Clinical Nutrition 40 (2021) 3883–3889

Contents lists available at ScienceDirect

Clinical Nutrition

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

Original Article

High-quality intake of carbohydrates is associated with lower prevalence of subclinical atherosclerosis in femoral arteries: The AWHS study

A. Muñoz-Cabrejas [a], M. Laclaustra [b, c, d, **], P. Guallar-Castillón [e, f, g], J.A. Casasnovas [a, c], E. Jarauta [a, c], H. Sandoval-Insausti [h], C. Donat-Vargas [e, f, i], B. Moreno-Franco [a, c, *]

[a] Universidad de Zaragoza, Zaragoza, Spain
[b] Agencia Aragonesa para La Investigación y El Desarrollo, ARAID, Zaragoza, Spain
[c] Instituto de Investigación Sanitaria Aragón, Hospital Universitario Miguel Servet, Zaragoza, Spain
[d] CIBERCV Instituto de Salud Carlos III. Madrid, Spain
[e] Department of Preventive Medicine and Public Health, School of Medicine, Universidad Autónoma de Madrid-IdiPaz, Madrid, Spain
[f] CIBERESP Instituto de Salud Carlos III, Madrid, Spain
[g] IMDEA-Food Institute. CEI UAM+CSIC, Madrid, Spain
[h] Department of Nutrition, Harvard T.H. Chan School of Public Health, Boston, MA, USA
[i] Unit of Nutritional Epidemiology, Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden

ARTICLE INFO

Article history:
Received 12 November 2020
Accepted 30 April 2021

Keywords:
Carbohydrates
Atherosclerosis
Cardiovascular disease
Carbohydrate quality index

SUMMARY

Background and aims: High-quality of the carbohydrates consumed, apart from their total amount, appear to protect from cardiovascular disease (CVD). However, the relationship between the quality of carbohydrates and the early appearance of atherosclerosis has not yet been described. Our objective was to estimate the association between the quality of dietary carbohydrates and subclinical atherosclerosis in femoral and carotid arteries.
Methods: Cross-sectional study of femoral and carotid atherosclerosis assessed using ultrasounds of 2074 middle-aged males, 50.9 (SD 3.9) years old, with no previous CVD, and pertaining to the Aragon Workers' Health Study (AWHS) cohort. Food frequency questionnaires were used to calculate a carbohydrate quality index (CQI) defined as: consumption of dietary fiber, a lower glycemic index, the ratio of whole grains/total grains, and the ratio of solid carbohydrates/total carbohydrates. The presence of plaques across four CQI intervals was studied using adjusted logistic regression models.
Results: The CQI showed a direct inverse association with subclinical atherosclerosis in femoral territories. Participants with a higher consumption of high-quality carbohydrates (13–15 points) were less likely to have femoral plaques when compared with participants in the lowest index interval (4–6 points) (OR = 0.59; 95% CI = 0.39, 0.89; p = 0.005). No association was found between the CQI and the presence of subclinical atherosclerosis in carotid territories. A lower consumption of high-quality carbohydrates tended to be associated with a greater atherosclerosis extension, considered as the odds for having more affected territories (p = 0.011).
Conclusions: Among middle-aged males, a high-quality intake of carbohydrates is associated with a lower prevalence of femoral artery subclinical atherosclerosis when compared with a lower consumption. Thus, indicating an early relationship between the quality of carbohydrates and the development of CVD.

Abbreviations: AWHS, Aragon Workers' Health Study; BMI, Body Mass Index; CEICA, Clinical Research Ethics Committee of Aragon; CHD, Coronary Heart Disease; CQI, Carbohydrate Quality Index; CVD, Cardiovascular Disease; FFQ, Food Frequency Questionnaire; GI, Glycemic Index; HDL-c, High-Density Lipoprotein Cholesterol; LDL-c, Low-Density Lipoprotein Cholesterol; Non HDL-c, Non High-Density Lipoprotein Cholesterol; OR, Odds Ratio; RR, Relative Risk; SD, Standard Deviation.

* Corresponding author. Department of Preventive Medicine and Public Health, Universidad de Zaragoza. C/Domingo Miral s/n, 50009 Zaragoza, Spain.
** Corresponding author. Unidad de Investigación Traslacional, Instituto de Investigación Sanitaria de Aragón, Avda Isabel La Católica 1-3, 50009 Zaragoza, Spain.
E-mail addresses: martin.laclaustra@unizar.es (M. Laclaustra), mbmoreno@unizar.es (B. Moreno-Franco).

https://doi.org/10.1016/j.clnu.2021.04.049

1. Introduction

Atherosclerosis is a multifactorial process responsible for a large proportion of cardiovascular disease (CVD) [1]. In addition to being the leading cause of death and disability in the world, CVD is also responsible for an important socioeconomic burden [1–3].

Behavioral and metabolic risk factors play a key role in the etiology and progression of atherosclerosis [1,4]. Accordingly, prevention efforts against CVD focus on preventable cardiovascular risk factors, such as modifying dietary patterns [1,5–7].

One dietary pattern of recent interest is the study of the type of carbohydrates and their quality. Carbohydrate quality is a multidimensional entity integrating several parameters and, as such, its elements can act in a synergic way. This is why, recent studies have assessed the relationship between carbohydrate quality and CVD through studying isolated indicators, mainly fiber intake, whole-grain consumption, and glycemic index (GI) or glycemic load. Several studies have shown that the consumption of dietary fiber [8,9] and whole-grains [10–13] decreases the risk of CVD, while a high GI [14–16] increases it. Likewise, some studies have shown how fiber [17] or whole-grain intake [18,19], as well as a low dietary GI [20,21] reduced atherosclerotic plaques.

