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Exploring the relationship between grip strength and diabetic nephropathy among U.S. adults with type 2 diabetes mellitus: a cross-sectional NHANES analysis



Xue Chen¹, Yi Lin¹, Weisong Dong², Xiuxiu Wen³ and Yidan Zuo^{4*}

Abstract

Aim To examine the relationship between grip strength (GS) and diabetic nephropathy (DN).

Materials and methods Data on patients with type 2 diabetes mellitus collected between 2011 and 2014 were obtained from National Health and Nutrition Examination Survey (NHANES). Demographic characteristics (sex, age, race, marital status, and educational level), clinical measures (smoking status, drinking status, body mass index [BMI], glycated hemoglobin [HbA1c], urinary albumin creatinine ratio [UACR], diabetes duration, and hypertension), and grip strength assessments were collected. The relationship between GS and DN was analyzed using a logistic regression model. Subgroup analyses were showed as forest plots, conducted while accounting for confounding variables. Restricted cubic splines were applied to investigate nonlinear correlations. A sensitivity analysis was conducted to assess the robustness of the findings.

Results This study included 1,539 participants. In the multivariate logistic regression model, the odds ratios (ORs) were 0.96 (95% CI, 0.94–0.98) in male and 0.94 (95% CI, 0.91–0.98) in female. Compared with those in the lowest quartiles, participants in the uppermost GS quartiles were less susceptible to DN in male [OR 0.35 (95% CI, 0.20–0.62)] and female [OR 0.37 (95% CI, 0.20–0.67)] (p for trend < 0.001). After adjusting for all variables, the ORs were 0.96 (95% CI, 0.91–0.98) in female. Compared with those in the lowest quartiles, participants in the uppermost GS quartiles were less susceptible to DN in male [OR 0.37 (95% CI, 0.20–0.67)] (p for trend < 0.001). After adjusting for all variables, the ORs were 0.96 (95% CI, 0.94–0.98) in male and 0.94 (95% CI, 0.91–0.98) in female. Compared with those in the lowest quartiles, participants in the uppermost GS quartiles were less susceptible to DN in male [OR 0.35 (95% CI, 0.20–0.62)] (p for trend < 0.001) and female [OR 0.37 (95% CI, 0.20–0.67)] (p for trend < 0.001). Subgroup analysis demonstrated a reliable connection between GS and DN (all p for interaction > 0.05). We discovered a nonlinear relationship between GS and DN in both male and female participants (all p for nonlinearity < 0.05). More precisely, the data revealed L-shaped relationship and inverted-S relation in male and female participants, respectively.

Conclusion The results of this cross-sectional study using NHANES data indicated a potential negative association between GS and DN. Additional extensive studies are necessary to elucidate these trends.

Keywords Diabetic nephropathy, Grip strength, Type 2 diabetes mellitus, NHANES

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Introduction

Diabetic nephropathy (DN), a major complication of diabetes, is characterized by elevated levels of albumin in the urine and/or a reduced estimated glomerular filtration rate (eGFR) [1]. DN is the primary cause of chronic kidney disease (CKD) in many nations, leading to endstage renal disease (ESRD), which is characterized by significantly impaired kidney function requiring dialysis or kidney transplantation for survival [2]. Patients with DN have an approximately 30-fold higher risk of all-cause mortality, compared patients with diabetes without DN, posing a significant danger to human health [3]. Thus, identifying the risk factors for DN is crucial for early prevention and intervention.

Grip strength (GS) is an inexpensive and simple assessment tool used to measure muscle strength [4]. In patients with CKD, GS is a crucial prognostic indicator and an independent predictor of renal outcomes [5]. Furthermore, recent findings confirmed that decreased GS is associated with an increased likelihood of developing diabetes, DN, and diabetic foot diseases [6–8]. Prior studies have shown that individuals with diabetes who have a higher GS tend to have a reduced risk of cardiovascular disease and overall mortality [9].

