Clinical Nutrition 34 (2015) 302–308

Contents lists available at ScienceDirect

Clinical Nutrition

journal homepage: http://www.elsevier.com/locate/clnu

Original article

Meal patterns in healthy adults: Inverse association of eating frequency with subclinical atherosclerosis indexes☆

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ARTICLE INFO

Article history:
Received 18 December 2013
Accepted 29 April 2014

Keywords:
Cardiovascular disease
Meal frequency
Premature atherosclerosis
Carotid atherosclerosis
Arterial stiffness
Dietary patterns

SUMMARY

Background & aims: Meal patterns and their relationship with cardiovascular disease are insufficiently examined with important clinical implications. Our aim was to investigate associations between eating frequency (EF) and early markers of atherosclerosis.

Methods: In this cross-sectional study, we consecutively recruited 164 healthy subjects (46.8 ± 9.3years, 62 men). EF among other dietary parameters and markers of subclinical atherosclerosis, including flow mediated dilatation (FMD), pulse wave velocity (PWV), intima media thickness (IMT) and the presence of plaques in the carotid arteries were evaluated in all volunteers.

Results: EF was positively associated with total energy intake (EI) and a favorable profile in terms of adiposity, glucose tolerance and blood lipids. Subjects with an increased EF (> median), had significantly lower IMT ($p = 0.024$) and prevalence of plaques (5.3% vs. 21.3%, $p = 0.003$), as compared to those below median. IMT and the prevalence of plaques were also significantly lower in those with increased EF compared with subjects with low EF belonging to the same group of energy intake (EI) by EI median. By multivariate regression analysis, carotid plaques remained significantly associated with EF (OR: 0.71, 95% CI 0.56–0.89), while IMT also remained significantly associated with EF after adjustment for age and dietary factors (beta: −0.010, 95% CI: −0.020 to −0.0002), but not after adding obesity-related risk factors.

Conclusion: Increased EF is associated with lower prevalence of subclinical atherosclerosis in the carotid arteries in apparently healthy individuals. Whether consumption of the same amount of energy in more eating episodes favorably affects cardiovascular risk should be further investigated.

1. Introduction

Meal patterns represent complex interactions between food and environment, where caloric, macro- and micronutrients' intake interact with personality traits, social determinants and circadian rhythmicity. In 1964, Fabry and colleagues found an inverse relationship between prevalence of overweight subjects and habitual meal frequency [1]. Following this observation, several studies have shown that eating frequency (EF) is negatively associated with body weight and fat in children, men and postmenopausal women [2–4]. However, this issue is still under investigation, as there is also evidence for no association between the number of eating episodes and markers of adiposity [5,6]. In relation to other cardiovascular risk factors, increasing EF could be beneficial in improving blood lipid profile [7,8] and may reduce postprandial insulin and glucose

Abbreviations: BMI, body mass index; HDL, high density lipoprotein; LDL, low density lipoprotein; HOMA, homeostasis model assessment; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; FMD, flow mediated dilatation; PWV, pulse wave velocity; IMT, intima media thickness; SFA, saturated fatty acids; MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids.

☆ The work was performed in both Alexandra University Hospital and Harokopio University.

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http://dx.doi.org/10.1016/j.clnu.2014.04.022
0261-5614/

responses in non-diabetic and diabetic individuals [7]. Furthermore, EF is negatively associated with insulin resistance and the risk of developing metabolic syndrome [9], whereas grazing has also been related to a lower risk of peripheral arterial disease [10].

Although the study of Powel et al., imply associations between EF and risk of development of symptomatic peripheral atherosclerosis, currently there are no data on the potential associations between EF and early vascular damage. The latter can be assessed by measuring markers of subclinical atherosclerosis, like arterial stiffness, endothelial function and carotid atherosclerosis [11]. These markers have been developed to non-invasively identify and quantify accelerated atherosclerosis both in research and, to some extent, in clinical practice. They are considered surrogates of cardiovascular disease, risk and generalized atherosclerosis [12,13]. Clinically significant improvements of these surrogates through drug treatment and/or lifestyle changes, including diet, may have a beneficial effect on the progress of atherosclerosis and individual's cardiovascular risk profile [13]. From a nutritional point of view, EF may affect a number of dietary factors, such as total energy intake, macronutrients intake and diet quality, acting synergistically with them for modifying the process of atherosclerosis. As a result, EF may well belong to a network of intimately interwoven risk factors, whose dynamic interaction may indicate that a purely data-driven, multivariate stepwise model may not describe adequately the phenomenon [14]. In an attempt to overcome this problem, we created a conceptual framework and an hierarchical approach [15]. Several levels of parameters were recognized, with each level possibly exerting its effects upon all the following, "higher" levels. Five distinct levels were recognized i.e., immutable demographic factors and long-term habits, dietary factors, eating frequency, obesity-related risk factors and presence of atherosclerosis as well as surrogate indices (Fig. 1). Thus, the scope of the present analysis was to investigate potential associations between EF, i.e. the number of eating episodes (measured per three days) and early markers of atherosclerosis, through a hierarchical model.

