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Effects of vegetarian versus Mediterranean diet on kidney function: Findings from the CARDIVEG study

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Abstract

Background: The aim of the present study was to assess the effects of a lacto-ovo-vegetarian diet (VD), compared to a Mediterranean diet (MD), on kidney function in a group of subjects with medium-to-low cardiovascular risk profile.

Methods: We analysed 107 subjects (82 women, 25 men; median age 52) who followed a VD (n = 54) and a MD (n = 53) for 3 months in the CARDIVEG study, a randomized, open, crossover trial that compared the effects of these 2 diets on cardiovascular disease risk.

Results: The effect of the two diets on kidney function markers was evaluated by conducting a general linear model for repeated measurements adjusted for possible confounding factors such as age, sex, physical activity, alcohol, smoking, hypertension, LDL cholesterol, glucose and body weight change. A significant reduction in creatinine (−5.3%; $P < .001$), urea nitrogen levels (−9%; $P = .001$), blood urea nitrogen (BUN) (−8.7%; $P = .001$) and BUN/creatinine ratio (−5.8%; $P < .001$), and an increase in estimated glomerular filtration rate (eGFR) (+3.5%; $P = .001$) was observed during the VD period. On the contrary, no significant changes were noted in the MD group. Variations obtained in the two dietary interventions were significantly different ($P < .0001$) for creatinine levels, BUN/creatinine and eGFR, for which opposite trends were observed in the VD and MD groups.

Conclusions: In a selected group of subjects with medium-to-low cardiovascular risk profile, a 3 month VD period determined significant improvements in kidney function markers. Further trials are needed to confirm these results.

KEYWORDS

fibre, kidney function, protein, vegetarian diet

Trial Registration: http://www.clinicaltrials.gov. Unique identifier: NCT02641834

1 | INTRODUCTION

Chronic kidney disease (CKD) is recognized as a major public health problem associated with a poor prognosis and mortality.[1] It exposes patients to the risk of numerous health complications and represents an independent cardiovascular risk factor. In a study examining over 1 million people, the rate of cardiovascular events progressively increased as estimated glomerular filtration rate (eGFR) declined.[2] Even mild to moderate kidney impairment was associated with an increased cardiovascular mortality.[3]

The knowledge of the nutritional aspects of kidney diseases, ranging from understanding the metabolic imbalances associated with nutritional disorders to optimizing diet in patients with CKD, has seen great progress in the last decades. Current evidence suggests that the adoption of plant-based diets, such as the Mediterranean diet (MD) or the lacto-ovo-vegetarian diet (VD), has potential benefits in both primary prevention and early stages of CKD.[4] These benefits might be mediated by reduced protein and sodium intake, decreased phosphorus load and increased intake of fibre, vitamins, antioxidants and chemicals that have been linked to improved outcomes in patients with CKD. Moreover, plant-based diets might also help to prevent and manage some of the metabolic complications of CKD such as dyslipidaemia, hypertension, inflammation and bone disorders.[5]

In the general population and in cohorts of patients with CKD, observational studies have shown that adherence to a MD or patterns of diet that are consistent with VD are associated with lower CKD prevalence and reduced risk for incident CKD.[6,7] However, only a few randomized clinical trials of these diets have been conducted, reporting contrasting results. A small 90 day study of a MD in 40 patients with CKD reported improvements in lipid profile and inflammatory parameters,[8] while a 1 year MD intervention in a cohort of the PREDIMED study showed no effect on kidney function in elderly individuals with a high cardiovascular risk.[9] Lastly, a randomized crossover trial reported that patients with CKD who followed a VD for 8 weeks showed similar levels of protein catabolic rate, albumin, lipids and calcium to those who followed an animal-based low-protein diet.[10]

The aim of the present study was to compare, in the framework of the CARDIVEG study, the effectiveness of a VD and a similar isocaloric MD in improving kidney function in a group of subjects with medium-to-low cardiovascular risk profile.

