Dietary patterns and cardiovascular risk in postmenopausal women: Protocol of a cross-sectional and prospective study

K. Stamatelopoulos[a], C. Papavagelis[b,1], A. Augoulea[b], E. Armeni[b], I. Karagkouni[b], E. Avgeraki[c], G. Georgiopoulos[a], M. Yannakoulia[c,2], I. Lambrinoudaki[b,*]

[a] Vascular Laboratory, Department of Clinical Therapeutics, Alexandra Hospital, Medical School, National and Kapodistrian University of Athens, Athens, Greece
[b] Menopause Clinic, 2nd Department of Obstetrics and Gynecology, National and Kapodistrian University of Athens, Aretaieio Hospital, Athens, Greece
[c] Department of Nutrition and Dietetics, Harokopio University, Athens, Greece

ABSTRACT

Objective: Aging and menopause are associated with an adverse cardiometabolic profile, predisposing to cardiovascular disease. Diet may also affect their cardiometabolic risk. The aim of this study is to assess dietary habits and patterns of postmenopausal women and their association with adiposity measures, cardiometabolic parameters and subclinical atherosclerosis.

Study protocol: The study will include two parts. The first part consists of cross-sectional evaluation of 750 postmenopausal women recruited consecutively from the Menopause Unit of an academic hospital. Dietary intake will be assessed by a food frequency questionnaire. Nutrient and food group intake will be calculated and adherence to the Mediterranean diet and other dietary patterns will be evaluated. A-priori and a-posteriori defined dietary patterns will be tested for associations with major and minor outcome measures. The second part consists of a prospective follow-up of all women recruited at baseline and re-assessment of the same variables after 3 years. Adherence to predefined or a-posteriori defined dietary patterns over these 3 years will be evaluated in association with changes in obesity indices and lipid levels, as well as in the progression of subclinical atherosclerosis.

Major outcome measures: Body mass index, lipid profile, carotid and femoral artery intima-media thickness and plaques.

Minor outcome measures: Waist circumference, waist-to-hip ratio, abdominal fat layers, incident hypertension and diabetes, homeostasis model assessment of insulin resistance (HOMA-IR), c-reactive protein and markers of subclinical arterial disease, including flow-mediated dilation, pulse wave velocity, augmentation index and ankle-brachial index.

Results: The study is expected to complete baseline enrolment by the end of 2018 and follow-up assessment by the end of 2021. The results of the study will address the question of whether dietary patterns and eating habits are associated with cardiometabolic risk as well as with accelerated subclinical arterial disease and arterial aging in postmenopausal women.

1. Introduction

Menopause, the permanent cessation of menses as a result of ovarian aging, occurs in a median age of 51 years in most populations. As longevity increases steadily worldwide, it is expected that women will spend nearly half of their lifetime beyond the menopausal transition [1]. Menopause is associated with unfavourable changes in adiposity measures, in the lipid profile, in blood pressure and in glucose metabolism, which increase the risk of cardiovascular disease later in life [2]. Although several medical approaches are successful in preventing or treating these conditions, a holistic approach encompassing diet and lifestyle modifications may be more efficacious and applicable on the long term [3].

Healthy dietary patterns that promote energy balance and prevent weight gain during the menopausal transition can be effective in reducing obesity rates among middle-aged women. Beyond the current

---

dietary guidelines for adults, the efficacy of existing dietary patterns, like the Mediterranean diet or the low-carbohydrate diet with regard to adiposity and metabolic management in postmenopausal women should be further investigated [4–6]. Postmenopausal women may have different metabolic characteristics compared to the general adult population, and therefore, other dietary patterns than the recommended may be more favourable for weight management and metabolic health. Adherence to a low-fat diet seems to be effective in reducing serum levels of total cholesterol and LDL-C in premenopausal women, but this effect is not evident in postmenopausal women [7]. Moreover, low-fat diet may decrease HDL-C serum levels, ameliorating thus the beneficial effect of the diet on atherosclerosis prevention [7].

Cardiovascular disease (CVD) is the leading cause of death in the postmenopausal population worldwide [8,9]. While it has not been clearly established whether the menopausal transition aggravates atherosclerosis independently of age, a growing body of evidence suggests that lifestyle, consisting of a healthy diet, regular exercise, and possibly other lifestyle patterns, such as adequate sleep, delays the atherosclerotic process [10,11]. A well-balanced diet low in saturated fat and salt and daily consumption of dairy products, fruit and vegetables is recommended by most authorities for maintaining cardiovascular health [12,13]. Specifically, cardiovascular mortality can be reduced by following either the Mediterranean dietary pattern, or the Dietary Approach to Stop Hypertension [14,15]. However, adherence to these diets may not be always feasible on a routine basis. Dietary patterns and habits differ substantially among countries and communities and adherence rates are influenced by cultural and sociodemographic parameters [16]. The identification, therefore, of prevalent dietary patterns among postmenopausal women and their association with cardiometabolic characteristics and evolving vascular disease of this population may have significant inferences with regard to public health policies and clinical practice.

