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Synergistic associations of physical activity and diet quality on cardiometabolic risk factors in overweight and obese postmenopausal women

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Abstract

Healthy diet and physical activity are associated with a lower cardiometabolic risk (CMR). Little is known about whether they interact to improve CMR. The purpose of the present study was to determine the synergistic associations of diet quality and physical activity energy expenditure (PAEE) on CMR factors. The present study was an *a posteriori* analysis of two cross-sectional studies on 124 inactive non-diabetic postmenopausal women with a BMI $\geq 27\,kg/m^2$. The following factors were measured: diet quality (assessed by the Canadian Healthy Eating Index (C-HEI) from a 3 d food record); PAEE (doubly labelled water); body composition (dual-energy X-ray absorptiometry, computed tomography scan); lipoprotein profile (total, HDL- and LDL-cholesterol (HDL-C and LDL-C), non-HDL-C, total cholesterol:HDL-C, TAG, apoA1, apoB, apoA1:apoB and LDL-C:apoB); insulin sensitivity (homeostasis model assessment of insulin resistance and hyperinsulinaemic–euglycaemic clamp); inflammatory markers (high-sensitivity C-reactive protein (hs-CRP), haptoglobin, orosomucoid, IL-6 and leucocyte count). The association of the interaction PAEE × C-HEI and CMR factors was evaluated by hierarchical regressions. Fat mass-adjusted ANCOVA determined the interaction between PAEE and the C-HEI. In hierarchical regressions, the interaction PAEE × C-HEI was a correlate of more favourable values of HDL-C, apoB, apoA1:apoB and LDL-C:apoB ratios, and hs-CRP, while only PAEE was a negative correlate of haptoglobin. Compared with those in the low-PAEE/low-C-HEI group, women in the high-PAEE/high-C-HEI group had 10% higher HDL-C, 13% lower apoB, 11% larger LDL particles and 28% lower hs-CRP concentrations ($P<0{\cdot}05$). PAEE and the C-HEI have a synergistic association with the CMR profile. These results support the integration of both diet quality and physical activity in the management of CMR.

Key words: Inflammation: Physical activity energy expenditure: Healthy Eating Index: Diet quality: Obesity: Women

Obesity has reached pandemic proportions and is associated with several metabolic disorders including dyslipidaemia, insulin resistance and chronic subclinical inflammation, which all contribute to an increased risk of type 2 diabetes (T2D) and CVD[1]. Moreover, they are all components of cardiometabolic risk (CMR)[2]. Interventions intended to prevent or delay the development of these chronic diseases (T2D and CVD) include lifestyle modifications focused on improving dietary habits, physical activity and weight management. Healthy diets are characterised by a high consumption of dietary fibres and PUFA, moderate alcohol consumption, and a low intake of red meat and sugar-sweetened beverages[3,4]. These diets are

Abbreviations: BP, blood pressure; C-HEI, Canadian Healthy Eating Index; CAO, Complications Associated with Obesity; CMR, cardiometabolic risk; CRP, C-reactive protein; EI, energy intake; hs-CRP, high-sensitivity C-reactive protein; HDL-C, HDL-cholesterol; HEI, Healthy Eating Index; HOMA-IR, homeostasis model assessment of insulin resistance; LDL-C, LDL-cholesterol; MONET, Montreal-Ottawa New Emerging Team; NHANES III, Third National Health and Nutrition Examination Survey; PAEE, physical activity energy expenditure; T2D, type 2 diabetes; TEE, total energy expenditure.

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associated with lower CMR as evidenced by a healthier plasma lipoprotein profile, glucose and inflammatory markers, as well as a lower incidence of the metabolic syndrome, T2D and CVD, independently of adiposity and physical activity[5–9]. While the latter studies have focused on specific aspects of the diet (i.e. specific nutrients), others have investigated the relationship between the overall diet quality, which is a reflection of the global effect of food intake, and CMR factors[10,11].

The Healthy Eating Index (HEI) is a widely used diet quality index that evaluates the adherence of individuals to the US dietary intake recommendations[12]. A higher HEI is associated with lower BMI, C-reactive protein (CRP), glucose and glycated Hb (HbA_{1C}), as well as with a better endothelial function[10,13,14]. Similarly, independent of adiposity and energy intake (EI), high levels of physical activity are associated with a better plasma lipoprotein profile[15] and lower subclinical inflammation[16], the metabolic syndrome, T2D risk[17,18] and mortality[19].

We have recently shown that higher levels of physical activity energy expenditure (PAEE) are negatively associated with a better inflammatory profile (reduced serum concentration of CRP and haptoglobin) in overweight and obese sedentary postmenopausal women[16]. As previously stated by Joosten *et al.*[20], healthy lifestyle behaviours (higher diet quality, physical activity and weight loss) 'are often intercorrelated and may be most effective when present in combination'. To our knowledge, there has been no report examining the effect of the combination of overall diet quality and physical activity on CMR factors in comparison with their effects taken separately. Therefore, the objective of the present study was to investigate whether diet quality, as assessed by the Canadian HEI (C-HEI), and PAEE have synergistic associations on a large panel of clinical and biochemical CMR factors in overweight and obese sedentary women. We hypothesised that higher PAEE in combination with higher diet quality would have a synergistic beneficial association with CMR factors than higher PAEE or higher diet quality alone.

Subjects and methods

Subjects

The cohort examined in the present cross-sectional *a posteriori* analysis was pooled from two hypoenergetic dietary intervention studies in similar populations. The two studies included non-diabetic overweight and obese postmenopausal women who were examined by our research team from 2003 to 2007: the Montreal-Ottawa New Emerging Team (MONET) Study (n 137)[21] and the Complications Associated with Obesity (CAO) Study (n 59)[16]. Subjects from both studies were recruited through newspaper advertisements. The study was conducted according to the guidelines laid down in the Declaration of Helsinki and both studies were approved by the University of Montreal ethics committee. All subjects gave a written informed consent before the study started.

