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Original article

Longitudinal association of dietary carbohydrate quality with visceral fat deposition and other adiposity indicators

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SUMMARY

Background & aims: The quality of dietary carbohydrates rather than total carbohydrate intake may determine the accumulation of visceral fat; however, to date, few studies have examined the impact of diet on adiposity using specific imaging techniques. Thus, the aim of this prospective study was to investigate the association between concurrent changes in carbohydrate quality index (CQI) and objectively-quantified adiposity distribution over a year.
Methods: We analyzed a cohort of 1476 participants aged 55–75 years with overweight/obesity and metabolic syndrome (MetS) from the PREDIMED-Plus randomized controlled trial. Dietary intake information was obtained at baseline, 6- and 12-months from a validated 143-item semi-quantitative food-frequency questionnaire, and CQI (range: 4 to 20) was calculated based on four dietary criteria: total dietary fibre, glycemic index, wholegrain/total grain carbohydrate ratio, and solid/total carbohydrate ratio. Overall and regional adiposity (total body fat, visceral fat and android-to-gynoid fat ratio) was quantified using dual-energy X-ray absorptiometry at all three time points. Multiple adjusted linear

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mixed-effects models were used to assess associations between concurrent changes in repeatedly measured CQI and adiposity over time.

Results: After controlling for potential confounding factors, a 3-point increment in CQI over 12-month follow-up was associated with a decrease in visceral fat (β −0.067 z-score, 95% CI -0.088; −0.046, p < 0.001), android-to-gynoid fat ratio (−0.038, −0.059; −0.017, p < 0.001), and total fat (−0.064, −0.080; −0.047, p < 0.001). Fibre intake and the ratio of wholegrain/total grain showed the strongest inverse associations with all adiposity indicators.

Conclusions: In this prospective cohort of older adults with overweight/obesity and MetS, we found that improvements in dietary carbohydrate quality over a year were associated with concurrent favorable changes in visceral and overall fat deposition. These associations were mostly driven by dietary fibre and the wholegrain/total grain ratio.

Trial registration: The trial was registered at the International Standard Randomized.

Controlled trial: (ISRCTN: http://www.isrctn.com/ISRCTN89898870) with number 89898870 and registration date of 24 July 2014, retrospectively registered.

1. Introduction

Obesity prevalence is increasing worldwide [1] and has been widely associated with a range of serious metabolic and cardiovascular diseases (CVD), among others [2]. At the same time, abdominal obesity, measured by waist circumference, a proxy of visceral fat, is increasing at an even greater rate than overall obesity alone [3]. In this sense, it seems that excess visceral fat, which appears with increasing age [4,5] but also with unhealthy dietary patterns [6,7] and lifestyle behaviors [8], could be an important contributor to chronic diseases, particularly type 2 diabetes (T2D), insulin resistance [9], metabolic syndrome (MetS) [10], and CVD [11].

It is well known that diet plays a role in body fat accumulation [12,13]; however, recent evidence indicates that, beyond quantity, the quality of certain nutrients may have an independent effect [3,14]. Intake of high quality dietary carbohydrates, characterized by individual indicators, such as fibre-rich foods (wholegrains, pulses and fruit) and a low glycemic index and glycemic load [14,15], has been associated with a lower risk of overweight/obesity [16,17] and cardiometabolic diseases [14,17], as well as reduced visceral fat in adults [3,6,7]. Thus, it seems that combined effects of carbohydrate quality domains could be a better determinant of health than carbohydrate quantity alone, warranting for further understanding of its role in body fat deposition.

The carbohydrate quality index (CQI) was proposed in 2015 by the “Seguimiento University of Navarra” (SUN) cohort as a dietary quality metric which integrates four different dimensions (glycemic index, fibre intake, the degree of carbohydrate processing, and solid or liquid form) [16]. However, so far, only a few studies have used this multidimensional approach to evaluate the link between carbohydrate quality and health outcomes [3,17–21]. In a recent longitudinal analysis in the PREDIMED-Plus study evaluated as a cohort, a higher CQI was associated with decreased body weight and waist circumference, as well as with an improvement in a range of cardiovascular risk factors in overweight/obese adults with MetS [18]. Moreover, similar results have been reported in other studies [16,19], whereby an inverse association between dietary CQI and both overall and abdominal obesity was reported. However, only a few studies have been published in which the impact of dietary factors on adiposity was directly measured using imaging techniques [6,7,22].

Thus, in this study we aimed to carry out a prospective analysis of a subset of participants in the PREDIMED-Plus trial to determine the dynamic association between changes in overall dietary carbohydrate quality and changes in objectively-measured visceral and overall adiposity distribution, using three repeated measurements of diet and adiposity throughout a 1-year follow-up time.

2. Methods

2.1. Study design

This prospective cohort study is based on data collected during the first year of the PREDIMED-Plus (PREvención con DIeta MEDiterránea Plus) randomized controlled trial (RCT). The trial's design and methods have been previously described elsewhere [23–25] and are available at http://predimedplus.com. Briefly, the PREDIMED-Plus is a 6-year parallel-group, multicenter and CVD primary prevention trial ongoing in Spain. The aim of the trial is to assess the effects of an intensive weight-loss intervention (intervention group) based on an energy-reduced (er) Mediterranean Diet (MedDiet), physical activity (PA) promotion, and behavioral support on the prevention of CVD events, in comparison to usual care and dietary counselling only with an energy-unrestricted MedDiet (control group). The PREDIMED-Plus study protocol was approved by the Research Ethic Committees from all the participating centers and the trial was registered at the International Standard Randomized Controlled Trial (ISRCTN) with the code 89898870.

2.2. Study population

For the PREDIMED-Plus trial, participants were recruited between September 2013 and December 2016 in 23 centers all over Spain. A total of 6874 people met the eligibility criteria and were randomly allocated in a 1:1 ratio to either the intervention or control group, using a computer-based system with stratification by center, sex, and age. Couples sharing the same household were randomized together, and the couple was used as a unit of randomization. Eligible participants were older adults of both genders (men aged 55–75 years and women 60–75 years) without previous cardiovascular events, who were overweight or obese (BMI ≥ 27 kg/m^2 and <40 kg/m^2) and met at least three characteristics of the MetS: hypertension, hypertriglyceridemia, lower high-density lipoprotein (HDL) cholesterol, hyperglycemia, or central obesity [26]. All participants provided written informed consent.

The current analysis encompasses a subsample of participants who underwent dual-energy X-ray absorptiometry (DXA) scans for body composition assessment in 7 recruiting centers which had access to a DXA scanner at baseline (n = 1569). Within each center, all participants, or a random sub-sample (depending on the center), were invited for DXA scans. The size of the difference between participants with DXA measurements and rest of the participants enrolled in the PREDIMED-Plus trial (n = 5305) in terms of principal socio-demographic, health-related and lifestyle factors was relatively low (relative differences between included and non-included subjects <10%). However, participants who underwent DXA were somehow more physically active (relative difference = 11.9%), although the size of the difference for the measure of physical fitness (chair-stand test) was low between both groups (relative difference <10%) (Supplementary Table 1).

For this analysis, the following exclusion criteria were considered: missing data on variables of interest at baseline (n = 49) and values of total energy intake outside the ranges previously proposed by Willett [27] (<500 or >3500 kcal for women, <800 or >4000 kcal for men) at baseline and follow-up (n = 44). Finally, a total of 1476 participants were included in the final analyses. A flowchart detailing participants' selection and the exclusion criteria is shown in Supplementary Fig. 1.

2.3. Dietary assessment and carbohydrate quality index

Participants' dietary intake was assessed at baseline and during follow-up (at 6 and 12 months) during face-to-face interviews conducted by trained dietitians-nutritionists using the Spanish version of the validated 143-item semiquantitative Food-Frequency Questionnaire (FFQ) [28,29]. The average intake of each item (foods and beverages) was calculated by multiplying a common portion size by frequency of consumption (9 possible responses ranging from never to >6 times/day). Spanish food composition tables [30] were used to derive nutrients (including total carbohydrates, protein, fat and fat subtypes), fibre, alcohol (all in g/d) and total energy intake (kcal/day), as well as to determine consumption of specific food groups. The glycemic index of the diet was also estimated as the glycemic load of the diet multiplied by 100 and divided by the grams of total carbohydrates consumed per day. For this, the glycemic load of the diet was calculated by summing the glycemic loads of individual FFQ items, which were calculated by multiplying the known amount of available carbohydrate contained in the specified serving size of each item by the glycemic index values of that item from the International Tables of Glycemic Index [31] (with glucose as the reference food) and then divided by 100. The intake of foods obtained from FFQ was also used to calculate consumption of ultra-processed foods (UPF) according to NOVA classification system [32]. In addition, adherence to the erMedDiet was assessed using the validated 17-point score [33]. This questionnaire includes a few items to better capture the potential caloric restriction that should be applied to a MedDiet pattern as a means for weight loss.

