International Journal of Nutrition Sciences

ORIGINAL ARTICLE

The Association between Low-Carbohydrate Diet Score and Conventional Risk Factors of Cardiovascular Diseases in Iranian Adult Population: A Cross-Sectional Study

Zahra Makhtoomi[1], Sepideh Alijani[2], Zainab Shateri[3], Milad Rajabzadeh-dehkordi[4,5], Moein Askarpour[4,6], Abbas Rezaianzadeh[7], Masoumeh Ghoddusi Johari[8], Mehran Nouri[9*], Shiva Faghih[5,10*]

1. Department of Medical Sciences, Shahrood Branch, Islamic Azad University, Shahrood, Iran
2. Student Research Committee, Department of Biochemistry and Diet Therapy, Faculty of Nutrition and Food Sciences, Tabriz University of Medical Sciences, Tabriz, Iran
3. Department of Nutrition and Biochemistry, School of Medicine, Ilam University of Medical Sciences, Ilam, Iran
4. Student Research Committee, Shiraz University of Medical Sciences, Shiraz, Iran
5. Department of Community Nutrition, School of Nutrition and Food Sciences, Shiraz University of Medical Sciences, Shiraz, Iran
6. Department of Clinical Nutrition, School of Nutrition and food Sciences, Shiraz University of Medical Sciences, Shiraz, Iran
7. Department of Epidemiology, School of Health and Nutrition, Shiraz University of Medical Sciences, Shiraz, Iran
8. Breast Diseases Research Center, Shiraz University of Medical Sciences, Shiraz, Iran
9. Infertility and Reproductive Health Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, Iran
10. Nutrition Research Center, Shiraz University of Medical Sciences, Shiraz, Iran
Co-first author: Sepideh Alijani and Zahra Makhtoomi equally contributed to this work.

ARTICLE INFO

Corresponding authors:
Shiva Faghih, PhD;
Department of Community Nutrition, School of Nutrition and Food Sciences,
Shiraz University of Medical Sciences, Shiraz, Iran.
Tel: +98-71-37251001
Email: shivafaghih@gmail.com
Mehran Nouri, PhD;
Infertility and Reproductive Health Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, Iran.
Tel: +98-9378542652
Email: mehran_nouri71@yahoo.com

ABSTRACT

Background: Cardiovascular diseases (CVDs) are the leading cause of global morbidity and mortality. The findings of previous studies on the association between a low-carbohydrate diet (LCD) and cardiovascular risk factors are inconsistent. Therefore, the aim of the present study was to investigate the relationship between LCD score (LCDS) and conventional cardiovascular risk markers in the adult Iranian population.

Methods: This cross-sectional study was conducted on participants in the Kharameh Cohort Study in southern Iran. According to the inclusion and exclusion criteria, 6,611 subjects were enrolled. A valid 130-item food frequency questionnaire was used to evaluate the food intake of individuals. The association of LCDS with indicators such as high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglycerides (TG), fasting blood sugar (FBS), non-HDL-C, LDL-C to HDL-C ratio, and waist circumference (WC) was evaluated. Multivariate logistic regression models were used to evaluate the association between the risk factors of CVD and LCDS.

Results: The findings showed that individuals in the highest LCDS tertile had lower odds of having an increased WC (odds ratio (OR)=0.83, 95% confidence interval (95% CI): 0.74-0.94), and TG (OR=0.68, 95% CI: 0.59-0.79), and higher odds of having an increased HDL-C (OR=0.84, 95% CI: 0.74-0.95) in the adjusted model. No other variables exhibited a statistically significant relationship with LCDS.

Conclusion: In this cross-sectional study among Iranian adults, adherence to LCDS was associated with improved CVD risk factors, such as WC, HDL-C, and TG. Further studies are needed to confirm the results.

Introduction

Cardiovascular diseases (CVDs) are the leading cause of global morbidity and mortality and are responsible for approximately 30% of all deaths worldwide (1). The main risk factors for these diseases include high levels of low-density lipoprotein cholesterol (LDL-C), abdominal obesity, diabetes, hypertension, smoking, excessive alcohol consumption, psychosocial factors, insufficient consumption of fruits and vegetables, and lack of regular physical activity (2-4). Several dietary approaches have been shown to reduce cardiovascular events. Consuming polyunsaturated fats instead of saturated fats has been shown to prevent cardiovascular events in men, and consuming fish oil and a Mediterranean diet has increased survival (5, 6). However, increased carbohydrate intake may negatively affect glucose metabolism and lipoprotein concentrations (7, 8). In a low-carbohydrate diet (LCD), energy from carbohydrates is less than 45% (9) and LCDs have been considered a way to lose weight (10). However, the effect of LCDs on cardiovascular risk factors is inconsistent. Some studies have shown an increase in LDL-C with LCDs, while others have shown little change. Also, an increase in high-density lipoprotein cholesterol (HDL-C) and a decrease in triglycerides (TG) have been demonstrated with LCDs (11-13).

