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Association between polyunsaturated fatty acids and progression among patients with diabetic kidney disease

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ABSTRACT

Aims: Diabetic kidney disease (DKD) is the major complication of diabetes mellitus (DM) and one of the leading causes of end-stage renal disease. Early detection and treatment are contributing to delay the progression of DKD. Dietary management has potential benefits for DKD, especially the intake of polyunsaturated fatty acids (PUFAs). However, there is a lack of sufficient evidence, so we aimed to explore the association between PUFAs intake and DKD progression.

Methods: In the National Heath and Nutrition Examination Survey (NHANES) between 2011–2018, a cross-sectional study was conducted among adults with T2DM. DKD was diagnosed with urine albumin to creatinine ratio (ACR) $\geq$ 30 mg/g or estimated glomerular filtration rate (eGFR) $<$ 60 ml/min/1.73 m^2. Using Survey package of R to arrange the collected PUFAs intake data in order from small to large and divide them into four equal parts, which were expressed as Q1, Q2, Q3 and Q4 respectively. To investigate the association between PUFAs intake and DKD, a weighted univariate logistic regression analysis was performed and the odds ratio (OR) and 95% confidence interval (CI) were calculated for the association with DKD and PUFAs quartiles.

Results: The study involved 3287 participants with T2DM, including 2043 non-DKD and 1244 DKD patients. The results showed that the intake of PUFAs was a protective factor for DKD ($p = 0.022$), and with the increase of the PUFAs, renal function improved in DKD patients, the adjusted mean of eGFR and Scr changing from 57 (41, 86) in Q1 to 71 (55, 101) ml/min in Q4 (*p 0.001), 103 (73, 131) in Q1 to 90 (68, 117) in Q4 ($p = 0.031$), respectively.

Conclusion: Our study indicated that intake of more PUFAs may contribute to delay DKD progression, while different n-6/n-3 ratios need to be explored to protect the kidney.

1. Introduction

Diabetic kidney disease (DKD) is the major microvascular complication of diabetes mellitus (DM), generating a large economic burden and accelerating the progression of kidney failure [1]. About 40% type 2 diabetes mellitus(T2DM) patients progress to DKD, and the incidence of DKD continues to increase [2]. DKD has already become the leading cause of end-stage renal disease (ESRD) worldwide and imposed significant financial burden [3,4]. Early diagnosis and treatment of DKD are necessary, and dietary intervention is the most basic[5]. In general, dietary interventions for DKD advocate a low-protein diet, requiring a daily protein intake of less than 0.8 g/kg of body weight/day for non-dialysis patients, while the recommended daily protein intake for regular dialysis patients is higher than 1.2 g/kg of body weight/day [6]. Since DKD patients have significantly higher cardiovascular risks than non-diabetic patients with chronic kidney disease, attention has been paid to reducing risk through intake of polyunsaturated fatty acids (PUFAs) in addition to pharmacological interventions and protein control [4].

PUFAs are mainly divided into n-6 (omega-6) and n-3 (omega-3) families, linoleic (LA) and α-linolenic (ALA) are members of the key PUFA of the n-6 and n-3 families [7,8]. Fig. 1 shows the major categories

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and foods included in n-3 and n-6 PUFAs. PUFAs are beneficial for renal function, a higher dietary intake of PUFAs may delay the progression of renal disease [9,10]. Indeed, higher levels of plasma PUFAs are associated with lower levels of proinflammatory markers, such as interleukin 6 (IL-6), tumor necrosis factor α(TNFα) [11]. PUFAs may increase estimated glomerular filtration rate (eGFR) via anti-inflammatory property [9]. Therefore, patients with DKD are advised to use more PUFAs and monounsaturated fatty acids in place of saturated fatty acids (SFAs), trans-fat, and cholesterol [6]. However, evidence for the renal protective effect of PUFAs is less, a randomized, controlled clinical trial finds that n-3 PUFAs fail to decline urinary protein excretion [12]. n-3 PUFA may act synergistically with renin-angiotensin-aldosterone system (RAAS) therapy to protect kidney [12]. Therefore, more studies are needed to confirm the important role of PUFAs in the diet of DKD patients. Exploring the relationship between dietary nutrients and the occurrence and development of DKD can provide a theoretical basis for the potential influence of the diet on the treatment of DKD, and further develop personalized nutritional therapy for DKD patients.