Dietary intake information obtained from the FFQ was used to calculate the CQI, as previously described in the SUN and the PREDIMED-Plus cohorts [16,18,34]. This index is constructed based on the following four dietary criteria: total dietary fibre intake (g/d), glycemic index of the diet, wholegrain/total grain carbohydrate ratio, and solid/total carbohydrate ratio. To estimate total grains consumption, we summed up items containing wholegrains and their derived products (bread, rice, pasta, muesli and cookies), and refined grains and their derived products (white bread, breakfast cereals, rice, pasta, pizza, cookies and pastries). Liquid carbohydrates included milk and milkshakes, gazpacho, sugar-sweetened beverages and fruit juices, coffee and tea, and alcoholic drinks, whereas solid carbohydrate intake included the rest of the carbohydrates contained in solid foods. Ratio of solid carbohydrate/total carbohydrate was calculated as solid carbohydrates/(solid carbohydrates + liquid carbohydrates), and the ratio of wholegrain/total grain carbohydrate was calculated as wholegrains/(wholegrains + refined grains or their products). For each of these four dietary criteria, participants were categorized into quintiles. Each quintile received a value ranging from 1 to 5 (1 point for the first quintile to 5 points for the fifth quintile, except for the glycemic index, which was inversely weighted). Finally, all values were summed up to construct the CQI (ranging from 4 to 20), where higher values represent better carbohydrate quality.

2.4. Adiposity assessment

The study outcomes were adiposity depots quantified directly using DXA at baseline, 6 and 12 months. Participants underwent whole-body scans to obtain data on overall and regional (android and gynoid region) body composition (fat, lean and bone mass). Third-generation DXA scanners from General Electric (DXA Lunar Prodigy Primo and Lunar iDXA; GE Healtcare, Madison, WI) connected with enCore™ software were used by trained operators. DXA scans, including subject positioning and daily phantom calibration, were performed following manufacturer guidelines. We focused on visceral fat and android-to-gynoid ratio, as we previously found in the same sample of subjects that these indicators are better in predicting cardiometabolic risk than anthropometry and other DXA-derived parameters [35]. In order to determine visceral fat mass within the android region, scans were re-analyzed using the validated CoreScan software application (GE Healthcare) [36]. CoreScan uses algorithms that work through automated detection of the width of the subcutaneous fat layer on the lateral part of the abdomen and the anterior–posterior thickness of the abdomen, by x-ray attenuation of the abdominal cavity in the android region. The android-to-gynoid fat ratio was calculated by dividing the fat mass (g) from the specific regions. Total body fat is expressed as a % of the DXA-derived total body mass (sum of total bone, fat and muscle mass (g)).

2.5. Covariables assessment

At baseline, participants filled out a general questionnaire to provide information on socio-demographics, lifestyle and clinical conditions. Three categories were constructed to determine educational level (higher education or technician, secondary education, primary education or less) and smoking habits (current, never, ex-smoker), whereas history of overweight was categorized into five groups (during childhood, adolescence, adulthood, after childbirth, at menopause). Marital status was dichotomized into married or all others (including single, separated, widow (er) and divorced). Prevalence of T2D was used as a dichotomous variable (yes or no). Current type 2 diabetes was defined as previous diagnosis of diabetes, glycated hemoglobin (HbA1c) $\geq$ 6.5%, use of antidiabetic medication, or having fasting glucose >126 mg/dL in both the screening and baseline visit.

At baseline and at each follow-up visit, participants' height and weight were measured in light clothes and without shoes in duplicate (the average value was used for analysis) by trained staff using a wall-mounted stadiometer and calibrated scales, respectively. The BMI was calculated as weight (kg)/height (m) squared. Waist circumference (cm) was determined midway between the lowest rib and the iliac crest using a measuring tape. At each visit, questionnaires previously validated in the Spanish population were used to determine moving behaviors: the Minnesota-REGICOR short physical activity questionnaire [37] was used to collect data on leisure-time physical activity (PA) and the Nurses' Health Study questionnaire [38] determined sedentary behavior (SB). Total PA (metabolic equivalent of tasks (METs) min/week) and time spend on total SB (h/day) were computed as previously described [8].

2.6. Statistical analysis

Means and standard deviations (SD) for continuous variables, and numbers and percentages (%) for categorical variables were calculated for descriptive analysis of the participants' socio-demographic, lifestyle and health-related characteristics. Differences in characteristics by sex-specific tertiles of dietary CQI were evaluated applying one-way ANOVA or X^2 test, as appropriate.

Linear mixed-effects models were used to assess associations between CQI (independent variable) and each adiposity indicator (dependent variables normalized into a sex-specific z-scores), both measured every 6 months over the first year of follow-up. We fitted a 3-level mixed linear model with random intercepts at recruiting center, cluster family and participant level. The CQI was evaluated as continuous (per 3-point increment, equivalent of SD at baseline) and using sex-specific tertiles, with the first tertile (T1, lowest CQI) as the reference category. Tests for linear trend across tertiles of CQI were performed by modelling the median value of each tertile category as continuous variable. Models were initially minimally adjusted for age, sex, study arm (control or intervention) and follow-up time (0, 6 or 12 months). Furthermore, models were adjusted for baseline educational level, marital status, smoking, T2D prevalence (all categorical), height, as well as repeatedly measured PA, SB, total energy and alcohol intake (all continuous). Covariates were selected using a causal directed acyclic graph approach (Supplementary Fig. 2) implemented in the DAGitty free web application [39]. Additionally, in order to ascertain the real magnitude of changes, the main analyses were rerun with all adiposity indicators expressed in absolute values.

To assess the robustness of our findings, several sensitivity analyses were performed using a multivariable-adjusted model. Models were additionally adjusted for repeatedly measured intake of carbohydrates (g/day), in order to check whether our associations occurred beyond carbohydrates quantity. The potential influence of factors related to diet quality was addressed by an additional and simultaneous adjustment for repeatedly measured intake (g/day) of monounsaturated fatty acids (FA), polyunsaturated FA, saturated FA and trans FA, and protein; or adjustment in separate models either for adherence to erMedDiet or UPF consumption (all continuous variables). We also rerun the models after excluding total energy intake. To potentially attenuate reverse causality bias, we controlled for several health-related conditions by further adjustment of our multivariable-adjusted model used in main analysis for the number of MetS criteria diagnosed at inclusion (continuous), as well as for history of overweight, which was self-reported at baseline (categorical). Furthermore, models were additionally adjusted for repeatedly measured total fat mass (absolute value) and body weight, in order to assess the association of CQI on regional fat distribution independently of overall fat. Finally, we ran the model in which the missing follow-up data on repeatedly measured variables was imputed using the last observation carried forward (LOCF) method, which consists on replacement of a missing value by per subject previously observed value. Number of missing data in outcome variables was ~33% at 6-month and ~21% at 12-month visit, due to failure to attend the DXA.

Potential effect modification by baseline categories of age (<66 or ≥66 years), sex (men or women), study arm (control or intervention), T2D prevalence (yes or no), overall obesity (obese when BMI ≥30 kg/m^2 or overweight when BMI <30 kg/m^2), abdominal obesity (yes if waist circumference ≥102 cm (men) and ≥88 cm (women) or no), PA (<2098 or ≥2098 METs min/week), SB (very sedentary ≥6 h/day or not very sedentary <6 h/day), and carbohydrates intake (<232 or ≥232 g/day) was explored by modeling multiplicative interaction term between these variables and CQI (continuous). Median values were used for categories of age, PA, SB, and carbohydrates intake. Analyses were performed separately within each stratum when a significant interaction was detected.

Lastly, some additional analyses were performed. We tested association for adiposity indicators using two CQI alternatives. For this purpose, CQI was recalculated interchanging the ratio of solid/total carbohydrate by intake of sugar-sweetened beverages (sweetened soft drinks and commercial fruit juices (g/day)) or the ratio of wholegrain/total grain carbohydrate by intake of wholegrains (g/day). Furthermore, we checked whether the associations varied depending on baseline CQI values (low − below the median, or high − at or above the median) and CQI change over a year (<median change or ≥median change in CQI). For that, we constructed a 4-category CQI variable based on the levels of CQI at baseline and CQI change at 1 year.

We also evaluated the associations between concurrent changes in each CQI component (in quintiles) and all adiposity outcomes (sex-specific z-scores). For these analyses, multivariable-adjusted models were used, and tests for linear trend across quintiles of each component were performed by modelling the median value of each quintile category as continuous variable. These models were additionally run after mutual adjustment for the individual components of the CQI (as categorical variables in quintiles).

Statistical analyses were performed using Stata v15.0 program, and statistical significances was set at $p < 0.05$. We used the PREDIMED-Plus longitudinal database generated on the 22nd December 2020.