Previous study reported that lower GS associated with retinal capillary density decline [10]. A recent Mendelian randomization study demonstrated that GS was negatively associated with risk of DN [11]. However, the relationship between GS and DN in patients with diabetes has not been fully explained by the available evidence. Therefore, the present study analyzed data from a large sample extracted from the National Health and Nutrition Examination Survey (NHANES) to comprehensively evaluate the correlation between GS and the risk of DN in American adults.

Methods

Study population

The NHANES database, created by the National Center for Health Statistics (NCHS), is a nationwide survey aimed at evaluating the health and dietary habits of individuals living outside of institutions in the US. The present study initially considered 2,091 participants with type 2 diabetes mellitus from the NHANES 2011–2014. The exclusion criteria were: (1) current pregnant, (2) age < 20 years, (3) missing data on urinary albumin creatinine ratio (UACR), (4) missing GS data, (5) missing covariate data. Finally, the analyses included 1,538 participants (Fig. 1).



Fig. 1 The flow chart of study participants

Definition of GS

The NHANES Muscle Strength/Grip Test Procedure Manual provides comprehensive instructions for assessing the GS. Following a brief preparation that involved explaining and demonstrating the protocol, adjusting the grip size of the dynamometer, and completing a practice trial, the participants were instructed to use one hand to squeeze the dynamometer with maximum force and to exhale during the squeeze to prevent buildup of intrathoracic pressure. Every hand underwent three tests, switching hands between each trial and allowing a 60-s break between measurements on the same hand. GS was defined as the maximum GS of both hands and was expressed in kilograms (kg).

Definition of diabetes and DN

Diabetes was diagnosed when one of the following conditions was met: self-reported diabetes, fasting plasma glucose level \geq 7.0 mmol/L, glycated hemoglobin (HbA1c) \geq 6.5%, 2-h OGTT blood glucose \geq 11.1 mmol/L, random plasma glucose \geq 11.1 mmol/L, or the use of diabetes medication or insulin. Participants with UACR \geq 30 mg/g were classified as having DN [1].

Covariates

The demographic parameters included sex, age, race, marital status, and educational level. Additionally, various anthropometric and laboratory covariates were considered, including smoking status, drinking status, body mass index (BMI), HbA1c, diabetes duration, and hypertension.

Smoking status was categorized as "now" for responses of "Every day" or "Some days" to the survey question "Do you now smoke cigarettes"; if the response was "Not at all", then the participants were asked if they had "Smoked at least 100 cigarettes in life". Responses of "Yes" and "No" were categorized as "former" and "never", respectively.

Smoking status was categorized as "now" for a response of ">0" to the survey question "How often have you consumed alcohol over the past 12 mos?". If the response was "0," the participants were asked if they "Had at least 12 alcohol drinks/lifetime"; responses of "Yes" and 'No' were categorized as "former" and never," respectively.

Missing responses to the survey question "Age when first told you had diabetes" were recorded as "0".

Hypertension was defined as the prescription of antihypertensive medications, systolic blood pressure \geq 140 mmHg, or diastolic blood pressure \geq 90 mmHg.

Statistical analysis

Demographic features are presented as averages (standard deviation) for continuous variables and proportions (%) for categorical variables. Continuous variables with non-normal distributions are expressed as medians and interquartile ranges and were compared using the Mann-Whitney U test. Categorical variables were analyzed using the chi-square test, whereas normal continuous variables were analyzed using one-way analysis of variance (ANOVA). The relationship between GS and DN was analyzed using a logistic regression model. Subgroup analyses were showed as forest plots, conducted while accounting for confounding variables. Restricted cubic splines were used to investigate nonlinear correlations. The initial 2,091 participants with type 2 diabetes mellitus from NHANES 2011–2014 were included in the sensitivity analysis. Statistical significance was determined by a two-sided P < 0.05. All analyses were conducted using R version 4.4.0.