In recent years, only a few studies have assessed overall carbohydrate quality integrating all previously defined indicators in a single index, known as the carbohydrate quality index (CQI) [22]. A high adherence to this index has shown a reduction in CVD as well as in some cardio-metabolic factors, which eventually can determine the development of CVD [23–25]. Nevertheless, no previous studies have assessed at what point in life this link is established, for example, in early adulthood indicated by the presence of subclinical atherosclerosis, or late in adulthood.

Subclinical atherosclerosis can be measured in several body locations, including carotid, femoral, and coronary arteries. However, without medical explorations it can remain clinically undetected throughout life, or until an acute clinical event occurs [26,27]. Among the subclinical locations, femoral plaques are the earliest and the most prevalent peripheral atherosclerotic indicators, that are available for detection using non-invasive techniques in the middle-aged population [28,29]. Hence, femoral subclinical atherosclerosis has the strongest association with traditional CVD risk factors, as well as being a strong marker of coronary lesions [28].

To our knowledge, the association of the quality of carbohydrates consumed with subclinical atherosclerosis in peripheral arteries has not previously been investigated. As a result, our objective was to estimate the impact that the quality carbohydrate consumption could have on the presence of subclinical atherosclerosis in femoral and carotid arteries. We studied this association with a sample of male factory workers from Spain.

2. Materials and methods

2.1. Study design and population

The association between carbohydrate quality and subclinical atherosclerosis was cross-sectionally studied with participants from the Aragon Workers' Health Study (AWHS), whose design and methodology have been previously described [30]. The AWHS is a prospective cohort study based on data from the annual physical examinations of workers in an automotive assembly plant with the aim to characterize risk factors for metabolic abnormalities and subclinical atherosclerosis. Between 2011 and 2014, study participants aged 39–59 and free of CVD at baseline underwent subclinical atherosclerosis imaging as well as an interview with questionnaires on cardiovascular and lifestyle factors, including diet. Of the 2616 participants who attended these extended examinations, we excluded the following participants: females due to their small number (n = 132), those with missing data on subclinical atherosclerosis imaging exams (n = 316), and those with missing data on diet, and on CVD risk factors (BMI, blood pressure, cholesterol, and smoking) (n = 94). The final sample comprised 2074 males (Supplemental Fig. 1). All participants gave their written informed consent. The study was approved by the Clinical Research Ethics Committee of Aragon (CEICA).

2.2. Data collection

2.2.1. Atherosclerosis imaging

The presence of plaques in carotid and femoral arteries was assessed using a Philips IU22 ultrasound system (Philips Healthcare, Bothell, WA). Ultrasound images were acquired with linear high-frequency 2-dimensional probes (Philips Transducer L9-3, Philips Healthcare), using the Bioimage Study protocol for the carotid arteries [31], as well as a specifically designed protocol for the femoral arteries [32]. Inspection sweeps were obtained on the right and left side of the carotid (common, internal, external, and bulb) and femoral territories. Plaque was defined as a focal structure protruding ≥0.5 mm into the lumen, or reaching a thickness ≥50% of the surrounding intima-media thickness. All measurements were analyzed using electrocardiogram gated frames corresponding to the end-diastole (R-wave) [33].

2.2.2. Diet assessment and carbohydrate quality index (CQI) calculation

Data used in the analysis were obtained with a previously validated food frequency questionnaire (FFQ) [34]. This questionnaire collects data on the frequency of consumption of 136 food items, including questions about the consumption of supplements and special diets. The FFQ gathers the average annual consumption for each food included, considering nine frequencies from "never or almost never" to "more than six times a day". Additionally, dietary energy, macronutrient, and micronutrient intake were derived using Spanish food composition tables [35,36].

To assess carbohydrate quality, we calculated the CQI [22], considering the following components: dietary fiber intake (g/d), GI, whole grain/total grain ratio, and solid carbohydrate/total carbohydrate ratio. Dietary fiber intake was directly derived from the FFQ. GI was calculated as a weighted GI based on the individual GI for each food item and using a previously proposed formula [25]. The GI for individual food items were obtained from various sources, including international food tables [36,37]. We estimated whole-grain consumption as the sum of 'whole bread consumption', 'integral cereal consumption', and 'whole wheat cookies consumption'. The intake of total grains was calculated by summing the intake of whole grains, refined grains, and their products (including refined bread, breakfast refined cereals, white rice, refined pasta, pizza and different biscuits, as well as pastry products). Liquid carbohydrates were calculated by summing up carbohydrates from sugar-sweetened beverages and fruit juice, and solid carbohydrates accounted for the carbohydrate content of the rest of the foods.

Before calculating the score, each component was pre-processed as follows [22]: for dietary fiber intake, and solid carbohydrate/total carbohydrate ratio, the participants were categorized into quartiles, and then, the belonging category ordinal was used as the component value (ranging from 1 to 4); for the GI, where lower values increase the final score, the quartile order was reversed (so that, those in the fourth quartile received 1 point, and those in the first quartile received 4 points); and for the whole grain/total grain ratio, participants were categorized into three groups, those that did not consume whole grains received 1 point, and the rest were divided into two equally sized groups and received 2 and 3 points. Finally, the CQI was constructed by summing up all the component scores (ranging from 4 to 15). We classified participants into four 3-point intervals of this final score. Higher CQI values mean better quality of the carbohydrate consumed (Table 1).

The components of CQI were categorized into four groups due to their moderate variability in this sample of middle-aged participants that prevented using the five groups originally described [22] in some components (Supplemental Table 1).