3. Results

Characteristics of participants at baseline, 6 and 12 months' follow-up can be found in Supplementary Table 2. The baseline subsample encompassed 701 (47.5%) women and 775 (52.5%) men with a mean age of 65.3 years (SD 5.0 years), and with highly prevalent overall obesity (74.9%) and abdominal obesity (93.4%). On average, the CQI value was of 11.8 (SD 3.4) at baseline. Over the follow-up period, improvements in body composition and lifestyle factors were observed compared to baseline data (both study arms combined) ($p < 0.05$ for all). Slightly higher CQI ($p = 0.024$) was observed at both the 6 and 12 month follow-up. Statistically significant differences were observed over time in all CQI components, although the most relevant changes in magnitude were the increase in consumption of carbohydrates proceeding from wholegrains and a decrease in refined grains, as well as an increase in dietary fibre intake. A slight change was observed for the ratio of solid to total carbohydrates.

Baseline socio-demographic, lifestyle and health-related characteristics of participants according to baseline sex-specific tertiles of CQI are shown in Table 1. Participants with the highest CQI (T3, mean CQI 15.9 (SD 1.4)) were less likely to be active smokers and more highly educated, compared to those with the lowest CQI (T1, mean CQI 8.3 (SD 1.6)). They also showed healthier lifestyle, in terms of higher energy consumed from unsaturated FA, but lower from trans FA, lower intake of alcohol, lower consumption of UPF, and being more adherent to MedDiet and physically active. All indicators of carbohydrate quality improved across the successive tertiles of CQI; however, no significant differences in the intake of total carbohydrates were observed across tertiles of CQI. In addition, participants in the highest tertile had lower visceral and total fat mass and higher lean mass. Interestingly, in the analysis by sex (Supplementary Table 3), only mass of visceral fat improved across the successive tertiles of CQI in men and women, although without reaching statistical significance.

The main associations between concurrent changes in CQI and fat distribution are shown in Table 2. In a multivariable-adjusted model, a 3-point increment in CQI (equivalent to SD at baseline) was associated with a decrease in visceral fat (β −0.067 z-score, 95% CI -0.088;-0.046, $p < 0.001$), android-to-gynoid fat ratio (−0.038, −0.059;-0.017, $p < 0.001$), and total fat (−0.064, −0.080;-0.047, $p < 0.001$) during 12-month follow-up. Furthermore, the comparison of the highest versus the lowest tertiles of CQI (Table 2)

Table 1
Baseline characteristics of study participants according to baseline sex-specific tertiles of CQI.

	Total	Tertiles of CQI			p-value
		T1 (low)	T2 (medium)	T3 (high)	
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	
n	1476	550	501	425	
Socio-demographic factors					
Women, n (%)	701 (47.5)	291 (52.9)	187 (37.3)	223 (52.5)	<0.001
Age (years)	65.3 (5.0)	65.5 (5.1)	64.8 (5.1)	65.7 (4.6)	0.019
Higher education, n (%)	319 (21.6)	107 (19.5)	108 (21.6)	104 (24.5)	0.029
Married, n (%)	1125 (76.2)	420 (76.4)	380 (75.9)	325 (76.5)	0.971
Current smokers, n (%)	187 (12.7)	92 (16.7)	56 (11.2)	39 (9.2)	<0.001
Lifestyle factors					
Total energy intake (kcal/day)	2384 (532)	2323 (516)	2432 (555)	2406 (518)	0.003
Carbohydrate intake (% of energy intake)	39.9 (6.4)	40.0 (6.9)	40.1 (6.3)	39.5 (5.7)	0.338
Protein intake (% of energy intake)	16.5 (2.7)	16.3 (2.6)	16.4 (2.7)	17.0 (2.7)	<0.001
Fat intake (% of energy intake)	40.4 (6.0)	40.0 (6.3)	40.1 (6.1)	41.1 (5.6)	0.008
Polyunsaturated FA (% of energy intake)	6.8 (1.9)	6.5 (1.8)	6.8 (1.8)	7.2 (1.9)	<0.001
Monounsaturated FA (% of energy intake)	21.1 (4.2)	20.9 (4.3)	20.9 (4.3)	21.7 (4.0)	0.002
Saturated FA (% of energy intake)	10.1 (2.0)	10.2 (2.1)	10.1 (2.0)	10.0 (1.8)	0.155
Trans FA (% of energy intake)	0.23 (0.13)	0.25 (0.14)	0.23 (0.12)	0.21 (0.12)	<0.001
Alcohol intake (g/day)	11.5 (15.3)	12.9 (18.8)	12.4 (15.5)	8.7 (12.3)	<0.001
Solid carbohydrates (g/day)	215 (65)	205 (63)	222 (71)	220 (59)	<0.001
Liquid carbohydrates (g/day)	23.8 (16.7)	27.9 (17.4)	24.0 (17.4)	18.2 (12.9)	<0.001
Ratio of solid carbohydrate/total carbohydrate	0.89 (0.06)	0.88 (0.07)	0.90 (0.06)	0.92 (0.05)	<0.001
Refined carbohydrates (g/day)	85.5 (56.4)	108.0 (51.1)	92.1 (57.8)	48.6 (40.8)	<0.001
Wholegrain carbohydrates (g/day)	24.8 (34.4)	2.9 (8.1)	20.7 (26.4)	57.9 (38.5)	<0.001
Ratio of wholegrain/total grain	0.25 (0.30)	0.03 (0.10)	0.22 (0.26)	0.56 (0.26)	<0.001
Fiber intake (g/day)	25.7 (8.2)	20.3 (5.4)	25.7 (6.6)	32.7 (7.7)	<0.001
Glycemic index	54.2 (5.4)	56.4 (4.6)	54.2 (4.8)	51.5 (5.6)	<0.001
CQI (index range 4–20)	11.8 (3.4)	8.3 (1.6)	12.0 (1.3)	15.9 (1.4)	<0.001
Adherence to erMedDiet (17p score)	8.35 (2.6)	7.36 (2.3)	8.30 (2.5)	9.7 (2.6)	<0.001
UPF consumption (% of total intake g/day)	8.45 (7.65)	9.26 (8.34)	8.53 (7.82)	7.31 (6.29)	0.0004
Physical activity (METs min/week)	2677 (2313)	2315 (1955)	2896 (2529)	2889 (2419)	<0.001
Sedentary behavior (h/day)	5.9 (1.8)	5.9 (1.9)	6.0 (1.8)	5.7 (1.8)	0.052
Health-related factors					
Weight (kg)	86.3 (12.7)	85.5 (12.7)	87.9 (13.1)	85.4 (12.2)	0.002
Height (cm)	162.7 (9.4)	161.9 (9.8)	164.4 (9.2)	161.9 (8.8)	<0.001
BMI (kg/m^2)	32.5 (3.3)	32.6 (3.3)	32.5 (3.3)	32.5 (3.3)	0.900
Overall obesity prevalence, n (%)	1105 (74.9)	419 (76.2)	368 (73.5)	318 (74.8)	0.595
History of overweight from childhood, n (%)	103 (7.0)	41 (7.5)	37 (7.4)	25 (5.9)	0.011
WC (cm)	107.3 (9.2)	107.1 (8.8)	108.0 (9.7)	106.7 (9.1)	0.069
Abdominal obesity prevalence, n (%)	1378 (93.4)	516 (93.8)	471 (94.0)	391 (92.0)	0.407
Visceral fat (g)	2307 (888)	2326 (903)	2390 (891)	2184 (854)	0.002
Android-to-gynoid fat ratio	0.79 (0.2)	0.78 (0.2)	0.81 (0.2)	0.78 (0.2)	0.019
Total fat mass (%)	40.4 (6.9)	41.2 (6.8)	39.3 (6.8)	40.8 (6.9)	<0.001
Total lean mass (%)	56.5 (6.6)	55.8 (6.5)	57.6 (6.5)	56.1 (6.6)	<0.001
Type 2 diabetes prevalence, n (%)	386 (26.2)	133 (24.2)	128 (25.6)	125 (29.4)	0.170
Number of MetS factors	3.63 (0.75)	3.66 (0.75)	3.60 (0.73)	3.62 (0.76)	0.429