Consequently, the purpose of our study is to investigate the relationship between PUFAs and DKD in the National Health and Nutrition Examination Survey (NHANES) and determine the association of dietary intake of PUFAs with renal function.

2. Materials and methods

2.1. Data and sample sources

The data we used were from the NHANES, which was based on repeated cross-sectional surveys conducted by the National Center for Health Statistics (NCHS). NHANES used a complex stratified, multistage probabilistic approach to sample the U.S. population to ensure adequate representation, and collected baseline population data, health and nutrition status through questionnaires and home visits. The protocol was approved by the NCHS Research Ethics Review Board, and all participants signed informed consent. Detailed data could be found at https://www.cdc.gov/nchs/nhanes/. In this study, we combined the four NHANES cycles from 2011–2018, a total of 39156 participants were involved in the four cycles. We screened 23825 participants over the age of 18, 3144 with missing total PUFAs, 331 without albumin-to-creatinine ratio (ACR), 1021 without serum creatinine (Scr), 3293 participants with DM, and 6 with pregnancy. Eventually, 3287 participants were included in the study (Fig. 2).

2.2. Variable definitions

DM was defined as (1) the fasting plasma glucose (FPG) $\geq$ 7.0 mmol/L, or (2) Glycohemoglobin (GHB) $\geq$ 6.5%, or (3) previously diagnosed with diabetes by a physician. eGFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation (ml/min/1.73 m^2). The diagnosis of DKD was ACR $\geq$ 30 mg/g or eGFR $<$ 60 ml/min/1.73 m^2.

2.3. Other variable definitions

Age, gender, race, education, smoking status were self-reported by participants. Body mass index (BMI) was equal to weight (kg) divided by squared height (m^2). And BMI was classified as obesity ($\geq$30 kg/m^2), overweight (25–29.9 kg/m^2), normal weight (18.5–24.9 kg/m^2), and underweight ($<$ 18.5 kg/m^2). Smoking status was classified as never (smoked $<$ 100 cigarettes in their lifetime), former (smoked $>$ 100 cigarettes in their lifetime, but currently did not smoke), and current (smoked $>$ 100 cigarettes in their lifetime, and currently still smoke). Hypertension was defined as systolic blood pressure (SBP) $\geq$ 140 mmHg and/or diastolic blood pressure (DBP) $\geq$ 90 mmHg after repeated examination, or a previously reported diagnosis by doctor. Hyperlipidemia was defined by total cholesterol (TC) $\geq$ 240 mg/dL, triglycerides (TG) $\geq$ 200 mg/dL, low density lipoprotein (LDL-C) $\geq$ 160 mg/dL, high density lipoprotein (HDL-C) $<$ 40 mg/dL or a prior diagnosis of hyperlipidemia.

2.4. Covariates screening

This study included covariates that may affect the association between PUFAs and DKD. Demographics included age, gender, race, BMI, education level, smoking status, waist circumference, SBP, and DBP. Laboratory examination covered glycohemoglobin, plasma fasting