As described previously[16,21], postmenopausal women were included in the two studies if they (1) had biological confirmation of the menopause status and were not on hormone replacement therapy, (2) had a BMI $\geq 27\,kg/m^2$ ($30–40\,kg/m^2$ for the CAO study), (3) aged between 46 and 70 years, (4) were non-smokers and (5) were inactive (<3 h of structured exercises per week for the CAO study and <2 h for the MONET study). The exclusion criteria were as follows: (1) diabetes (fasting glucose >7·1 mmol/l or 2 h plasma glucose >11·1 mmol/l after a 75 g oral glucose tolerance test), (2) untreated thyroid disease, (3) chronic liver or renal disease, (4) asthma requiring therapy with steroids, (5) cardiovascular or peripheral vascular disease, (6) previous 3 months use of hormone replacement therapy, oestrogen, narcoleptics, steroids, or lipid-lowering or antihypertensive agents, (7) dyslipidaemia or hypertension requiring immediate medical intervention (total cholesterol >8 mmol/l, systolic blood pressure (BP) >160 mmHg or diastolic BP >100 mmHg), (8) history of alcohol or drug abuse, (9) abnormal blood laboratory values (haematocrit <32 or >48 %; creatinine >130 μmol/l), (10) use of drugs or medications to stimulate weight loss, psychoactive drugs and adrenergic agonists by any route, (11) body-weight fluctuation ±3 kg in the last 3 months (±2 kg for the MONET study and ±3 kg for the CAO study) and (12) known history of inflammatory disease as well as cancer.

Of the 196 subjects recruited in the two studies, 124 subjects (eighty-eight from MONET study and thirty-six from CAO study) had a complete set of baseline data for all components of energy expenditure, cardiorespiratory fitness, dietary intake and CMR factors and were thus included in the present analysis.

Diet quality

For each 3 d food record, a score of diet quality was established using the index previously adapted for the Canadian population by Shatenstein *et al.*[22]: the C-HEI. It has a maximum score of 100 based on nine components: four major food groups assess the food guide servings (grain products, vegetables and fruits, milk products, and meat and alternatives, according to the 1997 Canada's Food Guide for Healthy Eating), three components assess total fat, saturated fat and cholesterol intake, one component assesses Na intake and one component assesses the variety of food consumed. The number of servings for each four food groups was calculated based on the information given by the 1997 Canada's Food Guide for Healthy Eating. Nutrient intake (total fat, saturated fat, cholesterol and Na) was computed using the Food Processor SQL program (see the Covariates subsection). Each component is scored from 0 to 10, except for vegetables and fruits that scored from 0 to 20; all components are summed to yield a score between 0 and 100. The criteria (minimum and maximum) followed to score each component of the C-HEI are presented in Table 1. A score of 100 indicates that the dietary guidelines for the nine components have been fully met and a score of 0 indicates a complete lack of adherence.

Energy expenditure and cardiorespiratory fitness

Total energy expenditure (TEE) was assessed by doubly labelled water and resting energy expenditure (REE) was determined by indirect calorimetry, as described previously[23]. PAEE was calculated from the following equation[24]:

$$PAEE = (TEE \times 0{\cdot}90) - REE,$$

Table 1. Criteria used to establish the Canadian Healthy Eating Index score*

Components†	Score range (points)	Criteria for maximum score, by age‡	Criteria for minimum score
Intake of grain products	0–10	18–49 years: 9 servings ≥ 50 years: 6 servings	0 servings
Intakes of vegetables and fruits	0–20	18–49 years: 7 servings ≥ 50 years: 5 servings	0 servings
Intakes of milk products	0–10	2 portions	0 servings
Intakes of meat and alternatives	0–10	18–49 years: 2·5 servings ≥ 50 years: 2 servings	0 servings
Total fat intake (%)	0–10	< 30 % of energy from fat	≥ 45 % of energy from fat
Saturated fat intake (%)	0–10	< 10 % of energy from saturated fat	≥ 15 % of energy from saturated fat
Cholesterol intake	0–10	≤ 300 mg	≥ 450 mg
Dietary Na intake	0–10	≤ 2400 mg	≥ 4800 mg
Diversity	0–10	≥ 1 servings from each of four food groups of the CFGHE	< 1 serving from each of four food groups of the CFGHE

CFGHE, Canada's Food Guide for Healthy Eating.
* Adapted from Shatenstein *et al.*[22].
† The first four components are based on the 1997 CFGHE; evaluation considers daily intakes.
‡ Proportional scores are computed for intakes situated between the maximum and minimum criteria.

where thermic effect of food was assumed as 10 % of TEE[25].

Cardiorespiratory fitness (VO_2 peak) was assessed by a graded exercise test on an ergocycle Ergoline 900 (Ergoline), as described previously[16]. Briefly, the highest value obtained during the test was considered as the peak VO_2 (litres/min). That value was then divided by the body weight to give the relative VO_2 peak (litres/min per kg). Expired gas was analysed during the exercise protocol using an Ergocard (software version 6; MediSoft) cardiopulmonary exercise test station. A successful VO_2 peak was obtained when three of the following criteria were reached: respiratory exchange ratio above 1·1; heart rate within 10 beats/min of the maximal predicted heart rate value (220 − age); volitional cessation of exercise by the subject; plateau in oxygen consumption for 60 s.

Cardiometabolic risk factors

Venous blood samples were collected at baseline before a 75 g oral glucose tolerance test and every 30 min for 2 h thereafter. Measurements of fasting insulin levels were analysed by RIA specific for human insulin (Linco), fasting glucose, plasma total cholesterol, HDL-cholesterol (HDL-C) and TAG on the Cobas Integra 400 (Roche Diagnostic), and apoA1 and apoB by immunonephelometry on an Image analyser (Beckman Coulter). LDL-cholesterol (LDL-C) was calculated according to the Friedewald equation[26]. Non-HDL-C and total cholesterol:HDL-C were also calculated. The size of LDL particles was estimated as the LDL-C:apoB ratio[27].

