Original Article

Comparison of Three Diet Quality Indices for Patients with Chronic Kidney Disease

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Abstract

Background: Patients with chronic kidney disease (CKD) have specific dietary needs due to recommended dietary restrictions. However, there is no specific index for evaluating the quality of diet in patients with CKD.

Objective: To define and compare three specific diet quality indices in patients with CKD.

Methods: Two hundred twenty-one subjects with CKD were selected for this cross-sectional study. The patients' Dietary intake was assessed with a validated food frequency questionnaire. Total protein intake per body weight (TP/BW), animal protein intake per body weight (AP/BW) and animal protein to vegetable protein ratio (AP/VP) were defined as diet quality indices. Renal function was measured by blood urea nitrogen (BUN) and serum creatinine (Cr).

Results: Patients in the highest tertile of TP/BW and tertile of AP/BW consumed more amounts of nutrients which should be limited in CKD (i.e., sodium, potassium and phosphorus). Subjects in the last tertile of AP/BW had higher BUN and Cr. A marginally significant increased risk of higher stage of CKD across the tertiles of AP/BW was observed after adjusting for potential confounders (OR = 2.20, 95% CI: 1.06, 4.56; *P* = 0.08).

Conclusion: The results showed that AP/BW is a good diet quality index and is marginally associated with being in higher stages of CKD.

Keywords: Chronic kidney disease, diet quality, dietary protein

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Introduction

The high prevalence of chronic kidney disease (CKD) has raised concerns in both developed and developing countries. According to the NHANES data, 13.1% of the American population suffer from CKD.[1] In Iran, the prevalence of CKD among adults has been reported as 18.9%.[2] Patients with CKD are at greater risk for all-cause mortality.[3]

Dietary intake has an important role in medical management of CKD, and dietary protein is one of the most important parts of dietary intervention in patients with CKD. Studies have reported that adherence to a high protein diet may increase the risk of renal hypertrophy, glomerular hyperfiltration and renal blood flow in healthy subjects.[4] Therefore, a low protein diet is recommended to patients with CKD.[5] Observational evidence shows that high intake of dietary protein may worsen CKD control.[6] A meta-analysis revealed that a low protein diet could decrease the risk of death from renal disease in subjects with CKD.[7]

The source of dietary protein is another controversial issue. Several studies have reported that consumption of vegetable protein, especially soy products, may have beneficial effects on renal function.[8–14] On the other hand, it has been recommended that more than 50% of ingested protein should be selected from sources of high biological value (i.e., animal proteins such as egg, milk and meat).[15] Therefore, assessment of dietary quality among patients with CKD has been made difficult by these inconsistent findings and recommendations. Moreover, patients with CKD should restrict dietary sodium, potassium and phosphorus because of insufficient renal ability to excrete excess amounts of these minerals.[5] Therefore, the recommended diet for these patients has lower amounts of sources of these nutrients such as fruits, vegetables, legumes, dairies and whole grains.[16]

These restrictions are in contrast with nutritional recommendations for healthy subjects. For instant, HEI-2010 has suggested a diet rich in fruits, vegetables, whole grains and low fat dairies[17] and we cannot assess diet quality of the subjects with CKD by general recommendations for healthy subjects. Therefore, the aim of this study was to introduce three specific diet quality indices based on the amount and source of dietary protein for patients with CKD. Also, we checked the validity of these indices to predict being in higher stages of CKD by biochemical variables.

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Materials and Methods

Subjects

This is a cross-sectional study conducted in 2015 in Isfahan, Iran. We used the following formula to calculate sample size: $n = [Z_{1-\alpha/2}+Z_{1-\beta}]^2/[0.5*\log(1+r/1-r)]$. According to this formula ($r = 0.2$, $\alpha = 0.05$ and $\beta = 0.20$), 193 patients were recruited for the study. Among subjects who referred to nephrology clinics, patients with CKD were diagnosed. A nephrologist calculated estimated glomerular filtration rate (eGFR) for each subject (18) and eGFR < 60 mL/min/1.73m^2 was considered as CKD.[19] Two hundred twenty-one subjects with CKD were selected using convenience sampling method. CKD was categorized as stage 3 ($30 \leq$ eGFR ≤ 59 mL/min/1.73m^2), stage 4 ($15 \leq$ eGFR ≤ 29 mL/min/1.73m^2) and stage 5 (eGFR < 15 mL/min/1.73m^2).[19] Other diseases (e.g., diabetes and nephrolithiasis) were treated by relevant specialists. Written consent was provided by all patients. The Ethics Committee of Isfahan University of Medical Sciences approved the study protocol (Code: IR.MUI.REC.1394.3.192). Financial support was provided by the Research Council of the Food Security Research Center, Isfahan University of Medical Sciences, Isfahan, Iran.