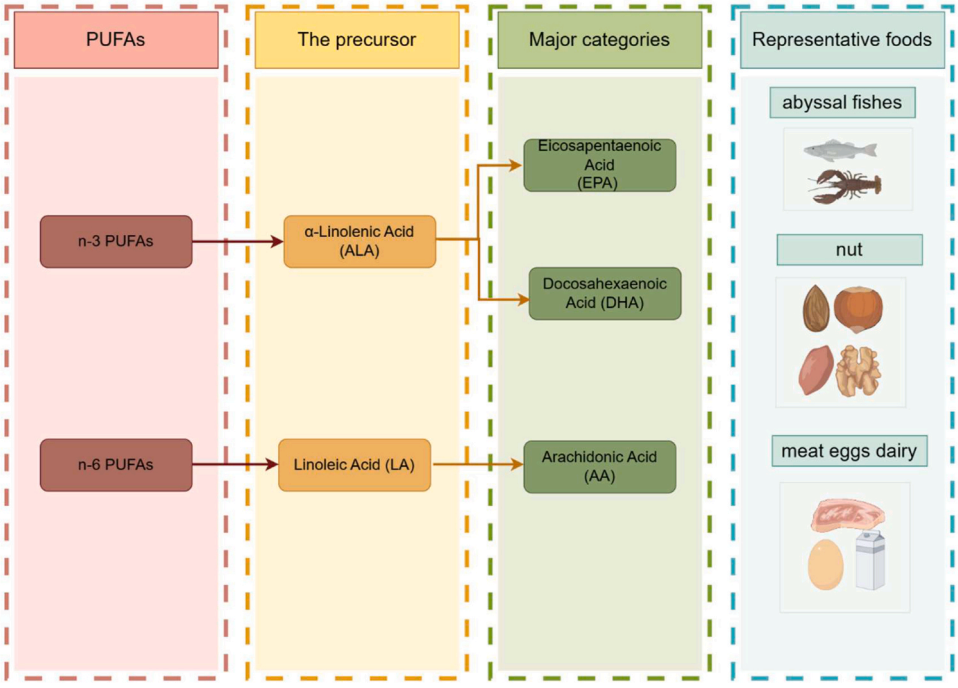

Fig. 1. The information about polyunsaturated fatty acids (By Figdraw).

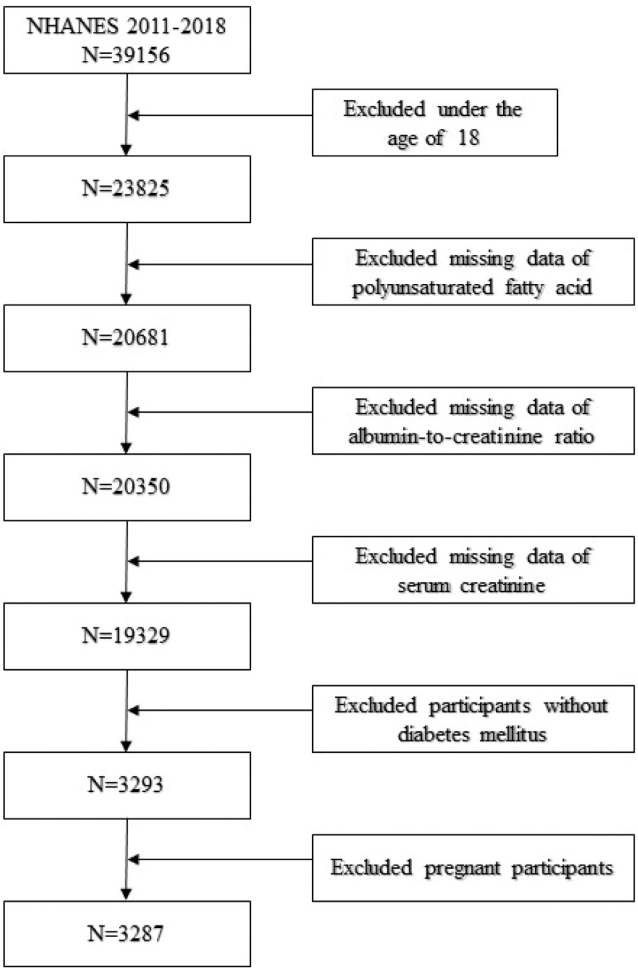

Fig. 2. The flowchart for screening participants from NHANES 2011–2018.

glucose, Scr, eGFR, blood urea nitrogen (BUN), serum uric acid (UA), ACR, albumin (ALB), aspartate aminotransferase (AST), alanine aminotransferase (ALT), HDL, LDL, TC, TG. Other factors included hypertension and hyperlipidemia.