2.2.3. Sociodemographic, clinical, and biological data

Age, sex, type of work (blue collar or white collar), clinical, and laboratory data were obtained in the annual medical examination performed in the factory, including BMI, waist circumference, blood pressure, medical history, and the current use of medication. Laboratory measurements were performed on blood samples collected in fasting (>8 h) conditions. Fasting serum glucose, triglycerides, total cholesterol, and high-density lipoprotein cholesterol (HDL-c) were measured by spectrophotometry (Chemical Analyzer ILAB 650, Instrumentation Laboratory). Low-density lipoprotein cholesterol (LDL-c) levels were calculated using the Friedewald equation when triglycerides were lower than 400 mg/dl. We defined arterial hypertension as having systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg, or self-reported use of antihypertensive medication [38]. Dyslipidemia was defined as having total cholesterol ≥240 mg/dl, LDL-c ≥160 mg/dl, HDL-c <40 mg/dl, or self-reported use of lipid-lowering drugs [39]. Diabetes was defined as fasting plasma ≥126 mg/dl or self-reported treatment with hypoglycemic medication [38]. Smoking habits were categorized as never smoker or ever smoker if the participant had smoked at least 50 cigarettes in their lifetime.

Physical activity was assessed using the validated Spanish version [40] of the questionnaire on the frequency of engaging in physical activity used in the Nurses' Health Study [41] and the Health Professionals' Follow-up Study [42]. To compute the volume of activity performed by each participant, a metabolic cost was assigned to each activity using Ainsworth's compendium for physical activities [43], and multiplied by the time the participant reported practicing that activity. From the sum of all activities, we obtained a value of overall weekly METs-h.

2.3. Statistical methods/analysis

Descriptive analysis of baseline characteristics of the study participants classified by CQI categories were reported as mean and standard deviation (SD) for continuous variables or as percentage for categorical variables. The association between CQI categorized into four groups (4–6, 7–9, 10–12, and 13–15 points) and the presence of atherosclerotic plaques in femoral arteries (right and/or left, accounted jointly as one circulatory affected territory), carotid arteries (right and/or left, accounted jointly as one circulatory affected territory), and at any of these territories (sum of previous two) was examined using logistic regression (for sum > 0 in the later). Additionally, four approaches were used to describe and statistically test study atherosclerosis extension: 1) Average number of affected territories 0, 1, or 2 was calculated to describe the extension; 2) the percentage of presence of at least one (one or more) affected territory was also calculated (calculating odds ratios —OR— for presence of one or more affected territories vs no affected territories with logistic regression, which is the same as the one described above for atherosclerosis at any territory); 3) the percentage of participants with two affected territories (calculating OR for presence of 2 affected territories vs 0 or 1 affected territory with logistic regression); and 4) calculating ordinal OR with ordinal logistic regression of atherosclerosis extension. Models were adjusted for age, type of work, BMI, smoking status, hypertension, dyslipidemia, diabetes, total energy (Kcal/day), protein intake (g/day), total fat intake (g/day), alcohol intake (g/day), and total METs-h/week. P values below 0.05 were considered statistically significant. R statistical software (ver. 3.4.4) was used for the analysis.

Additionally, an alternative analysis with CQI index categorized in quintiles (Supplemental Table 1) was performed for demonstrating robustness and to facilitate comparison with previous work.

3. Results

The sample included 2074 males with a mean age of 50.9 (SD 3.9) years. Compared with individuals in the lowest CQI interval, participants with the highest one had a slightly higher probability to be white collar workers and showed a higher concentration of HDL-c, and a lower concentration of triglycerides. Likewise, they were less likely to be smokers (Table 2).

Concerning to lifestyle behaviours, participants with the highest CQI consume less carbohydrates and more protein than the lowest CQI interval. Moreover, they practice more physical activity (higher METs-h/week) (Supplemental Table 2).

The prevalence of the presence of atheroma plaques among participants was 56.7% in femoral territory. There was a significant inverse association between CQI index and the presence of plaques in this territory. Compared with participants with the lowest CQI, those with the highest CQI had less prevalence of femoral plaques (60.4% vs. 51.4%). Fully adjusted odds for femoral plaques among participants with the highest CQI were reduced to 0.59 (95% CI: 0.39, 0.89) times the odds of those with the lowest CQI (Table 3, Fig. 1). Overall, there was a linear dose–response in the protective direction. Assessing the association of CQI as a continuous variable with the presence of femoral plaques, the odds for having femoral plaques were reduced by 5.6% (95% CI: 1.8%, 9.3%; p = 0.005) for each unit of CQI increase.

The prevalence of atheroma plaques among participants in the carotid territory was 36.6%. Data showed a downward trend as the quality of the carbohydrates consumed increased, but statistical significance was not reached (Fully adjusted OR of the highest vs. the lowest CQI was: 0.90; 95% CI: 0.60, 1.36) (Table 3).

In addition, we assessed the association of CQI with the number of affected territories, interpreted as atherosclerosis extension

Table 1
Components and algorithm used to calculate the carbohydrate quality index.

Components of carbohydrate quality index	Index range (points) (4–15)	Scores according to the groups of the component (cut-off points)			
Dietary fiber intake (g/d)	1–4	G1 = 1 (0, 20.1]	G2 = 2 (20.1, 24.4]	G3 = 3 (24.4,29.3]	G4 = 4 (29.3, max)
Glycemic index	1–4	G1 = 4 (0, 48.8]	G2 = 3 (48.8,51.9]	G3 = 2 (51.9,54.0]	G4 = 1 (54.0, max)
Ratio of whole grains/total grains	1–3	G1 = 1 0		G2 = 2 (0,0.246]	G3 = 3 (0.246, max)
Ratio of solid carbohydrates/total carbohydrates	1–4	G1 = 1 (0, 0.947]	G2 = 2 (0.947,0.977]	G3 = 3 (0.977,0.996]	G4 = 4 (0.996, max)

Max = Maximum.

Table 2
Baseline characteristics of the AWHS participants according to the carbohydrate quality index categories.