Dietary assessment

The patients' dietary intake during the previous year was assessed with a validated food frequency questionnaire (FFQ) completed by trained assistants. This semi-quantitative FFQ covered 168 food items frequently consumed by Iranians. Reported food consumption was converted to g/day using household measures and then analyzed by Nutritionist IV software (N-Squared Computing, Salem, OR). The results of validation study have been presented elsewhere.[20,21] Subjects who reported < 800 or > 4200 kcal/d were excluded.

Diet quality indices

Three specific diet quality indices were defined based on the amount and source of dietary protein: *1)* Total protein intake per body weight (TP/BW), calculated by summing protein content of all consumed foods. The amount of protein intake for each individual was converted to grams per kilogram body weight (g/kg). *2)* Animal protein intake per body weight (AP/BW), calculated by summing protein content of all consumed foods from animal sources. The amount of animal protein intake for each individual was converted to grams per kilogram body weight (g/kg). *3)* Animal protein to vegetable protein ratio (AP/VP), calculated by dividing animal protein by animal protein minus total protein (animal protein/ [total protein – animal protein]). We did not include body weight in this index because it is a ratio and, therefore, numerator and denominator were multiplied by the same number.

Biochemical measures

A blood specimen was taken after 12-hour overnight fasting. Obtained specimens were centrifuged at 3000×g for 10 min. Blood urea nitrogen (BUN) level was measured using urease enzyme. A standard spectrophotometric assay was conducted to assess the concentration of serum creatinine (Cr). All kits were produced by Pars Azmoon Inc.

Other variables

The patients' general characteristics were obtained through interviews. We provided a questionnaire consisting of questions regarding income, occupation, education and region of residence to evaluate socioeconomic status. Weight was measured with a digital scale to the nearest 0.1 kg. Height was assessed by self reported measures. By dividing weight (kg) by square of height (m^2), body mass index was calculated.

Statistical analysis

We tested normal distribution of variables using Kolmogorov-Smirnov test and histogram curve. Qualitative (sex ratio, CKD stage, physical activity level [low, moderate and high], and tertiles of socioeconomic status) and quantitative (age, body mass index, BUN, creatinine and eGFR) variables were compared across the tertiles of diet quality indices using Chi-square test and analysis of variance (ANOVA), respectively. Energy-adjusted nutrient intakes across the tertiles of diet quality indices were compared with analysis of covariance (ANCOVA). Logistic regression was run to calculate odds ratio and 95% confidence interval of being in higher stages of CKD. The risk of being in higher stages of CKD was presented in crude and 3 adjusted models. The first model was adjusted for age, physical activity and socioeconomic status. Further adjustment was considered for systolic and diastolic blood pressure in the second model. The third model was additionally adjusted for total energy intake and body weight (body weight was adjusted only in case of animal protein to vegetable protein ratio). Quantitative variables are reported as mean ± standard deviation. We used SPSS version 20 (IBM) to analyze the data.

Results

Table 1 displays the general characteristics of subjects with CKD across the tertiles of three diet quality indices. The percent of males was significantly different across tertiles of AP/BW ($P = 0.04$) and tertiles of AP/VP ratio ($P = 0.03$). We also observed a significant difference in body mass index across tertiles of TP/BW and tertiles of AP/BW ($P < 0.01$ for both). There was no significant difference in age, socioeconomic status, physical activity and CKD stage across tertiles of three diet quality indices.

Table 2 shows energy adjusted dietary intake of selected nutrients which should be limited in renal diseases among subjects with chronic kidney disease across tertiles of three diet quality indices. We observed significantly higher intake of fat, cholesterol, saturated fatty acid, potassium, phosphorus and sodium among subjects of the highest tertile of TP/BW and tertile of AP/BW ($P < 0.01$ for all). Regarding the tertiles of AP/VP, there was a significant difference in cholesterol ($P = 0.02$), saturated fatty acid ($P = 0.01$) and phosphorus ($P < 0.01$).

Tables 3 presents the mean of biochemical values of subjects with CKD across tertiles of three diet quality indices. We did not observe a significant difference in BUN, Cr and eGFR across tertiles of TP/BW ($P = 0.05$ for BUN and Cr; $P = 0.41$ for eGFR) and tertiles of AP/VP ($P = 0.09$ for BUN; $P = 0.69$ for Cr and P=0.14 for eGFR). Although subjects in the last tertile of AP/BW had higher BUN ($P = 0.03$) and Cr ($P = 0.04$), there was no significant difference in eGFR ($P = 16$).