Macronutrient intake scoring is more commonly used when assessing carbohydrate intake because it allows for examining the relationship between disease risk and different intake levels (14). Also, as mentioned, there are contradictory findings regarding the relationship between LCDs and CVD risk factors. Therefore, the present study aimed to investigate the association between LCD score (LCDS) and conventional cardiovascular risk markers in adult population in southern Iran.

Materials and Methods

The participants included in this cross-sectional study were those in the Prospective Epidemiological Research Studies in Iran (PERSIAN) (12). The Cohort of Kharameh is a part of the PERSIAN Cohort in Kharameh, southern Iran that was undertaken between 2014 and 2017. This study was performed on a total of 10,663 individuals with an age range of 40-70 years. The number of participants excluded for cardiovascular diseases, diabetes, and other diseases was 4,015. The missing data was 6, and the over-nutrition and under-nutrition reports were 31. Eventually, 6,611 subjects entered the final analysis (Figure 1). Some information, such as demographic information, medical history, and physical

activity, was prepared. The measurements, such as weight, height, hip circumference (HC), and waist circumference (WC), were determined. Additionally, HDL-C, LDL-C, TG, fasting blood sugar (FBS), and total cholesterol (TC) (15) were measured.

A valid 130-item food frequency questionnaire was used to evaluate the food intake of individuals (15). The grams of the food items were providede. For obtaining energy, micro- and macro-nutrients, Nutritionist IV software (version 7.0) was utilized. The dietary glycemic index (GI) was computed as GI×available carbohydrate/total available carbohydrate. The term "available carbohydrate" refers to carbohydrate minus dietary fiber (16). Glycemic load (GL) (17) was calculated using the formula of total GI multiplied by total available carbohydrates divided by 100. This study was approved by the Medical Research and Ethics Committee Of Shiraz University of Medical Sciences (IR.SUMS.REC.1399.1115), Shiraz, Iran and the informed consents were completed by all participants. All experiments were performed in accordance with relevant guidelines and regulations.

To calculate the LCDS, the participants were divided into 11 classes for each carbohydrate, vegetable protein, refined grains, monounsaturated fatty acids (MUFAs), fiber, GL, and n3/n6 polyunsaturated fatty acids (PUFAs) (18). For fiber, MUFA, vegetable protein, and n3/n6 PUFA, adults received 10 points in the highest class, and 0 points in the lowest level. The sequence of levels was opposite for categories such as GL, refined grains, and carbohydrates (lowest level: 10 points and the highest level: 0 points). The percentage of energy instead of absolute intake was used to decrease bias.
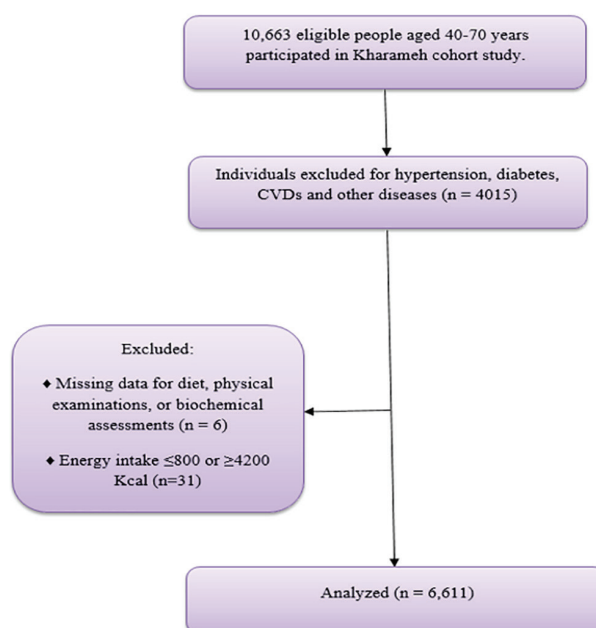

Figure 1: The study flowchart.