N = 2074	Overall	Carbohydrate Quality Index				*p* for trend
		4-6 points	7-9 points	10-12points	13-15 points	
		n = 293	n = 941	n = 665	n = 175	
Age, years	50.9 (3.9)	50.4 (4.2)	51.0 (3.9)	51.0 (3.8)	50.9 (3.7)	0.183
White collar, %	11.7 [242]	9.2 [27]	10.4 [98]	14.3 [95]	12.6 [22]	0.022
BMI, kg/m^2	27.6 (3.3)	27.4 (3.4)	27.6 (3.2)	27.7 (3.3)	27.6 (3.5)	0.289
Waist circumference, cm	97.3 (8.8)	96.8 (8.9)	97.6 (8.7)	97.2 (9.0)	96.7 (9.0)	0.655
Systolic blood pressure, mm Hg	125.4 (13.9)	125.0 (13.3)	125.7 (13.7)	124.9 (14.1)	126.4 (15.4)	0.824
Diastolic blood pressure, mm Hg	82.4 (9.4)	82.5 (9.2)	82.6 (9.2)	82.0 (9.5)	82.7 (10.2)	0.636
Total cholesterol, mg/dl	220.1 (36.3)	220.6 (38.7)	218.9 (34.9)	221.9 (36.7)	219.0 (38.1)	0.607
HDL-c, mg/dl	53.0 (11.4)	52.0 (10.7)	51.9 (10.9)	54.6 (11.9)	54.8 (12.1)	<0.001
Non-HDL-c, mg/dl	167.1 (35.1)	168.6 (37.9)	166.9 (33.6)	167.3 (35.4)	164.2 (37.0)	0.331
LDL-c, mg/dl	137.9 (31.3)	137.6 (33.8)	137.2 (30.4)	138.7 (30.9)	138.9 (33.7)	0.406
Triglycerides, mg/dl	150.2 (97.2)	157.8 (92.2)	153.7 (104.9)	144.7 (87.0)	139.5 (98.3)	0.008
Fasting glucose, mg/dl	97.7 (17.5)	96.5 (16.7)	97.6 (18.1)	97.8 (16.4)	99.9 (19.4)	0.075
Ever-smokers, %	77.1 [1600]	81.2 [238]	78.0 [734]	74.4 [495]	76.0 [133]	0.031
Hypertension, %	37.4 [776]	34.8 [102]	37.7 [355]	37.3 [248]	40.6 [71]	0.325
Dyslipidemia, %	49.2 [1020]	49.1 [144]	48.5 [456]	49.0 [326]	53.7 [94]	0.426
Diabetes, %	5.6 [116]	5.1 [15]	5.6 [53]	4.8 [31]	9.1 [16]	0.318

BMI: body mass index; HDL-c: High-density lipoprotein cholesterol; Non-HDL-c: non-High-density lipoprotein cholesterol; LDL-c: Low-density lipoprotein cholesterol. Values are mean (standard deviation) or % [number]. P value for trend from unadjusted regression models.

Table 3
Association between the carbohydrate quality index categories and the presence of plaques in peripheral arteries in AWHS participants.

Participants (N = 2074)	Carbohydrate Quality Index				*p* for trend[b]
	4–6 points OR (95%CI)	7–9 points OR (95%CI)	10–12 points OR (95%CI)	13–15 points OR (95%CI)	
	293	941	665	175	
Femoral plaques, % (n)	60.4% (n = 177)	58.0% (n = 546)	54.6% (n = 363)	51.4% (n = 90)	
Age-adjusted	Ref.	0.84 (0.64, 1.11)	0.73 (0.55, 0.97)	0.64 (0.43, 0.94)	0.005
Multivariable-adjusted[a]	Ref.	0.84 (0.62, 1.11)	0.74 (0.54, 1.00)	0.59 (0.39, 0.89)	0.005
Carotid plaques, % (n)	36.5% (n = 107)	37.7% (n = 355)	35.2% (n = 234)	36.0% (n = 63)	
Age-adjusted	Ref.	0.99 (0.75, 1.31)	0.89 (0.67, 1.20)	0.93 (0.62, 1.38)	0.280
Multivariable-adjusted[a]	Ref.	1.00 (0.75, 1.33)	0.90 (0.67, 1.23)	0.90 (0.60, 1.36)	0.271

AWHS, Aragon Workers' Health Study; OR, odds ratio; CI, confidence interval.
N, total number of participants; n, number of subjects with plaques.
[a] Adjusted for age, type of work (blue collar or white collar), BMI, smoking status (ever smoker or never smoker), hypertension, dyslipidemia, diabetes, total energy (Kcal/day), protein intake (g/day), total fat intake (g/day), alcohol intake (g/day), and total METs-h/week.
[b] *P* for trend is calculated using CQI as continuous variable.

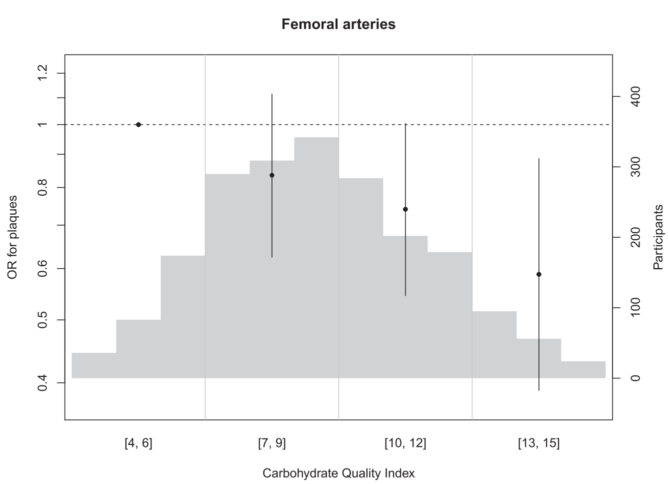

Fig. 1. Odds Ratios (95% Confidence Interval) for the presence of femoral plaques according to carbohydrate quality index categories.