2. Materials and methods

2.1. Study population

One hundred sixty four volunteers (62 males and 102 females), who attended a secondary prevention program for free vascular examination in the outpatients' clinic of Alexandra University Hospital, Athens, Greece, were recruited over a period of 12 months. All subjects were apparently healthy. Exclusion criteria were: medical history of coronary artery disease, diabetes mellitus (defined as taking hypoglycemic medication or as fasting glucose ≥7 mmol/l (126 mg/dl) and/or 2 h post-load glucose ≥ 11.1 mmol/l during screening), liver or endocrine diseases, autoimmune disease, cancer or active infection, alcohol consumption (≥30 g alcohol/day) and dieting at the time of the study. The study protocol complied with the Declaration of Helsinki and it was approved by the Hospital scientific committee. All subjects gave their written consent before entering the study.

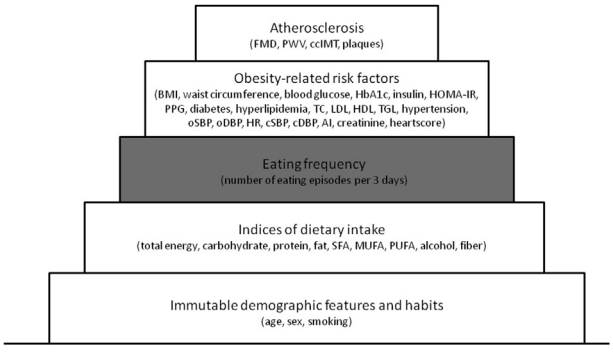

Fig. 1. Description of the hierarchical model. AI, augmentation index, BMI, body mass index, cSBP, central systolic blood pressure, cDBP, central diastolic blood pressure, FMD, flow mediated dilatation, HbA1c, glycosylated hemoglobin, HDL, high density lipoprotein, HOMA-IR, homeostasis model assessment, HR, heart rate, IMT, intima media thickness, LDL, low density lipoprotein, MUFA, monounsaturated fatty acids, oDBP, office diastolic blood pressure, oSBP, office systolic blood pressure, PPG, postprandial glucose, PUFA, polyunsaturated fatty acids, PWV, pulse wave velocity, SFA, saturated fatty acids, TC, total cholesterol, TGL, triglycerides.

2.2. Study protocol

The study had a cross-sectional design. All participants were instructed to follow a 12 h fast and abstain from alcohol, coffee or caffeinated beverages and smoking one day before their hospital visit. They were asked to visit once the vascular laboratory at 8.00 a.m. Women of reproductive age were examined during the early follicular phase of the menstrual cycle. Anthropometric and clinical measurements, ultrasound scanning for assessing vascular function, blood sample collection, and dietary assessment were performed in all study participants.

2.3. Anthropometric measurements and risk factor assessment

Weight and height were measured using a calibrated scale and tapeline. Waist circumference (cm) was measured at the maximal abdominal circumference between the xiphoid process and the iliac crest.

Smoking condition was considered the daily use of more than 1 cigarette per day. Arterial hypertension was defined as systolic arterial pressure ≥140 mm Hg and/or diastolic arterial pressure ≥90 mm Hg (average of 2 measurements, 1 min apart) in each of 2 consecutive office visits or treatment for hypertension. Blood pressure measurements were taken using an automated oscillometric device (Omron 705 IT; Omron Healthcare Europe BV, Hoofddorp, The Netherlands). Hyperlipidemia was defined as history of hypolipidemic treatment or total blood cholesterol level ≥200 mg/dL. A second definition for hyperlipidemia was also used, based on LDL levels (hypolipidemic treatment or LDL >115 mg/dl) in order to take into consideration the main treatment target in dylipidemia management according to latest European Society of Cardiology (ESC) guidelines [16]. We also took into account the latest American Society of Cardiology guidelines, with no significant alterations in our outcome [17]. The European Society of Cardiology online Heart Score (HS) calculator was used for the computation of the 10-year mortality risk (MR) adjusted for the Greek population [18].

2.4. Blood assays

Glycosylated hemoglobin was evaluated by HPLC method (HiAuto A1C Analyzer HA-8140 Menarini) and insulin concentrations by ELISA method (Boehringer Mannheim). Plasma glucose, total cholesterol, triglycerides and HDL cholesterol blood concentrations were measured using standard analyzers. As no study participant had TG levels, above 500 mg/dl, LDL-cholesterol was calculated by the Friedewald equation [19]. Insulin resistance was estimated by HOMA-IR, [HOMA-IR = (fasting glucose [mmol/l]) × insulin [mU/l]/22] [20].

2.5. Vascular measurements

Flow Mediated Dilatation (FMD) was measured using a B-Mode high-resolution ultrasound machine (Acuson 128xp California,