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Relationship between high sodium and low PUFA intake and carotid atherosclerosis in elderly women

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ABSTRACT

Several biologically active molecules including nutrients can affect the vascular endothelium which becomes dysfunctional and, as a consequence, predisposes to atherosclerosis. However, the impact of the intake of sodium and polyunsaturated fatty acids on carotid atherosclerosis in a population of elderly women has scarcely been studied. Our aim was to investigate the association between carotid intima-media thickness and atherosclerotic plaque and nutrient intake in asymptomatic elderly women. Carotid atherosclerosis was determined by duplex ultrasound in 108 elderly women. Dietary intake was assessed by a combination of a 24-hour recall and a 7-day food record. A physical examination and laboratory tests were performed. We found an association between the C-IMT and polyunsaturated fatty acid (negative, B = −0.014; p = 0.03; CI −0.027/−0.001) and sodium (positive, r = 0.16; P = 0.09) intake. When linoleic acid was added to the multivariable regression analysis instead of polyunsaturated fatty acids, C-IMT was associated with linoleic acid (B = −0.017; p = 0.02; CI −0.032/−0.003). In normotensive women we found a positive association between the C-IMT and sodium intake. The atherosclerotic plaque prevalence increased with the increase in sodium intake (66% *vs* 90% Tertile I *vs* Tertile III; p = 0.02). Iin conclusion, A low salt diet to a level of about 1.5 g/d and a polyunsaturated fatty acid intake of > 9 g/d were found to be associate with a low atherosclerotic plaque prevalence in an elderly female population. Sodium and polyunsaturated fatty acids-mediated functional changes of the carotid endothelium may be implicated in atherosclerosis development.

1. Introduction

It is well known that endothelial cells regulate the flow of various blood cells, molecules as well as nutrient substances (Cines et al., 1998). When the endothelium is perturbed by physical forces or particular biologically active molecules, it becomes dysfunctional and creates a prothrombotic microenvironment involved in the pathogenesis of atherosclerosis (Cines et al., 1998). The association of markers of immunological, inflammatory and procoagulant functions with both the carotid intima-media thickness (C-IMT) and atherosclerotic plaque is consistent with the contribution of several inflammatory cells, immunological factors and nutrients to the atherosclerotic process (Mosca et al., 2011; Mason and Libby, 2015; Hennig et al., 1996).

Animals studies have provided evidence that dietary sodium impairs endothelial function increasing cellular oxidative stress without alterations in blood pressure (Hennig et al., 1996; Matavelli et al., 2007; Zhu et al., 2007; Nurkiewicz and Boegehold, 2007). An increase in serum E-selectin, a marker of endothelial dysfunction, has been reported after *trans* fatty acids consumption in both genders (Bendsen et al., 2011; Baer et al., 2004).

On the other hand, certain nutrients, which have antioxidant and/or membrane stabilizing proprieties, can protect the endothelial cells (Hennig et al., 1996). A high dietary fiber intake has been reported to be inversely associated with carotid atherosclerosis (Buil-Cosiales et al., 2009). Vitamins A, E and C, and lycopene have been found to be inversely associated with C-IMT (Riccioni et al., 2008; Odermarsky et al., 2009).

However, to date, reports aimed at identifying the relationship between nutrient intake and carotid atherosclerosis in elderly female populations are scarce. Nevertheless, the incidence of new coronary events is highest among adults over 65 years of age and this group accounts for 83% of coronary heart disease (CHD) deaths (Rosamond

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et al., 2008). An unhealthy diet along with a sedentary lifestyle increases the prevalence of central obesity and lipid abnormalities among older adults (Ford et al., 2004), and these factors may increase CHD risk. In addition, increased chronological age alone should not exclude any patient from receiving the benefits of such pharmacological or dietary treatments. Thus, in the present study, we investigated the association between C-IMT and carotid atherosclerotic plaques, determined by duplex ultrasound, and cardiovascular risk factors including unhealthy dietary habits, in asymptomatic elderly women.

2. Methods

This study included participants recruited in the study entitled: “Effect of the Mediterranean Diet on cognitive function in the elderly” which ran from February 2013 to August 2016 at the “Mater Domini” University Hospital in Catanzaro and was funded by Italian Ministry of Health. The protocol was approved by the “Mater Domini” University Hospital ethics committee in Catanzaro (projects codes 2011.48; 2011 year of approval). Written informed consent was obtained from all participants. The investigation conforms to the principles outlined in the Declaration of Helsinki.

The participants were invited to participate in the study by newspapers advertisements. All subjects were white, community-dwelling individuals aged ≥65 years and had a Mini Mental State Examination (MMSE) score > 20 (Mazza et al., 2017). Participants were not suffering from any debilitating diseases (such as stage 2–5 chronic kidney disease, congestive heart failure, dementia, end stage liver failure, cancer,) as ascertained from their medical history, a physical and neurological examination and laboratory tests. They had no previous history of cardiovascular disease or thyroid dysfunction or excessive alcohol consumption (> 20 g of alcohol per day; 350 mL (12 oz) of beer, 120 mL (4 oz) of wine, and 45 mL (1.5 oz) of hard liquor each contain 10 g of alcohol), and did not take any dietary supplements and psychotropic drugs.