2.5. Statistical analysis

Due to the complex sampling of the survey, appropriately weighted analyses were used to analyze NHANES data. The weighted t-test or weighted chi-square test was used for the continuous and categorical variables, respectively, to compare the differences in baseline characteristics between DM and DKD patients. Categorical variables were expressed as proportions (%). And continuous variables were expressed as the mean and standard deviation (SD). A weighted univariate logistic regression model was used to evaluate the association between PUFAs and eGFR. The Survey package of R was used to arrange the collected PUFAs intake data in order from small to large and divide them into four equal parts, which were expressed as Q1, Q2, Q3 and Q4 respectively. The correlation indexes of renal function corresponding to PUFAs quartile interval were analyzed statistically. The models were adjusted for age, sex, race, BMI, waist circumference, education level, smoking status, hyperlipidemia, hypertension, ACR, GHB, FPG, Scr, uric acid (UA), urea nitrogen (BUN), HDL-C, LDL-C, TC, TG. And compare the *p*-values for linear trend to assess the association between renal function and the intake of PUFAs. The odds ratio (OR) and 95% confidence interval (CI) were calculated for the association with DKD and PUFAs quartiles. The lowest quartile was always used as the reference value. A *p*-value < 0.05 characterized significant results.

3. Results

3.1. Baseline characteristics of participants

A total of 3287 T2DM participants were enrolled, including 2043 non-DKD and 1244 DKD patients. The average age of DKD patients was 64.05 years, with 590 (47.4%) male and 654 (52.6%) female patients. Age, race, waist circumference, SBP, DBP, education level, hypertension, smoking status, GHB, FPG, Scr, eGFR, BUN, UA, ACR, ALB, TG, and PUFAs intake were significantly different between the two groups ($p < 0.05$). There was no difference in gender, BMI, hyperlipidemia, AST, ALT, HDL, LDL, and TC between T2DM patients with and without DKD. Compared to those without DKD, participants with DKD were older (56.74 vs. 64.05 years, $p < 0.001$), had thicker waist circumferences (110.37 vs. 113.19 cm, $p = 0.0025$), and had a higher proportion of people with hypertension (59.6 vs. 74.8%, $p < 0.001$) and less PUFAs intake (18.81 vs. 17.58 gm/d, $p = 0.03461$). The baseline characteristics of all patients were shown in Table 1.

Table 2 showed the biochemical characteristics in DKD patients adjusted by the quartile of total PUFAs intake. With the increase of the PUFAs, renal function improved in DKD patients, the adjusted mean of eGFR changing from 57 (41, 86) in Q1 to 71 (55, 101) ml/min in Q4 ($p < 0.001$), and the adjusted mean of Scr changing from 103 (73, 131) in Q1 to 90 (68, 117) in Q4 ($p = 0.031$). However, in this study, the correlation between ACR and PUFAs was no significant. Therefore, whether PUFA intake could ameliorate proteinuria remains to be explored.

3.2. The association of PUFAs and renal function

We evaluated the relationship between PUFAs intake and renal function by creating multiple models. Table 3 showed that without controlling for any confounding variables, PUFAs intake was associated with the progression of renal function (OR = 1.48, 95% CI: 1.13–1.94, $p = 0.005$). However, when the model was adjusted, there was no statistical difference between DKD and PUFAs intake. Moreover, according to univariate logistic analysis, although there was a difference in PUFAs intake between DKD and DM patients, this variable may be a protective factor to DKD (OR = 1.00, 95% CI: 1.00–1.00, $p = 0.022$, Table 4). And age, race, education level, smoke, hypertension, waist circumference, GHB, FPG, ACR, Scr, UA, BUN were correlated with the progression of DM to DKD ($p < 0.05$, Table 4).