2 | MATERIALS AND METHODS

2.1 | Study population

Data presented were obtained from 107 clinically healthy subjects (82 women, 25 men; median age 52) who followed a VD and a MD as a first dietary intervention in the CARDIVEG study, a randomized, open, crossover trial that compared the effects of these 2 diets on cardiovascular disease risk.[11] The study design and the characteristics of the participants were described in detail previously.[12] Briefly, 118 subjects with low-to-moderate cardiovascular risk profile (<5% at 10 years, according to the European Society of Cardiology) were recruited from the Clinical Nutrition Unit of Careggi University Hospital, Florence, Italy. People with serious illness or unstable condition, who took medications for any reason, who were pregnant or nursing, who excluded meat, poultry or fish from their diet in the last 6 months or participated in a weight loss treatment programme in the last 6 months, were excluded.

Study procedures were approved by the Ethics Committee of the Tuscany Region, Careggi University Hospital (SPE 15.054), registered at clinicaltrials.gov (identifier: NCT02641834) and adhered to the principles of the Declaration of Helsinki and the Data Protection Act. Written informed consent was obtained from all participants enrolled in the study. Reporting of the study conforms to broad EQUATOR guidelines.[13]

2.2 | Dietary interventions

VD and MD were hypocaloric with respect to the energy needs of the participants, but isocaloric between them. Both diets consisted of about 50%-55% of energy from carbohydrate, 25%-30% from total fat and 15%-20% from protein. VD was characterized by abstinence from meat and meat products, poultry, fish and seafood, but included eggs and dairy products, as well as all the other food groups. MD was characterized by the consumption of all the food groups including meat, poultry and fish. Participants were provided with a detailed 1-week menu plan and information on the foods that could be included and those that could not. Dietary profiles were calculated on the basis of the portion sizes recommended by the Italian Recommended Dietary Allowances.[14] There were no differences in the frequency of servings per week for fruits and vegetables, cereals and olive oil. However, in the case of VD, a higher frequency of consumption per week of legumes (5 vs 2.5 servings), nuts (2 vs 1), dairy products (21.5 vs 18.5) and eggs (2 vs 1) was reported compared to MD. Participants were instructed not to alter their lifestyle or exercise habits, and no weight loss goal was given.

2.3 | Data collection

Participants were interviewed and examined at the Clinical Nutrition Unit of Careggi University Hospital (Florence)

through the use of standardized methods. Details regarding demographics, risk factors, comorbidities and lifestyle habits were obtained from all the participants. Weight and height were measured using a stadiometer. Body mass index (BMI) was calculated as the weight (kg)/height (m^2), and body composition was determined by a bioelectrical impedance analysis device (TANITA, model TBF-410). All measurements were performed both at the beginning and at the end the intervention period, between 6:30 AM and 9:30 AM after an overnight fasting period.

Before starting the study, participants were asked to complete a 3 days dietary record (2 weekdays and 1 weekend day) that was analysed by a dietician using a nutrition-specific database. Compliance to the VD was assessed through a 24 hours dietary recall interview and a modified version of the National Health and Nutrition Examination Survey (NHANES) Food Questionnaire.[15] Participants who reported no consumption of meat, meat products, poultry, fish and seafood were considered adherent to the VD. Adherence to the MD was assessed using the Medi-Lite adherence score,[16] considering adherents the participants who reported ≥10 points in a scale ranging from 0 to 18.

2.4 | Laboratory measurements

Venous blood samples were collected at the beginning and at the end of the intervention period in evacuated plastic tubes (Vacutainer; Becton Dickinson). Samples were centrifuged at 3,000 rpm for 15 minutes (4°C) and stored in aliquots at –80°C until further analyses. Kidney function parameters (uric acid, urea and creatinine) were measured according to conventional laboratory standard methods. To convert urea to blood urea nitrogen (BUN), we multiplied by 0.467, while GFR was estimated (eGFR) using the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) Equation [17] Mild kidney impairment was defined as eGFR<90 mL/minute/1.73m^2.

2.5 | Statistical analysis

The study was originally designed to have adequate statistical power (power >80% and $P < .05$) to measure meaningful changes in body weight, BMI and fat mass, that is primary outcomes of the study. Continuous variables were presented as means and standard deviations (SDs) or medians and ranges, as appropriate. Categorical variables were presented as frequencies and percentages. Changes (from pre- to post-intervention) within each group were calculated using the Wilcoxon test, while differences between groups were estimated using the Mann-Whitney U test. The $\chi 2$ tests were used for categorical variables.