Results

Table 1 showed the participants' characteristics according to DN status and sex. Among the 1,538 included participants, 791 (51.4%) were male and 747 (48.6%) were female. Overall, 448 (29.1%) participants had DN, including 239 (30.2%) male and 209 (28.0%) female participants. Male participants with DN were more likely to be older and hypertensive, have a higher BMI, higher HbA1c, longer diabetes duration, and lower GS compared with participants without DN. Female participants with DN were more likely to be older, and have higher proportions of being unmarried, smoking, hypertension, higher HbA1c, longer diabetes duration, and lower GS compared with participants without DN.

Table 2 showed the results of logistic regression analysis of the association between GS and DN. In model 1, the odds ratios (ORs) were 0.96 [95%confidence interval (CI), 0.94-0.97] for male and the 0.93 (95%CI, 0.91-0.96) for female. Compared with those in the lowest quartiles, participants in the uppermost GS quartiles were less susceptible to DN in both male [OR 0.35 (95%CI, 0.22-0.54)] (p for trend < 0.001) and female [OR 0.30 (95%CI, 0.18–0.48)] (p for trend < 0.001). The relationship between GS and DN remained consistent across various models and the trend was robust. In model 3, after adjusting for all variables, the ORs were 0.96 (95%CI, 0.94-0.98) in male and 0.94 (95%CI, 0.91-0.98) in female. Compared with those in the lowest quartiles, participants in the uppermost GS quartiles were less susceptible to having DN in both male [OR 0.35 (95%CI, 0.20–0.62)] (p for trend < 0.001) and female [OR 0.37 (95%CI, 0.20-(0.67) (p for trend < 0.001). The variance inflation factors (VIF) was shown in Supplementary Table 1. Variables with VIF < 2 showed no collinearity.

Figure 2 showed the results of the restricted cubic spline analyses, including the ORs and 95%CIs for the association between GS and DN. A nonlinear relation-ship between GS and DN was observed in both male and female (all p for nonlinearity < 0.05). More precisely, the