(Supplemental Table 3). The mean count of affected territories decreases as CQI increased. In multivariable logistic regression models we found that the CQI was negatively associated with the presence of two affected territories (p for trend = 0.017). Although the presence of any atherosclerosis (one or more affected territories) showed a similar downward tendency in adjusted models, statistical significance was not reached in this case. This was further tested and proved with the most appropriate statistical modeling, which should be considered the conclusive test for this association, in an ordinal logistical regression model (p = 0.011).

Likewise, when we assess associations between CQI (with components scores in five groups, Supplemental Table 1) and presence of atheroma plaques, results obtained were similar on trend and significance (Supplemental Table 4, Supplemental Table 5, Supplemental Fig. 2). However, with this scoring, which was suboptimal for the variability in our sample, those response was not linear.

4. Discussion

In this study, we found a consistent and inverse association between the CQI and the presence of subclinical atherosclerosis in femoral territories. However, this association was not shown in the carotid territories, probably because, at the age of the participants, subclinical atherosclerosis appears more frequently in femoral arteries. Nonetheless, CQI was also associated with lower atherosclerosis extension. Thus, our results suggest that consuming carbohydrates from whole grains instead of foods from refined flours, those with a low glycemic index, consumed as a solid food, and associated with dietary fiber and reducing consumption of liquid carbohydrates and those with high glycemic index could potentially reduce the risk of subclinical atherosclerosis. These findings support the premise that the quality of dietary carbohydrates is likely to play an important role as a determinant of cardiovascular health.

Previously to the first definition of the CQI [22], its components had demonstrated significant clinical benefits in reducing the risk of CVD. In this sense, two meta-analyses [44,45] have shown that the consumption of dietary fiber, naturally present in fruit and vegetables, is inversely associated with the risk of coronary heart disease (CHD). Besides, other meta-analyses indicate that a high whole-grain intake has a protective effect against CHD [10], and it is associated with a reduced risk of all-cause mortality as well as CVD mortality [11]. Interestingly, the study of Steffen et al. [18] has shown a beneficial effect of whole-grains and both fruit and vegetable consumption on the risk of all-cause mortality and incident coronary artery disease, but not on ischemic stroke. Also, the study of Juan et al. [13] observed that the consumption of whole-grains was not associated with a reduction in ischemic stroke, although a high consumption of whole-grain cold breakfast cereal and bran decreased this risk. Finally, Livesey et al. [16], showed a relationship between the GI and CHD risk with a relative risk of 1.24 per each 10 U GI increase.

Several studies have assessed the effects of different components of the CQI in the development of atherosclerosis, when studying the early steps in the natural history of CVD. With regard to this, Mellen et al. [19] showed an inverse association between whole-grain intake and the carotid intima media thickness. Furthermore, Erkkilä et al. [17] demonstrated that the progression of coronary atherosclerosis was slowed down by a high intake of cereal fiber as well as whole-grain products in postmenopausal females, with established coronary artery disease. The association between the GI and atherosclerosis is more controversial. Some studies, like those carried out by Choi et al. [46] and Peng et al. [21], have shown a direct relationship between the GI and carotid stenosis, or coronary artery calcium. However, Goñi et al. [20] showed no association between the GI and the carotid intima media thickness. Likewise, Dearborn et al. showed no association between the GI and high-risk plaque features. In addition, the relationship between the GI and the maximum wall thickness was described as non-linear.

The association between CQI and atherosclerosis may stem from the effects that some quality aspects of dietary carbohydrates have on the traditional cardiovascular risk factors, although evidence is sparse beyond the diabetes realm. Two studies have shown how a high GI diet unfavorably affected CVD risk factors and therefore, the substitution of a high with a low GI dietary carbohydrates may reduce the risk of CVD [14,15]. Additionally, a recent systematic review and meta-analysis [47] concluded that the consumption of a high intake of dietary fiber or whole grains was associated with a reduced incidence of type 2 diabetes.

The study of Zazpe et al. [22] defined the CQI in literature for the first time, allowing scientist to compare participants with different carbohydrate quality intakes. This index has allowed to identify important associations in participants with high quality intake of carbohydrates. In the SUN project, among a Mediterranean cohort of 17,424 middle-aged adults, a higher CQI showed a significant inverse association with CVD incidence. This study also found that participants in the higher CQI and with more than 50% of energy intake coming from carbohydrates had the lowest risk of CVD [23]. In early stages of CVD development, the impact of a high adherence to CQI and specific cardiovascular risk factors have already been reported. The KNHANES survey showed an inverse association between a high CQI and the prevalence of traditional CVD risk factors like obesity and hypertension [25]. In addition, the PREDIMED-Plus randomized trial found that, after 12 months, improvements in CQI were strongly associated with concurrent favorable CVD risk factor changes, which persisted over time in overweight/obese adults with metabolic syndrome. Blood pressure, fasting blood glucose, and glycated hemoglobin, as well as triglycerides levels, all decreased as the CQI improved. Additionally, HDL-c levels showed significant increases as CQI changes improved [24]. However, the relationship between the CQI and subclinical atherosclerosis had not yet been studied, and presently there are no former studies focusing on femoral arteries.

Our findings extend the knowledge of the benefits of a high CQI on CVD events, showing benefits in the early stages of the atherosclerosis process. Atherosclerosis develops throughout our lifespan, from childhood to adulthood [48], and the quality of carbohydrates is already relevant from middle age onwards. The CQI association could be confirmed statistically with femoral plaques while only a mild association tendency appeared with carotid plaques. This is probably due to the age range of our sample, which is mainly composed of middle-aged men. When middle aged, subclinical atherosclerosis appears primarily in the femoral arteries, where, in addition, atherosclerosis is more strongly associated with known CVD risk factors [28,29].