As shown in Table 4, patients who completed more than high school had a 6% lower risk of developing DKD than those who did not complete high school ($p = 0.032$). Compared with current smoking patients, patients who had a former smoking history had 11% increased risk ($p = 0.001$). And patients with non-hypertension had 1% lower odds of DKD ($p < 0.001$). Furthermore, with a per unit increase in GHB, FPG, BUN, the likelihood of developing DKD increased by 5%, 2%, 7%, respectively (all $p < 0.001$).

4. Discussion

With the raising morbidity of DKD, especially the obesity epidemic fueled the trend, so that except drug intervention, the potential influence of diet on DKD has gradually received attention. Fatty acids are ubiquitous organic molecules that are involved in providing energy to the body and are important components of cell membranes. And consuming certain types and amounts of fatty acids through a particular diet may prevent and attenuate the occurrence of diseases[13]. It is found that intake of SFAs can lead to an increase in LDL, which increases the risk of cardiovascular disease. Simultaneously, in the case of the same calories, the body hoards less fat than SFAs when consuming superfluous unsaturated fatty acids (UFAs) [14]. In addition to increasing LDL and atherogenic lipoprotein particle concentrations, high intake of SFAs may also lead to inflammatory responses, affect heart rhythm,

Table 1
Baseline characteristics of T2DM patients with and without DKD in the NHANES 2011–2018.

Characteristics	Non-DKD (n = 2043)	DKD (n = 1244)	*p*-value
Age (years)	56.74 ± 0.46	64.05 ± 0.52	<0.001
Gender (%)			0.7667
Female	46.3 (42.1, 50.8)	47.4 (43.1. 52.2)	
Male	53.7 (49.2, 57.9)	52.6 (47.8, 56.9)	
Race (%)			<0.001
Mexican American	10.7 (7.5, 13.8)	9.8 (6.8, 12.5)	
Other Hispanic	7.1 (5.7, 8.4)	5.1 (3.7, 6.5)	
Non-Hispanic White	58.4 (53.8, 63.1)	59.8 (55.1, 64.1)	
Non-Hispanic Black	13.2 (10.5, 15.6)	15.9 (12.9, 19.3)	
Non-Hispanic Asian	6.9 (5.6, 8.4)	4.6 (3.3, 5.9)	
Other Race - Including Multi-Racial	3.7 (2.7, 4.8)	4.8 (3.0, 6.9)	
BMI			0.3106
Underweight	0.2(−0.1, 0.3)	0.3(−0.2, 0.7)	
Normal weight	11.0(9.0, 13.1)	10.7(8.2, 13.1)	
Overweight	27.8(24.8, 30.6)	23.9(21.0, 26.9)	
Obesity	61.0(57.3, 64.9)	65.1(61.7, 68.5)	
Waist Circumference (cm)	110.37 ± 0.76	113.19 ± 0.84	0.0025
SBP (mmHg)	127.04 ± 0.63	136.44 ± 1.16	<0.001
DBP (mmHg)	71.07 ± 0.53	69.25 ± 0.61	0.03086
Education level (%)			0.04764
>high school	56.2 (52.0, 60.5)	48.9(44.9, 53.0)	
< =high school /GED or equivalent	43.8(39.5, 48.0)	51.1(46.9, 55.0)	
Hypertension			<0.001
Yes	59.6(56.2, 63.2)	74.8(71.3, 78.0)	
No	40.4(36.8, 43.8)	25.2(22.0, 28.7)	
Hyperlipidemia			0.6692
Yes	59.4(56.9, 62.3)	60.3(57.1, 63.9)	
No	40.6(37.7, 43.1)	39.7(36.1, 42.9)	
Smoking status (%)			0.002785
Current	16.2(13.8, 18.9)	13.9(10.8, 17.1)	
Former	31.0(27.4, 34.2)	41.0(37.1, 45.2)	
Never	52.8(49.2, 56.3)	45.1(40.5, 49.2)	
Glycohemoglobin (%)	7.03 ± 0.06	7.56 + 0.10	<0.001
Plasma fasting glucose (mmol/L)	8.42 ± 0.12	9.12 + 0.20	0.00015
Serum creatinine (μmol/L)	72.76 ± 1.08	103.18 ± 4.29	<0.001
eGFR (ml/min/1.73 m^2)	96.00 ± 1.02	74.56 ± 1.66	<0.001
Blood urea nitrogen (mmol/L)	5.10 ± 0.09	6.97 ± 0.19	<0.001
Serum uric acid (μmol/L)	328.95 ± 3.73	372.82 ± 5.33	<0.001
ACR (mg/g)	10.20 ± 0.21	345.57 ± 42.60	<0.001
ALB (g/L)	41.70 ± 0.19	40.32 ± 0.20	<0.001
AST (U/L)	26.57 ± 0.65	24.06 ± 0.58	0.8685
ALT (U/L)	28.44 ± 0.87	25.11 ± 0.91	0.84
HDL (mmol/L)	1.24 ± 0.02	1.24 ± 0.02	0.1042
LDL (mmol/L)	2.72 ± 0.05	2.72 + 0.06	0.9897
TC (mmol/L)	4.70 ± 0.06	4.73 ± 0.07	0.4897
TG (mmol/L)	1.59 ± 0.05	1.67 ± 0.05	0.01031
PUFAs intake (gm/d)	18.81 ± 0.52	17.58 ± 0.38	0.03461