Abbreviations: BMI – body mass index; CQI – carbohydrate quality index; erMedDiet – energy-restricted Mediterranean Diet; FA – fatty acids; MetS – Metabolic syndrome; METs – metabolic equivalents of tasks; UPF – ultra-processed foods; WC – waist circumference.
Values shown are mean (SD) unless otherwise specified. Ratio of solid carbohydrate/total carbohydrate was calculated as solid carbohydrates/(solid carbohydrates + liquid carbohydrates); ratio of wholegrain/total grain carbohydrate was calculated as wholegrains/(wholegrains + refined grains or their products). Overall obesity was defined as body mass index ≥30.0 kg/m^2, and abdominal obesity as waist circumference ≥88 cm in women or ≥102 cm in men. Total lean and total fat mass were expressed as percentages of DXA-derived total body mass (sum of total bone, fat and muscle mass (g)). Current type 2 diabetes was defined as previous diagnosis of diabetes, glycated hemoglobin (HbA1c) ≥ 6.5%, use of antidiabetic medication, or having fasting glucose >126 mg/dL in both the screening and baseline visit.
Sex-specific ranges for tertiles of CQI: men – T1: 4–9, T2: 10–13, and T3: 14–20; women – T1: 4–11, T2: 12–14, and T3: 15–20.
P-values for comparisons between baseline tertiles of CQI were calculated by one-way ANOVA test for continuous variables and $\chi 2$ test for categorical variables.

again revealed reductions in regional and overall adiposity during the follow-up, with a significant dose–response relation (p for trend <0.05 for all comparisons): visceral fat (β −0.155 z-score, 95% CI -0.209; −0.100), android-to-gynoid fat ratio (−0.060, −0.114; −0.005), and total fat (−0.152, −0.194; −0.110). In terms of absolute values, a 3-point increment in CQI was associated with a decrease of 50.9 g (95% CI -67.0; −34.8, p < 0.001) [or 53.6 cm^3 (−70.7; −36.5, p < 0.001)] in visceral fat and 424 g (−519; −331, p < 0.001) in total fat mass during 1 year of follow-up (Supplementary Table 4).

Regarding the sensitivity analysis (Table 3), the main results did not substantially change when alternative assumptions were tested. However, in those models whereby CQI was considered a continuous variable, further adjustment for adherence to the erMedDiet somewhat attenuated point estimates, although statistically significant associations remained with all adiposity indicators, except for the android-to-gynoid fat ratio. Additional adjustment for body weight and total fat mass also decreased the magnitude of the inverse associations for all adiposity indicators, although associations remained statistically significant. A similar pattern was seen when CQI was coded in tertiles, except for the android-to-gynoid fat ratio, for which statistical significance for linear trend was lost under some of the scenarios tested.

Baseline age, T2D prevalence, obesity status, PA and SB did not modify the association between CQI and any of the adiposity indicators, thus stratified analyses by these variables were not

Table 2
Association between concurrent changes in CQI and fat distribution (z-scores) during follow-up.

	Continuous		Tertiles of increment in CQI			
	CQI (per 3-point increment)		T1 (low)	T2 (medium)	T3 (high)	
	β (95% CI)	p-value	β (95% CI)	β (95% CI)	β (95% CI)	p for trend
Visceral fat z-score						
Minimally-adjusted	−0.073 (−0.094; −0.052)	<0.001	reference	−0.062 (−0.109; −0.015)	−0.170 (−0.225; −0.116)	<0.001
Multivariable-adjusted	−0.067 (−0.088; −0.046)	<0.001	reference	−0.057 (−0.104; −0.010)	−0.155 (−0.209; −0.100)	<0.001
Android-to-gynoid fat ratio z-score						
Minimally-adjusted	−0.039 (−0.060; −0.018)	<0.001	reference	−0.041 (−0.087; 0.005)	−0.064 (−0.117; −0.010)	0.031
Multivariable-adjusted	−0.038 (−0.059; −0.017)	<0.001	reference	−0.041 (−0.087; 0.006)	−0.060 (−0.114; −0.005)	0.047
Total fat mass z-score						
Minimally-adjusted	−0.069 (−0.086; −0.053)	<0.001	reference	−0.083 (−0.119; −0.048)	−0.165 (−0.207; −0.124)	<0.001
Multivariable-adjusted	−0.064 (−0.080; −0.047)	<0.001	reference	−0.077 (−0.113; −0.041)	−0.152 (−0.194; −0.110)	<0.001

Abbreviations: CQI − carbohydrate quality index.
Visceral fat (g), android-to-gynoid fat ratio, and total fat mass (% of DXA-derived total body mass (sum of total bone, fat and muscle mass)) were normalized into sex-specific z-scores for analysis.
Analyses were performed using linear mixed-effects models with random intercepts at recruiting center, cluster family and patient level. Minimally adjusted model was adjusted for age, sex, study arm and follow-up time. Multivariable-adjusted model was further adjusted for baseline variables, such as educational level, marital status, smoking habits, type 2 diabetes prevalence, height, as well as repeatedly measured physical activity, sedentary behavior, total energy and alcohol intake.
In the continuous model, beta represents changes in adiposity indicators expressed as sex-specific z-scores, associated with 3-point increment in CQI. In the categorical model, beta represents changes in adiposity indicators expressed as sex-specific z-scores in each sex-specific tertile of CQI *versus* tertile 1 (reference category).

conducted. However, a significant interaction between CQI and sex was observed in the case of the android-to-gynoid fat ratio (p for interaction = 0.038); stratified analyses showed a negative association between CQI and android-to-gynoid fat ratio among men (β −0.057 z-score, 95% CI -0.087; −0.027, p < 0.001) but not among women (−0.014, −0.044; 0.016, p = 0.360). Moreover, a significant effect modification by study arm was detected for all adiposity indicators (p for interaction for visceral fat = 0.003, android-to-gynoid fat ratio = 0.046, and total fat mass = 0.006). Furthermore, we found that the associations were only evident in the intervention group (visceral fat: β −0.093 z-score, 95% CI −0.122; −0.063, p < 0.001; android-to-gynoid fat ratio: −0.056, −0.086; −0.026, p < 0.001; total fat mass: −0.072, −0.097; −0.048, p < 0.001) but not in the control arm of the trial (visceral fat: −0.023, −0.055; 0.009, p = 0.151; android-to-gynoid fat ratio: −0.011, −0.043; 0.020, p = 0.481; total fat mass: −0.020, −0.042; 0.002, p = 0.078) (data not shown in tables).

In additional analysis, we found that our results were practically unchanged when CQI alternatives were tested (Supplementary Table 5). Furthermore, we found that for all adiposity indicators the associations were stronger among those participants with higher values (≥ median) of both CQI at baseline and CQI change at 1 year (Supplementary Table 6). Finally, when evaluating each CQI component separately (Fig. 1), we found that fibre intake and the ratio of wholegrain/total grain presented the strongest and statistically significant negative associations with all adiposity indicators (all p-values <0.01). After mutual adjustment for individual CQI components, fibre intake remained as the component which was most strongly associated with adiposity, and the point estimates for the associations with the ratio of wholegrain/total grain were attenuated, but p for linear trend remained statistically significant, except for android-to-gynoid fat ratio (Supplementary Fig. 3).

4. Discussion

This prospective analysis aimed to determine the association of changes in the carbohydrate quality index, a multidimensional score assessing carbohydrate intake quality, on adiposity distribution using a direct quantifying method in older adults with overweight/obesity and MetS. Overall, we found that a CQI increase was associated with a decrease in regional and overall adiposity. These associations were independent of changes in carbohydrates quantity and other macronutrients, but were attenuated (although they remained statistically significant) after adjusting for changes in adherence to the MedDiet as well as for changes in total fat mass and body weight. To the best of our knowledge, no previous studies have assessed the link between changes in the overall quality of carbohydrates and changes in overall and regional adiposity accretion using a prospective design. Of note, this relationship was ascertained by analyzing dynamic changes in diet and adiposity throughout a 1-year follow-up time with three repeated measurements of diet and adiposity, in the context of an intervention study aimed at weight loss.

Evidence so far has shown that the quality of dietary carbohydrates, rather than the quantity, may have a greater impact on a health and overall mortality [3,40]. A variety of methods have been proposed to assess dietary carbohydrate quality, serving as useful tools to determine the potential risk of suffering conditions such as T2D, CVD and MetS [3,40]. However, most studies have used individual components instead of a clearly defined multidimensional measurement that accounts for several quality indicators [18]. In this sense, the use of the CQI as a tool to determine dietary carbohydrate quality is a recent and interesting addition to these approaches, whereby a higher CQI indicates better carbohydrate quality and is thus associated to a lower risk of obesity [16,18,19], CVD [18,41], breast cancer [20] and all-cause mortality [21]. Martínez-González et al. [18] carried out a longitudinal analysis in the same population herein studied (PREDIMED-Plus) and reported that improvements in CQI throughout a 1-year period were associated to a reduction in CVD risk factors, including waist circumference and body weight. Furthermore, the SUN project, an ongoing, longitudinal cohort carried out in a Spanish population of younger and healthier subjects, also reported that the CQI was inversely associated with risk of overweight/obesity over an 8-year time frame [16]. In contrast, Sawicki et al. [3] reported marginal associations between CQI and changes in waist circumference, and none with weight gain, throughout a period of 18 years in the US middle-aged to older cohort from the Framingham Offspring Study. The discrepancies might be related to different methodological aspects or cohort characteristics.