The score of every item was collected, and the total score ranged from 0 to 70 points. A score of 0 described the minimum consumption of fat and protein and the maximum consumption of carbohydrates, while 70 points indicated the maximum protein and fat intake and the minimum carbohydrate intake. A higher score demonstrated that more LCD or "LCDS" was being followed (19-21).

Socio-demographic information (sex, medical history, and age) and some information such as duration of exercise, sleep, eating, and work in a day were collected using a checklist (22). Anthropometric indices such as weight, WC, and HC were measured with an accuracy of 0.1 cm. Also, height was assessed without shoes. Blood pressure was determined using a German sphygmomanometer. A 20 mL blood sample was collected from each participant, and their laboratory indicators were investigated. Glucose, TC, and TG were measured by Pars Azmoon test kits. The enzymatic method was employed to assess TC, TG, and HDL-C levels. LDL-C level was determined applying the Friedwald's formula (23). The crude and multivariable-adjusted odds ratios (ORs) and 95% confidence intervals (95% CIs) across the tertiles of LCDS were also presented (24).

Data analysis was done using SPSS software (version 20.0, Chicago, IL, USA). The Kolmogorov-Smirnov test was utilized to evaluate the normality of the data. One-way analysis of variance (ANOVA) and Chi-Square tests were used to assess the differences of continuous and categorical variables among different tertiles of LCDS, respectively. The Kruskal-Wallis test was used to determine the differences across tertiles of LCDS. Multivariate logistic regression models were used to examine any association between the risk factors of CVD and tertiles of LCDS. A p value less than 0.05 was considered statistically significant.

Results

Out of 10,663 people eligible to participate in the study, only data from 6,611 participants were included in the analysis. For various reasons, other participants were excluded from the study (Figure 1). According to Table 1, there were significant differences in relation to gender ($p<0.001$), weight ($p<0.001$), WC ($p=0.001$), educational level ($p=0.005$), physical activity ($p=0.005$), systolic blood pressure ($p=0.028$), TG ($p<0.001$), HDL-C ($p<0.001$), and the ratio of LDL-C to HDL-C ($p=0.034$) between LCDS tertiles. No significant difference was detected in other variables ($p>0.05$). Higher LCDS was associated with higher intakes of protein, carbohydrates, fat, fiber, cholesterol, saturated fatty acids (SFAs), MUFAs, PUFAs, whole grains, fruits, vegetables, nuts, legumes, dairy, meats, and processed meats ($p<0.001$, for all variables). Also, higher LCDS were related to a lower intake of energy, refined grains, and sweets ($p<0.001$, for all variables; Table 2).

Table 1: Baseline characteristics of the study participants.

Variable	Low Carbohydrate Diet Score			
	T_1 (n=2361)	T_2 (n=2172)	T_3 (n=2078)	*P* value
Gender, Female (%)	44.0	51.6	57.7	<0.001
Age (year)	50.16±7.60	50.13±7.83	49.88±7.84	0.443
Weight (kg)	69.23±12.17	68.76±12.14	67.18±12.08	<0.001
BMI (kg/m^2)	25.56±4.42	25.63±4.34	25.44±4.47	0.360
WC (cm)	94.06±12.16	94.04±11.91	92.85±11.77	0.001
HC (cm)	100.52±8.10	100.57±8.15	100.14±8.48	0.180
Education (year)	4.73±4.18	5.00±4.57	5.17±4.87	0.005
Physical activity (MET/day)	39.37±6.79	38.88±6.30	38.81±5.83	0.005
Systolic blood pressure (mm Hg)	111.23±15.39	111.00±14.84	110.07±14.80	0.028
Diastolic blood pressure (mm Hg)	70.56±9.62	70.44±9.10	70.16±9.27	0.348
FBS (mg/dL)	90.90±17.04	91.58±17.61	91.01±14.63	0.345
TG (mg/dL)	127.52±76.01	126.59±88.71	117.92±67.25	<0.001
TC (mg/dL)	187.40±40.42	187.77±40.59	189.19±39.96	0.308
LDL-C (mg/dL)	114.79±34.67	114.74±33.34	116.85±33.43	0.069
HDL-C (mg/dL)	47.20±12.49	47.97±13.36	48.92±12.09	<0.001
Non-HDL-C	140.21±39.06	139.79±39.28	140.27±38.08	0.909
LDL-C to HDL-C ratio	2.57±0.96	2.53±0.91	2.50±0.86	0.034

BMI: Body mass index; WC: Waist circumference; HC: Hip circumference; FBS: Fasting blood sugar; TG: Triglyceride; TC: Total cholesterol; LDL-C: Low-density lipoprotein cholesterol; HDL-C: High-density lipoprotein cholesterol; MET: metabolic equivalent of task; T: Tertile. Values were mean±SD for continuous and percentage for categorical variables. Using one-way ANOVA for continuous and chi-square test for categorical variables. A *p* value less than 0.05 was considered statistically significant.

