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Original article

Cross-sectional associations between macronutrient intake and chronic kidney disease in a population at high cardiovascular risk

Andrés Díaz-López [a,b], Mònica Bulló [a,b,*], Josep Basora [a,b], Miguel Ángel Martínez-González [b,c], Marta Guasch-Ferré [a,b], Ramon Estruch [b,d], Julia Wärnberg [c,e], Lluís Serra-Majem [f], Fernando Arós [g,h], José Lapetra [b,i], Emilio Ros [b,j], Xavier Pintó [h,k], María Isabel Covas [b,l], Jordi Salas-Salvadó [a,b,*]

[a] Human Nutrition Unit, IISPV, Universitat Rovira i Virgili, Reus, Spain
[b] CIBERobn Physiopathology of Obesity and Nutrition, Institute of Health Carlos III, Madrid, Spain
[c] Department of Preventive Medicine and Public Health, University of Navarra, Pamplona, Spain
[d] Department of Internal Medicine, Hospital Clínic, IDIBAPS, University of Barcelona, Spain
[e] Department of Preventive Medicine, University of Málaga, Spain
[f] Department of Clinical Sciences, University of Las Palmas de Gran Canaria, Spain
[g] Department of Cardiology, Hospital Txagorritxu, Vitoria, Spain
[h] Redes Temáticas de Investigación Cooperativa RD06/0045, ISCIII, Spain
[i] Primary Care Division of Sevilla, San Pablo Health Center, Sevilla, Spain
[j] Lipid Clinic, Service of Endocrinology and Nutrition, IDIBAPS, Hospital Clínic, Barcelona, Spain
[k] Atherosclerosis Unit, Department of Internal Medicine, IDIBELL-Hospital Universitari de Bellvitge, Barcelona, Spain
[l] Cardiovascular Risk and Nutrition Research Group, IMIM, Barcelona, Spain

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SUMMARY

Background & aims: The aim was to examine the associations between macronutrient intake and the prevalence of chronic kidney disease (CKD) or microalbuminuria (MiA) in individuals at high cardiovascular risk.
Methods: Cross-sectional analyses conducted in 2123 nondiabetic individuals from the PREDIMED study. Dietary data were collected using a food-frequency questionnaire. Analysis of covariance was used to assess associations between quartiles of nutrient intake and estimated glomerular filtration rate (eGFR) or urinary albumin-to-creatinine ratio (ACR). The odds ratio (OR) for the presence of CKD or MiA according to quartiles of nutrient intake was assessed by logistic regression models.
Results: Individuals in the highest quartile of *n*-6 polyunsaturated fatty acid (PUFA) intake showed lower average eGFR. Individuals in the top quartile of fiber intake had a decreased risk of CKD [OR: 0.68; 95% CI: 0.48–0.95]. Conversely, subjects in the highest quartile of *n*-6 PUFA intake showed an increased risk of CKD [OR: 1.44; 95% CI: 1.03–2.01]. No significant associations were found between the intake of other macronutrients and eGFR, urinary ACR or risk of CKD or MiA.
Conclusions: A high fiber intake was associated with a decreased risk of CKD, while a high *n-6* PUFA intake was inversely associated with eGFR and directly associated with an increased risk of CKD.

1. Introduction

Chronic kidney disease (CKD), defined by the presence of microalbuminuria (MiA) or a reduced glomerular filtration rate (GFR), is recognized as a major global public health problem,[1] increasing the risk of cardiovascular disease (CVD) and mortality,[2] especially in older populations. Age may be interpreted as increased exposure time to traditional CVD risk factors such as hypertension, diabetes, smoking and dyslipidemia, all of which are positively associated with the progression of kidney disease. Hence,

Abbreviations: CKD, chronic kidney disease; MiA, microalbuminuria; GFR, glomerular filtration rate; CVD, cardiovascular disease; PUFA, polyunsaturated fatty acids; ACR, albumin-to-creatinine ratio; PREDIMED, PREvención con DIeta MEDiterránea; CHD, coronary heart disease; FFQ, food-frequency questionnaire; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; NA, normoalbuminuric; ARB, angiotensin-type 2 receptor blockers; ACE-I, angiotensin converting enzyme inhibitors; LDL, low density lipoprotein; HDL, high density lipoprotein.

* Corresponding authors. Human Nutrition Unit, Universitat Rovira i Virgili, C/Sant Llorenç 21, 43201 Reus, Spain. Tel.: +34 977759312; fax: +34 977759322.
E-mail address: jordi.salas@urv.cat (J. Salas-Salvadó).

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in recent years CKD has received considerable attention, and several epidemiological studies have investigated the effect of diet on CKD, primarily under the hypothesis that diet is one of the most important factors linked to chronic diseases, including CKD. These studies have been conducted in different populations in an attempt to evaluate the association between dietary patterns and kidney function.[3,4] They have shown that greater adherence to a healthy dietary pattern is inversely associated with MiA or estimated glomerular filtration rate (eGFR) decline, two widely used measures for assessing kidney function. However, other epidemiological studies have appraised individual nutrients or foods and have suggested that dietary intake of some macronutrients may be involved in the development of CKD.[5–8]