To test the effects of the VD and MD on kidney function markers, a general linear model, adjusted for age, sex, physical activity (absent/light, moderate), alcohol consumption (<1 AU/day, 1-2 AU/day; >2 AU/day), smoking (yes, no), hypertension (yes, no), LDL cholesterol (≤115 mg/dL, >115 mg/dL), glucose (<110 mg/dL, 110-126 mg/dL) and body weight change, was conducted. Because these tests assume normal data distribution, nondistributed data were transformed into logs, and further analyses were performed with the processed data. However, to facilitate interpretation, the log data were again converted to the original scale (antilog) and presented as geometric means with 95% CIs. Finally, a linear regression analysis was conducted to evaluate the relationship between changes in kidney function markers and changes in dietary composition, after adjustment for age, sex and body weight change. Outcomes were analysed through on-treatment procedures. P values < .05 were considered statistically significant. The statistical package PASW 20.0 for Macintosh (SPSS Inc) was used.

3 | RESULTS

3.1 | Baseline characteristics of the study population

One hundred and seven participants completed the first 3 months of dietary intervention and were included in the analysis. Table 1 presents the baseline demographic and clinical characteristics of study participants, according to the randomization. No significant differences for demographic characteristics and cardiovascular traditional risk factors were found between the participants who started with the VD and the MD. With regard to kidney function parameters, no participant was diagnosed with chronic kidney disease, and the proportion of mild eGFR impairment was not significantly different between the VD and MD groups.

3.2 | Nutritional profiles

Total energy and macronutrients' intake at baseline and after the dietary intervention period are reported in Table 2. At baseline, participants randomized to the VD had a dietary profile consisting of about 2,125 kcal/day, 47% carbohydrates, 36% fat and 16% protein, with 1.12 g/kg/day of protein. Participants randomized to the MD reported a dietary profile that included 2,039 kcal/day, 47% carbohydrates, 36% fat and 17% protein, with 1.05 g/kg/day of protein. There were no significant differences between the two groups.

TABLE 1 Baseline characteristics of the study population according to the randomization

Characteristics	VD (n = 54)	MD (n = 53)	*P* value
Age, yr	51 (24-70)	52 (21-75)	.607
Females, n (%)	43 (79.6)	39 (73.6)	.460
Body weight, kg	82.2 ± 16.1	84.0 ± 16.6	.599
BMI, kg/m^2	29.8 ± 4.6	30.7 ± 4.6	.294
Alcohol consumption			
<1 AU/day	46 (85.2)	42 (79.2)	.685
1-2 AU/day	7 (13.0)	9 (17.0)	
>2 AU/day	1 (1.9)	2 (3.8)	
Smoking habit, n (%)	4 (7.4)	11 (20.8)	.138
Absent or light physical activity, n (%)	48 (88.9)	48 (90.6)	.609
Blood pressure >140/90 mmHg, n (%)	11 (20.4)	13 (24.5)	.606
Total cholesterol >190 mg/dL, n (%)	43 (79.6)	40 (75.5)	.606
LDL cholesterol >115 mg/dL, n (%)	42 (77.8)	39 (73.6)	.613
Triglycerides >150 mg/dL, n (%)	15 (27.8)	17 (32.1)	.627
Fasting glucose 110–126 mg/dL, n (%)	5 (9.3)	8 (15.1)	.356
Kidney function			
Creatinine >1.2 mg/dL	0	1 (1.9)	.311
BUN >20 mg/dL	17 (31.5)	13 (24.5)	.382
eGFR <90 mL/min/1.73 m^2	6 (11.1)	9 (17.0)	.423

Note: Data are reported as median (min-max range), mean ± SD or number and percentage as appropriate.

Abbreviations: AU, Alcoholic Unit; BMI, Body Mass Index; BUN, Blood Urea Nitrogen; Egfr, Estimated Glomerular Filtration RateMD Mediterranean Diet; LDL, Low-Density Lipoprotein; VD, denotes Lacto-Ovo-Vegetarian Diet.