Visceral fat constitutes only a small proportion of total fat (in our population accounted for 8.5% in men and 5% in women), but the available evidence indicates that it plays an important role in certain chronic diseases, such as T2D, MetS, CVD and cancer [9–11]. Yet, it remains unclear whether modifications in particular lifestyle

Table 3
Sensitivity analysis. Association between concurrent changes in CQI and fat distribution (z-scores) during follow-up.

A. Visceral fat z-score	Continuous		Tertiles of increment in CQI			
	CQI (per 3-point increment)		T1 (low)	T2 (medium)	T3 (high)	
	β (95% CI)	p-value	β (95% CI)	β (95% CI)	β (95% CI)	p for trend
Overall	−0.067 (−0.088; −0.046)	<0.001	reference	−0.057 (−0.104; −0.010)	−0.155 (−0.209; −0.100)	<0.001
Nutritional factors						
+ changes in intake of carbohydrates (g/day)	−0.070 (−0.091; −0.048)	<0.001	reference	−0.059 (−0.106; −0.012)	−0.160 (−0.214; −0.105)	<0.001
+ changes in intake of MUFA, PUFA, SFA, trans FA, and protein (g/day)	−0.058 (−0.080; −0.036)	<0.001	reference	−0.044 (−0.091; 0.004)	−0.132 (−0.188; −0.076)	<0.001
+ changes in adherence to erMedDiet (17p score)	−0.038 (−0.062; −0.015)	0.001	reference	−0.018 (−0.067; 0.030)	−0.084 (−0.143; −0.024)	0.012
+ changes in UPF consumption (% of total intake g/day)	−0.061 (−0.083; −0.040)	<0.001	reference	−0.048 (−0.095; −0.001)	−0.142 (−0.197; −0.087)	<0.001
Excluding total energy intake (kcal/day)	−0.065 (−0.086; −0.044)	<0.001	reference	−0.053 (−0.099; −0.006)	−0.149 (−0.204; −0.095)	<0.001
Health conditions						
+ number of MetS factors	−0.067 (−0.088; −0.046)	<0.001	reference	−0.056 (−0.103; −0.010)	−0.154 (−0.209; −0.100)	<0.001
+ history of overweight	−0.067 (−0.088; −0.046)	<0.001	reference	−0.057 (−0.104; −0.010)	−0.155 (−0.209; −0.100)	<0.001
+ changes in body weight (kg)	−0.030 (−0.049; −0.010)	0.002	reference	−0.013 (−0.056; 0.029)	−0.069 (−0.118; −0.020)	0.013
+ changes in total fat mass (g)	−0.028 (−0.046; −0.010)	0.003	reference	−0.009 (−0.049; 0.031)	−0.060 (−0.107; −0.014)	0.018
Dealing with missing follow-up data using LOCF	−0.053 (−0.071; −0.035)	<0.001	reference	−0.034 (−0.072; 0.004)	−0.119 (−0.163; −0.074)	<0.001

B. Android-to-gynoid fat ratio z-score	Continuous		Tertiles of increment in CQI			
	CQI (for 3-point increment)		T1 (low)	T2 (medium)	T3 (high)	
	β (95% CI)	p-value	β (95% CI)	β (95% CI)	β (95% CI)	p for trend
Overall	−0.038 (−0.059; −0.017)	<0.001	reference	−0.041 (−0.087; 0.006)	−0.060 (−0.114; −0.005)	0.047
Nutritional factors						
+ changes in intake of carbohydrates (g/day)	−0.039 (−0.060; −0.018)	<0.001	reference	−0.041 (−0.088; 0.005)	−0.061 (−0.115; −0.006)	0.044
+ changes in intake of MUFA, PUFA, SFA, trans FA, and protein (g/day)	−0.030 (−0.052; −0.008)	0.008	reference	−0.029 (−0.076; 0.018)	−0.037 (−0.093; 0.018)	0.257
+ changes in adherence to erMedDiet (17p score)	−0.019 (−0.042; 0.005)	0.120	reference	−0.012 (−0.060; 0.036)	−0.007 (−0.066; 0.052)	0.981
+ changes in UPF consumption (% of total intake g/day)	−0.036 (−0.057; −0.014)	0.001	reference	−0.036 (−0.083; 0.011)	−0.053 (−0.108; 0.002)	0.086
Excluding total energy intake (kcal/day)	−0.037 (−0.058; −0.016)	0.001	reference	−0.039 (−0.085; 0.007)	−0.057 (−0.111; −0.003)	0.056
Health conditions						
+ number of MetS factors	−0.038 (−0.059; −0.017)	<0.001	reference	−0.040 (−0.086; 0.007)	−0.058 (−0.113; −0.004)	0.051
+ history of overweight	−0.036 (−0.060; −0.017)	<0.001	reference	−0.041 (−0.088; 0.005)	−0.060 (−0.114; −0.006)	0.044
+ changes in body weight (kg)	−0.029 (−0.050; −0.007)	0.008	reference	−0.029 (−0.075; 0.017)	−0.037 (−0.091; 0.017)	0.239
+ changes in total fat mass (g)	−0.028 (−0.049; −0.007)	0.008	reference	−0.028 (−0.074; 0.017)	−0.036 (−0.089; 0.018)	0.254
Dealing with missing follow-up data using LOCF	−0.030 (−0.048; −0.013)	0.001	reference	−0.027 (−0.065; 0.010)	−0.044 (−0.088; 0.001)	0.084

C. Total fat mass z-score	Continuous		Tertiles of increment in CQI			
	CQI (per 3-point increment)		T1 (low)	T2 (medium)	T3 (high)	
	β (95% CI)	p-value	β (95% CI)	β (95% CI)	β (95% CI)	p for trend
Overall	−0.064 (−0.080; −0.047)	<0.001	reference	−0.077 (−0.113; −0.041)	−0.152 (−0.194; −0.110)	<0.001
Nutritional factors						
+ changes in intake of carbohydrates (g/day)	−0.064 (−0.080; −0.047)	<0.001	reference	−0.077 (−0.113; −0.041)	−0.152 (−0.194; −0.110)	<0.001
+ changes in intake of MUFA, PUFA, SFA, trans FA, and protein (g/day)	−0.055 (−0.072; −0.038)	<0.001	reference	−0.065 (−0.101; 0.029)	−0.131 (−0.173; −0.088)	<0.001
+ changes in adherence to erMedDiet (17p score)	−0.034 (−0.052; −0.016)	<0.001	reference	−0.039 (−0.076; −0.003)	−0.083 (−0.128; −0.038)	0.001
+ changes in UPF consumption (% of total intake g/day)	−0.058 (−0.075; −0.041)	<0.001	reference	−0.069 (−0.104; −0.033)	−0.140 (−0.182; −0.098)	<0.001
Excluding total energy intake (kcal/day)	−0.062 (−0.078; −0.045)	<0.001	reference	−0.073 (−0.109; −0.038)	−0.147 (−0.189; −0.105)	<0.001
Health conditions						
+ number of MetS factors	−0.064 (−0.080; −0.047)	<0.001	reference	−0.077 (−0.113; −0.042)	−0.153 (−0.195; −0.111)	<0.001
+ history of overweight	−0.064 (−0.080; −0.047)	<0.001	reference	−0.077 (−0.113; −0.042)	−0.152 (−0.194; −0.111)	<0.001
+ changes in body weight (kg)	−0.015 (−0.028; −0.002)	0.028	reference	−0.021 (−0.050; 0.007)	−0.043 (−0.077; −0.009)	0.020
Dealing with missing follow-up data using LOCF	−0.052 (−0.065; −0.038)	<0.001	reference	−0.061 (−0.090; −0.033)	−0.122 (−0.156; −0.088)	<0.001

Abbreviations: FA – fatty acids; CQI – carbohydrate quality index, erMedDiet – energy-restricted Mediterranean diet; LOCF – last observation carried forward; MetS – metabolic syndrome; MUFA – monounsaturated fatty acids, PUFA – polyunsaturated fatty acids, SFA – saturated fatty acids; UPF – ultra-processed foods.
Visceral fat (g), android-to-gynoid fat ratio, and total fat mass (% of DXA-derived total body mass (sum of total bone, fat and muscle mass)) were normalized into sex-specific z-scores for analysis.
Analyses were performed using linear mixed-effects models with random intercepts at recruiting center, cluster family and patient level, after adjusting in full model for baseline variables, such as age, sex, study arm, educational level, marital status, smoking habits, type 2 diabetes prevalence, height, as well as repeatedly measured physical activity, sedentary behavior, total energy and alcohol intake, and follow-up time.
In the continuous model, beta represents changes in adiposity indicators expressed as sex-specific z-scores, associated with 3-point increment in CQI. In the categorical model, beta represents changes in adiposity indicators expressed as sex-specific z-scores in each sex-specific tertile of CQI *versus* tertile 1 (reference category).