Insulin sensitivity was estimated using the fasting homeostasis model assessment (HOMA-IR) according to the formula of Matthews *et al.*[28]. Insulin sensitivity was also determined by measuring the glucose disposal rate during a hyperinsulinaemic–euglycaemic clamp, as described previously[29]. Glucose disposal rates during the clamp were expressed as mg/min per kg fat-free mass.

Serum high-sensitivity CRP (hs-CRP), orosomucoid and haptoglobin were assessed by immunonephelometry on an Image analyser (Beckman Coulter), IL-6 was measured using high-sensitivity commercial ELISA kits (Quantikine) and leucocyte count was assessed in an automated cell counter using an $A^C{\cdot}T$ 5diff AL analyser (Beckman Coulter). In the present study, four women with hs-CRP > 10 mg/l were excluded from the analysis as such an elevated hs-CRP suggests an acute inflammatory state[30].

Sitting BP was determined after the subjects had rested quietly for 10 min, using a Dinamap automatic machine (Welch Allyn).

Covariates

Body weight was measured to the nearest 0·1 kg using a calibrated scale (Balance Industrielle Montréal) and subjects' height was measured with a standard stadiometer (Perspective Enterprises). Then, BMI was calculated as body weight (kg)/height (m^2)[31]. Measurements of total lean body mass and fat mass were done by dual-energy X-ray absorptiometry with a LUNAR Prodigy system (software version 6.10.019; General Electric Lunar Corporation), while visceral adipose tissue (VAT) and subcutaneous adipose tissue were measured by abdominal computed tomography scan (General Electric Medical Systems), as described previously[16,21].

Food and nutrient intakes were assessed with a 3 d food record at baseline, during a weight stabilisation period, as described previously[32]. Briefly, subjects were instructed by a registered dietitian on how to record food intake, including condiments and beverages, over two weekdays and one weekend day while maintaining their usual habits. Analyses were conducted with the Food Processor SQL program (Food Processor SQL Edition, version 9.6.2, 2004; ESHA Research), using the 2001 Canadian Nutrient Data File and the US Department of Agriculture database (when foods were not available in the Canadian Nutrient Data File). Mean intake of 3 d for energy from total and saturated fat, cholesterol and Na intake was calculated for each subject.

Identification of energy intake in under-reporting subjects

The ratio of reported EI:TEE (EI:TEE) was used to identify subjects who under- or over-reported their EI. The cut-off point of EI:TEE < 0·80 was used to identify subjects who under-reported their EI, as described previously by Black &

Cole[33]. Subjects with a ratio of EI:TEE > 1·20 were identified as over-reporters, as reported previously[34], and those with a ratio between 0·80 and 1·20 were considered as normal reporters.

Statistical analysis

The synergistic associations of PAEE and the C-HEI with clinical and biochemical CMR factors were determined using hierarchical regressions. This test allows the selection of independent variables from one group (or bloc) of variables at a time using a stepwise approach. The selection of variables in bloc 2 does not affect the variables selected from bloc 1; the selected variables of bloc 1 are kept in the model. In the final model, all variables selected in each bloc become part of the model even if they are no longer significant. In our hierarchical regression analyses, CMR factors were entered as dependent variables and independent variables were entered in the models as follow: bloc 1 (stepwise) included BMI, total fat mass and VAT to control for the potential effect of body composition on the relationships between PAEE/C-HEI and CMR factors, and bloc 2 (stepwise) included PAEE, C-HEI and their interaction (PAEE × C-HEI), adjusted to the mean. This step (adjusted to the mean) was achieved as follows: 'individual value' minus the mean of the cohort. These calculations were done for PAEE and C-HEI variables. The interaction term, PAEE × C-HEI, was calculated as follows: PAEE (adjusted to the mean) × C-HEI (adjusted to the mean). This approach stabilised the regression models. We also reran the hierarchical regression analysis with the addition of EI and age as independent variables in bloc 1 to determine their potential effect on the synergistic associations between PAEE and the C-HEI with CMR factors. HOMA-IR, IL-6 and hs-CRP were log-transformed in the hierarchical regression because they were not normally distributed.

The magnitude of the synergistic associations between PAEE and the C-HEI with CMR factors was further determined by dividing the subjects into four groups according to their PAEE levels and C-HEI score (high and/or low levels of PAEE and the C-HEI). The median of the whole cohort for PAEE and the C-HEI was used as cut-off points (median of PAEE = 4008 kJ/d (958 kcal/d), median of the C-HEI = 83·3). ANOVA was used to compute raw means of PAEE, C-HEI, anthropometric parameters and CMR factors by PAEE and C-HEI groups and to identify pairwise mean differences among the groups.

ANCOVA adjusted for total fat mass (or BMI, for clinical relevance, or VAT instead of fat mass) was used to calculate least square means of CMR factors identified as significant correlates of PAEE × C-HEI (HDL-C, apoB, hs-CRP, apoA1:apoB and LDL-C:apoB) in the hierarchical regression and to compute pairwise mean differences among the PAEE/C-HEI groups. As for the hierarchical regressions, hs-CRP was log-transformed in the ANCOVA analyses because it was not normally distributed. In secondary analyses, the ANCOVA models were additionally adjusted for age and EI. The percentage of the difference between the low-PAEE/low-C-HEI group and the three other groups for HDL-C, apoB and hs-CRP concentrations and the ratios apoA1:apoB and LDL-C:apoB were calculated as follows:

$$\text{Percentage difference} = (\text{individual data} - \text{mean of the low-PAEE/low-C-HEI group})/\text{mean of the low-PAEE/low-C-HEI group} \times 100,$$

where the 'individual data' represent the value of each subject of the three other groups (low-PAEE/high-C-HEI, high-PAEE/low-C-HEI and high-PAEE/high-C-HEI) for HDL-C, apoB, hs-CRP, apoA1:apoB or LDL-C:apoB variables.