After the 3 months dietary intervention, total energy and fat intake decreased significantly ($P < .05$) in both groups. In contrast, the contribution of carbohydrates as a percentage of total energy increased. Protein intake showed an opposite trend: in the VD group, the contribution of protein as a percentage of total energy decreased by 8.3%, while in the MD group it increased by 7.5%. In terms of grams of protein per kilogram of body weight per day, VD participants showed a decrease in consumption of 34.8%, while MD participants showed a decrease of 17.1%. Fibre intake significantly increased in both groups, with a 54.5% increase in the VD group and 56% increase in the MD group. Significant differences between groups were observed for changes in protein ($P < .05$) and fibre intake ($P < .001$).

3.3 | Effects of VD and MD on kidney function parameters

The effect of the two diets on kidney function markers was evaluated by conducting a general linear model for repeated measurements adjusted for possible confounding factors such as age, sex, physical activity, alcohol, smoking, hypertension, LDL cholesterol, glucose and body weight change. As reported in Table 3, a significant reduction in creatinine (−5.3%; $P < .001$), urea nitrogen levels (−9%; $P = .001$), BUN (−8.7%; $P = .001$), and BUN/creatinine ratio (−5.8%; $P < .001$) and an increase in eGFR (+3.5%; $P = .001$) was observed during the VD period. On the contrary, no significant changes were noted in the MD group. Variations obtained in the two dietary intervention were significantly different ($P < .0001$) for creatinine levels, BUN/creatinine and eGFR, for which opposite trends were observed in the VD and MD groups (Figure 1).

To explore possible associations between changes in kidney function markers and changes in dietary composition, a linear regression analysis with kidney function markers as dependent variables and variations of protein intake and fibre intake as independent was conducted. After adjustment for possible confounding factors such as age, gender and body weight change, no significant associations ($P > .05$) were found for all the variables analysed.

4 | DISCUSSION

This randomized controlled trial is the first to assess markers of kidney function in a group of subjects with medium-to-low cardiovascular risk profile who followed a dietary intervention with VD and MD. After 3 months, VD resulted in a significant decrease in creatinine, urea nitrogen levels, BUN and BUN/creatinine ratio, and an increase in eGFR, while MD did not affect kidney function markers.

Kidney disease has a major effect on global health, both as a direct cause of morbidity and mortality and as an independent risk factor for cardiovascular disease.[1,18] Emerging evidence supports the role of dietary factors in the prevention and management of CKD; however, so far, no specific diet has been recognized as able to prevent or ameliorate this condition. According to recent findings, diet may positively influence kidney function due to its ability to affect the cardiovascular risk factors involved in the onset and maintenance of impaired kidney function.[19] In this regard, VD and MD have attracted increasing attention. These dietary profiles are both aimed at discouraging consumption of refined cereals, processed foods, meat and meat products, while maximizing the consumption of whole, plant-based foods. Although the benefits of both diets on several

TABLE 2 Changes in total energy and macronutrients' intake after the dietary intervention periods