Table 2: Nutrient and food intakes between tertiles of low-carbohydrate diet score.

Variable	T_1 (n=2361)	T_2 (n=2172)	T_3 (n=2078)
	Median (25-75)	Median (25-75)	Median (25-75)
Nutrient			
Energy (kcal/d)	2548.7 (2097.7-3044.9)	2449.9 (1992.8-2924.5)	2235.1 (1809.8-2710.9)
Protein (% Energy)	11.18 (8.79-13.73)	12.42 (10.14-15.01)	14.07 (11.54-17.27)
Carbohydrate (% Energy)	64.74 (54.02-78.84)	63.75 (52.43-79.31)	67.59 (54.26-83.81)
Fat ((% Energy)	8.52 (6.67-10.74)	10.14 (8.36-12.27)	15.27 (9.96-14.90)
Fiber (g/day)	21.90 (18.77-25.78)	23.93 (20.97-27.74)	25.83 (22.48-29.50)
Cholesterol (g/day)	195.43 (147.24-253.54)	228.47 (183.62-285.88)	266.31 (215.80-329.81)
SFA (% Energy)	6.63 (4.90-8.52)	8.05 (6.45-10.02)	9.96 (7.78-12.35)
MUFA (% Energy)	5.32 (3.96-7.01)	6.65 (5.19-8.20)	8.15 (6.46-10.12)
PUFA (% Energy)	3.04 (2.15-4.11)	3.69 (2.71-4.75)	4.45 (3.26-5.70)
Food Item			
Whole Grains (g/day)	77.22 (13.63-202.30)	113.41 (46.01-254.26)	144.5 (74.53-264.68)
Refined Grains (g/day)	471.30 (341.50-595.06)	401.15 (295.61-490.37)	311.74 (228.22-398.44)
Fruits (g/day)	260.76 (169.71-388.49)	297.72 (199.20-421.34)	315.84 (222.20-446.31)
Vegetables (g/day)	416.61 (312.05-546.30)	451.81 (345.16-586.69)	490.32 (381.65-629.09)
Nuts (g/day)	2.67 (0.76-4.98)	3.73 (1.80-6.89)	4.62 (2.56-8.80)
Legumes (g/day)	21.04 (12.08-33.00)	25.00 (15.90-37.94)	29.89 (19.5-46.20)
Dairy (g/day)	172.98 (104.31-261.36)	200.75 (134.47-287.45)	215.22 (145.23-310.44)
Meats (g/day)	41.77 (24.89-63.13)	51.15 (33.60-74.03)	61.30 (42.58-85.57)
Processed Meats (g/day)	1.12 (0.42-3.27)	1.42 (0.03-4.08)	2.04 (0.52-5.23)
Sweets (g/day)	61.09 (36.35-96.02)	47.20 (30.04-67.55)	43.42 (27.93-59.59)
Sweetened beverages (g/day)	45.70 (14.17-95.81)	44.61 (17.17-94.17)	46.76 (22.19-85.52)

SFA: Saturated fatty acids; PUFA: Polyunsaturated fatty acids; MUFA: Monounsaturated fatty acids; T: tertile.*Using Kruskal-Wallis test. A p value less than 0.05 was considered statistically significant.

Table 3: The crude and multivariable-adjusted odds ratios and 95% CIs across the tertiles of low-carbohydrate diet score.