hemostasis, apolipoprotein CIII production, and high-density lipoprotein function [15]. This also increases the risk of disease progression and cardiovascular complications in DKD patients. Nutritionists recommend limiting SFAs intake to less than 10% of the total daily energy of the general healthy population and further for patients with hyperglycaemia and hyperlipidemia [15]. Therefore, the substitution of UFAs for SFAs is

Table 3
Association between PUFAs intake and DKD patients.

Model	OR	95% CI[a]	*p*-value
Model 1[a]			
PUFAs intake	1.48	1.13–1.94	0.005
Model 2			
PUFAs intake	1.13	0.94–1.36	0.2
Model 3			
PUFAs intake	1.00	0.85–1.18	> 0.9

[a]Model 1 did not adjust for any confounding factors.
[b] Model 2 adjusted for gender, age, race, BMI status, waist circumference, education levels, smoking status, hypertension, and hyperlipidemia.
[c] Model 3 adjusted for gender, age, race, BMI status, waist circumference, education levels, smoking status, hypertension, and hyperlipidemia, GHB, FPG, ACR, Scr, UA, BUN, HDL, LDL, TC, TG.
[a] CI = Confidence Interval

Table 4
Univariate logistic regression models of DKD.

Characteristic	OR	95% CI[a]	*p*-value
Age	1.01	1.01,1.01	<0.001
Gender (versus female)			0.8
male	0.99	0.93,1.06	
Race (versus Mexican American)			<0.001
Other Hispanic	0.95	0.89,1.02	
Non-Hispanic White	1.02	0.96,1.09	
Non-Hispanic Black	1.07	1.00,1.14	
Non-Hispanic Asian	0.93	0.85,1.02	
Other Race - Including Multi-Racial	1.08	0.96,1.22	
Education level (versus<=high school/GED)			0.032
>high school	0.94	0.88,0.99	
Smoking status (versus current)			0.001
Former	1.11	1.03,1.19	
Never	1.00	0.93,1.07	
BMI status (versus underweight)			0.3
Normal weight	0.86	0.54,1.38	
Overweight	0.84	0.53,1.34	
Obesity	0.88	0.56,1.40	
Hypertension (versus yes)			<0.001
No	0.86	0.83,0.90	
Hyperlipidemia (versus yes)			0.7
No	0.99	0.95,1.03	
PUFAs intake	1.00	1.00,1.00	0.022
Waist Circumference	1.00	1.00,1.00	0.001
GHB	1.05	1.04,1.07	<0.001
FPG	1.02	1.01,1.03	<0.001
ACR	1.00	1.00,1.00	<0.001
Scr	1.00	1.00,1.00	<0.001
UA	1.00	1.00,1.00	<0.001
BUN	1.07	1.06,1.07	<0.001
HDL	0.95	0.90,1.01	0.10
LDL	1.00	0.97,1.03	>0.9
TG	1.02	1.00,1.05	0.094
TC	1.01	0.99,1.02	0.5

[a] CI = Confidence Interval

Table 2
Adjusted mean of markers of renal function across quartiles of PUFAs intake.