Variables	Male				Female			
	Total	Non-DN	DN	Р	Total	Non-DN	DN	Ρ
	(<i>n</i> = 791)	(n=552)	(n=239)		(n=747)	(<i>n</i> = 538)	(n=209)	
Age, years	60.69 (13.34)	59.76 (13.36)	62.83 (13.06)	0.003	60.05 (13.67)	58.71 (13.73)	63.49 (12.93)	< 0.001
Age groups				0.202				0.001
< 60 years	323 (40.83)	234 (42.39)	89 (37.24)		317 (42.44)	249 (46.28)	68 (32.54)	
≥60 years	468 (59.17)	318 (57.61)	150 (62.76)		430 (57.56)	289 (53.72)	141 (67.46)	
Race				0.450				0.251
Non-Hispanic White	280 (35.40)	205 (37.14)	75 (31.38)		262 (35.07)	183 (34.01)	79 (37.80)	
Non-Hispanic Black	216 (27.31)	147 (26.63)	69 (28.87)		214 (28.65)	148 (27.51)	66 (31.58)	
Mexican-American	108 (13.65)	75 (13.59)	33 (13.81)		101 (13.52)	78 (14.50)	23 (11.00)	
Other	187 (23.64)	125 (22.64)	62 (25.94)		170 (22.76)	129 (23.98)	41 (19.62)	
Marital status				0.443				0.042
Married	517 (65.36)	366 (66.30)	151 (63.18)		332 (44.44)	252 (46.84)	80 (38.28)	
Other	274 (34.64)	186 (33.70)	88 (36.82)		415 (55.56)	286 (53.16)	129 (61.72)	
Education level				0.136				0.360
Below high school	233 (29.46)	151 (27.36)	82 (34.31)		239 (31.99)	164 (30.48)	75 (35.89)	
High school	172 (21.74)	122 (22.10)	50 (20.92)		185 (24.77)	137 (25.46)	48 (22.97)	
Above high school	386 (48.80)	279 (50.54)	107 (44.77)		323 (43.24)	237 (44.05)	86 (41.15)	
Smoking status				0.051				0.037
Never	343 (43.36)	252 (45.65)	91 (38.08)		448 (59.97)	338 (62.83)	110 (52.63)	
Former	310 (39.19)	214 (38.77)	96 (40.17)		190 (25.44)	128 (23.79)	62 (29.67)	
Now	138 (17.45)	86 (15.58)	52 (21.76)		109 (14.59)	72 (13.38)	37 (17.70)	
Drinking status				0.946				0.050
Never	79 (9.99)	54 (9.78)	25 (10.46)		206 (27,58)	153 (28.44)	53 (25.36)	
Former	236 (29 84)	166 (30.07)	70 (29 29)		176 (23 56)	114 (21 19)	62 (29 67)	
Now	476 (60 18)	332 (60 14)	144 (60 25)		365 (48.86)	271 (50 37)	94 (44 98)	
BMI ka/m ²	31 34 (6 81)	31 27 (6 81)	31 53 (6 82)	0.622	33 51 (8 18)	33.82 (8.22)	32 73 (8 03)	0 102
BMI aroups	51.51 (0.01)	51127 (0.017)	31.33 (0.02)	0.011	55151 (6116)	55102 (0122)	52.75 (0.03)	0.169
$< 25 \text{ kg/m}^2$	112 (14 16)	71 (12 86)	41 (17 15)	0.011	104 (13 92)	67 (12 45)	37 (17 70)	0.105
$25-30 \text{ kg/m}^2$	281 (35 52)	214 (38 77)	67 (28.03)		170 (22 76)	123 (22.86)	47 (22 49)	
$> 30 \text{ kg/m}^2$	398 (50 32)	267 (48 37)	131 (54.81)		473 (63 32)	348 (64 68)	125 (59.81)	
HbA1c %	7 29 (1 71)	7 12 (1 61)	7.68 (1.89)	< 0.001	7 20 (1.83)	7 02 (1 66)	7 66 (2 13)	< 0.001
HbA1c	7.29 (1.7.1)	7.12 (1.01)	7.00 (1.05)	< 0.001	7.20 (1.05)	7.02 (1.00)	7.00 (2.13)	< 0.001
< 7%	455 (57 52)	346 (62 68)	109 (45 61)	< 0.001	453 (60.64)	349 (64 87)	104 (49 76)	< 0.001
> 7%	336 (42.48)	206 (37 32)	130 (54 39)		204 (30 36)	189 (35 13)	101 (19.70)	
Diabetes duration	550 (+2.40)	200 (37.32)	150 (54.55)	< 0.001	274 (37.30)	105 (55.15)	105 (50.24)	< 0.001
	341 (43 11)	272 (10 28)	60 (28 87)	< 0.001	340 (45 52)	271 (50 27)	60 (33 01)	< 0.001
3 10 years	273 (28 10)	272 (49.20)	73 (20.57)		104 (25 07)	271 (30.37)	43 (20.57)	
> 10 years	223 (20.19)	120 (27.17)	73 (30.54)		194 (23.97) 212 (20.51)	116 (21.56)	43 (20.37)	
	227 (20.70)	150 (25.55)	97 (40.59)	< 0.001	213 (20.31)	110 (21.50)	97 (40.41)	< 0.001
Ne	247 (21 22)		45 (10.02)	< 0.001	207 (27 71)	175 (22 52)	22 (15 21)	< 0.001
NO	247 (31.23)	202 (30.59)	45 (18.83)		207 (27.71)	1/5 (32.53)	32 (15.31)	
res	544 (68.77)	350 (03.41)	194 (81.17)	.0.001	540 (72.29)	303 (07.47)	177 (84.69)	.0.001
GS, Kg	41.48 (9.50)	42.02 (9.15)	38.85 (9.79)	< 0.001	20.81 (6.38)	27.55 (6.35)	24.91 (6.08)	< 0.001
GS, groups		112 (20.20)	00 (27 (2)	< 0.00 I	100 (25 20)	112 (20.02)	77 (26.04)	< 0.001
QI	202 (25.54)	112 (20.29)	90 (37.66)		189 (25.30)	112 (20.82)	//(36.84)	
Q2	198 (25.03)	141 (25.54)	57 (23.85)		189 (25.30)	135 (25.09)	54 (25.84)	
Q3	194 (24.53)	145 (26.27)	49 (20.50)		187 (25.03)	140 (26.02)	47 (22.49)	
04	197 (24.91)	154 (27.90)	43 (17.99)		182 (24.36)	151 (28.07)	31 (14.83)	