Variable	LCDS			
	T_1 (n=2361)	T_2 (n=2172)	T_3 (n=2078)	P_{trend}
WC (cm)				
Crude Model	Ref.	1.00 (0.89, 1.12)	0.85 (0.76, 0.96)	0.012
Adjusted Model[a]	Ref.	0.98 (0.87, 1.11)	0.83 (0.74, 0.94)	0.006
Adjusted Model[b]	Ref.	1.03 (0.86, 1.21)	0.91 (0.76, 1.08)	0.318
FBS (mg/dL)				
Crude Model	Ref.	1.44 (0.90, 2.31)	0.80 (0.46, 1.39)	0.524
Adjusted Model[c]	Ref.	1.45 (0.90, 2.32)	0.82 (0.47, 1.43)	0.589
TG (mg/dL)				
Crude Model	Ref.	0.86 (0.75, 0.98)	0.66 (0.57, 0.76)	<0.001
Adjusted Model[c]	Ref.	0.87 (0.76, 0.99)	0.68 (0.59, 0.79)	<0.001
LDL-C (mg/dL)				
Crude Model	Ref.	1.09 (0.96, 1.24)	1.08 (0.94, 1.23)	0.234
Adjusted Model[c]	Ref.	1.07 (0.94, 1.22)	1.06 (0.93, 1.21)	0.365
HDL-C (mg/dL)				
Crude Model	Ref.	0.98 (0.87, 1.10)	0.85 (0.75, 0.96)	0.012
Adjusted Model[b]	Ref.	0.97 (0.86, 1.09)	0.84 (0.74, 0.95)	0.007
Non-HDL-C				
Crude Model	Ref.	1.01 (0.90, 1.14)	1.04 (0.92, 1.17)	0.514
Adjusted Model[c]	Ref.	1.00 (0.89, 1.13)	1.05 (0.93, 1.19)	0.383
LDL-C to HDL-C Ratio				
Crude Model	Ref.	0.99 (0.88, 1.11)	0.92 (0.81, 1.03)	0.191
Adjusted Model[c]	Ref.	1.04 (0.92, 1.17)	1.02 (0.90, 1.15)	0.699

LCDS: Low-carbohydrate diet score; WC: Waist circumference; FBS: Ffasting blood sugar; TG: Triglyceride; LDL-C: Low-density lipoprotein cholesterol; HDL-C: High-density lipoprotein cholesterol; T, tertile; Ref, reference. Adjusted Model[a]: Adjusted for age, physical activity, and education. Adjusted Model[b]: Adjusted for age, physical activity, education, and BMI. Adjusted Model[c]: Adjusted for gender, age, physical activity, education, and BMI. These values are shown as odds ratio (95% CIs). Obtained from logistic regression. A p value less than 0.05 was considered statistically significant.

The crude and multivariable-adjusted odds ratios (ORs) and 95% confidence intervals (95% CIs) across the tertiles of LCDS were shown in Table 3. There were no significant differences for FBS, LDL-C, non-HDL-C, and LDL-C to HDL-C ratio in the crude and adjusted models among the LCDS tertiles ($p > 0.05$). However, in the crude model, individuals in the highest LCDS tertile had lower odds of having a high WC (OR=0.85, 95% CI: 0.76-0.96), TG (OR=0.66, 95% CI: 0.57-0.76), and higher odds of increased HDL-C (OR=0.85, 95% CI: 0.75-0.96). Also, after adjusting for confounders, people in the highest LCDS tertile had lower odds of having a high WC (OR=0.83, 95% CI: 0.74-0.94), TG (OR=0.68, 95% CI: 0.59-0.79), and higher odds of increased HDL-C (OR=0.84, 95% CI: 0.74-0.95).

Discussion

The present cross-sectional study indicated a significant association between WC, TG, and HDL-C with LCDs. Also, individuals in the highest tertile of LCDS consumed lower amounts of energy, refined grains, and sweets and higher amounts of protein, carbohydrates, fats, fiber, cholesterol, SFAs, MUFAs, PUFAs, whole grains, fruits, vegetables, nuts, legumes, dairy, meats, and processed meats. As can be perceived from the findings, the lowest amount of carbohydrate intake (second tertile) was higher than the definition of a low-carbohydrate diet (less than 45%). Therefore, if LCDS was related to CVD risk factors, in the current study, this carbohydrate intake could influence the association of LCDS with cardiovascular risk factors.

This study found no significant association between FBS, LDL-C, non-HDL-C, and LDL-C to HDL-C ratio with LCDS. The important role of diet on cell function has been described before (25, 26). A study by Shirani *et al.* on Iranian women showed no significant relationship between LCDS and high FBS (27). Another study on obese adults revaeled no significant association between FBS and LDL-C with LCDS tertiles (28). Also, in another study by Freedland *et al.* on the effect of LCD with walking among prostate cancer patients, it was shown that LCD with walking did not impact non-HDL-C (29). So, these findings were in line with previous studies.