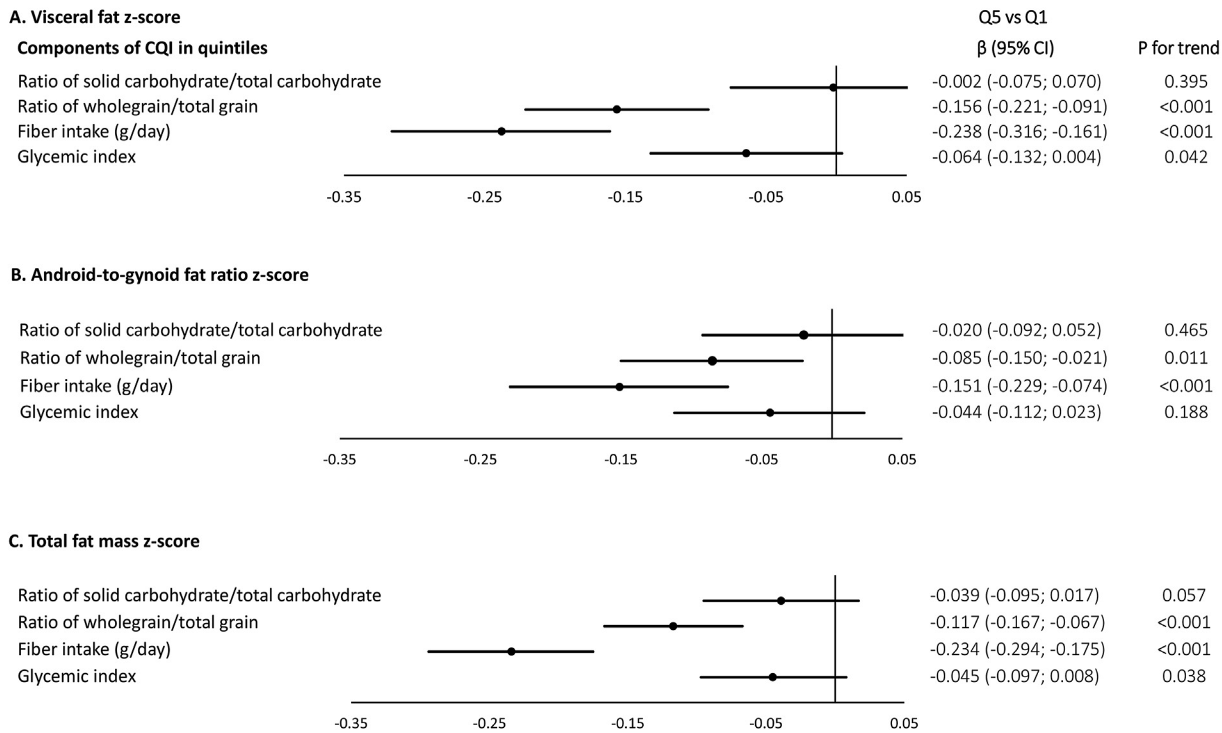

Fig. 1. Association between concurrent changes in components of CQI and fat distribution (z-scores) during follow-up. Abbreviations: CQI − carbohydrate quality index. Visceral fat (g), android-to-gynoid fat ratio, and total fat mass (% of DXA-derived total body mass (sum of total bone, fat and muscle mass)) were normalized into sex-specific z-scores for analyses. Ratio of solid carbohydrate/total carbohydrate was calculated as solid carbohydrates/(solid carbohydrates + liquid carbohydrates); ratio of wholegrain/total grain carbohydrate was calculated as whole grains/(wholegrains + refined grains or their products). Analyses were performed using linear mixed-effects models with random intercepts at recruiting center, cluster family and patient level, after adjusting in full model for baseline variables, such as age, sex, study arm, educational level, marital status, smoking habits, type 2 diabetes prevalence, height, as well as repeatedly measured physical activity, sedentary behavior, total energy and alcohol intake, and follow-up time. Beta represents changes in adiposity indicators, expressed as sex-specific z-scores, in quintile 5 *versus* quintile 1 (reference category) of each CQI component.

factors can alter fat from specific anatomic sites [42]. Thus, one of the most important findings from this study is that moving towards better CQI is associated with a decrease in visceral fat, and these improvements are of similar magnitude and independent of changes in total body fat. Although it is true that further adjustment for changes in total fat or body weight substantially attenuated this association, suggesting that a reduction in overall adiposity could be partially responsible for the association, manipulation of carbohydrate quality may also specifically induce mobilization of visceral fat, and possibly via mechanisms beyond its effects on overall adiposity. Our group and other authors have previously reported the presence of unique associations of certain food groups, such as ultra-processed foods [22], fruit and vegetables [6], whole and refined grains [7], with visceral fat beyond overall obesity.

It is worth to underline that strategies to decrease visceral fat are highly warranted, but the clinical significance of the magnitude of decrease we found for this depot in our study (−50.9 g or −53.6 cm^3 per each 3-point increment in CQI) is unclear. Lack of robust reference ranges affects the interpretation of visceral fat in clinical practice and research settings [43]. The direct comparison with previous studies addressing link between diet and objectively-measured specific fat depots is severely hampered by type of imaging technique used (different tissue segmentation and units), as well as subject's and study characteristics. In a small RCT with DXA device, a 12-week weight loss intervention based on portion-controlled reduced-energy diet among overweight/obese subjects resulted in the decrease of 14.2 g of visceral fat [44]. In a recent CENTRAL magnetic resonance imaging RCT [42], authors found that a decrease of 0.58 cm^2 of visceral fat in subjects with abdominal obesity or dyslipidemia after a 18-month intervention with Mediterranean/low-carbohydrate diet vs low-fat diet, was associated with improved cardiometabolic markers. Undoubtedly, more large and well-conducted longitudinal studies and RCTs are warranted to shed light on the clinical importance of results found on this particular fat depot.

Due to the sexual dimorphism in body composition [45], sex-adjusted models were used for all analyses and the interaction between CQI and sex on adiposity was assessed. However, given that after menopause the pattern of fat accumulation in women mirrors that of men [45], we found little evidence for sex-specific modification effect in our study. The exception was for android-to-gynoid fat ratio, for which we found a stronger and significant association with CQI only in men, but not in women. This might be due to chance finding due to the multiple comparisons performed in this study.

The mechanism behind the association between carbohydrates quality and better metabolic facets has been previously discussed [3,16,17,46], suggesting that a variety of factors related to individual quality dimensions play a role, including the satiating effect, capacity of slowing food digestion and absorption, changes in the gut microbiota profile, and the fact that individuals presenting higher CQI values have a healthier diet overall (as seen in this paper through higher adherence to MedDiet at baseline of participants in tertile 3 and reported by others [18]). Notably, when looking at the individual components of the CQI, we observed that our associations were mostly driven by fibre, and the ratio of wholegrains/total grains carbohydrates. In line with our findings, the authors of recent series of systematic reviews and meta-analyses of prospective studies and clinical trials concluded that both dietary fibre and wholegrains may serve as key markers of overall carbohydrate quality in relation to a range of non-communicable disease outcomes [40]. The benefits of fibre include the capacity to increase faecal bulk and to shorten transit time, leading to decreased nutrient absorption, or energy reduction, which could affect total fat, and ultimately visceral fat accumulation [47]. The slower food digestion and absorption may also reduce postprandial glucose and insulin responses, which can in turn influence satiety as well as lipid metabolism, favouring fat oxidation and lipolysis rather than its storage [40,48]. The mode of action of these beneficial fibre effects is not fully elucidated, but gut microbiota and short-chain fatty acids may be implicated [49].

The results for wholegrains/total grains ratio were similar to those for fibre, suggesting that the beneficial effects of wholegrains on adiposity could be predominantly due to cereal fibre content. However, further adjustment for fibre and other CQI components preserved the associations with visceral and total fat, although the point estimates diminished, suggesting that other attributes of wholegrains, such as antioxidants (i.e. vitamin E), minerals (i.e. magnesium, potassium, selenium, and zinc) and bioactive compounds (i.e. polyphenols) or particle size, may also enhance glucose and insulin metabolism, and thereby prevent body fat accumulation [7,48]. All in all, the potential mechanisms by which carbohydrate quality may be related to overall and regional adiposity is speculative and warrants future studies.

