Nutrition, Metabolism & Cardiovascular Diseases (2015) **25**, 569–574

Available online at www.sciencedirect.com

Nutrition, Metabolism & Cardiovascular Diseases

journal homepage: www.elsevier.com/locate/nmcd

Does the Mediterranean diet counteract the adverse effects of abdominal adiposity?

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Received 1 November 2014; received in revised form 3 February 2015; accepted 2 March 2015
Available online 11 March 2015

KEYWORDS
Waist-to-height ratio;
Mediterranean diet;
Dietary intervention;
Cardiovascular disease

Abstract *Background and aim:* We tested the hypothesis that an intervention with a Mediterranean diet (MeDiet) could mitigate the well-known harmful effects of abdominal obesity on cardiovascular health.
Methods and results: We assessed the relationship between baseline waist-to-height ratio (WHtR) and major cardiovascular events during a median follow-up of 4.8 years in the Prevention with Mediterranean Diet (PREDIMED) randomized primary prevention trial, which tested a MeDiet against a control diet (advice on a low-fat diet). We also examined whether the MeDiet intervention was able to counteract the detrimental cardiovascular effects of an increased WHtR. The trial included 7447 participants (55–80 years old, 57% women) at high cardiovascular risk but free of cardiovascular disease (CVD) at enrollment.

An increased risk of CVD events (myocardial infarction, stroke, or cardiovascular death) was apparent for the highest versus the lowest quartile of WHtR (multivariable-adjusted hazard ratio: 1.98) (95% confidence interval: 1.10–3.57; linear trend: $p = 0.019$) only in the control-diet group, but not in the two groups allocated to intervention with MeDiet (p for interaction = 0.034). This apparent interaction suggesting that the intervention counterbalanced the detrimental cardiovascular effects of adiposity was also significant for body mass index (BMI) ($p = 0.01$) and waist circumference ($p = 0.043$).

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http://dx.doi.org/10.1016/j.numecd.2015.03.001

Conclusions: The MeDiet may counteract the harmful effects of increased adiposity on the risk of CVD.

Introduction

Excess body weight is likely to be associated with clinical cardiovascular disease (CVD) even at moderate levels of overweight. Sound biological plausibility and recent empirical studies support that the adverse consequences of obesity are mainly attributable to abdominal fat accumulation [1–5]. We assessed the association between adiposity indexes and CVD in the Primary Prevention of Cardiovascular Disease with a Mediterranean Diet (PREDIMED) study, a randomized nutrition intervention trial comparing a Mediterranean diet (MeDiet) supplemented with extra-virgin olive oil (EVOO) and a MeDiet supplemented with nuts against a control low-fat diet for the primary prevention of CVD in older subjects at high cardiovascular risk [6]. We tested the hypothesis that the MeDiet would counteract or mitigate the detrimental effects of abdominal obesity. Although the final results of the PREDIMED trial [8] supported that a MeDiet was able to prevent CVD, there is scarce information from randomized trials on whether the MeDiet can specifically attenuate the harmful effects of increased abdominal fat.

Methods

The design, objectives, and methods of the PREDIMED trial were previously published [6]. Briefly, PREDIMED was a randomized, multicenter, cardiovascular primary prevention trial conducted in Spain (www.predimed.es) from October 2003 to December 2010, which compared three dietary interventions: two MeDiets, one supplemented with EVOO and the other supplemented with mixed nuts, versus a control (low-fat) diet.

The Institutional Review Boards at all study locations approved the protocol. The trial was registered at http://www.controlled-trials.com/ISRCTN 35739639.

Subjects

By study design, all participants were at high cardiovascular risk because of the presence of type-2 diabetes or at least three risk factors, but had no CVD at enrollment [6]. Of 7447 recruited participants, 43% were men (aged 55–80 years) and 57% were women (aged 60–80 years).

The procedures and specific details of the intervention have been previously described [7,8]. Of note, energy restriction was not part of the nutritional intervention.

Measurements

Registered nurses previously trained and certified to implement the PREDIMED protocol directly measured weight, height, and waist circumference (WC) of participants, as previously described [6,7,9]. Height (m) and weight (kg) were measured with light clothing and no shoes with calibrated scales and a wall-mounted stadiometer, respectively; body mass index (BMI) was calculated as the weight in kilograms divided by the square of the height in meters; WC was measured midway between the lowest rib and the iliac crest using an anthropometric tape; and waist-to-height ratio (WHtR) was calculated as WC divided by height, both in centimeters.

Outcome

The main outcome was a composite primary end point including myocardial infarction, stroke, or death from cardiovascular causes. Repeated contacts with participants and family physicians, a yearly review of medical records, and consultation (every 6 months) of the National Death Index provided the basic information used by the end-point adjudication committee to classify the events. Members of this committee were blinded to study-group assignments and to the anthropometric indexes of participants.

Assessment of confounders

Medical, socio-demographic, and lifestyle variables were collected in a baseline interview. We used the Minnesota validated physical activity questionnaire to assess leisure-time physical activity [10,11]. Dietary habits were ascertained through a semi-quantitative 137-item food frequency questionnaire previously validated in Spain [12].

Statistical analyses

We used Cox regression models to assess the hazard ratios (HRs) and their 95% confidence intervals (CIs) for total CVD events across quartiles of WHtR (quartiles two and three were merged to simplify the results), BMI (cutoff points: 25 and 30 kg/m [2]), and WC. We adjusted for the following potential confounders measured at baseline: age, sex, smoking, diabetes, hypertension status, dyslipidemia status, intervention group, metabolic equivalents (METs)-min/d (adding a quadratic term to account for a nonlinear association with cardiovascular events), and family history of early-onset coronary artery disease. We evaluated the interaction between baseline indexes of adiposity and the intervention using the likelihood ratio test, after merging the two active arms of the trial that received the MeDiet intervention in a single category. For WHtR, we used the 75th percentile as the cutoff point to dichotomize the WHtR (one degree of freedom). To better