As mentioned, our findings demonstrated a significant association between LCDS and WC. These results were consistent with similar studies. A study by Sali *et al.* illustrated that WC significantly decreased in the higher tertile of LCDS compared to the lower tertile of LCDS (30). In another study by Gholami *et al.*, it was detected that the odds of high visceral fat levels decreased among women with high adherence to LCDs (31). Also, a meta-analysis

study revealed that LCDs caused a significant reduction in WC by 5.74 cm (32). WC was shown to be a consistent risk factor for CVDs (33), and WC accurately reflected obesity-related health risks (34). Ebbeling *et al.* found that LCDS may affect total and resting energy expenditure (35). LCDs have also been shown to cause fat mass loss (36). Thus, LCDs may have influenced WC through the effects mentioned above.

In addition, the findings demonstrated that with the increase of LCDS, TG decreased, and HDL-C increased. A systematic review by Meng *et al.* showed that LCD could reduce TG (37). Also, a randomized clinical trial revealed that LCD decreased TG (36). Moreover, some studies have shown a positive relationship between LCD and HDL-C (28, 38). Dietary carbohydrate is one of the important factors regulating the metabolism of fatty acids and induces lipogenesis by stimulating insulin secretion. When carbohydrate intake is restricted in the diet, even with high consumption of SFAs (such as LCD), access to insulin ligands, fructose, and glucose, and insulin secretion is reduced. As a result, there would be a decrease in lipogenesis, the secretion of very LDL-C (VLDL-C), and an increase in the oxidation of fats (39). These mechanisms explain the increase in HDL-C and the decrease in TG observed in the present study. Also, as mentioned earlier, the findings showed that people with the highest level of LCDS had lower weight and energy intake and higher fiber and whole grains, all of which decreased serum TG levels.

The current study had several limitations. First, we could not specify the cause-and-effect relationship due to the cross-sectional design. Second, there might be confounding factors that were not included in the study, which were always possible in observational studies. Third, although the FFQ is the best tool for collecting dietary data in epidemiological studies, it relies on the participants' memory. However, the large sample size and adjustment of the effect of many important confounders were the strengths of this study.

Conclusion

The findings showed that adherence to LCDS could possibly improve some risk factors of CVDs, including WC, HDL-C, and TG. Therefore, the consumption of whole grains, fruits, vegetables, nuts, legumes, and dairy products is recommended for cardiovascular health and the prevention of CVDs. Further studies are needed to confirm these results.

Acknowledgment

Funding

Authors' Contribution

Conflict of Interest

None declared.

References

1   World Health Organization. Cardiovascular disease: Prevention and control. Global strategy on diet, physical activity and health. 2007.

2   Walden R, Tomlinson B. Cardiovascular disease. In: Herbal Medicine: Biomolecular and Clinical Aspects. 2nd edition. Boca Raton (FL): CRC Press/Taylor & Francis; 2011. Chapter 16. 2012. PMID: 22593934.

3   Ntentie FR, Nguedjo MW, Nkougni JT, et al. Nutrition Transition, Malnutrition and Cardiometabolic Risk Factors in the Far North Region of Cameroon. *Int J Nutr Sci*. 2023;8:91-101. DOI: 10.30476/IJNS.2023.97849.1226.

4   Aghasadeghi K, Zarei-Nezhad M, et al. The Prevalence of Coronary Risk Factors In Iranian Lor Migrating Tribe. *Arch Iran Med*. 2008;11:322-325. PMID: 18426325.

5   Sacks FM, Katan M. Randomized clinical trials on the effects of dietary fat and carbohydrate on plasma lipoproteins and cardiovascular disease. *Am J Med*. 2002;113:13-24. DOI: 10.1016/s0002-9343(01)00987-1. PMID: 12566134.

6   Khoramnazari R, Salehi M, Kojuri J. The Effect of Whole Wheat and White Breads on Serum Lipid Profile, Malondialdehyde, and C-Reactive Protein in Over-Weight and Obese Patients with Coronary Stent. *Int J Nutr Sci*. 2017;2:203-208.

7   Jeppesen J, Schaaf P, Jones C, et al. Effects of low-fat, high-carbohydrate diets on risk factors for ischemic heart disease in postmenopausal women. *Am J Clin Nutr*. 1997;65:1027-33. DOI: 10.1093/ajcn/65.4.1027. PMID: 9094889.

8   Mittendorfer B, Sidossis LS. Mechanism for the increase in plasma triacylglycerol concentrations after consumption of short-term, high-carbohydrate diets. *Am J Clin Nutr*. 2001;73:892-9. DOI: 10.1093/ajcn/73.5.892. PMID: 11333842.