	VD pre (n = 54)	VD post (n = 54)	Delta changes	MD pre (n = 53)	MD post (n = 53)	Delta changes	*P* ($\Delta_{VD\ vs.}$ Δ_{MD})[b]
Total energy, kcal/day	2124.8 (1979.2-2270.4)	1519.5 (1492.9-1546.1)[a]	−605.3 (−743.2; −467.4)	2038.6 (1883.6-2193.6)	1538.8 (1515.8-1561.9)[a]	−499.8 (−655.2; −344.4)	.140
Carbohydrates, % of energy	47.5 (45.2-49.8)	54.1 (54.1-54.2)[a]	6.64 (4.33; 8.96)	46.8 (44.2-49.4)	52.3 (52.2-52.4) [a]	5.52 (2.95; 8.08)	.493
Carbohydrates, g/day	250.8 (231.3-270.4)	219.4 (215.6-223.3)[a]	−31.4 (−50.1; −12.7)	232.6 (214.5-250.7)	214.8 (211.4-218.2)	−17.8 (−36.2; 0.63)	.331
Fat, % of energy	36.7 (35-38.4)	30.4 (30.3-30.5)[a]	−6.27 (−7.94; −4.59)	37.4 (35.4-39.5)	29.1 (28.9-29.2[a]	−8.3 (−10.4; −6.31)	.125
Fat, g/day	86.8 (78.8-94.7)	51.4 (50.5-52.3)[a]	−35.4 (−43.1; −27.6)	83.5 (75.6-91.5)	49.7 (48.9-50.3)[a]	−33.9 (−41.9; −25.9)	.672
Protein, % of energy	16.8 (15.5-18)	15.4 (15.3-15.5)	−1.4 (−2.61; −0.10)	17.3 (16.2-18.4)	18.6 (18.5-18.7)[a]	1.3 (0.19; 2.43)	.005
Protein, g/day	90.1 (80.9-99.3)	58.6 (57.6-59.6)[a]	−31.5 (−40.4; −22.5)	86.3 (77.4-95.3)	71.5 (70.5-72.6)[a]	−14.8 (−23.8; −5.75)	.002
Protein pro/kilo, g/kg/day	1.12 (1.00-1.23)	0.73 (0.70-0.76)[a]	−0.39 (−0.49; −0.29)	1.05 (0.95-1.16)	0.87 (0.84-0.91)[a]	−0.18 (−0.28; −0.08)	.002
Dietary fibre, g/1000 kcal	15.6 (9.6-21.6)	24.1 (24-24.2)[a]	8.5 (2.48; 14.5)	12.5 (8.9-16.1)	19.5 (19.4-19.69[a]	7 (3.46; 10.5)	<.001

Note: Data are reported as mean and 95% confidence intervals

Abbreviations: MD, Mediterranean DietVD denotes Lacto-Ovo-Vegetarian Diet.

[a]$p<0.05$ for changes within each group (from pre- to post-intervention).

[b]Changes between groups.

TABLE 3 Changes in kidney function parameters after the dietary intervention periods

	VD pre (n = 54)	VD post (n = 54)	Delta changes	MD pre (n = 53)	MD post (n = 53)	Delta changes	P ($\Delta_{VD\ vs.}$ Δ_{MD}) [b]
Creatinine, g/dL	0.76 (0.74-0.78)	0.72 (0.69-0.74)[a]	–0.04 (−0.06; −0.02)	0.75 (0.72-0.78)	0.76 (0.74-0.79)	0.01 (−0.01; 0.04)	<.0001
Urea nitrogen, mg/dL	32.2 (30.4-33.9)	29.3 (27.4-31.1)[a]	–2.91 (−4.59; −1.23)	34.2 (32.0-36.5)	32.3 (30.1-34.6)	–1.91 (−4.23; 0.42)	.412
BUN, mg/dL	15.0 (14.2-15.8)	13.7 (12.8-14.5)[a]	–1.36 (−2.14; −0.57)	16.0 (14.9-17.0)	15.1 (14.0-16.1)	–0.89 (−1.97; 0.19)	.412
Uric acid, g/dL	4.16 (3.95-4.38)	4.06 (3.85-4.27)	–0.10 (−0.22; 0.02)	4.37 (4.11-4.63)	4.44 (4.14-4.73)	0.07 (−0.13; 0.27)	.075
BUN/creatinine	75.9 (73.7-78.1)	71.5 (68.9-74.1)[a]	–4.35 (−6.39; −2.31)	75.1 (71.7-78.3)	76.4 (73.6-79.2)	1.34 (−1.01; 3.69)	<.0001
eGFR, ml/min/1.73 m^2	96.5 (94.2-98.9)	99.9 (97.4-102.3)[a]	3.37 (1.37; 5.37)	97.0 (93.9-100.1)	95.7 (93.0-98.5)	–1.27 (−3.7; 1.13)	<.0001

Note: Data are reported as mean and 95% confidence intervals.

Abbreviations: MD Mediterranean Diet; VD denotes Lacto-Ovo-Vegetarian Diet.

General linear model for repeated measurements adjusted for age, sex, physical activity, alcohol, smoking, hypertension, LDL cholesterol, glucose and weight change.

[a]$p<0.05$ for changes within each group (from pre- to post-intervention).

[b]Changes between groups.