The aim of this study is to assess the dietary habits and patterns of postmenopausal women in Greece and their cross-sectional and prospective association with adiposity, cardiometabolic parameters, and subclinical atherosclerosis.

2. Methods

2.1. Design and sampling procedure

This ongoing study recruits consecutively screened postmenopausal women, who visit the Menopause Clinic of Aretaieio Hospital, University of Athens since September 2014. The flowchart of the study as well as the inclusion and exclusion criteria are presented in detail in Fig. 1. Briefly, exclusion criteria include the presence of diabetes, CVD, chronic kidney disease, depression, physical inability or eating disorders. Women with morbid obesity (BMI > 40 kg/m2) are also excluded from the study, as this state is by itself a strong risk factor of cardiovascular disease and diabetes, that might prohibit us to detect associations with less strong covariates, such as dietary patterns. Finally, women with significant fluctuation of body weight (> 10%) over the past 12 months are not included, as these women might strongly underestimate or overestimate their food records.

Menopause is defined by the absence of menses for at least 12 consecutive months and the simultaneous presence of serum FSH > 25 mIU/ml and serum estradiol < 50 pg/ml. All study measurements are performed in one day at baseline and at 3 years after the first assessment and include anthropometric and blood pressure measurements, fasting blood sample collection, dietary assessment and evaluation of subclinical atherosclerosis. Blood samples are centrifuged and both plasma and serum are stored at −80 °C until assessment. All women give their written consent. Institutional Review Board approval was obtained by the Ethics Committee of Aretaieio Hospital (approval number B - 22/19-12-2013).

2.2. Anthropometric measurements

Body weight (in kilograms), height (in centimeters), waist and hip circumference (in centimeters), Mid-Upper Arm Circumference (MUAC) (in centimeters) and triceps skin-fold thickness (in millimeter) are recorded in all participants. Body weight is measured by using a digital weight scale, standing without shoes in the minimum clothing possible. Height is measured using a stadiometer with a fixed vertical backboard and an adjustable head piece. Participants stand with the heels together and toes apart, look straight ahead and have relaxed shoulders and their arms at sides. The back of the head, shoulder blades, buttocks, and heels make contact with the backboard. The head placement in the Frankfort horizontal plane is deemed essential in order to estimate precisely the individual's height. The aforementioned head position can be achieved when the horizontal line from the ear canal to the lower border of the orbit of the eye is parallel to the floor and perpendicular to the vertical backboard [17]. Body mass index (BMI) (kg/m^2) is estimated by dividing weight (kg) by standing height squared (m^2). Women are classified as underweight, normal weight, overweight and obese according to the BMI criteria [18]. Waist circumference is measured at the midpoint between the bottom of the rib cage and the top of the lateral border of the iliac crest during minimal respiration. Hip circumference is measured approximately 10 cm below the lateral border of the iliac crest, and the Waist-to-Hip ratio (WHR) is estimated using the values resulting from the above measurements. MUAC is measured at the midpoint between the tip of the shoulder and the tip of the elbow of the left upper arm. Regarding triceps skin-fold thickness, a skinfold caliper was used, in order to measure the width of a fold of skin taken over the triceps muscle.

3. Outline of the cross-sectional and prospective arm of the study

Patient recruitment is expected to be completed within 2018. The first part of the study includes cross-sectional analysis of potential associations between dietary habits, level of physical activity and baseline prevalence of cardiovascular risk factors as well as prevalence of subclinical vascular disease. The second part of the study includes a follow up evaluation of the participants over the next 3 years. During this time, participants will be contacted annually by the staff of the Menopause clinic to ensure compliance. The formal follow-up re-assessment will be performed for each individual patient at 36 months post – inclusion in the study. The assessment will include the same the clinical evaluation, laboratory tests and measurements of subclinical vascular disease as performed at baseline. The adherence to predefined or a-posteriori defined dietary patterns will be evaluated in association with the changes in obesity indices and the progression of markers of subclinical atherosclerosis. Finally, we have predicted a 10% loss to follow-up, based on our clinic records of routine repeat annual or biennial patient visits.

3.1. Medical history and risk factor assessment

A detailed medical history is recorded for every woman, using questionnaires regarding demographic and lifestyle parameters, cardiovascular risk, medical, surgical, obstetrical and gynecological history. Blood pressure is measured twice (1 min apart) by oscillometry using the automated Omron 705IT device (Omron) after resting in the sitting position for 5 min, and the average of these measurements is calculated [19]. Hypertension is defined as systolic arterial pressure (SBP) ≥140 mmHg and/or diastolic arterial pressure (DBP) ≥ 90 mmHg, after 2 blood pressure measurements in each of 2 consecutive office visits or the intake of antihypertensive medication. Hyperlipidemia is defined as total blood cholesterol level above 200 mg/dL or the intake of hypolipidemic medication. Diabetes is defined as fasting serum glucose levels > 126 mg/dL or HβA1c > 6.5%.