., 2005. Cardiorespiratory fitness is inversely associated with the incidence of metabolic syndrome: a prospective study of men and women. Circulation 112 (4), 505–512.
Lee, S., Kuk, J.L., Katzmarzyk, P.T., Blair, S.N., Church, T.S., Ross, R., 2005 Aprr. Cardiorespiratory fitness attenuates metabolic risk independent of abdominal subcutaneous and visceral fat in men. Diabetes Care 28 (4), 895–901.
Lee, D.C., Sui, X., Ortega, F.B., et al., 2011 Mayy. Comparisons of leisure-time physical activity and cardiorespiratory fitness as predictors of all-cause mortality in men and women. Br. J. Sports Med. 45 (6), 504–510.
Lovejoy, J.C., Champagne, C.M., de Jonge, L., Xie, H., Smith, S.R., 2008 Junn. Increased visceral fat and decreased energy expenditure during the menopausal transition. Int. J. Obes. 32 (6), 949–958.
Mercuro, G., Saiu, F., Deidda, M., Mercuro, S., Vitale, C., Rosano, G.M.C., 2006. Impairment of physical exercise capacity in healthy postmenopausal women. Am. Heart J. 151 (4), 923–927.
Minder, C.M., Shaya, G.E., Michos, E.D., et al., 2014 Feb 15. Relation between self-reported physical activity level, fitness, and cardiometabolic risk. Am. J. Cardiol. 113 (4), 637–643.
Owens, J.F., Matthews, K.A., Wing, R.R., Kuller, L.H., 1990. Physical activity and cardiovascular risk: a cross-sectional study of middle-aged premenopausal women. Prev. Med. 19 (2), 147–157.
Pearson, T.A., 1999 Aprr. Cardiovascular disease in developing countries: myths, realities, and opportunities. Cardiovasc. Drugs Ther. 13 (2), 95–104.
Riou, M.E., Abdulnour, J., Brochu, M., Prud'homme, D., Rabasa-Lhoret, R., Doucet, E., 2014 Febb. Light physical activity is a better determinant of lower adiposity during the menopausal transition. Climacteric 17 (1), 79–86.
Rosano, G.M., Vitale, C., Marazzi, G., Volterrani, M., 2007 Febb. Menopause and cardiovascular disease: the evidence. Climacteric 10 (Suppl. 1), 19–24.
Soules, M.R., Sherman, S., Parrott, E., et al., 2001 Decc. Executive summary: stages of reproductive aging workshop (STRAW). Climacteric 4 (4), 267–272.
Sui, X., LaMonte, M.J., Blair, S.N., 2007. Cardiorespiratory fitness as a predictor of nonfatal cardiovascular events in asymptomatic women and men. Am. J. Epidemiol. 165 (12), 1413–1423.
Tremblay, M.S., Warburton, D.E., Janssen, I., et al., 2011 Febb. New Canadian physical activity guidelines. Appl. Physiol. Nutr. Metab. 36 (1), 36–46.
Vainionpaˆaˆ, A., Korpelainen, R., Kaikkonen, H., Knip, M., Leppaˆluoto, J., Jaˆmsaˆ, T., 2007. Effect of impact exercise on physical performance and cardiovascular risk factors. Med. Sci. Sports Exerc. 39 (5), 756–763.
Vanhees, L., Lefevre, J., Philippaerts, R., et al., 2005. How to assess physical activity? How to assess physical fitness. Eur J Cardiovasc Prev Rehabil. 12 (2), 102–114.
Warburton, D.E., Charlesworth, S., Ivey, A., Nettlefold, L., Bredin, S.S., 2010. A systematic review of the evidence for Canada's physical activity guidelines for adults. Int. J. Behav. Nutr. Phys. Act. 7, 39.
Wong, S.L., Katzmarzyk, P.T., Nichaman, M.Z., Church, T.S., Blair, S.N., Ross, R., 2004. Cardiorespiratory fitness is associated with lower abdominal fat independent of body mass index. Med. Sci. Sports Exerc. 36 (2), 286–291.
Yu, R., Yau, F., Ho, S.C., Woo, J., 2013. Associations of cardiorespiratory fitness, physical activity, and obesity with metabolic syndrome in Hong Kong Chinese midlife women. BMC Public Health 13, 614.