Considering the importance of under-reporting EI in overweight and obese individuals[34], differences in C-HEI scores between under- and over-reporters with normal reporters were determined using unpaired Student's *t* test.

Data are presented as means and standard deviations for continuous variables and as percentages (with error bars representing standard deviations) for categorical variables. All statistical analyses were performed using Statistical Package for the Social Sciences software (version 17.0.1, 2008; SPSS) and significance was set at $P < 0{\cdot}05$ (two-sided).

Results

Characteristics of the cohort

As shown in Table 2, women included in the present analysis had a mean age of 58 (SD 5) years and a mean BMI of 33·0 (SD 4·6) kg/m^2, with thirty-four women having a BMI between 27 and <30 kg/m^2 and ninety women having a BMI ≥30 kg/m^2. Values for glycaemia, blood lipids and BP were within the normal range. The mean C-HEI score for the whole cohort was 83·2 (SD 0·8) with 64·5 % of the women having a diet quality classified as 'good' (C-HEI score >80), 35·5 % having a 'needs improvement' diet (C-HEI score 51–80) and none having a 'poor' diet (C-HEI score <51). The mean score for each component of the C-HEI score is presented in Fig. 1. Because of the large number of subjects (>69 %) meeting the recommended intake for four out of nine components of the C-HEI index (vegetables and fruits 76·6 %; meats and alternatives 79·0 %; cholesterol 69·4 %; dietary variety 77·4 %), we used only the total C-HEI score in further analyses. The mean PAEE of the whole cohort was 3976 (SD 1266) kJ/d (950 (SD 303) kcal/d) (Table 2) with a wide range of values (824–7100 kJ/d (197–1697 kcal/d)).

Associations between the physical activity energy expenditure × Canadian Healthy Eating Index interaction with cardiometabolic risk factors

In hierarchical regression analyses, the interaction PAEE × C-HEI and VAT explained 13 % of the variance observed in HDL-C ($P < 0{\cdot}005$), while PAEE × C-HEI, BMI and VAT explained 24 % of the variance in log hs-CRP ($P < 0{\cdot}05$) (Table 3). Furthermore, the interaction PAEE × C-HEI was the only correlate of apoB ($P < 0{\cdot}01$), LDL-C:apoB ($P < 0{\cdot}01$) and apoA1:apoB ($P < 0{\cdot}01$) levels. PAEE independently predicted the inter-individual variance in haptoglobin ($P < 0{\cdot}05$), while the C-HEI was not associated with any of the CMR factors. Total fat mass was an independent correlate of total cholesterol, resting diastolic BP and orosomucoid ($P < 0{\cdot}05$). BMI independently explained

Table 2. Raw means of cardiometabolic risk factors, energy expenditure and cardiorespiratory fitness among the physical activity energy expenditure (PAEE)/Canadian Healthy Eating Index (C-HEI) groups

(Mean values and standard deviations)

	Total (*n* 124)		Low PAEE/low C-HEI (*n* 33)		Low PAEE/high C-HEI (*n* 29)		High PAEE/low C-HEI (*n* 29)		High PAEE/high C-HEI (*n* 33)	
Characteristics	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
PAEE (kcal/d)	950	303	698	175	707	163	1170*†	187	1223*†	166
PAEE (kJ/d)	3976	1266	2920	732	2957	684	4894*†	782	5119*†	696
C-HEI	83·2	9·2	76·8	5·9	90·3*‡	3·6	74·3	7·0	91·0*‡	3·6
Age (years)	57·7	4·7	58·0	4·5	58·7	4·7	56·6	4·8	57·5	4·9
Anthropometric parameters										
Body weight (kg)	86·7	14·9	86·5	15·9	83·0	14·1	91·5	15·4	86·0	13·5
BMI (kg/m^2)	33·0	4·6	32·5	4·7	31·8	3·9	35·1	5·0	32·8	4·2
Total fat mass (kg)	40·2	9·9	40·5	10·0	37·2	8·8	43·7	9·8	39·7	10·1
Total lean body mass (kg)	43·4	6·6	42·6	6·9	42·7	7·1	44·8	7·5	43·5	4·9
VAT (cm^2)	190	52	189	44	180	47	200	61	189	54
SAT (cm^2)	484	123	486	120	439	109	530	117	482	133
Systolic BP (mmHg)	123	14	124	13	123	14	122	16	122	11
Diastolic BP (mmHg)	77	8	78	7	76	10	77	9	77	7
Blood lipids and lipoproteins										
Total cholesterol (mmol/l)	5·35	0·82	5·39	0·74	5·28	0·94	5·16	0·79	5·53	0·78
HDL-C (mmol/l)	1·45	0·34	1·43	0·29	1·39	0·34	1·38	0·29	1·58†‡	0·38
LDL-C (mmol/l)	3·15	0·70	3·17	0·67	3·08	0·71	3·05	0·67	3·28	0·75
TAG (mmol/l)	1·64	0·78	1·66	0·78	1·85	0·95	1·60	0·75	1·47	0·62
Total cholesterol:HDL-C	3·83	0·86	3·88	0·86	3·90	0·81	3·84	0·76	3·71	1·02
Non-HDL-C (mmol/l)	3·90	0·79	3·95	0·75	3·89	0·83	3·78	0·70	3·96	0·88
apoB (g/l)	0·99	0·21	1·04	0·21	1·01	0·23	0·99	0·18	0·94*	0·21
apoA1 (g/l)	1·44	0·23	1·45	0·17	1·40	0·21	1·41	0·22	1·51	0·28
LDL-C:apoB	3·20	0·57	3·07	0·48	3·05	0·38	3·11	0·61	3·53*†‡	0·64
apoA1:apoB	1·52	0·43	1·45	0·36	1·45	0·38	1·46	0·34	1·70*†‡	0·56
Glucose homeostasis										
Fasting glycaemia (mmol/l)	5·24	0·54	5·35	0·57	5·28	0·48	5·07*	0·49	5·26	0·57
Fasting insulin (pmol/l)	109·0	49·3	108·2	37·8	107·5	48·9	117·0	72·3	104·1	33·9
Glucose disposal rate (mg/kg per min)§	11·5	3·6	11·6	3·5	10·7	3·1	11·6	4·4	12·2	3·3
HOMA-IR	3·7	1·9	3·8	1·5	3·7	2·0	3·8	2·6	3·5	1·3
Inflammatory markers										
IL-6 (pg/ml)	1·46	0·94	1·60	1·00	1·29	0·64	1·48	0·67	1·45	1·30
hs-CRP (mg/l)‖	2·95	2·08	3·18	17·99	2·70	14·54	3·37	18·15	2·53	13·86
Orosomucoid (g/l)	0·85	0·19	0·86	0·22	0·87	0·20	0·87	0·17	0·81	0·16
Haptoglobin (g/l)	1·33	0·48	1·50	0·56	1·36	0·47	1·27	0·42	1·18*	0·39
Leucocyte count (× 10^9/l)	5·86	1·38	5·72	1·30	5·84	1·42	6·18	1·27	5·73	1·56
Energy expenditure										
TEE (kcal/d)	2550	418	2260	288	2252	321	2840†	349	2846†	237
TEE (kJ/d)	10 670	1747	9458	1203	9424	1345	11 885*†	1461	11 912*†	993
REE (kcal/d)	1345	205	1336	225	1320	202	1387	225	1339	167
REE (kJ/d)	5628	856	5992	942	5524	845	5803	942	5602	700
VO_2 peak (ml/min per kg)	17·1	3·6	16·1	4·0	17·6	4·4	17·0	2·8	17·8	2·8