Finally, this evidence provides grounds for specific recommendations on improving dietary carbohydrates quality in CVD primary prevention campaigns. CQI could also be used to inform about poor quality diets, to encourage specific qualitative changes in diets, as well as to monitor the success of these changes. Therefore, public health dietary recommendations should include improving the quality of dietary carbohydrates, rather than only limiting their intake quantity. In addition, it is worthwhile educating the general public to the benefits of food with high-quality carbohydrates, while at the same time, being able to identify this food.

Our study has several strengths, among which having been carried out with standardized protocols stands out. The study also used high-quality data collection methods to obtain information on subclinical atherosclerosis, both in femoral as well as carotid territories. However, it has also several limitations. First, the cross-sectional design does not allow to establish causality nor the temporality of the associations found, although in this case, dietary intake was not modified by the presence of subclinical disease. Second, our sample of females is too small to analyze separately, so we only included a middle-aged male sample. In addition, this is a sample of working men who all work in the same car assembly plant, thus, the results may not be directly generalized to other populations. Third, although the dietary assessment was conducted using FFQ by trained interviewers, we cannot rule out the presence of some misclassification [49]. However, the scientific literature supports that the FFQ is a feasible tool to evaluate food habits in epidemiological studies [34,50]. Fourth, even though we adjusted for the major potential confounders, residual confounding is still possible. Lastly, the use of the CQI could make the comparison with previous results difficult.

5. Conclusions

Our results suggest a protective effect of the consumption of high-quality carbohydrates on the presence of subclinical atherosclerosis in the femoral territory.

Sources of support

This study was supported in part by CIBERCV and grants PIE16/00022, PI18/01929, PI19/00020, PI19/00948 and PI20/00144 from the Instituto de Salud Carlos III (co-supported by the European

Regional Development Fund 'Investing in your future'). ML's research activity is funded by Agencia Aragonesa para la Investigación y el Desarrollo (ARAID).

Conflicts of interest

None.

Acknowledgements

The authors thank the study participants, doctors and healthcare professionals at the Opel factory. The authors also thank the AWHS technical staff.

The authors' contributions were as follows - AMC: Data curation, Writing-Original draft preparation, Writing - Review & Editing. ML: Methodology, Software, Formal analysis, Writing-Original draft preparation, Writing - Review & Editing. PGC: Conceptualization, Writing-Original draft preparation, Writing - Review & Editing. BMF: Conceptualization, Data curation, Writing-Original draft preparation, Writing - Review & Editing. PGC: Writing - Review & Editing. JAC: Writing - Review & Editing. EJ: Writing - Review & Editing. HSI: Writing - Review & Editing. CDV: Writing - Review & Editing.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clnu.2021.04.049.

References

[1] Mendis S, Puska P, Norrving B, World Health Organization. World heart federation, world stroke organization. In: Global atlas on cardiovascular disease prevention and control. Geneva: The World Health Organization in collaboration with the World Heart Federation and the World Stroke Organization; 2011.

[2] Roth GA, Johnson C, Abajobir A, Abd-Allah F, Abera SF, Abyu G, et al. Global, regional, and national burden of cardiovascular diseases for 10 causes, 1990 to 2015. J Am Coll Cardiol 2017;70:1–25. https://doi.org/10.1016/j.jacc.2017.04.052.

[3] World Health Organization. Global status report on noncommunicable diseases 2014. Geneva: World Health Organization; 2014.

[4] World Health Organization. Prevention of cardiovascular disease : guidelines for assessment and management of total cardiovascular risk. Geneva: World Health Organization; 2007. https://doi.org/10.1016/0091-7435(73)90043-1.

[5] Piepoli MF, Hoes AW, Agewall S, Albus C, Brotons C, Catapano AL, et al. European Guidelines on cardiovascular disease prevention in clinical practice. Eur Heart J 2016 2016;37:2315–81. https://doi.org/10.1093/eurheartj/ehw106.

[6] U.S. Department of Health and Human Services and U.S. Department of Agriculture. In: 2015-2020 dietary guidelines for Americans. 8th ed. Rockville, USA: U.S. Department of Health and Human Services and U.S. Department of Agriculture; 2015. https://doi.org/10.1097/NT.0b013e31826c50af.

[7] World Health Organization. Global action plan for the prevention and control of noncommunicable diseases 2013-2020. Geneva: World Health Organization; 2013. https://doi.org/9789241506236.

[8] Estruch R, Martínez-González MA, Corella D, Basora-Gallisá J, Ruiz-Gutiérrez V, Covas MI, et al. Effects of dietary fibre intake on risk factors for cardiovascular disease in subjects at high risk. J Epidemiol Community Health 2009;63:582–8. https://doi.org/10.1136/jech.2008.082214.

[9] Buil-Cosiales P, Martinez-Gonzalez MA, Ruiz-Canela M, Díez-Espino J, García-Arellano A, Toledo E. Consumption of fruit or fiber-fruit decreases the risk of cardiovascular disease in a mediterranean young cohort. Nutrients 2017;9:1–13. https://doi.org/10.3390/nu9030295.

[10] Tang G, Wang D, Long J, Yang F, Si L. Meta-analysis of the association between whole grain intake and coronary heart disease risk. Am J Cardiol 2015;115:625–9. https://doi.org/10.1016/j.amjcard.2014.12.015.

[11] Zhang B, Zhao Q, Guo W, Bao W, Wang X. Association of whole grain intake with all-cause, cardiovascular, and cancer mortality: a systematic review and dose-response meta-analysis from prospective cohort studies. Eur J Clin Nutr 2018;72:57–65. https://doi.org/10.1038/ejcn.2017.149.

