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Dietary fat composition and cardiac events in patients with type 2 diabetes

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ABSTRACT

Objective: To evaluate associations of dietary fat composition with the development of cardiac events in patients with type 2 diabetes, without ischemic heart disease who were followed for at least 12 months.
Methods: In this prospective cohort study the usual diet of patients was retrospectively assessed by a 3-day weighed diet record (WDR). Compliance with the WDR technique was assessed by comparing protein intake estimated from 3-day WDR and 24-h urinary nitrogen output. The following were considered cardiac events: myocardial infarction, myocardial revascularization procedures, congestive heart failure, new-onset angina pectoris, and sudden death.
Results: A total of 227 patients with type 2 diabetes (aged 59 ± 10 years; 46.0% male), were followed during 4.6 years. In a multivariate Cox regression analysis, the intake of polyunsaturated fatty acids had a protective effect for cardiac events (HR = 0.31, 95% CI: 0.11–0.89; $P = 0.03$) adjusted for age, gender, duration of diabetes, smoking, compliance with WDR, using hypolipidemic agents, and the presence of hypertension and diabetic nephropathy. When the fat intake was divided into quartiles, the highest intake of α-linolenic acid (>1.25% of energy) was negatively associated with cardiac events (HR = 0.58, 95% CI: 0.39–0.85; $P = 0.006$), adjusted for the same covariates..
Conclusion: In patients with type 2 diabetes without ischemic heart disease, a high intake of polyunsaturated fatty acids, especially alpha linolenic acid, was protective for the development of cardiac events..

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1. Introduction

Cardiovascular disease (CVD) is the main cause of morbidity and mortality in patients with diabetes mellitus. Coronary artery disease is more frequent and more severe in diabetic than non-diabetic patients [1]. Diabetes itself, particularly due to sustained hyperglycemia, greatly contributes to the severity of atherosclerotic disease [2]. Additionally, the known high frequency of associated cardiovascular risk factors in patients with diabetes, such as obesity, dyslipidemia, and hypertension, can also explain the severity of CVD in diabetes. A cross-sectional, multicenter study including 927 Brazilian outpatients with type 2 diabetes showed a 36% prevalence of coronary artery disease, a 33% of peripheral artery disease, and a 73% of hypertension in these patients [3].

Though hypolipidemic agents have shown the same effectiveness for type 2 diabetic patients and nondiabetic patients, the absolute rates of atherosclerotic cardiovascular disease events remained elevated in patients with diabetes [4]. This reinforces the importance of cardiovascular prevention measures based especially on lifestyle interventions, such as dietary changes; these measures should be implemented to mitigate cardiovascular risk factors.

Dietary intervention involves the management of the intake of nutrients associated with cardiovascular protection and risk factors [5]. Current recommendations for the prevention and treatment of CVD in diabetes suggest a diet rich in fruits, vegetables, whole grains, walnuts, and low-fat dairy products, and salt restriction both for normotensive and hypertensive patients [6,7]. The specific recommendations are: reduction in saturated fatty

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acids (SFAs) and cholesterol intake; restriction of *trans* fatty acids (FA) intake; increase in total fiber intake and increase in consumption of fish (as a source of polyunsaturated FA (PUFA) [6,7]. However, the scientific evidence for these recommendations is generally based on studies conducted with non-diabetic subjects. Furthermore, the effects of dietary fat intake on CVD prevention could be different in patients with and without diabetes, since diabetes has been associated with lipid abnormalities and a prothrombotic profile [8].

The aim of the present study was to evaluate the association between dietary fat composition and the development of cardiac events in patients with type 2 diabetes and without ischemic heart disease. In addition, the role of adherence to current cardiovascular dietary recommendations in the prevention of cardiac events was evaluated.

2. Patients and methods

2.1. Patients

We carried out a retrospective data analysis of patients with type 2 diabetes belonging to a prospective cohort study. The patients included in the study were from the Diabetes research outpatient clinic at Hospital de Clínicas de Porto Alegre (Rio Grande do Sul, Brazil) and were followed for at least 12 months. At baseline, the patient exclusion criteria were: presence of ischemic heart disease, body mass index (BMI) > 40 kg/m^2, serum creatinine >1.5 mg/dl, heart failure, symptomatic autonomic neuropathy (gastroparesis or diabetic diarrhea), dietary counseling by a registered dietitian during the previous 12 months, and inability to perform the weighed diet records (WDR). The study was approved by the Hospital Ethics Committee; all patients signed a written informed consent form.