Characteristic	Q1 (1.10–10.47) N = 355[a]	Q2 (10.47–15.16) N = 284[a]	Q3 (15.16–22.55) N = 312[a]	Q4 (22.55–112.96) N = 293[a]	*p*-value
eGFR	57 (41, 86)	73 (53, 101)	68 (52, 97)	71 (55, 101)	<0.001
ACR	52 (32, 197)	81 (32, 312)	62 (27, 150)	54 (34, 156)	0.5
BUN	6.8 (5.0, 9.3)	5.7 (4.6, 8.2)	6.2 (5.0, 8.9)	6.1 (4.3, 8.2)	0.4
Scr	103 (73, 131)	88 (67, 110)	94 (72, 119)	90 (68, 117)	0.031
UA	357 (292, 428)	357 (309, 440)	351 (292, 416)	387 (297, 431)	0.4

[a] Median (IQR)

advocated.

N-3 and n-6 are two classes essential PUFAs. α-Linolenic acid (ALA) is the most commonly n-3 PUFAs precursor through dietary oils of plants and animals, such as the seeds of flax, canola, chia seeds, perilla, and walnuts[16]. Whereas eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) derived from marine food such as fish and fish oils, as well as algae [17]. ALA, DHA, and EPA are all essential fatty acids that are supplemented through dietary intake. Sources of n-6 PUFAs are eggs, meat, some dietary oils from plants and processed foods. The role of PUFAs has been gradually appreciated recently, especially their anti-inflammatory effects. Long-term exposure to hyperglycemia in patients with DM can lead to low-grade inflammation in the body, reducing total fat intake and taking lower saturated fat and more UFAs can improve inflammation and metabolic syndromes [18].

It is well known that n-3 PUFAs have cardioprotective effects and can prevent the occurrence of cardiovascular death in DKD patients [19]. And there is evidence indicating that n-3 PUFAs have proven protective effects in delaying the progression of renal dysfunction [9,20]. Similarly, the protective effect of PUFAs in the kidney has also been confirmed in vivo [21]. It is proved that n-3 PUFAs alleviate proteinuria and renal tubulointerstitial fibrosis through maintaining podocyte integrity and anti-inflammatory effects [21]. However, there is no shortage of opinion on the role of n-6 PUFAs. The function of n-6 PUFAs remains controversial. N-6 PUFAs help regulate the metabolic function of body, and promote the immune response (initiate the inflammatory response to fight off germs), and promote platelet aggregation. However, the proinflammatory effect can lead to the progression of DKD [22]. In particular, arachidonic acid (AA), a metabolite of LA, is considered to have pro-inflammatory property, potentially harmful to glucose metabolism, weight regulation and eating behavior, and ultimately aggravating DM [23]. However, some scholars hold the opposite view in the effect of N-6 PUFAs. A pooled analysis of 39 prospective cohort studies found that LA has long-term benefits for T2DM, and AA is harmless [24]. Mainly consuming LA in the diet improved glucose, insulin resistance and insulin secretion [25]. This may be related to the incorporation of LA with phospholipids to change membrane fluidity and regulate insulin receptor activity [26]. Moreover, higher levels of AA biomarkers are associated with lower rates of coronary heart disease [27]. There is no evidence that AA contributes to the development of T2DM, and high levels of dietary n-6 PUFAs are not harmful [24]. In response to the above, as more evidence attributing n-6 PUFAs to an adverse effect, there is also evidence to refute the pro-inflammatory effects of n-6 PUFAs. Would increasing the intake of n-3 PUFAs and decreasing n-6 PUFAs delay the progression of disease? This topic is taken seriously. Because of the double sided nature of n-6 PUFAs, scholars have focused on the ratio of n6/n3 PUFAs.