[12] Helnæs A, Kyrø C, Andersen I, Lacoppidan S, Overvad K, Christensen J, et al. Intake of whole grains is associated with lower risk of myocardial infarction: the Danish Diet, Cancer and Health Cohort. Am J Clin Nutr 2016;103:999–1007. https://doi.org/10.3945/ajcn.115.124271.

[13] Juan J, Liu G, Willett WC, Hu FB, Rexrode KM, Sun Q. Whole grain consumption and risk of ischemic stroke results from 2 prospective cohort studies. Stroke 2017;48:3203–9. https://doi.org/10.1161/STROKEAHA.117.018979.

[14] Barclay AW, Petocz P, McMillan-Price J, Flood VM, Prvan T, Mitchell P, et al. Glycemic index, glycemic load, and chronic disease risk - a metaanalysis of observational studies. Am J Clin Nutr 2008;87:627–37. https://doi.org/10.1093/ajcn/87.3.627.

[15] McKeown NM, Meigs JB, Liu S, Rogers G, Yoshida M, Saltzman E, et al. Dietary carbohydrates and cardiovascular disease risk factors in the framingham offspring cohort. J Am Coll Nutr 2009;28:150–8. https://doi.org/10.1080/07315724.2009.10719766.

[16] Livesey G, Livesey H. Coronary heart disease and dietary carbohydrate, glycemic index, and glycemic load: dose-response meta-analyses of prospective cohort studies. Mayo Clin Proc Innov Qual Outcomes 2019;3:52–69. https://doi.org/10.1016/j.mayocpiqo.2018.12.007.

[17] Erkkilä AT, Herrington DM, Mozaffarian D, Lichtenstein AH. Cereal fiber and whole-grain intake are associated with reduced progression of coronary-artery atherosclerosis in postmenopausal women with coronary artery disease. Am Heart J 2005;150:94–101. https://doi.org/10.1016/j.ahj.2004.08.013.

[18] Steffen LM, Jacobs DR, Stevens J, Shahar E, Carithers T, Folsom AR. Associations of whole-grain, refined-grain, and fruit and vegetable consumption with risks of all-cause mortality and incident coronary artery disease and ischemic stroke: the Atherosclerosis Risk in Communities (ARIC) study. Am J Clin Nutr 2003;78:383–90. https://doi.org/10.1093/ajcn/78.3.383.

[19] Mellen PB, Liese AD, Tooze JA, Vitolins MZ, Wagenknecht LE, Herrington DM. Whole-grain intake and carotid artery atherosclerosis in a multiethnic cohort: the Insulin Resistance Atherosclerosis Study. Am J Clin Nutr 2007;85:1495–502. https://doi.org/10.1093/ajcn/85.6.1495.

[20] Ruiz NG, Martínez González MÁ, Salvadó JS, Cosiales PB, Espino JD, Vila EM, et al. Association between dietary glycemic index and glycemic load and intima media thickness in a population at high cardiovascular risk: a subgroup analysis in the predimed trial. Nutr Hosp 2015;32:2319–30. https://doi.org/10.3305/nh.2015.32.5.9650.

[21] Peng M, Li X, Liu Y, Zou M, Xia Y, Xu G. Dietary glycemic index and glycemic load in relation to atherosclerotic stenosis of carotid and cardiovascular risk factors in ischemic stroke patients. J Atherosclerosis Thromb 2020:1–8. https://doi.org/10.5551/jat.53843.

[22] Zazpe I, Sánchez-Taínta A, Santiago S, De La Fuente-Arrillaga C, Bes-Rastrollo M, Martínez JA, et al. Association between dietary carbohydrate intake quality and micronutrient intake adequacy in a Mediterranean cohort: the SUN (Seguimiento Universidad de Navarra) project. Br J Nutr 2014;111:2000. https://doi.org/10.1017/S0007114513004364. 9.

[23] Zazpe I, Santiago S, Gea A, Ruiz-Canela M, Carlos S, Bes-Rastrollo M, et al. Association between a dietary carbohydrate index and cardiovascular disease in the SUN (Seguimiento Universidad de Navarra) Project. Nutr Metabol Cardiovasc Dis 2016;26:1048–56. https://doi.org/10.1016/j.numecd.2016.07.002.

[24] Martínez-González MA, Fernandez-Lazaro CI, Toledo E, Díaz-López A, Corella D, Goday A, et al. Carbohydrate quality changes and concurrent changes in cardiovascular risk factors: a longitudinal analysis in the PREDIMED-Plus randomized trial. Am J Clin Nutr 2019:1–16. https://doi.org/10.1093/ajcn/nqz298.

[25] Kim DY, Kim SH, Lim H. Association between dietary carbohydrate quality and the prevalence of obesity and hypertension. J Hum Nutr Diet 2018;31:587–96. https://doi.org/10.1111/jhn.12559.

[26] Herrington W, Lacey B, Sherliker P, Armitage J, Lewington S. Epidemiology of atherosclerosis and the potential to reduce the global burden of atherothrombotic disease. Circ Res 2016;118:535–47. https://doi.org/10.1161/CIRCRESAHA.115.307611.

[27] Frostegård J. Immunity, atherosclerosis and cardiovascular disease. BMC Med 2013;11:117. https://doi.org/10.1186/1741-7015-11-117.

[28] Laclaustra M, Casasnovas JA, Fernández-Ortiz A, Fuster V, León-Latre M, Jiménez-Borreguero LJ, et al. Femoral and carotid subclinical atherosclerosis association with risk factors and coronary calcium: the AWHS study. J Am Coll Cardiol 2016;67:1263–74. https://doi.org/10.1016/j.jacc.2015.12.056.