All patients underwent a standardized clinical, nutritional and laboratory examination at baseline. A three-day WDR was carried out, 24-h urine was collected, and on the 3rd day (after patients fasted overnight), blood samples were also collected. During the re-evaluation period, patients were submitted to the same clinical and laboratory examinations.

The follow-up was determined as the period between the first assessment and the date of a first cardiac outcome, death, or the last medical evaluation. Patients were divided into two groups according to the presence of cardiac outcomes at the end of the study.

2.2. Methods

2.2.1. Dietary assessment

Diet was assessed using a 3-day WDR technique (two nonconsecutive weekdays and one day of the weekend). Patients were issued commercial scales (1–125 g) and measuring cups (25–250 mL; Pirex) and given a detailed explanation and demonstration of the procedures by a trained, registered dietitian. Next, patients performed a training session for a one-day WDR. The 3-day WDR was performed over two to three weeks and before nutritional recommendations for all patients (Fig. 1).

Compliance with the WDR technique was assessed by comparison of protein intake estimated from the 3-day WDR (PI-WDR) and from the 24-h urinary nitrogen output (PI-N) performed on the third day of the WDR period [9]. According to Vaz et al. [9], patient compliance with the WDR protocol is established if the PI-WDR/PI-N ratio remain between 0.79 and 1.26.

The analysis of dietary nutrients from the 3-day WDRs was performed using the Nutribase Clinical Nutritional Manager software (version 7.14, 2007). The mean values of each nutrient consumed during the 3-day WDR were calculated. Nutritional data for frequently consumed foods were updated if necessary, and/or complemented with data obtained from local manufacturers of industrialized foods.

Patients were classified as adherent or non-adherent according to reaching or not each dietary fat goal based on American Diabetes Association (ADA) recommendations [6]. The items of ADA fat intake recommendations are: SFA below 7% of energy/day; cholesterol below 200 mg/day; increasing the intake PUFA, and reducing the intake of *trans* FAs. Besides using established cutoff points values of ADA dietary recommendations, we also categorized patients as adherent or non-adherent according to the fat intake of all studied sample: above or below the mean (for PUFA) or median (for *trans* FAs), and according to the quartiles of nutrient intake (for PUFA).

2.2.2. Anthropometric measurements

The body weight and height of patients (without shoes or coats) were collected with an anthropometric scale; measurements were recorded to the nearest 100 g for weight, and to the nearest 0.1 cm for height. Waist circumference was measured midway between the lowest rib and the iliac crest, near the umbilicus.

2.2.3. Clinical evaluation at baseline and end-of-study

The clinical assessment emphasized cardiovascular evaluation (blood pressure, WHO cardiovascular questionnaire, resting electrocardiogram, and evaluation of peripheral arterial pulses) and renal function.

Patients were classified as “nonsmoker” or “smoker” (smoker in the past or currently a smoker). Physical activity was classified into four levels based on a standardized questionnaire, which was adapted to local habits [10].

Mean blood pressure was calculated based on two separate measures using a digital sphygmomanometer (OMRON® Automatic Blood Pressure Monitor, Model HEM-705CP, Vernon Hills, Illinois 60061). Hypertension was defined as blood pressure ≥140/90 mmHg or use of antihypertensive drugs on at least two separate occasions.

Presence of baseline ischemic heart disease, an exclusion criterion, was defined as: presence of angina and/or possible infarction, using a World Health Organization (WHO) cardiovascular questionnaire as previously standardized in patients with type 2 diabetes by our group [11], or abnormalities on resting electrocardiogram (Minnesota Codes: Q and QS patterns [1-1 to 1-3]; S-T junction and segment depression [4-1 to 4-4]; T-wave items [5-1 to 5-3], or complete left bundle branch block [7-1]). In those cases, the ischemic heart disease was always confirmed by exercise electrocardiogram or radionuclide myocardial perfusion imaging with stress (exercise or pharmacological) compatible with the presence of myocardial ischemia [12].

Peripheral vascular disease was determined based on the presence of intermittent claudication and/or absence of posterior tibial pulse at clinical examination. The presence of cerebrovascular disease was established if there was a history of cerebrovascular accident (ischemic stroke) and/or compatible findings (sequelae).

Renal function was evaluated by serum creatinine and urinary albumin excretion [12]. The diagnosis of increased urinary albumin, microalbuminuria (24-h urinary albumin excretion between 30 and 300 mg) or macroalbuminuria (24-h urinary albumin excretion ≥300 mg), was confirmed by a second measurement [12,13].

2.2.4. Cardiac outcomes

Cardiac endpoints were defined when a new cardiac event occurred (myocardial infarction [Minnesota codes 1-1 to 1-3 or 7-1

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