Several limitations to this study need to be acknowledged. First, due to the observational nature of the study, causality cannot be inferred. Second, the cohort is based on older people with overweight/obesity and MetS from a Mediterranean area, which can limit the generalizability of our findings to the general population. However, the described health profile of our population (overweight/obesity and/or MetS) is quite common in current Western societies [50–53]. On the other hand, the extrapolation of these findings to the general population could be affected by the fact that half of the study cohort was exposed to a weight-loss program. Third, the use of self-reported dietary data is subject to measurement error. However, we undertook some actions to improve measurement precision: the FFQ used was previously validated in a Spanish population; the FFQ was administered repeatedly (every 6 months) to the participants by trained dietitians during face-to-face interviews; participants with implausible total energy intake values were excluded from analyses; and all models were adjusted for changes in total energy intake. Lastly, the social desirability bias inherent to most nutritional studies is also a limitation, since dietary assessment methods based on self-reports may be affected by the natural tendency to respond in a manner to avoid criticism or judgement and to seek social approval [54].

Despite these limitations, the strengths of this study include the prospective, multicenter design, a relatively large sample size, control for a wide set of confounders, and performance of a series of sensitivity and stratified analyses. Unlike most of the previous research on carbohydrate quality and obesity, we used a multidimensional quality metric, being a more comprehensive tool than individual quality markers, to capture interactive effects of food components on health outcomes. Moreover, adiposity was determined by means of a precise imaging technique. Of note, the advantage and novelty of this study is that both exposure and outcome were repeatedly measured at the same three time points, potentially decreasing the risk of reverse causality.

In summary, in this prospective study among older adults at high CVD risk from Mediterranean area, we found that changes towards better overall carbohydrate quality, as assessed by a multidimensional approach, were associated with favourable changes in visceral and overall adiposity distribution. These findings contribute to an extensive literature on carbohydrates, emphasizing the importance of carbohydrate quality (increasing dietary fibre and wholegrains, reducing liquid carbohydrates, and preferring lower glycemic index foods) over quantity to reduce the risk of obesity and the development of other chronic diseases. Furthermore, we also found that the observed associations were mostly driven by fibre and the wholegrains/total grains ratio. Thus, special focus on the promotion of fibre-rich foods, including fruits, vegetables, legumes and nuts, and the substitution of refined grains by wholegrains, may be important dietary recommendations to adopt in clinical practice to promote a healthier body composition.

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Author's contributions

RZ-C, AC, DR and JK, conceived the study, analyzed the data, interpreted the results and wrote the article. All authors were involved in project design and conduction, participants recruitment, data collection, manuscript revision and read and approved the final manuscript.

Conflict of interest

Ramón Estruch reports receiving personal fees for educational conferences from Fundacion Cerveza y Salud, Spain, Instituto Cervantes, Alburquerque, USA; Instituto Cervantes, Milan, Italy, Instituto Cervantes, Tokyo, Japan, Fundacion Bosch i Gimpera, Spain; nonfinancial support for educational conferences from Wine and Culinary International Forum; Fees of Educational Conferences from Pernaud Richart, Mexico, Fundacion Dieta Mediterranea, Barcelona, Spain; non-financial support for travels from ERAB, Belgium, personal fees for organizing an European Conference from

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List of abbreviations

BMI	Body-mass index
CQI	Carbohydrate quality index
CVD	Cardiovascular diseases
DXA	Dual-energy X-ray absorptiometry
ER	Energy-restricted
FFQ	Food Frequency Questionnaire
LOCF	Last observation carried forward
MedDiet	Mediterranean diet
MetS	Metabolic syndrome
PA	Physical activity
PREDIMED-Plus	PREvención con DIeta MEDiterránea Plus
SB	Sedentary behavior
T2D	Type 2 Diabetes

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clnu.2022.08.008.

References

[1] World Health Organization. WHO/Europe | obesity - data and statistics. https://www.euro.who.int/en/health-topics/noncommunicable-diseases/obesity/data-and-statistics. [Accessed 12 November 2020].

[2] Powell-Wiley TM, Poirier P, Burke LE, Després JP, Gordon-Larsen P, Lavie CL, et al. Obesity and Cardiovascular Disease: A Scientific Statement From the American Heart Association. Circulation 2021;143:e984–1010. https://doi.org/10.1161/CIR.0000000000000973.

[3] Sawicki CM, Lichtenstein AH, Rogers GT, Jacques PF, Ma J, Saltzman E, et al. Comparison of indices of carbohydrate quality and food sources of dietary fiber on longitudinal changes in waist circumference in the Framingham offspring cohort. Nutrients 2021;13:1–16. https://doi.org/10.3390/NU13030997.

[4] Hunter GR, Gower BA, Kane BL. Age related shift in visceral fat. Int J Body Compos Res 2010;8:103–8.

[5] Kuk JL, Saunders TJ, Davidson LE, Ross R. Age-related changes in total and regional fat distribution. Ageing Res Rev 2009;8:339–48. https://doi.org/10.1016/j.arr.2009.06.001.

[6] Van Eekelen E, Geelen A, Alssema M, Lamb HJ, De Roos A, Rosendaal FR, et al. Sweet snacks are positively and fruits and vegetables are negatively associated with visceral or liver fat content in middle-aged men and women. J Nutr 2019;149:304–13. https://doi.org/10.1093/jn/nxy260.

[7] McKeown NM, Troy LM, Jacques PF, Hoffmann U, O'Donnell CJ, Fox CS. Whole- and refined-grain intakes are differentially associated with abdominal visceral and subcutaneous adiposity in healthy adults: the Framingham Heart Study. Am J Clin Nutr 2010;92:1165–71. https://doi.org/10.3945/ajcn.2009.29106.

[8] Galmes-Panades AM, Konieczna J, Abete I, Colom A, Rosique-Esteban N, Zulet MA, et al. Lifestyle factors and visceral adipose tissue: results from the PREDIMED-PLUS study. PLoS One 2019;14. https://doi.org/10.1371/journal.pone.0210726.

[9] Machann J, Stefan N, Wagner R, Fritsche A, Bell JD, Whitcher B, et al. Normalized indices derived from visceral adipose mass assessed by magnetic resonance imaging and their correlation with markers for insulin resistance and prediabetes. Nutrients 2020;12:1–14. https://doi.org/10.3390/nu12072064.

[10] Kahn CR, Wang G, Lee KY. Altered adipose tissue and adipocyte function in the pathogenesis of metabolic syndrome. J Clin Invest 2019;129:3990–4000. https://doi.org/10.1172/JCI129187.

[11] Britton KA, Massaro JM, Murabito JM, Kreger BE, Hoffmann U, Fox CS. Body fat distribution, incident cardiovascular disease, cancer, and all-cause mortality. J Am Coll Cardiol 2013;62:921–5. https://doi.org/10.1016/j.jacc.2013.06.027.

[12] Kayode OO. Diet and Obesity. Psychology and Pathophysiological Outcomes of Eating [Internet]. In: Takada A, Himmerich H, editors. London: IntechOpen; 2021. https://www.intechopen.com/chapters/77412. [Accessed 12 November 2021].

[13] Swinburn B, Caterson I, Seidell J, James W. Diet, nutrition and the prevention of excess weight gain and obesity. Publ Health Nutr 2004;7:123–46. https://doi.org/10.1079/phn2003585.

[14] Sievenpiper JL. Low-carbohydrate diets and cardiometabolic health: the importance of carbohydrate quality over quantity. Nutr Rev 2020;78:69. https://doi.org/10.1093/NUTRIT/NUZ082.

[15] 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.

[16] Santiago S, Zazpe I, Bes-Rastrollo M, Sánchez-Tainta A, Sayón-Orea C, De La Fuente-Arrillaga C, et al. Carbohydrate quality, weight change and incident obesity in a Mediterranean cohort: the SUN Project. Eur J Clin Nutr 2015;69:297–302. https://doi.org/10.1038/ejcn.2014.187.

[17] 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.

[18] Martínez-González MA, Fernandez-Lazaro CI, Toledo E, Diáz-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 2020;111:291–306. https://doi.org/10.1093/ajcn/nqz298.

[19] Suara SB, Siassi F, Saaka M, Rahimi Foroshani A, Sotoudeh G. Association between Carbohydrate Quality Index and general and abdominal obesity in women: a cross-sectional study from Ghana. BMJ Open 2019;9. https://doi.org/10.1136/bmjopen-2019-033038.

[20] Romanos-Nanclares A, Gea A, Martínez-González MÁ, Zazpe I, Gardeazabal I, Fernandez-Lazaro CI, et al. Carbohydrate quality index and breast cancer risk in a Mediterranean cohort: the SUN project. Clin Nutr 2021;40:137–45. https://doi.org/10.1016/J.CLNU.2020.04.037.

[21] Fernandez-Lazaro CI, Zazpe I, Santiago S, Toledo E, Barbería-Latasa M, Martínez-González MÁ. Association of carbohydrate quality and all-cause mortality in the SUN Project: a prospective cohort study. Clin Nutr 2021;40:2364–72. https://doi.org/10.1016/J.CLNU.2020.10.029.