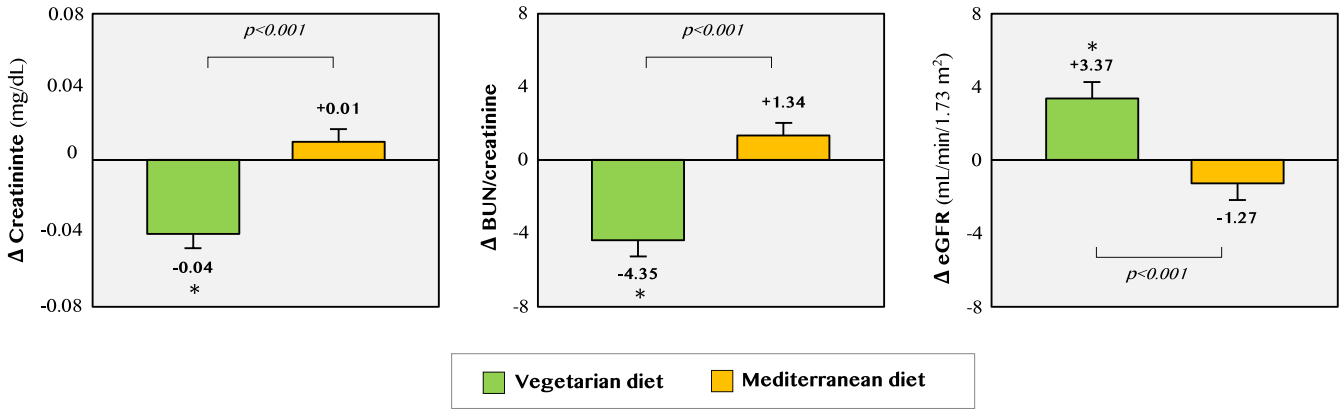

FIGURE 1 Delta change of creatinine, BUN/creatinine ratio and eGFR after the VD and MD periods

health outcomes have been widely demonstrated,[20] their relationship with kidney function and CKD remains poorly understood and is still being debated. Nephrologists traditionally did not recommend plant-based diets because they were considered dangerous for CKD patients, due to their high potassium content and possible nutritionally inadequacy.[5] However, as VD generally offers protein quantities that are consistent with low-protein diets (i.e., 0.6-0.8 g/kg/day) and high amounts of fibre, recently it has been postulated that it may have additive positive effects on kidney function.[5]

In our study, VD was effective in improving kidney function parameters even after adjustment for possible confounding factors such as weight change, lipid profile, systolic pressure and fasting blood glucose, suggesting that this dietary pattern may have a direct influence on kidney function protection, at least in the short-term. These results are in line with several observational studies, conducted in apparently healthy young or middle-aged individuals from different populations, which have shown better kidney function parameters and/or lower prevalence of CKD among vegetarians than among omnivores. A study

in Thailand revealed a significantly lower level of BUN, BUN/creatinine ratio and a lower urinary protein excretion rate in vegans compared to nonvegans,[21] while a recent cross-sectional study in China reported that vegetarians had better kidney function parameters than nonvegetarians, also after adjustment for possible confounding factors.[22] In another cross-sectional study on 55,113 participants from Taiwan, VD was significantly associated with lower prevalence of CKD,[23] and similar findings were reported in two prospective cohort studies after 6.1 years [24] and 24 years [25] of follow-up.

In the MD group, no significant changes were observed. The impact of a MD intervention was investigated also in the context of the PREDIMED study, and the authors obtained similar results to this study.[9] These findings, however, are in contrast to some observational studies that suggested a relationship between adherence to the MD and improved kidney function.[6,7,26] In our study, MD and VD groups differed only in terms of changes in protein and fibre intake. In fact, the intake of protein per kilogram of body weight per day decreased with both dietary interventions, but the decrease in the VD group was twice as large as in the MD group. In contrast, fibre intake increased more (in terms of percentages) in the MD group. Although this might suggest possible relationships between protein, fibre intake and kidney markers, correlation analyses showed no significant associations. This could be explained by several factors. Firstly, all participants had a protein intake in line with recommended dietary intake standards, regardless of dietary interventions. Furthermore, it is difficult to say whether it was the lower intake or the different source of protein during the VD period that led to better kidney function. Indeed, although there is no conclusive evidence yet, it appears that proteins in VD are less fermentable and have been associated with reduced production, exposure and absorption of uremic toxins such as indoxyl sulphate, p-cresyl sulphate and trimethylamine oxidase.[27] A similar effect was observed for dietary fibre, the consumption of which was associated with increased production of short-chain fatty acids and improved integrity of tight junctions, resulting in reduced intestinal permeability of uremic toxins.[28] In addition to this, as reported in a meta-analysis of controlled feeding studies, increased fibre intake appears to be associated with a reduction in urea and creatinine levels in a dose-dependent manner.[29] In our study, it should be noted that although the increase in fibre intake was greater in the MD group, the daily fibre intake was higher in those following VD, and this may partially explain the results.