Table 1 Baseline characteristics of participants

DN, diabetic nephropathy; BMI, body mass index; HbA1c, glycated hemoglobin A1c, GS, grip strength; male grip quartiles: Q1: 14.3, 35.4; Q2: 35.5,41.5; Q3: 41.6, 47.5; Q4: 47.6, 70.5; female grip quartiles: Q1: 7.7, 22.5; Q2: 22.6, 26.5; Q3: 26.6, 30.9; Q4: 31.0, 46.2

	GS	GS	GS	GS	P _{trend}	GS	Р
	Q1	Q2	Q3	Q4		Continuous	
	OR (95% CI)	OR (95% CI) OR (95% CI)		OR (95% CI)		OR (95% CI)	
Male							
Model 1	Ref	0.50 (0.33,0.76)	0.42 (0.27,0.64)	0.35 (0.22,0.54)	< 0.001	0.96 (0.94,0.97)	< 0.001
Model 2	Ref	0.53 (0.34,0.81)	0.46 (0.29,0.74)	0.38 (0.22,0.64)	< 0.001	0.96 (0.94,0.98)	< 0.001
Model 3	Ref	0.50 (0.32,0.79)	0.46 (0.28,0.75)	0.35 (0.20,0.62)	< 0.001	0.96 (0.94,0.98)	< 0.001
Female							
Model 1	Ref	0.58 (0.38,0.89)	0.49 (0.31,0.76)	0.30 (0.18,0.48)	< 0.001	0.93 (0.91,0.96)	< 0.001
Model 2	Ref	0.66 (0.42,1.03)	0.54 (0.33,0.87)	0.31 (0.17,0.55)	< 0.001	0.94 (0.91,0.97)	< 0.001
Model 3	Ref	0.67 (0.42,1.08)	0.57 (0.34,0.94)	0.37 (0.20,0.67)	< 0.001	0.94 (0.91,0.98)	0.001

Table 2	Logistic re	egression	analysis	s on the	association	between	GS and	DN

GS, grip strength; DN, diabetic nephropathy; OR, odds ratio; CI, confidence interval

Model 1: crude model

Model 2: adjusted for age, race, marital status and education

Model 3: model 2 + smoking status, drinking status, BMI, HbA1c, diabetes duration, and hypertension



Fig. 2 Restricted cubic spline of OR and 95% CI for the association between GS and DN (A) Male and (B) Female

associations showed L-shaped and inverted S-shaped relationships in male and female participants, respectively. In male participants, the risk of DN decreased with increasing GS, but when GS went to 35.9 kg, the risk of DN remained essentially unchanged with increasing GS. In female participants, the risk of DN remained essentially unchanged with increasing GS when GS up to 19.3 kg, increased with GS when GS exceeded 19.3 kg up to 34.1 kg, and remained essentially unchanged with increasing GS above 34.1 kg.