VAT, visceral adipose tissue; SAT, subcutaneous adipose tissue; BP, blood pressure; HDL-C, HDL-cholesterol; LDL-C, LDL-cholesterol; HOMA-IR, homeostasis model assessment of insulin resistance; hs-CRP, high-sensitivity C-reactive protein; TEE, total energy expenditure; REE, resting energy expenditure; VO_2 peak, cardiorespiratory fitness.

* Mean values were significantly different from those of the low-PAEE/low-C-HEI group ($P<0·05$; ANOVA).

† Mean values were significantly different from those of the low-PAEE/high-C-HEI group ($P<0·05$; ANOVA).

‡ Mean values were significantly different from those of the high-PAEE/low-C-HEI group ($P<0·05$; ANOVA).

§ Glucose disposal rate calculated from the hyperinsulinaemic–euglycaemic clamp.

‖ *n* 120 in the whole cohort, *n* 32 in the low-PAEE/low-C-HEI group, *n* 29 in the low-PAEE/high-C-HEI and high-PAEE/low-C-HEI groups, *n* 30 in the high-PAEE/high-C-HEI group.

18 % of the variance in IL-6 ($P<0·001$), while VAT was an independent correlate of total cholesterol:HDL-C ($P<0·05$), resting systolic BP ($P<0·05$), fasting insulin ($P<0·001$), log HOMA-IR ($P<0·001$), glucose disposal rate ($P<0·01$) and leucocyte count ($P<0·01$). Both VAT and BMI were independent correlates of fasting glycaemia ($P<0·05$). LDL-C and non-HDL-C were not associated with any of the independent variables included in the model. Additional adjustment for EI and age did not alter the primary findings (see Supplemental Table 1 of the supplementary material; available online at http://www.journals.cambridge.org/bjn), with the exception of orosomucoid for which VAT became a correlate instead of total fat mass ($P=0·044$). These two variables were not predictors of any of the CMR factors.

Results of ANOVA showed no differences among the four PAEE/C-HEI groups for age, anthropometric measures and systolic and diastolic BP (Table 2). As expected, women in the two high-PAEE groups had higher levels of TEE ($P<0·05$), while no difference was observed for resting energy expenditure and cardiorespiratory fitness among the groups (Table 2). In fat mass-adjusted ANCOVA analyses, women in the high-PAEE/high-C-HEI group had the highest concentrations of HDL-C and levels of LDL-C:apoB and apoA1:apoB, and the lowest levels

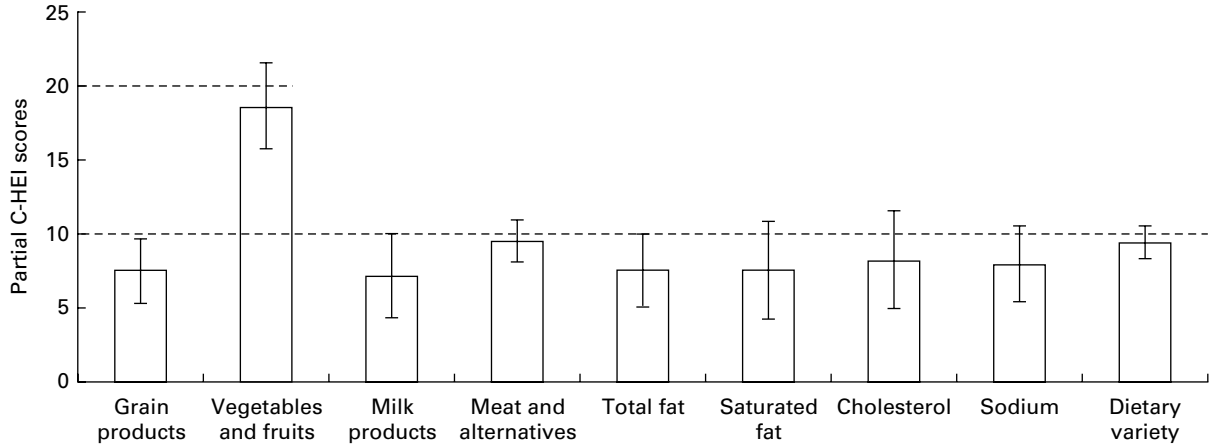

Fig. 1. Scores of the components of the Canadian Healthy Eating Index (C-HEI) in the whole cohort. Values are means, with standard deviations represented by vertical bars. The dashed lines represent the maximum score for each component.