[22] Konieczna J, Morey M, Abete I, Bes-Rastrollo M, Ruiz-Canela M, Vioque J, et al. Contribution of ultra-processed foods in visceral fat deposition and other adiposity indicators: prospective analysis nested in the PREDIMED-Plus trial. Clin Nutr 2021;40:4290–300. https://doi.org/10.1016/j.clnu.2021.01.019.

[23] Martínez-González MA, Buil-Cosiales P, Corella D, Bulló M, Fitó M, Vioque J, et al. Cohort profile: design and methods of the PREDIMED-Plus randomized trial. Int J Epidemiol 2019;48:387–388o. https://doi.org/10.1093/ije/dyy225.

[24] Sayón-Orea C, Razquin C, Bulló M, Corella D, Fitó M, Romaguera D, et al. Effect of a nutritional and behavioral intervention on energy-reduced mediterranean diet adherence among patients with metabolic syndrome. JAMA 2019;322:1486. https://doi.org/10.1001/jama.2019.14630.

[25] Schröder H, Cárdenas-Fuentes G, Angel Martínez-González M, Corella D, Vioque J, Romaguera D, et al. Effectiveness of the physical activity intervention program in the PREDIMED-Plus study: a randomized controlled trial behalf of the PREDIMED-Plus investigators. Int J Behav Nutr Phys Act 2018;15:110. https://doi.org/10.1186/s12966-018-0741-x.

[26] Alberti KGMM, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, et al. Harmonizing the metabolic syndrome: a joint interim statement of the international diabetes federation task force on epidemiology and prevention; National heart, lung, and blood institute; American heart association; World heart federation; International atherosclerosis society; and international association for the study of obesity. Circulation 2009;120:1640–5. https://doi.org/10.1161/CIRCULATIONAHA.109.192644.

[27] Willett W. Nutritional epidemiology. Oxford University Press; 2013.

[28] De La Fuente-Arrillaga C, Vzquez Ruiz Z, Bes-Rastrollo M, Sampson L, Martinez-González MA. Reproducibility of an FFQ validated in Spain. Publ Health Nutr 2010;13:1364–72. https://doi.org/10.1017/S1368980009993065.

[29] Fernández-Ballart JD, Piñol JL, Zazpe I, Corella D, Carrasco P, Toledo E, et al. Relative validity of a semi-quantitative food-frequency questionnaire in an elderly Mediterranean population of Spain. Br J Nutr 2010;103:1808–16. https://doi.org/10.1017/S0007114509993837.

[30] Moreiras O, Carbajal Á, Cabrera L, Cuadrado C. Tablas de composición de alimentos. Guía de prácticas. 19th ed. Madrid: Ediciones Pirámide; 2018.

[31] Atkinson FS, Foster-Powell K, Brand-Miller JC. International tables of glycemic index and glycemic load values: 2008. Diabetes Care 2008;31:2281–3. https://doi.org/10.2337/dc08-1239.

[32] Monteiro CA, Cannon G, Levy R, Moubarac J-C, Jaime P, Martins AP, et al. NOVA. The star shines bright (food classification. Public health). World Nutr 2016;7:28–38.

[33] Schröder H, Zomeño MD, Martínez-González MA, Salas-Salvadó J, Corella D, Vioque J, et al. Validity of the energy-restricted mediterranean diet adherence screener. Clin Nutr 2021;40:4971–9. https://doi.org/10.1016/J.CLNU.2021.06.030.

[34] Sánchez-Tainta A, Zazpe I, Bes-Rastrollo M, Salas-Salvadó J, Bullo M, Sorlí JV, et al. Nutritional adequacy according to carbohydrates and fat quality. Eur J Nutr 2016;55:93–106. https://doi.org/10.1007/s00394-014-0828-3.

[35] Konieczna J, Abete I, Galmés AM, Babio N, Colom A, Zulet MA, et al. Body adiposity indicators and cardiometabolic risk: cross-sectional analysis in

participants from the PREDIMED-Plus trial. Clin Nutr 2019;38:1883–91. https://doi.org/10.1016/j.clnu.2018.07.005.
[36] Kaul S, Rothney MP, Peters DM, Wacker WK, Davis CE, Shapiro MD, et al. Dual-energy X-ray absorptiometry for quantification of visceral fat. Obesity 2012;20:1313–8. https://doi.org/10.1038/oby.2011.393.
[37] Molina L, Sarmiento M, Peñafiel J, Donaire D, Garcia-Aymerich J, Gomez M, et al. Validation of the regicor short physical activity questionnaire for the adult population. PLoS One 2017;12:168148. https://doi.org/10.1371/journal.pone.0168148.
[38] Martínez-González MA, López-Fontana C, Varo JJ, Sánchez-Villegas A, Martinez JA. 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.
[39] Textor J, van der Zander B, Gilthorpe MS, Liśkiewicz M, Ellison GT. Robust causal inference using directed acyclic graphs: the R package "dagitty". Int J Epidemiol 2016;45:1887–94. https://doi.org/10.1093/IJE/DYW341.
[40] 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.
[41] 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.
[42] Gepner Y, Shelef I, Schwarzfuchs D, Zelicha H, Tene L, Meir AY, et al. Effect of distinct lifestyle interventions on mobilization of fat storage pools: CENTRAL magnetic resonance imaging randomized controlled trial. Circulation 2018;137:1143–57. https://doi.org/10.1161/CIRCULATIONAHA.117.030501.
[43] Swainson MG, Batterham AM, Hind K. Age- and sex-specific reference intervals for visceral fat mass in adults. Int J Obes 2020;44:289–96. https://doi.org/10.1038/s41366-019-0393-1.
[44] Liu FX, Flatt SW, Nichols JF, Pakiz B, Barkai HS, Wing DR, et al. Factors associated with visceral fat loss in response to a multifaceted weight loss intervention. J Obes Weight Loss Ther 2017;7(4):346. https://doi.org/10.4172/2165-7904.1000346.
[45] Wells JCK. Sexual dimorphism of body composition. Best Pract Res Clin Endocrinol Metabol 2007;21:415–30. https://doi.org/10.1016/J.BEEM.2007.04.007.
[46] Zazpe I, Santiago S, Toledo E, Bes-Rastrollo M, De La Fuente-Arrillaga C, Martínez-González MA. Diet quality indices in the SUN cohort: observed changes and predictors of changes in scores over a 10-year period. J Acad Nutr Diet 2021;121:1948–60. https://doi.org/10.1016/j.jand.2021.03.011.
[47] Davis JN, Alexander KE, Ventura EE, Toledo-Corral CM, Goran MI. Inverse relation between dietary fiber intake and visceral adiposity in overweight Latino youth. Am J Clin Nutr 2009;90:1160–6. https://doi.org/10.3945/AJCN.2009.28133.
[48] Sawicki CM, Jacques PF, Lichtenstein AH, Rogers GT, Ma J, Saltzman E, et al. Whole- and refined-grain consumption and longitudinal changes in cardiometabolic risk factors in the Framingham offspring cohort. J Nutr 2021;151:2790–9. https://doi.org/10.1093/JN/NXAB177.
[49] Den Besten G, Van Eunen K, Groen AK, Venema K, Reijngoud DJ, Bakker BM. The role of short-chain fatty acids in the interplay between diet, gut microbiota, and host energy metabolism. J Lipid Res 2013;54:2325–40. https://doi.org/10.1194/JLR.R036012.
[50] Aranceta-Bartrina J, Pérez-Rodrigo C, Alberdi-Aresti G, Ramos-Carrera N, Lázaro-Masedo S. Prevalence of general obesity and abdominal obesity in the Spanish adult population (aged 25–64 Years) 2014–2015: the ENPE study. Rev Española Cardiol (English Ed) 2016;69:579–87. https://doi.org/10.1016/J.REC.2016.02.009.
[51] Cuesta M, Fuentes M, Rubio M, Bordiu E, Barabash A, Garcia De La Torre N, et al. Incidence and regression of metabolic syndrome in a representative sample of the Spanish population: results of the cohort di@ bet. es study. BMJ Open Diab Res Care 2020;8:23. https://doi.org/10.1136/bmjdrc-2020-001715.
[52] Saklayen MG. The global epidemic of the metabolic syndrome. Curr Hypertens Rep 2018;20. https://doi.org/10.1007/S11906-018-0812-Z.
[53] Stierman B, Afful J, Carroll MD, Chen TC, Davy O, Fink S, et al. National health and nutrition examination survey 2017–march 2020 prepandemic data files-development of files and prevalence estimates for selected health outcomes. Natl Health Stat Report 2021;158. https://doi.org/10.15620/cdc:106273.
[54] Hebert JR, Ma Y, Clemow L, Ockene IS, Saperia G, Stanek EJ, et al. Gender differences in social desirability and social approval bias in dietary self-report. Am J Epidemiol 1997;146:1046–55. https://doi.org/10.1093/OXFORDJOURNALS.AJE.A009233.