Table 4 shows the risk of higher stage of CKD across tertiles of the three diet quality indices. The risk was reported in crude and 3 adjusted models. We did not observe any significantly increased risk of higher stage of CKD in crude and adjusted models across the tertiles of TP/BW. There was no significantly higher risk for higher stage of CKD in multivariate adjusted model across

Table 1. General characteristics of subjects with chronic kidney disease across tertiles of three diet quality indices.

Variables	Tertiles of total protein intake per body weight			*P* Value[1]	Tertiles of animal protein intake per body weight			*P* Value[1]	Tertiles of animal protein to vegetable protein ratio			*P* Value[1]
	T1 (≤ 0.65 gr/kg) N = 74	T2 (0.66–0.87 gr/kg) N = 74	T3 (>0.87 gr/kg) N = 73		T1 (≤ 0.27 gr/kg) N = 74	T2 (0.28–0.38 gr/kg) N = 74	T3 (>0.38 gr/kg) N = 73		T1 (≤ 0.61) N = 73	T2 (0.62–1.01) N = 75	T3 (>1.01) N = 75	
Age (y)	57.62 ± 14.71[2]	58.31 ± 13.90	53.74 ± 16.74	0.15	58.57 ± 13.70	55.27 ± 14.45	55.86±17.32	0.37	55.51 ± 14.13	57.80 ± 16.57	56.37 ± 14.93	0.65
Male (%)	60.8	68.9	78.1	0.08	75.7	58.1	74.0	0.04	74.0	76.0	57.5	0.03
SES (%)												
Low	14.9	20.3	19.2		17.6	21.6	15.1		20.5	20.0	13.7	
Moderate	67.6	63.5	65.8	0.92	62.2	64.9	69.9	0.67	60.3	69.3	67.1	0.42
High	17.6	16.2	15.1		20.3	13.5	15.1		19.2	10.7	19.2	
BMI (kg/m²)	27.83 ± 4.79	26.33 ± 3.88	23.33 ± 2.89	<0.01	27.53 ± 4.57	26.30 ± 4.32	23.66 ± 3.10	<0.01	26.51 ± 4.73	25.37 ± 3.84	25.65 ± 4.41	0.25
Physical activity level (%)												
Low	60.8	66.2	58.9		64.9	58.1	63.0		60.3	58.7	67.1	
Moderate	36.5	32.4	35.6	0.63	33.8	37.8	32.9	0.78	37.0	38.7	28.8	0.74
High	2.7	1.4	5.5		1.4	4.1	4.1		2.7	2.7	4.1	
CKD Stage (%)[3]												
3	67.6	70.3	63.0		71.6	70.3	58.9		74.0	69.3	57.5	
4	32.4	29.7	32.9	0.16	28.4	29.7	37.0	0.09	26.0	28.0	41.1	0.16
5	0.0	0.0	4.1		0.0	0.0	4.1		0.0	0.9	0.5	

[1]Calculated by chi-square test (for qualitative variables) or analysis of variance (for quantitative variables)
[2]Qualitative and quantitative variables are expressed as percentage and mean ± SD, respectively.
[3]Calculated by MDRD equation
BMI = body mass index, CKD = chronic kidney disease, SES = socioeconomic status.

Table 2. Dietary intake of selected nutrients which should be limited in renal disease among subjects with chronic kidney disease across tertiles of three diet quality indices.

Variables	Tertiles of total protein intake per body weight			*P* Value[1]	Tertiles of animal protein intake per body weight			*P* Value[1]	Tertiles of animal protein to vegetable protein ratio			*P* Value[1]
	T1 (≤ 0.65 gr/kg) N = 74	T2 (0.66-0.87 gr/kg) N = 74	T3 (>0.87 gr/kg) N = 73		T1 (≤ 0.27 gr/kg) N = 74	T2 (0.28–0.38 gr/kg) N = 74	T3 (>0.38 gr/kg) N = 73		T1 (≤ 0.61) N = 73	T2 (0.62–1.01) N = 75	T3 (>1.01) N = 75	
Fat (g)	38.17±9.81[2]	41.04±8.18	51.26±14.48	<0.01	37.57±10.16	43.14±11.87	49.76±12.16	<0.01	41.95±12.88	45.52±13.36	42.86±10.71	0.23
Cholesterol (mg)	82.11±38.81	104.59±47.16	130.70±54.89	<0.01	87.36±52.57	97.61±44.79	132.46±45.03	<0.01	92.09±59.03	113.27±45.85	111.49±45.56	0.02
Saturated Fatty acid (g)	10.19±3.72	11.88±3.68	15.12±5.15	<0.01	9.70±3.96	12.48±4.81	15.00±3.65	<0.01	11.07±5.38	12.86±4.35	13.21±4.00	0.01
Potassium (mg)	1939.62±684.08	2292.81±698.21	2641.08±862.49	<0.01	1971.70±779.30	2300.92±619.61	2600.34±869.99	<0.01	2166.55±811.42	2331.56±696.35	2369.49±885.07	0.23
Phosphorus (mg)	635.44±197.77	792.94±191.69	1083.69±345.34	<0.01	615.07±198.17	817.36±192.49	1079.59±336.99	<0.01	722.05±260.38	875.45±333.02	910.16±315.41	<0.01
Sodium (mg)	642.18±42.11	756.71±41.83	1148.92±42.08	<0.01	618.98±44.26	880.04±44.28	1047.42±44.48	<0.01	803.67±521.07	854.02±386.07	885.88±335.21	0.40