Some limitations on this study should be mentioned. Firstly, the short duration of the study and the limited number of participants allow only initial possible interpretation of the result. Studies with a longer duration and a larger population are needed to confirm these preliminary findings. Secondly, kidney function markers were determined once at baseline and once after 3 months of intervention, with no repeated or periodic measurements. The known biological variability of these measurements may have led to misclassification; however, measurements were done in a core laboratory, thus highly reducing the variability. Thirdly, we did not directly measure GFR from creatinine clearance. However, we estimated it by using the CKD-EPI equation that is considered the most appropriate for obese population up to a BMI range of 40 kg/m.[230] Finally, we acknowledge that this study was not originally designed for these analyses, but the results suggest that more studies are warranted to assess possible differences in responses to VD and MD. The strengths of the study, on the other hand, include the comparability between the two diets in terms of total energy and macronutrients, and the high rate of adherence of the subjects of both groups to the assigned diet. Furthermore, the participants were all omnivores that modified their dietary habits for the intervention study and were not previously lacto-ovo-vegetarian. In addition, none of participants took medication or drugs, which could have influenced the results, for the duration of the study.

In conclusion, the results of this study suggest that VD has potential benefits for kidney function that are not directly explained by changes in dietary composition. This leads us to speculate that other aspects of this dietary pattern may be involved and lays the groundwork for possible future research to confirm the effects of VD on kidney function.

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CONFLICT OF INTEREST

None.

AUTHORS CONTRIBUTIONS

research idea and study design: MD, BC, GP, FS; data acquisition: MD, GP, IG, FS; data analysis/interpretation: MD, BC, FC, AG, BG, RM, FS; statistical analysis: MD, FS; supervision or mentorship: FS, AG, BG, RM. Each author contributed important intellectual content during manuscript drafting or revision and agrees to be personally accountable for the individual's own contributions and to ensure that questions pertaining to the accuracy or integrity of any portion of the work, even one in which the author was not directly involved, are appropriately investigated and resolved, including with documentation in the literature if appropriate.