A study indicated that rather than more n-3 PUFAs, a balanced dietary ratio of n6/n3 PUFAs improved inflammatory markers in subjects with obesity [28]. Studies have indicated that a single diet of n-3 PUFAs is not significant for some diseases, and there is a competition for desaturation enzymes between n-6 and n-3 PUFAs, the two cannot be converted into each other, so it is scientific to explore the optimal balance of n-6/n-3 ratio [29]. N-3 and n-6 provide substrates for the formation of lipid oxidation products, and the oxidation of them is related to the formation of 4-hydroxy-2-hexenal (4-HHE) and 4-hydroxy-2-nonenal (4-HNE), respectively. When there is excessive 4-HHE and 4-HNE in the body, the lysine, histidine, and cysteine are attacked, forming protein carbonylation [30]. And protein carbonylation is a reliable biomarker for measuring protein oxidation-induced damage and is also identified as a biomarker of DKD progression [31]. In addition to taking antioxidant applications, dietary adjustments may also play a role in reducing protein carbonylation [30]. This hints the important role of fatty acid intake in delaying disease progression.

In this study, we analyzed the dietary data on PUFAs intake, and associated PUFAs intake with DKD from the NHANES 2011–2018. And a total of 3287 participants were included. Through model construction and univariate logistic regression, it was found that PUFAs intake could induce the possibility of DM developing into DKD. And the intake of PUFAs was positively correlated with eGFR. In moderate circumstances, higher levels of PUFAs intake may be associated with elevated eGFR. When not adjusted for confounding factors, PUFAs intake was a protective factor for DKD progression. However, after adjusting for confounding factors, no significant association was observed between the intake of PUFAs and DKD progression. This did not rule out that it was related to the lack of effective dietary guidance for participants. And in addition to fatty acid control, other healthy diets or lifestyles also appear together, such as diets rich in vegetables, whole grains, and fruits were also associated with a reduced risk of chronic diseases such as DM and obesity [32].

Our study had some limitations. Firstly, we only analyzed the total dietary PUFAs intake without detailly dividing the different species of n-6 and n-3 PUFAs, nor did we analyze the correlation between the ratio of n-6/n-3 and the progression of DKD. Differences in lifestyle, differences in ethnic and cultural background will lead to differences in dietary structure, which will affect the proportion to n-6/n-3 PUFAs intake. Secondly, the different diet structures and lifestyles will also affect the progression of DKD, even if the intake of PUFAs is sufficient, unhealthy eating habits are easy to accelerate the development of DKD. Besides, with the passage of time, the improvement of living standards, the diet will also change, and the diet of the past time may be widely divergent with the present. Therefore, according to the latest dietary guidelines issued by the World Health Organization (WHO) and combined with the disease characteristics of DKD patients, we suggest that the diet structure of patients should replace the SFAs in the diet with PUFAs, limit the energy supply ratio of SFAs to 10% as far as possible, and replace part of pork, beef and mutton with fish, seafood and nuts[33]. Switching milk to low-fat or skim milk is recommended. In addition, trans-fatty acid intake should be limited, which means not only limiting the consumption of fried foods, but also avoiding heating plant oils to too high a temperature during cooking, which can also produce trans-fatty acids for too long. In addition, emphasis on the intake of high-fiber vegetables and whole wheat products to replace white rice noodles and so on to improve hyperglycemia.

In conclusion, our study showed that PUFAs intake may be beneficial in delaying DKD progression, and a more appropriate n-6/n-3 ratio needs to be explored.

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CRediT authorship contribution statement

Wu Liu and Shiyi Liu contributed equally to this work. Conceptualization, Wu Liu and Shiyi Liu; Investigation, Qiuyue Ren and Ronglu Yang; Methodology, Wu Liu; Supervision, Xiaoyu Jiang; Writing – original draft, Wu Liu; Writing – review & editing, Shiyi Liu, Shanshan Su and Xiaoyu Jiang.

Declaration of Competing Interest

The authors declared that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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