[1] Calculated by analysis of covariance
[2] Mean ± SD. All values are adjusted for total calorie intake.

Table 3. Mean of biochemical measures of subjects with chronic kidney disease across the tertiles of three diet quality indices.

Variables	Tertiles of total protein intake per body weight			*P* Value[1]	Tertiles of animal protein intake per body weight			*P* Value[1]	Tertiles of animal protein to vegetable protein ratio			*P* Value[1]
	T1 (≤ 0.65 gr/kg) N = 74	T2 (0.66-0.87 gr/kg) N = 74	T3 (>0.87 gr/kg) N = 73		T1 (≤ 0.27 gr/kg) N = 74	T2 (0.28–0.38 gr/kg) N = 74	T3 (>0.38 gr/kg) N = 73		T1 (≤ 0.61) N = 73	T2 (0.62–1.01) N = 75	T3 (>1.01) N = 75	
BUN (mg/dL)	29.76±13.48[2]	28.40±10.87	33.58±15.30	0.05	29.38±12.90	28.45±10.76	33.92±15.80[c]	0.03	28.14±11.37	30.59±14.37	32.98±14.12	0.09
Creatinine (mg/dL)	1.96±0.67	1.93±0.66	2.19±0.80	0.05	1.98±0.68	1.90±0.66	2.19±0.79[c]	0.04	1.97±0.75	2.03±0.69	2.07±0.73	0.69
eGFR[3] (mL/min/1.73m²)	37.97±12.72	39.12±12.13	36.37±12.63	0.41	38.94±12.47	38.98±12.17	35.55±12.69	0.16	39.78±12.40	37.99±12.13	35.72±12.79	0.14

BUN = blood urea nitrogen, FBS = fasting blood sugar, GFR = glomerular filtration rate, hs-CRP = high sensitivity reactive protein, LDL = low density lipoprotein.
[1]Calculated by analysis of variance
[2]mean±SD
[3]Calculated by MDRD equation
[a]Significant different between the first vs. last tertile
[b]Significant different between the first vs. second tertile
[c]Significant different between second vs. last tertile

Table 4. Odds ratio (95% CI) for higher stage of chronic kidney disease across tertiles of the three diet quality indices.

Models	Tertiles of total protein intake per body weight			*P* for trend	Tertiles of animal protein intake per body weight			*P* for trend	Tertiles of animal protein to vegetable protein ratio			*P* for trend
	T1 (≤ 0.65 gr/kg) N = 74	T2 (0.66–0.87 gr/kg) N = 74	T3 (>0.87 gr/kg) N = 73		T1 (≤ 0.27 gr/kg) N = 74	T2 (0.28–0.38 gr/kg) N = 74	T3 (>0.38 gr/kg) N = 73		T1 (≤ 0.61) N = 73	T2 (0.62–1.01) N = 75	T3 (>1.01) N = 75	
Crude	1 (Ref)	0.88 (0.44, 1.77)	1.22 (0.62, 2.41)	0.64	1 (Ref)	1.07 (0.52, 1.17)	1.86 (0.88, 3.50)	0.20	1 (Ref)	1.26 (0.61, 2.57)	2.10 (1.04, 4.22)	0.10
Model 1	1 (Ref)	0.86 (0.42, 1.76)	1.24 (0.62, 2.48)	0.58	1 (Ref)	1.12 (0.54, 2.30)	1.85 (0.92, 3.72)	0.12	1 (Ref)	1.33 (0.64, 2.77)	2.13 (1.05, 4.34)	0.10
Model 2	1 (Ref)	0.89 (0.43, 1.87)	1.35 (0.66, 2.73)	0.50	1 (Ref)	1.13 (0.54, 2.36)	2.00 (0.98, 4.02)	0.18	1 (Ref)	1.35 (0.64, 2.84)	2.36 (1.14, 4.89)	0.06
Model 3	1 (Ref)	1.21 (0.56, 2.64)	2.38 (0.97, 5.87)	0.13	1 (Ref)	1.19 (0.56, 2.49)	2.20 (1.06, 4.56)	0.08	1 (Ref)	1.30 (0.61, 2.76)	2.16 (1.02, 4.57)	0.12