Figure 3 showed the results of subgroup analysis. The subgroup analysis demonstrated a consistent and reliable connections between GS and DN across various subgroups. Notably, no significant interactions were observed for age, race, marital status, education level, smoking status, drinking status, BMI, HbA1c, diabetes duration, or hypertension, suggesting that the results of the different layers were consistent and reliable (all p for interaction > 0.05).

Table 3 shows the results of the sensitivity analyses of the association between GS and DN. In model 1, the ORs

were 0.96 (95% CI, 0.94-0.97) in male participants and 0.93 (95% CI, 0.91-0.96) in female participants. Compared with those in the lowest quartiles, participants in the uppermost GS quartiles were less susceptible to having DN among both male [OR 0.37 (95% CI, 0.25–0.55)] (p for trend < 0.001) and female [OR 0.27 (95% CI, 0.17-0.42)] (p for trend < 0.001) participants. The relationship between GS and DN remained consistent across various models, and the trend was robust. In model 3, after adjusting for all variables, the ORs were 0.95 (95% CI, 0.93-0.98) in male participants and 0.95 (95% CI, 0.91-0.98) in female participants. Compared with those in the lowest quartiles, participants in the uppermost GS quartiles were less susceptible to DN in both male [OR 0.42 (95% CI, 0.24-0.73)] (p for trend < 0.001) and female [OR 0.35 (95% CI, 0.19–0.64)] (p for trend < 0.001) participants.

Variable	Male OR (95% CI)		P for interaction	Female OR (95% CI)		P for interaction
Age		1	0.202			0.567
<60 years	0.97 (0.94 , 1.01)			0.95 (0.89 , 1.00)	·•	
>=60 years	0.94 (0.91, 0.96)	—		0.94 (0.90, 0.98)		(
Race			0.131			0.277
Non-Hispanic White	0.92 (0.88 , 0.95)			0.99 (0.94 , 1.05)		•
Non-Hispanic Black	0.97 (0.94 , 1.01)			0.92 (0.86 , 0.97)	•	
Mexican American	0.89 (0.80 , 0.98)			0.94 (0.84 , 1.05)		
Other	0.96 (0.91 , 1.01)			0.93 (0.84 , 1.02)		
Marital status			0.286			0.887
Married	0.96 (0.93 , 0.99)			0.94 (0.90 , 1.00)		
Other	0.93 (0.90 , 0.96)			0.93 (0.89 , 0.98)		
Education level			0.082			0.089
Below high school	0.96 (0.92 , 1.00)			0.99 (0.93 , 1.04)		
High school	0.92 (0.87 , 0.96)			0.86 (0.79 , 0.94)	i	
Above high school	0.95 (0.92 , 0.98)			0.93 (0.88 , 0.98)		
Smoking status			0.371			0.665
Never	0.93 (0.90 , 0.97)			0.93 (0.89 , 0.97)		
Former	0.94 (0.90 , 0.98)			0.96 (0.90 , 1.02)		• • • • • • • • • • • • • • • • • • • •
Now	0.98 (0.93 , 1.03)			0.99 (0.90 , 1.09)	H	•
Drinking status			0.086			0.134
Never	0.95 (0.86 , 1.03)			0.91 (0.84 , 0.98)		
Former	0.92 (0.88 , 0.96)			0.94 (0.88 , 1.01)	•	
Now	0.97 (0.94 , 0.99)			0.95 (0.90 , 1.00)	·	•
BMI			0.485			0.190
<25	0.96 (0.89 , 1.03)			0.88 (0.78 , 0.98)	· · · · · · · · · · · · · · · · · · ·	(
25-30	0.93 (0.89 , 0.97)			0.86 (0.78 , 0.94)	<+	
>=30	0.95 (0.92 , 0.98)			0.96 (0.92 , 1.00)		
HbA1c			0.604			0.290
<7.0%	0.95 (0.93 , 0.98)			0.93 (0.89 , 0.98)	⊢	
>=7.0%	0.94 (0.91 , 0.97)			0.95 (0.90 , 1.00)	•	
Diabetes duration			0.973			0.443
0-3 years	0.95 (0.92 , 0.99)	→		0.95 (0.90 , 1.00)	•	
3-10 years	0.93 (0.89 , 0.98)			0.92 (0.85 , 0.98)	••	
>10 years	0.95 (0.92 , 0.99)			0.94 (0.89 , 1.00)		
Hypertension			0.199			0.243
No	0.97 (0.92 , 1.02)			0.98 (0.90 , 1.06)	H	• • •
Yes	0.94 (0.92 , 0.96)	→		0.94 (0.90 , 0.97)		
	0.8	0.9 1	1.1		0.8 0.9	
		Low risk High risk	(Ĺ	ow risk High risk