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REFERENCES

1. GBD Chronic Kidney Disease Collaboration. Global, regional, and national burden of chronic kidney disease, 1990–2017: a systematic analysis for the global burden of disease study 2017. *Lancet*. 2020;395:709-733.
2. Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *N Engl J Med*. 2004;351:1296-1305.
3. Papademetriou V, Nylen ES, Doumas M, et al. Chronic kidney disease, basal insulin glargine, and health outcomes in people with dysglycemia: the ORIGIN study. *Am J Med*. 2017;130:1465.
4. Carrero JJ, González-Ortiz A, Avesani CM, et al. Plant-based diets to manage the risks and complications of chronic kidney disease. *Nat Rev Nephrol*. 2020;16:525-542.
5. Joshi S, Hashmi S, Shah S, et al. Plant-based diets for prevention and management of chronic kidney disease. *Curr Opin Nephrol Hypertens*. 2020;29:16-21.
6. Bach KE, Kelly JT, Palmer SC, et al. Healthy dietary patterns and incidence of CKD: a meta-analysis of cohort studies. *Clin J Am Soc Nephrol*. 2019;14:1441-1449.
7. Ajjarapu AS, Hinkle SN, Li M, et al. Dietary patterns and renal health outcomes in the general population: a review focusing on prospective studies. *Nutrients*. 2019;11:1877.
8. Mekki K, Bouzidi-bekada N, Kaddous A, et al. Mediterranean diet improves dyslipidemia and biomarkers in chronic renal failure patients. *Food Funct*. 2010;1:110-115.
9. Díaz-López A, Bulló M, Martínez-González MÁ, et al. Effects of mediterranean diets on kidney function: a report from the PREDIMED trial. *Am J Kidney Dis*. 2012;60:380-389.
10. Soroka N, Silverberg DS, Greemland M, et al. Comparison of a vegetable-based (soya) and an animal-based low-protein diet in predialysis chronic renal failure patients. *Nephron*. 1998;79:173-180.
11. Sofi F, Dinu M, Pagliai G, et al. Low-calorie vegetarian versus mediterranean diets for reducing body weight and improving cardiovascular risk profile: CARDIVEG study (cardiovascular prevention with vegetarian diet). *Circulation*. 2018;137:1103-1113.
12. Sofi F, Dinu M, Pagliai G, et al. Mediterranean versus vegetarian diet for cardiovascular disease prevention (the CARDIVEG study): study protocol for a randomized controlled trial. *Trials*. 2016;17:233.
13. Simera I, Moher D, Hoey J, et al. A catalogue of reporting guidelines for health research. *Eur J Clin Invest*. 2010;40:35-53.
14. Acquistucci R. Società Italiana di nutrizione umana, SICS. LARN, livelli di assunzione di riferimento di nutrienti e energia per la popolazione Italiana. IV revisione. SICS. 2014.
15. NHANES Food questionnaire (available at https://www.cdc.gov/nchs/data/nhanes/nhanes_03_04/tq_fpq_c.pdf. [Accessed January 14, 2021].
16. Sofi F, Dinu M, Pagliai G, et al. Validation of a literature-based adherence score to mediterranean diet: the MEDI-LITE score. *Int J Food Sci Nutr*. 2017;68:757-762.
17. Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. *Ann Intern Med*. 2009;150:604-612.
18. Hyun YY, Kim H, Oh KH, et al. eGFR and coronary artery calcification in chronic kidney disease. *Eur J Clin Invest*. 2019;49(6):e13101.
19. Kramer H. Diet and chronic kidney disease. *Adv Nutr*. 2019;10:S367-S379.
20. Dinu M, Pagliai G, Angelino D, et al. Effects of popular diets on anthropometric and metabolic parameters: an umbrella review of meta-analyses of randomized controlled trials. *Adv Nutr*. 2020;11:815-833.
21. Wiwanitkit V. Renal function parameters of Thai vegans compared with non-vegans. *Ren Fail*. 2007;29:219-220.
22. Xu K, Cui X, Wang B, et al. Healthy adult vegetarians have better renal function than matched omnivores: a cross-sectional study in China. *BMC Nephrol*. 2020;21:268.
23. Liu HW, Tsai WH, Liu JS, et al. Association of vegetarian diet with chronic kidney disease. *Nutrients*. 2019;11:279.
24. Asghari G, Momenan M, Yuzbashian E, et al. Dietary pattern and incidence of chronic kidney disease among adults: a population-based study. *Nutr Metab*. 2018;15:88.
25. Kim H, Caulfield LE, Garcia-Larsen V, et al. Plant-based diets and Incident CKD and kidney function. *Clin J Am Soc Nephrol*. 2019;14:682-691.
26. Chrysohoou C, Panagiotakos DB, Pitsavos C, et al. Adherence to the Mediterranean diet is associated with renal function among healthy adults: the ATTICA study. *J Ren Nutr*. 2010;20:176-184.
27. Mafra D, Borges N, Alvarenga L, et al. Dietary components that may influence the disturbed gut microbiota in chronic kidney disease. *Nutrients*. 2019;11:496.
28. Camerotto C, Cupisti A, D'Alessandro C, et al. Dietary fiber and gut microbiota in renal diets. *Nutrients*. 2019;11:2149.
29. Chiavaroli L, Mirrahimi A, Sievenpiper JL, et al. Dietary fiber effects in chronic kidney disease: a systematic review and meta-analysis of controlled feeding trials. *Eur J Clin Nutr*. 2015;69:761-768.
30. Lemoine S, Guebre-Egziabher F, Sens F, et al. Accuracy of GFR estimation in obese patients. *Clin J Am Soc Nephrol*. 2014;9:720-727.

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