of apoB and log hs-CRP ($P<0{\cdot}05$; Table 4). Adjustment of ANCOVA for BMI or VAT instead of fat mass resulted in similar differences among the groups, except for hs-CRP for which the adjustment of ANCOVA for BMI removed the difference between the high-PAEE/low-C-HEI and high-PAEE/high-C-HEI groups (data not shown). Moreover, further adjustments for age and EI (in addition to fat mass (or BMI)) did not affect the results (data not shown).

As shown in Fig. 2, compared with those in the low-PAEE/low-C-HEI groups, women in the high-PAEE/high-C-HEI group had higher levels of HDL-C by 10%, LDL-C:apoB by 11% and apoA1:apoB by 14%, and lower levels of apoB by 13% and hs-CRP by 28%. There was no statistical difference between women in the low-PAEE/low-C-HEI group with the two other groups for these five CMR factors.

Comparison of diet quality scores in under-, normal and over-reporters

In our cohort, seventy-three women were characterised as under-reporters, forty-four were normal reporters and seven were over-reporters. The mean C-HEI score of the under-reporters (83·8 (SD 9·3)) and the over-reporters (76·0 (SD 11·6)) were not different from that of the normal reporters (83·3 (SD 8·3)) (under- *v.* normal reporters: $P=0{\cdot}76$; over- *v.* normal reporters: $P=0{\cdot}10$).

Table 3. Hierarchical regression analysis on the association between cardiometabolic risk factors and physical activity energy expenditure (PAEE), Canadian Healthy Eating Index (C-HEI) and their interaction (PAEE × C-HEI)*

Dependent variable	Step	Independent variable	Constant	Coefficient	Total R^2	*P*
Total cholesterol	1	Total fat mass	6·117	−0·019	0·054	0·011
HDL-C	1	VAT	1·822	−0·002	0·128	0·001
	2	PAEE × C-HEI		$2{\cdot}289 \times 10^{-6}$		0·034
Total cholesterol:HDL-C	1	VAT	3·204	0·003	0·039	0·028
apoB	1	PAEE × C-HEI	0·993	$-1{\cdot}979 \times 10^{-6}$	0·066	0·004
LDL-C:apoB	1	PAEE × C-HEI	3·205	$6{\cdot}695 \times 10^{-6}$	0·100	<0·001
apoA1	1	VAT	1·622	−0·001	0·046	0·017
apoA1:apoB	1	PAEE × C-HEI	1·524	$4{\cdot}281 \times 10^{-6}$	0·070	0·003
Systolic BP	1	VAT	111·571	0·059	0·049	0·031
Diastolic BP	1	Total fat mass	70·516	0·161	0·038	0·031
Fasting glycaemia	1	VAT	5·329	0·004	0·105	<0·001
	2	BMI		−0·025		0·035
Fasting insulinaemia	1	VAT	2·777	0·068	0·242	<0·001
Log HOMA-IR	1	VAT	0·193	0·002	0·230	<0·001
Glucose disposal rate	1	VAT	14·797	−0·017	0·059	0·007
Log IL-6	1	BMI	−0·624	0·022	0·176	<0·001
Log hs-CRP	1	BMI	−7·727	0·027	0·242	<0·001
	2	VAT		0·001		0·059
	3	PAEE × C-HEI		$-2{\cdot}046 \times 10^{-6}$		0·041
Orosomucoid	1	Total fat mass	0·696	0·004	0·041	0·025
Haptoglobin	1	PAEE	1·329	0·000	0·054	0·010
Leucocyte count	1	VAT	4·468	0·007	0·077	0·002

HDL-C, HDL-cholesterol; VAT, visceral adipose tissue; LDL-C, LDL-cholesterol; BP, blood pressure; HOMA-IR, homeostasis model assessment of insulin resistance; hs-CRP, high-sensitivity C-reactive protein.

* Independent variables included in the model: bloc 1 (stepwise) – BMI, total fat mass and VAT; bloc 2 (stepwise) – PAEE (adjusted to the mean), C-HEI (adjusted to the mean) and PAEE × C-HEI (adjusted to the mean).

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Table 4. Adjusted means of cardiometabolic risk factors among the physical activity energy expenditure (PAEE)/Canadian Healthy Eating Index (C-HEI) groups

(Mean values and standard deviations)

	Low PAEE/low C-HEI (*n* 33)		Low PAEE/high C-HEI (*n* 29)		High PAEE/low C-HEI (*n* 29)		High PAEE/high C-HEI (*n* 33)	
Characteristics	Mean	SD	Mean	SD	Mean	SD	Mean	SD
HDL-C	1·43	0·06	1·37	0·06	1·40†	0·06	1·57†‡	0·06
apoB	1·04	0·04	1·00	0·04	1·00	0·04	0·94*	0·04
LDL-C:apoB	3·07	0·09	3·05	0·10	3·12	0·10	3·53*†‡	0·10
apoA1:apoB	1·45	0·07	1·45	0·08	1·46	0·08	1·70*†‡	0·08
Log hs-CRP§	0·39	0·05	0·37	0·06	0·43	0·06	0·26‡	0·06

HDL-C, HDL-cholesterol; LDL-C, LDL-cholesterol; hs-CRP, high-sensitivity C-reactive protein.
* Mean values were significantly different from those of the low-PAEE/low-C-HEI group ($P<0·05$; ANCOVA).
† Mean values were significantly different from those of the low-PAEE/high-C-HEI group ($P<0·05$; ANCOVA).
‡ Mean values were significantly different from those of the high-PAEE/low-C-HEI group ($P<0·05$; ANCOVA).
§ *n* 32 in the low-PAEE/low-C-HEI group and *n* 30 in the high-PAEE/high-C-HEI group.