2.1. Anthropometric measurements and cardiovascular risk factors assessment

Body weight was measured before breakfast after a 12 h overnight fast with the subjects lightly dressed subtracting 1 kg from the recorded body weight to adjust for the weight of clothes. Body weight was measured on a calibrated digital scale (model Tanita BC-418MA) accurate to 0.1 kg, and standing height was measured with a wall-mounted stadiometer (Montalcini et al., 2007). BMI was calculated with the following equation: weight (kg)/height (m)^2. Obesity was defined by the presence of a body mass index (BMI) ≥ 30 kg/m2. Waist circumferences and hip circumferences (WC and HC) were measured with a nonstretchable tape over the unclothed abdomen at the narrowest point between costal margin and iliac crest and over light clothing at the level of the widest diameter around the buttocks, respectively, as described in the past (Mazza et al., 2017).

Bioelectrical impedance analysis (BIA) was performed to estimate the percentage of Fat Mass (FM) (BIA-101, Akern srl, Florence, Italy) (Greco et al., 2014).

We assessed the presence of the classical cardiovascular (CV) risk factors, such as hyperlipidemia, hypertension, diabetes and smoking, from clinical records and patient interview (Mazza et al., 2017). Blood pressure was determined at the time of the visit (Mazza et al., 2017; Montalcini et al., 2007).

2.2. Dietary intake assessment

Dietary intake was assessed by a combination of a 24-hour recall and a 7-day food record (Mazza et al., 2017), and calculated using nutritional software MetaDieta 3.0.1 (Metedasrl, San Benedetto del Tronto, Italy). The primary limitation of the 24-hour recall is that recording consumption for a single day is seldom representative of a person's usual intake due to day-to-day variation. However, this method better helps the dietitian in estimating portion sizes of foods really consumed by participants. The patients were asked to report any ingredients, food and food waste in a food diary for a 7-day period. Each patient was trained by a skilled dietitian before starting the study. The dietitian showed how various foods should be recorded. The portion sizes used were based on the typical or natural portion consumed (*e.g.*, a slice of bread, one egg). When a typical portion size was not obvious, a commonly-used portion size was selected (*e.g.*, one cup). Furthermore, a 24-hour recall was performed *via* a face-to-face interview with a dietitian who used images associated with a comprehensive food list. The recall required 15–20 min to complete for each participant. The nutrient database used to calculate nutrient intake was derived primarily from INRAN (National Institute of Food Research) 2000 and IEO (European Institute of Oncology) 2008 (Mazza et al., 2017).This database includes over 5000 foods and brand name products, and is updated annually. Dietary intake data were entered directly into the software MetaDieta. Briefly, The software searches for foods and brand products by name and their variable ingredients occurs as data are entered, with the simultaneous immediate calculation of nutrients intake.

2.3. Biochemical evaluation

Venous blood was collected after fasting overnight into vacutainer tubes (Becton & Dickinson, Plymouth, England) and centrifuged within 4 h. Serum glucose, total cholesterol, high density lipoprotein (HDL)-cholesterol, triglycerides, creatinine, calcium, sodium and potassium were measured with Enzymatic colorimetric test. Low-density lipoprotein (LDL) cholesterol level was calculated by the Friedewald formula (Montalcini et al., 2005). 25-hydroxy vitamin D was measured by Radioimmunoassay. Quality control was assessed daily for all determinations.

2.4. Carotid atherosclerosis assessment

The subjects underwent B-mode ultrasonography of the extracranial carotid arteries by use of a duplex system (Toshiba Medical Systems Corporation, model TUS-A500, 1385, Shimoishigami, Otawara-Shi, Tochigi 324-8550, Japan) with a 5- to 12-MHz linear array multi-frequency transducer. All the examinations were performed by the same ultrasonographer. The right and left common, internal and external carotid arteries (including bifurcations) were evaluated with the subjects in supine position, with the head turned away from the sonographer and the neck extended with mild rotation. The C-IMT, defined as the distance between the intimal–luminal interface and the medial–adventitial interface, was measured in all patients as previously described (Montalcini et al., 2007). Briefly, in posterior approach and with the sound beam set perpendicular to the arterial surface, 1 cm proximal to the bifurcation, three longitudinal measurements of C-IMT were completed on the right and left common carotid arteries far wall, at sites free of any discrete plaques. The mean of the three right and left longitudinal measurements was then calculated. The coefficient variation of this method was 3.3%. According to The European Mannheim consensus, plaque was defined as a focal thickening that encroaches into the lumen by 0.5 mm or by 50% of the surrounding IMT or where IMT is > 1.5 mm (Touboul et al., 2006).

Stenosis was defined as a peak systolic velocity > 120 cm/s, and occlusion was defined as absence of Doppler signal. According to these criteria, subjects were considered as normal if no lesion was detected, or having carotid atherosclerosis when a plaque, stenosis or occlusion was detected in at least one segment of carotid tree (Montalcini et al., 2007).