9   Jovanovski E, Zurbau A, Vuksan V. Carbohydrates and endothelial function: is a low-carbohydrate diet or a low-glycemic index diet favourable for vascular health? *Clin Nutrv Res*. 2015;4:69-75. DOI: 10.1093/ajcn/73.5.892. PMID: 11333842.

10 Oh R, Gilani B, Uppaluri KR. Low carbohydrate diet. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan. PMID: 30725769.

11 Nordmann AJ, Nordmann A, Briel M, et al. Effects of low-carbohydrate vs low-fat diets on weight loss and cardiovascular risk factors: a meta-analysis of randomized controlled trials. *Arch Intern Med*. 2006;166:285-93. DOI: 10.1001/archinte.166.3.285. PMID: 16476868.

12 Bhanpuri NH, Hallberg SJ, Williams PT, et al. Cardiovascular disease risk factor responses to a type 2 diabetes care model including nutritional ketosis induced by sustained carbohydrate restriction at 1 year: an open label, non-randomized, controlled study. *Cardiovasc Diabetol*. 2018;17:56. DOI: 10.1186/s12933-018-0698-8. PMID: 29712560.

13 Lu M, Wan Y, Yang B, Huggins CE, Li D. Effects of low-fat compared with high-fat diet on cardiometabolic indicators in people with overweight and obesity without overt metabolic disturbance: a systematic review and meta-analysis of randomised controlled trials. *Br J Nutr*. 2018;119:96-108. DOI: 10.1017/S0007114517002902. PMID: 29212558.

14 Jafari-Maram S, Daneshzad E, Brett NR, et al. Association of low-carbohydrate diet score with overweight, obesity and cardiovascular disease risk factors: a cross-sectional study in Iranian women. *J Cardiovasc Thorac Res*. 2019;11:216. DOI: 10.15171/jcvtr.2019.36. PMID: 31579462.

15 Poustchi H, Eghtesad S, Kamangar F, et al. Prospective epidemiological research studies in Iran (the PERSIAN Cohort Study): rationale, objectives, and design. *Am J Epidemiol*. 2018;187:647-55. DOI: 10.1093/aje/kwx314. PMID: 29145581.

16 Foster-Powell K, Holt SH, Brand-Miller JC. International table of glycemic index and glycemic load values: 2002. *Am J Clin Nutr*. 2002;76:5-56. DOI: 10.1093/ajcn/76.1.5. PMID: 12081815.

17 Chen S, Chen Y, Ma S, et al. Dietary fibre intake and risk of breast cancer: a systematic review and meta-analysis of epidemiological studies. *Oncotarget*. 2016;7:80980. DOI: 10.18632/oncotarget.13140. PMID: 27829237.

18 Halton TL, Willett WC, Liu S, et al. Low-carbohydrate-diet score and the risk of

coronary heart disease in women. *N Engl J Med*. 2006;355:1991-2002. DOI: 10.1056/NEJMoa055317. PMID: 17093250.

19 Mirmiran P, Asghari G, Farhadnejad H, et al. Low carbohydrate diet is associated with reduced risk of metabolic syndrome in Tehranian adults. *Int J Food Sci Nutr*. 2017;68:358-65. DOI: 10.1080/09637486.2016.1242119. PMID: 27718762.

20 Askarpour M, Ramezan M, Jafari F, Nouri M, Fattahi MR, Safarpour AR, et al. The association between low carbohydrate diet and odds of metabolic syndrome in adults: A cross-sectional study. *Clin Nutr ESPEN*. 2023;55:238-43. DOI: 10.1016/j.clnesp.2023.03.020. PMID: 37202052.

21 Mohebati S, Shakeri M, Ranjbar S, et al. The association of dietary carbohydrate quality and quantity with obesity among Iranian adolescents: a case-control study. *BMC Pediatr*. 2024;24:176. DOI: 10.1186/s12887-024-04671-9. PMID: 38461264.

22 Kazemi Karyani A, Karmi Matin B, Soltani S, et al. Socioeconomic gradient in physical activity: findings from the PERSIAN cohort study. *BMC Public Health*. 2019;19:1312. DOI: 10.1186/s12889-019-7715-z. PMID: 31638932.

23 Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem*. 1972;18:499-502. PMID: 4337382.

24 Moazzen S, Cortes-Ibañez FO, van der Vegt B, et al. Diet quality indices and gastrointestinal cancer risk: results from the Lifelines study. *Eur J Nutr*. 2022;61:317-27. DOI: 10.1007/s00394-021-02648-3. PMID: 34338867.