Discussion

The main results from the present study show that the combination of higher diet quality and PAEE has modest but significant synergistic associations with the blood lipoprotein profile (HDL-C, apoB, apoA1:apoB and LDL-C:apoB) and subclinical inflammation (hs-CRP) in women even after adjustments for adiposity.

Accumulating evidence from interventional studies indicates that the adoption of a healthy diet and an active lifestyle, as well as weight loss, can improve the blood lipoprotein profile, glucose tolerance and subclinical inflammation, which reduce the risk for T2D[35–38]. For example, in the Diabetes Prevention Program, subjects with impaired glucose tolerance reduced their risk for T2D either by losing body weight, while keeping their sedentary lifestyle, or by improving physical activity, without any significant weight loss[18]. A few studies have investigated the separate effect of these lifestyle behaviours (diet, physical activity and weight loss) in comparison with their combination on the risk for T2D[18,37,39]. No significant effect of dietary modifications alone on T2D incidence has been reported in two of them[18,37]. Despite the cross-sectional design of the present study, the present results suggest that improving both diet quality and physical activity is associated with lower CMR (i.e. better blood lipoprotein profile and lower CRP) than improving either factor alone, independently of the level of adiposity. However, it should be noted that although a large panel of clinical and biochemical CMR factors were measured in the present study, some other important factors were not measured (e.g. socio-economic and psychological status). Nevertheless, the present findings suggest that a reduction in the development of obesity-related cardiometabolic complications in an obese but otherwise relatively healthy population may be possible with improvement in diet quality and physical activity, independently of adiposity. Further investigations using high-risk individuals for T2D and CHD are required to validate this hypothesis.

Kraus *et al.*[15] reported that physical activity was associated with favourable changes in the lipoprotein profile in sedentary overweight individuals. However, no association has been reported between diet quality (assessed by the original HEI), and total cholesterol, HDL-C and LDL-C[14,40,41]. To our knowledge, no study has investigated the association between diet quality and the number or size of atherogenic lipoproteins. We have previously reported that postmenopausal overweight and obese sedentary women with higher levels of PAEE have lower concentrations of inflammatory markers as well as healthier lipoprotein and blood lipid profiles (lower levels of TAG and apoB; larger LDL size)[16]. Here we have further reported that women in the high-PAEE/high-C-HEI group had higher concentrations of HDL-C and the apoA1:apoB ratio, lower concentrations of atherogenic particles (apoB), and larger LDL size (estimated by LDL-C:apoB) compared with women in the low-PAEE/low-C-HEI group. Thus, combining a higher diet quality to a higher PAEE seems to have a greater relationship with these lipoprotein parameters than a higher PAEE alone. Larger LDL particles are less atherogenic than smaller, denser ones[42], and HDL-C is inversely and independently related to the risk of CHD and mortality[43,44]. Moreover, the ratio apoA1:apoB reflects the balance between anti- and pro-atherogenic particles[45] and is predictive of cardiovascular events[46,47]. The present study is the first to show a favourable synergistic association of diet quality and PAEE with blood lipid and lipoprotein profiles in obese subjects. Of note, the lack of difference in TAG, total cholesterol and LDL-C levels between our groups may be secondary to selection bias, as the present study included relatively healthy obese postmenopausal women (total cholesterol $<7·8$ mmol/l and TAG $<4·5$ mmol/l), whereas there was no cut-off points for HDL-C, apoB or apoA1. Thus, limited variations within the normal range of cholesterol and TAG levels may have limited group differences.

The original HEI has been inversely associated with CRP[13] after adjustment for potential confounding factors such as physical activities. We previously showed that a high level of PAEE is associated with lower concentrations of hs-CRP and haptoglobin in overweight/obese postmenopausal women[16]. In the present analysis, only the women with a combination of high PAEE and C-HEI had lower hs-CRP and not those with high PAEE but low C-HEI. Thus, the effect of PAEE on CRP is dependent on the concomitant presence of a high diet quality, which was not evaluated in our previous study[16]. On the other hand, haptoglobin levels do not seem to be affected by diet quality as