Model 1: adjusted for age, physical activity and socioeconomic status; Model 2: model 1 + systolic and diastolic blood pressure; Model 3: model 2 + total energy intake and body weight (body weight was adjusted only in case of animal protein to vegetable protein ratio).

the tertiles of AP/VP. In contrast, we observed a marginally significantly increased risk across the tertiles of AP/BW after adjusting for potential confounders ($P = 0.08$).

Discussion

The results of the present study showed that patients in the highest tertile of TP/BW and tertile of AP/BW consumed more energy adjusted amounts of nutrients which should be limited in CKD. Also, we found that subjects in the last tertile of AP/BW had higher BUN and Cr. Moreover, a marginally significantly increased risk was observed for higher stage of CKD across the tertiles of AP/BW after adjusting for potential confounders. To the best of our knowledge, this is the first study to compare these three indices to assess diet quality and being in the higher stages of CKD.

Our findings revealed that patients who were in the highest tertile of TP/BW and tertile of AP/BW consumed more amounts of nutrients which should be limited in CKD. In contrast, AP/VP failed to show reasonable results. This finding showed that TP/BW and AP/BW indices could reflect dietary intake of important nutrients beside dietary protein. Therefore, they are more reliable than the other introduced diet quality index, i.e. AP/VP.

We observed an increased intake of sodium, phosphorus and potassium across tertiles of TP/BW and tertiles of AP/BW. Previous studies reported that the sodium and phosphorus content of an animal source rich diet is high.[22,23] In our study, a higher potassium intake was observed among those in the highest tertile of TP/BW and tertile of AP/BW because Iranians consume animal proteins, especially meats, with vegetables (e.g., carrots, tomatoes, potatoes and stewed leafy vegetables).

We found that subjects in the last tertile of AP/BW had higher BUN and Cr. A previous feeding study reported that meat intake may result in significant increase in Cr[24] and urea nitrogen.[25] Meat is rich in creatine phosphate, a source of energy for muscular contraction.[25] Therefore, the plasma and urinary concentrations of biochemical metabolite of creatine phosphate (i.e., creatinine) are increased after consuming a diet rich in meats.[25] In our study, TP/BW and AP/VP could not show any significant results regarding BUN and Cr. It seems that vegetable protein included in these two indices attenuates significant results.

We observed a marginally significantly increased risk across the tertiles of AP/BW after adjusting for potential confounders. Sex was not included in the multivariate adjusted model because it had been included in the MDRD equation.[18] A previous study observed that removing red meat from the diet may improve renal function.[26] Reported results from a large prospective cohort study showed that total protein intake was significantly associated with reduction in eGFR among women with mild renal failure.[27] Due to the high creatinine content of meats,[24] it seems that the effect of meat consumption, especially red meat, on renal disease is greater than other sources of animal protein.

Our findings showed that AP/VP was not as good a predictor as AP/BW. It should be kept in mind that two factors contribute to changes of a ratio: a) changes in numerator, b) changes in denominator. Higher AP/VP may be due to lower animal protein intake or higher vegetable protein consumption. It is not clear which one of these two factors is responsible for lower/higher AP/VP. Therefore, we could not explain the observed findings regarding this index.

The design of the present study was cross-sectional, which is the most important limitation of this study. These diet quality indices should be evaluated in prospective cohort studies. In the current study, we used two biochemical variables (i.e. BUN and Cr). Future studies should focus on other renal function indices such as proteinuria and urine creatinine.

The major strength of this study is introducing and comparing three novel indices of diet quality for patients with CKD. Also, the source of dietary protein was considered in introducing the indices. As nutritional recommendations for patients with CK suggest lower intake of fruits, vegetables, legumes, dairies and whole grains,[16] usual diet quality indices (e.g., HEI-2010 and DQIs) cannot be used for these patients. Therefore, the results of this study may be helpful to find a good diet quality index for individuals with CKD.

In conclusion, the result of the present study showed that animal protein intake per body weight is a good diet quality index and is marginally associated with higher stages of CKD.

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