25 Mehrabani D, Masoumi SJ, Masoumi AS, et al. Role of diet in mesenchymal stem cells' function: a review. *Int J Nutr Sci*. 2023;8:9-19. DOI:10.30476/ijns.2023.97788.1221.

26 Hedayati A, Homayuon M, Mobaracky A, et al. Lithium Chloride, Ketogenic Diet and Stem Cell Transplantation in Treatment of Bipolar Disorder. *Int J Nutr Sci*. 2024;9:80-82. DOI: 10.30476/ijns.2024.99601.1250.

27 Shirani F, Esmaillzadeh A, Keshteli AH, Adibi P, Azadbakht L. Low-carbohydrate-diet score and metabolic syndrome: an epidemiologic study among Iranian women. *Nutrition*. 2015;31(9):1124-30. DOI: 10.1016/j.nut.2015.04.013. PMID: 26233870.

28 Pour Abbasi MS, Shojaei N, Farhangi MA. Low-carbohydrate diet score is associated with improved blood pressure and cardio-metabolic risk factors among obese adults. *Physiol Rep*. 2022;10:e15375. DOI: 10.14814/phy2.15375. PMID: 35822420.

29 Freedland SJ, Howard L, Allen J, et al. A lifestyle intervention of weight loss via a low-carbohydrate diet plus walking to reduce metabolic disturbances caused by androgen deprivation therapy among prostate cancer patients: carbohydrate and prostate study 1 (CAPS1) randomized controlled trial. *Prostate Cancer Prostatic Dis*. 2019;22:428-37. DOI: 10.1038/s41391-019-0126-5. PMID: 30664736.

30 Sali S, Farhadnejad H, Asghari G, et al. Animal based low carbohydrate diet is associated with increased risk of type 2 diabetes in Tehranian adults. *Diabetol Metab Syndr*. 2020;12:87. DOI: 10.1186/s13098-020-00596-2. PMID: 33042230.

31 Gholami F, Martami F, Ghorbaninezhad P, et al. Association of low-carbohydrate diet score and carbohydrate quality with visceral adiposity and lipid accumulation product. *Br J Nutr*. 2023;129:843-853. DOI: 10.1017/S000711452200143X. PMID: 35570588.

32 Santos FL, Esteves SS, da Costa Pereira A, et al. Systematic review and meta-analysis of clinical trials of the effects of low carbohydrate diets on cardiovascular risk factors. *Obes Rev*. 2012;13:1048-66. DOI: 10.1111/j.1467-789X.2012.01021.x. PMID: 22905670.

33 Rexrode KM, Carey VJ, Hennekens CH, et al. Abdominal adiposity and coronary heart disease in women. JAMA. 1998;280:1843-8. DOI: 10.1001/jama.280.21.1843. PMID: 9846779.

34 Janssen I, Katzmarzyk PT, Ross R. Waist circumference and not body mass index explains obesity-related health risk. *Am J Clin Nutr*. 2004;79:379-84. DOI: 10.1093/ajcn/79.3.379. PMID: 14985210.

35 Ebbeling CB, Swain JF, Feldman HA, Wong WW, Hachey DL, Garcia-Lago E, et al. Effects of dietary composition on energy expenditure during weight-loss maintenance. JAMA. 2012;307:2627-34. DOI: 10.1001/jama.2012.6607. PMID: 22735432.

36 Bazzano LA, Hu T, Reynolds K, et al. Effects of low-carbohydrate and low-fat diets: a randomized trial. *Ann Intern Med*. 2014;161:309-18. DOI: 10.7326/M14-0180. PMID: 25178568.

37 Meng Y, Bai H, Wang S, et al. Efficacy of low carbohydrate diet for type 2 diabetes mellitus management: a systematic review and meta-analysis of randomized controlled trials. *Diabetes Res Clin Pract*. 2017;131:124-31. DOI: 10.1016/j.diabres.2017.07.006. PMID: 28750216.

38 Ha K, Joung H, Song Y. Low-carbohydrate diet and the risk of metabolic syndrome in Korean

adults. *Nutr Metab Cardiovasc Dis.* 2018;28:1122-32. DOI: 10.1016/j.numecd.2018.06.007. PMID: 30139686.

39 Volek JS, Fernandez ML, Feinman RD, et al. Dietary carbohydrate restriction induces a unique metabolic state positively affecting atherogenic dyslipidemia, fatty acid partitioning, and metabolic syndrome. *Prog Lipid Res.* 2008;47:307-18. DOI: 10.1016/j.plipres.2008.02.003. PMID: 18396172.