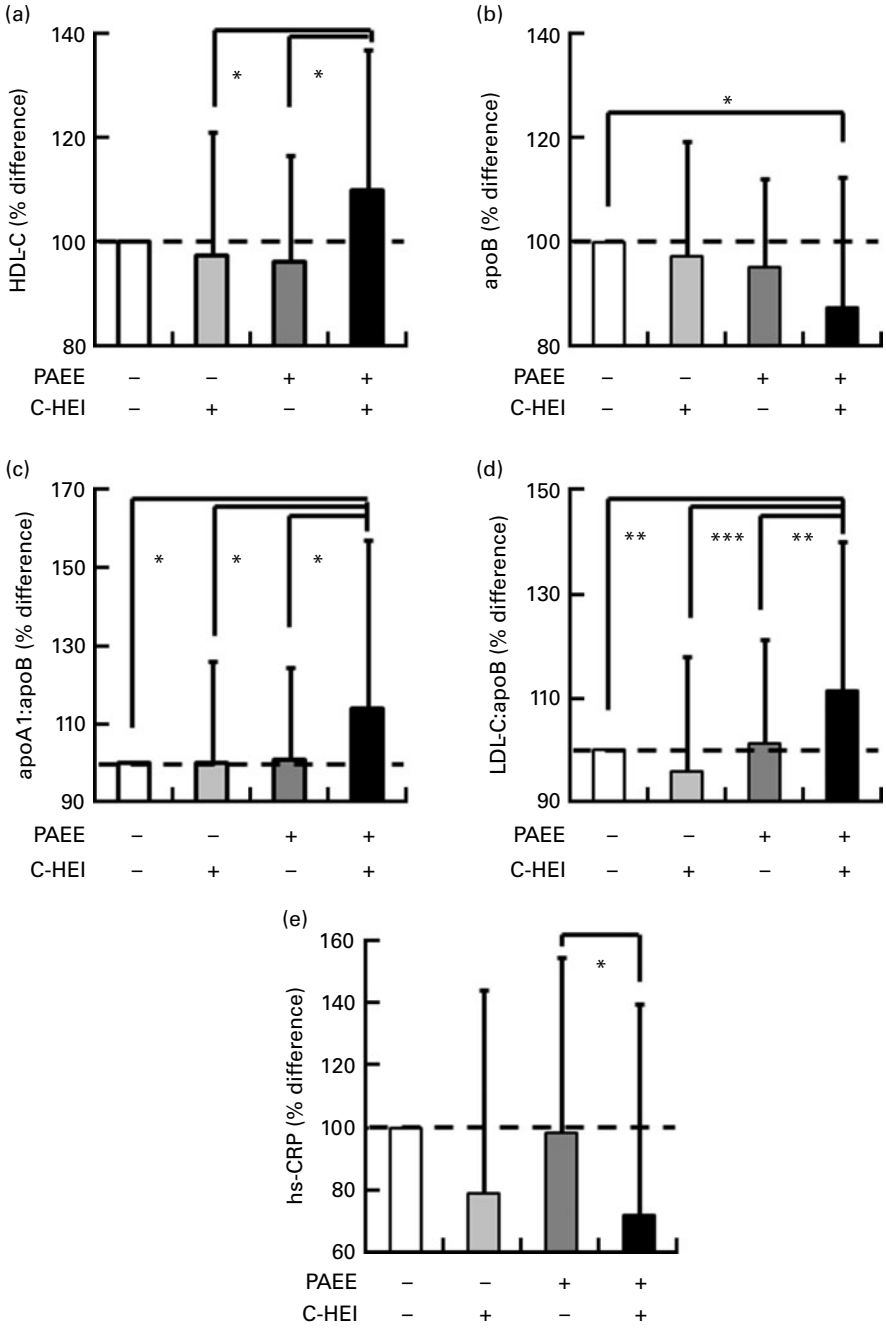

Fig. 2. Percentage of the difference among the four groups for (a)–(d) the blood lipoprotein profile and (e) the inflammatory marker high-sensitivity C-reactive protein (hs-CRP). The low-physical activity energy expenditure (PAEE)/low-Canadian Healthy Eating Index (C-HEI) group was used as the reference group for the percentage calculations. HDL-cholesterol (HDL-C), apoB, apoA1 and LDL-cholesterol (LDL-C) were measured in mmol/l and hs-CRP in mg/l. The symbols ' – ' means 'low' and ' + ' means 'high'. Values were significantly different: * $P<0{\cdot}05$, ** $P<0{\cdot}01$, *** $P<0{\cdot}001$.

PAEE remains its sole correlate in the present study. Of note, PAEE levels measured in a previous study included both structured exercise and non-exercise activities[48]. However, as the women included in the present study were inactive with less than 2–3 h of structured exercises per week, PAEE levels presented here represent mainly non-exercise activities (i.e. occupational and spontaneous physical activities).

While original HEI has been inversely associated with obesity in the Third National Health and Nutrition Examination Survey (NHANES III)[49,50], we found no differences in body composition or the degree of adiposity between the groups using the C-HEI. However, the NHANES III included large populations of both sexes ranging from normal body weight to obesity, while only overweight and obese postmenopausal women were included in the present analysis. Moreover, the present study included women without obesity-associated chronic disease and with high diet quality in comparison with those included in the NHANES III[49,50]. About two-thirds of the women had a 'good' diet quality score (mean score 83·5) compared with those (mean score 63) in the NHANES III.

Other studies have reported a lower mean HEI score (varying between 61 and 77) than the one observed in our cohort; the higher score has been reported in women from the Nurses' Health Study[10,13,22,40]. It should be noted, however, that women included in the present analysis were recruited to participate in a weight-loss study. Thus, a selection bias of more motivated and health-conscious cohort may have increased the diet quality of the present study.

Despite the beneficial effect of physical activity on BP and insulin sensitivity[51], we found no association between PAEE, C-HEI or their interaction with these parameters in our cohort. While no study has reported any association with insulin resistance, one study has reported a negative association between diet quality, as assessed by the HEI, and BP in men but not in women[52]. This absence of association could be secondary to a selection bias, as the present study excluded women with high BP (systolic BP $\leq$160 mmHg or diastolic BP $\leq$100 mmHg) and those with diabetes. This limited the variation in BP and the insulin resistance index might have reduced group differences in these parameters. Moreover, the relative small sample size in each group (n 29–33) may have limited the statistical power of the present analysis. Nevertheless, this further supports the needs to investigate the association between PAEE and the C-HEI with CMR factors in populations with a more disturbed profile such as hypertensive or T2D patients.

In conclusion, the present results indicate that both a good quality of food intake and greater physical activity levels are associated with a healthier cardiometabolic profile in inactive, overweight/obese postmenopausal women than either behaviour considered separately. Since the diet quality is based on the Canadian dietary guidelines, promotion of these guidelines together with the adoption of higher physical activity levels, including non-exercise-related daily activity, should be underlined in the management of obesity and its associated CMR factors. CMR benefits associated with the improvement of diet quality and physical activity should be tested in clinical trials. Greater benefits are expected in subjects with the poorest lifestyle behaviours.

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