Fig. 3 The association between GS and DN by subgroups

Table 3 The sensitivity analysis on the association between GS and DN

	GS	GS	GS	GS	P _{trend}	GS	Р
	Q1	Q2	Q3	Q4		Continuous	
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)		OR (95% CI)	
Male							
Model 1	Ref	0.60 (0.41,0.88)	0.35 (0.23,0.53)	0.37 (0.25,0.55)	< 0.001	0.96 (0.94,0.97)	< 0.001
Model 2	Ref	0.59 (0.39,0.88)	0.38 (0.24,0.58)	0.40 (0.24,0.65)	< 0.001	0.95 (0.93,0.97)	< 0.001
Model 3	Ref	0.62 (0.39,0.97)	0.39 (0.24,0.64)	0.42 (0.24,0.73)	< 0.001	0.95 (0.93,0.98)	< 0.001
Female							
Model 1	Ref	0.57 (0.38,0.85)	0.44 (0.29,0.65)	0.27 (0.17,0.42)	< 0.001	0.93 (0.91,0.96)	< 0.001
Model 2	Ref	0.63 (0.41,0.96)	0.47 (0.30,0.74)	0.28 (0.16,0.49)	< 0.001	0.94 (0.91,0.96)	< 0.001
Model 3	Ref	0.71 (0.44,1.14)	0.54 (0.33,0.90)	0.35 (0.19,0.64)	< 0.001	0.95 (0.91,0.98)	0.001

GS, grip strength; DN, diabetic nephropathy; OR, odds ratio; CI, confidence interval

Model 1: crude model

Model 2: adjusted for age, race, marital status and education

Model 3: model 2 + smoking status, drinking status, BMI, HbA1c, diabetes duration, and hypertension

Discussion

To the best of our knowledge, this is the first study to investigate the association of GS with DN risk in patients with type 2 diabetes mellitus. The results showed that a higher GS was associated with a lower DN risk in both male and female participants. The results of the subgroup analyses demonstrated the stability of this association. The GS had a threshold effect on DN, with the risk of DN no longer decreasing when the GS increased to a certain level.

In a recent study, patients with type 2 diabetes mellitus and sarcopenia had a 1.1-fold increased risk of severe diabetic nephropathy compared with patients without sarcopenia. Compared with the present study, which measured muscle function using GS, the previous study determined sarcopenia according to appendicular skeletal muscle mass (ASM) [12]. Prior research has shown that muscle strength is more crucial than muscle mass for forecasting health outcomes, and it is now widely accepted that muscle strength plays a greater role in determining sarcopenia than muscle mass [13, 14]. The latest recommendation from the European Working Group on Sarcopenia in Elderly Individuals identified weak muscle strength as the primary feature of sarcopenia and suggested GS as a substitute measure for overall strength [15]. Therefore, the current research, utilizing GS, offers a unique advantage in over the previous studies. The results of the present study showed that GS is negatively related to the risk of DN.