Clinical and observational studies have focused on dietary protein, with the hypothesis that restriction in protein intake and improved blood pressure control may delay the progression of CKD, possibly by reducing glomerular hyperfiltration. In adult patients with stage I or II CKD, there is no clear evidence to support a substantial effect of dietary protein intake on kidney function.[9] However, two recent meta-analyses of randomized trials conducted in individuals with stage III or IV CKD have reported that, compared to participants receiving a normal protein diet, individuals in the low-protein diet regime showed a significantly lower increase in the urinary albumin excretion rate, and a lower decline in eGFR or creatinine clearance during the intervention.[10,11]

Dietary fat[5,7] might also be important for the development of kidney disease, although the effects of different subtypes of fat on albuminuria or eGFR have not been well explored. To date, only two cross-sectional studies have analyzed the association between the type of fat and renal function. A high saturated fat intake was associated with an increased risk of MiA in one study.[7] In another study, high consumption of long-chain n-3 polyunsaturated fatty acids (PUFA) and α-linolenic acid were associated with reduced and increased risk of CKD, respectively.[12] Only one prospective study has examined the association between carbohydrate consumption and the prevalence and incidence of CKD. No significant associations were reported between carbohydrate or sugar intakes and CKD. However, compared to individuals in the reference quartile of dietary cereal fiber intake, participants in the top quartile had a 50% lower risk of CKD incidence.[13] Considering that relatively few studies have analyzed the association between macronutrient intake and kidney function in adults with normal-to-mild kidney disease, it is difficult to reach conclusions about the effect of macronutrient intake on kidney function. Therefore, the purpose of the present study was to cross-sectionally examine the association between macronutrient intake and the prevalence of CKD or MiA in nondiabetic individuals at high cardiovascular risk.

2. Materials and methods

2.1. Study population

The present cross-sectional analysis was performed with baseline data of a subsample of participants recruited from six Spanish centers [Reus-Tarragona, Pamplona, Basque Country, Barcelona Bellvitge and Clínico, Sevilla and the Canary Islands] of the PREDIMED (PREvención con DIeta MEDiterránea) study. The PREDIMED study is a large, parallel-group, randomized, multicenter, controlled trial designed to assess the effect of the Mediterranean diet on the primary prevention of CVD (http://www.predimed.org and www.predimed.es). Recruitment took place between October 2003 and January 2009, and 7447 participants were randomly assigned to three intervention groups: two Mediterranean diet groups (supplemented with virgin olive oil or nuts), and a control low-fat diet group. The design of the PREDIMED trial (http://www.controlled-trials.com/ISRCTN35739639) has been reported in detail elsewhere.[14] The Institutional Review Board of the recruitment centers approved the study protocol and participants gave their informed consent.

PREDIMED participants were eligible if they were men aged 55–80 years and women aged 60–80 years, who were free of CVD at baseline, and fulfilled at least one of the following two criteria: presence of type-2 diabetes and/or three or more of the following coronary heart disease (CHD) risk factors: family history of early-onset CHD, smoking, hypertension, dyslipidemia or overweight.[14]

All PREDIMED nondiabetic subjects recruited by the centers mentioned were included in the present study. Individuals whose data on urinary albumin-to-creatinine ratio (ACR) or eGFR was missing were excluded from the analysis ($n = 223$). Participants who had macroalbuminuria (ACR $\geq$355 mg/g in women and $\geq$250 mg/g in men; $n = 2$) or caloric intakes beyond the range we deemed plausible (for women 500–3500 kcal/d and for men 800–4000 kcal/d) were also excluded ($n = 24$). The effective sample size for statistical analyses was 2123 participants.

2.2. Dietary assessment

At baseline, diet was assessed by trained dieticians who administered a 137-item semi-quantitative food-frequency questionnaire validated for the PREDIMED study[15] to quantify usual dietary intake. Reproducibility of the FFQ used in PREDIMED for energy and nutrient intake, explored by the Pearson correlation coefficient (r) ranged 0.50–0.82, and the intraclass correlation coefficient (ICC) ranged from 0.63 to 0.90. The validity indexes of the FFQ in relation to the dietary records for energy and nutrient intake ranged (r) from 0.24 to 0.72, while the range of the ICC was between 0.40 and 0.84. Nutrient composition was estimated from Spanish food composition tables.[16]

2.3. Measurement of clinical and laboratory covariates

At baseline, all participants completed: (a) a 47-item questionnaire about education, lifestyle, history of illnesses and medication use; and, (b) a validated Spanish version of the Minnesota Leisure-Time Physical Activity Questionnaire evaluating physical activity.[14] In addition, anthropometric variables and blood pressure were determined. Blood and urine samples were also collected from all participants after an overnight fast. The aliquots of serum, plasma and urine were immediately prepared, coded, and shipped to a central laboratory. Serum levels of fasting glucose, total cholesterol, HDL-cholesterol and triglycerides were measured by standard enzymatic methods. LDL-cholesterol was calculated by Friedewald's formula. The clinical investigators and laboratory technicians were blinded to clinical data.

2.4. Assessment of kidney function

Serum creatinine was measured by enzymatic reaction using the modified Jaffé colorimetric method (coefficient of variation <4.0%). Urinary albumin and creatinine concentrations were determined in single spot urine using the modified Jaffé colorimetric method and by the Bromcresol green albumin method, respectively (coefficients of variation were <3.0% for urinary creatinine, and <10.0% for urinary albumin). All analyses were performed using a Roche Hitachi Modular-DDP clinical analyzer (Roche Diagnostics, Barcelona, Spain).

The eGFR was estimated indirectly from serum creatinine using the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) equation for Caucasian individuals.[17]