[29] Fernández-Friera L, Peñalvo JL, Fernández-Ortiz A, Ibañez B, López-Melgar B, Laclaustra M, et al. Prevalence, vascular distribution, and multiterritorial extent of subclinical atherosclerosis in a middle-aged cohort the PESA (Progression of Early Subclinical Atherosclerosis) study. Circulation 2015;131:2104–13. https://doi.org/10.1161/CIRCULATIONAHA.114.014310.

[30] Casasnovas JA, Alcalde V, Civeira F, Guallar E, Ibañez B, Jimenez Borreguero J, et al. Aragon workers ' health study – design and cohort description. BMC Cardiovasc Disord 2012;12. https://doi.org/10.1186/1471-2261-12-45.

[31] Muntendam P, Mccall C, Sanz J, Falk E, Fuster V. The BioImage Study : novel approaches to risk assessment in the primary prevention of atherosclerotic cardiovascular disease — study design and objectives. Am Heart J 2010;160:49–57. https://doi.org/10.1016/j.ahj.2010.02.021. e1.

[32] Junyent M, Gilabert R, Zambón D, Pocoví M, Mallén M, Cofán M, et al. Femoral atherosclerosis in heterozygous familial hypercholesterolemia influence of the genetic defect. Arterioscler Thromb Vasc Biol 2008;28:580–6. https://doi.org/10.1161/ATVBAHA.107.153841.

[33] Inaba Y, Chen JA, Bergmann SR. Carotid plaque , compared with carotid intima-media thickness , more accurately predicts coronary artery disease events : a meta-analysis. Atherosclerosis 2012;220:128–33. https://doi.org/10.1016/j.atherosclerosis.2011.06.044.

[34] Martin-Moreno JM, Boyle P, Gorgojo L, Mainsonneuve P, Fernandez-Rodriguez JC, Salvini S, et al. Development and validation of a food frequency questionnaire. Int J Epidemiol 1993;22:512–9.
[35] Moreiras O, Carvajal A, Cabrera L, Cuadrado C. Tablas de composición de alimentos. Madrid: Pirámide; 2011.
[36] Mataix J. Tabla de composición de alimentos (Food composition tables). Granada: Universidad de Granada; 2003.
[37] Moreiras O, Carvajal A, Cabrera L, Cuadrado C. Tablas de composición de alimentos. 19th editi. Madrid: Pirámide; 2018.
[38] Pearson TA, Palaniappan LP, Artinian NT, Carnethon MR, Criqui MH, Daniels SR, et al. American Heart Association Guide for Improving Cardiovascular Health at the Community Level , 2013 Update: a scientific statement for public health practitioners, healthcare providers, and health policy makers. Circulation 2013;127:1730–53. https://doi.org/10.1161/CIR.0b013e31828f8a94.
[39] Third report of the national cholesterol education program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III) final report. 2002. vol. 106.
[40] Martínez-González MA, López-Fontana C, Varo JJ, Sánchez-Villegas A, Martinez A. Validation of the Spanish version of the physical activity questionnaire used in the Nurses ' health study and the health professionals ' follow-up study. Publ Health Nutr 2005;8:920–7. https://doi.org/10.1079/PHN2005745.
[41] Chasan-Taber S, Rimm EB, Stampfer MJ, Spiegelman D, Colditz GA, Giovannucci E, et al. Reproducibility and validity of a self-administered physical activity questionnaire for male health professionals. Epidemiology 1996;7.
[42] Wolf AM, Hunter DJ, Colditz GA, Manson JE, Stampfer MJ, Corsano KA, et al. Reproducibility and validity of a self-administered physical activity questionnaire. Int J Epidemiol 1994;23:991–9.
[43] Ainsworth BE, Haskell WL, Herrmann SD, Meckes N, Jr DRB, Tudor-locke C, et al. Compendium of physical activities: a second update of codes and met values. Med Sci Sports Exerc 2011 2011;43:1575–81. https://doi.org/10.1249/MSS.0b013e31821ece12.
[44] Gan Y, Tong X, Li L, Cao S, Yin X, Gao C, et al. Consumption of fruit and vegetable and risk of coronary heart disease: a meta-analysis of prospective cohort studies. Int J Cardiol 2015;183:129–37. https://doi.org/10.1016/j.ijcard.2015.01.077.
[45] Wu Y, Qian Y, Pan Y, Li P, Yang J, Ye X, et al. Association between dietary fiber intake and risk of coronary heart disease: a meta-analysis. Clin Nutr 2015;34:603–11. https://doi.org/10.1016/j.clnu.2014.05.009.
[46] Choi Y, Chang Y, Ryu S, Cho J, Kim MK, Ahn Y, et al. Relation of dietary glycemic index and glycemic load to coronary artery calcium in asymptomatic Korean adults. Am J Cardiol 2015;116:520–6. https://doi.org/10.1016/j.amjcard.2015.05.005.
[47] Reynolds A, Mann J, Cummings J, Winter N, Mete E, Te Morenga L. Carbohydrate quality and human health: a series of systematic reviews and meta-analyses. Lancet 2019;393:434–45. https://doi.org/10.1016/S0140-6736(18)31809-9.
[48] Mendis S, Nordet P, Fernandez-Britto JE, Sternby N. Atherosclerosis in children and young adults: an overview of the world health organization and international society and federation of cardiology study on pathobiological determinants of atherosclerosis in youth study (1985-1995). Prev Contr 2005;1:3–15. https://doi.org/10.1016/j.precon.2005.02.010.
[49] Michels KB. A renaissance for measurement error. Int J Epidemiol 2001;30:421–2. https://doi.org/10.1093/ije/30.3.421.
[50] Hu FB, Rimm E, Smith-Warner SA, Feskanich D, Stampfer MJ, Ascherio A, et al. Reproducibility and validity of dietary patterns assessed with a food- frequency questionnaire. Am J Clin Nutr 1999;69:243–9. https://doi.org/10.1093/ajcn/69.2.243.