The mechanisms linking GS and DN remain poorly understood. Evidence suggests that low GS and DN share several risk factors, and that several pathways link them, such as insulin resistance, chronic inflammation, etc [16–18]. On the one hand, muscle is an endocrine organ capable of producing myokines such as irisin, which has been reported to alleviate insulin sensitivity [19, 20]. It was discovered that irisin, produced by muscles, plays a protective role in shielding the kidney from damage caused by diabetes mellitus [21]. Furthermore, higher muscular strength is linked to a lower risk of developing long-term diabetes [22]. As skeletal muscle is the primary location for insulin-facilitated glucose uptake, it could suggest that insulin resistance plays a significant role in the decline of muscle function [23]. On the other hand, some studies indicate that inflammation can contribute to complications such as diabetic retinopathy, nephropathy, and neuropathy [24]. Multiple studies have confirmed the inverse relationship between GS and levels of inflammation [25, 26]. Owing to the similarities in physiopathology between these two conditions, it is challenging to distinguish whether a low GS is the root cause of DN or a resulting complication. Moreover, the association between GS and DN may be bidirectional. Therefore, further studies are required to elucidate these underlying mechanisms.

Targeted comprehensive interventions are crucial owing to the complex progression of DN. Various strategies, including changes in diet, medications, and lifestyle habits, are used to lower the risk of developing DN [1]. Low-protein diets have been proven to be safe and effective, without causing harm to muscle atrophy, muscle mass, or overall health, which is significant. Resistance training can boost muscle strength, leading to better glucose control, lower HbA1c levels, and increased expression of important proteins in the insulin signaling pathway [27]. Resistance training is also successful in decreasing plasma pro-inflammatory markers such as C-reactive protein. Resistance training is anticipated to enhance muscle strength, ultimately leading to a reduction in urinary protein levels. At present, pharmaceuticals to reduce the progression of DN are limited. Possible treatments consist of angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARB), sodium-glucose cotransporter -2 (SGLT-2) inhibitors and novel non-steroidal mineral receptor antagonists [28]. Further investigations are required to elucidate the potential dangers and advantages of these therapies.

Our study has several strengths. This study's main advantage was being the initial extensive populationbased research to uncover the link between GS and DN in American adults. The questionnaire and laboratory datasets contain comprehensive demographic, lifestyle, nutritional, and medical data. Having this information allows us to more effectively manage potential confounding variables in the multivariate regression models. Additionally, the large sample size provided by the NHANES increased the ability to obtain meaningful findings.

Nevertheless, this study has some limitations. For instance, DN was diagnosed using a single UACR test, rather than 3 months of observation. However, as the prevalence of DN in this study was similar to that reported previously, the results are considered reliable. Furthermore, the NHANES utilizes a cross-sectional design, making it difficult to directly assess the causal relationship between GS and DN due to the lack of ability to evaluate temporal relationships in the data. Our population representation was ultimately restricted by the NHANES database. Thus, whether the association between GS and DN applies to other demographic groups remains unclear.

Conclusion

Our research found that higher GS appeared associated with lower risk of DN. Given the research methodology we used, additional extensive prospective studies and clinical trials are necessary to elucidate the relationship's characteristics and trends.

Supplementary Information

The online version contains supplementary material available at https://doi.or g/10.1186/s12902-025-01862-y.

Supplementary Material 1

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Author contributions

Xue Chen drafted of manuscript. Weisong Dong collected the data. Xue Chen, Xiuxiu Wen and Yi Lin analyzed and interpretated the data. Yi Lin revised the article. Yidan Zuo designed the study and revised the article. All authors reviewed the manuscript.

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Data availability

Publicly available datasets were analyzed in this study. Data can be found below: www.cdc.gov/nchs/nhanes/.

Declarations

Ethics approval and consent to participate

The study protocol was approved by the NCHS Ethics Review Board (https:// www.cdc.gov/nchs/nhanes/irba98.htm), and was performed in accordance with the Declaration of Helsinki, with all NHANES participants providing their written informed consent.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Clinical trial number

Not applicable.

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