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RESEARCH

Association of sarcopenia and pancreatic exocrine insufficiency in older adults type 2 diabetes mellitus patients

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Abstract

Background and aim An association between type 2 diabetes mellitus (T2DM) and pancreatic exocrine insufficiency (PEI) has been increasingly recognized. Sarcopenia is also common among older adults with T2DM, contributing to poor functional outcomes and increased frailty. Recent findings indicate a potential link between PEI and sarcopenia. The present study aimed to investigate the relationship between PEI and sarcopenia in older adults patients with T2DM, independent of other contributing factors.

Methods A total of 120 patients aged≥65 years with T2DM were enrolled in the study. Demographic characteristics, diabetes-related clinical data, and malnutrition risk were assessed. Muscle strength, muscle mass, physical performance, and fecal elastase-1 levels were measured. Sarcopenia was diagnosed according to the criteria defined by the European Working Group on Sarcopenia in Older People 2 (EWGSOP2).

Results PEI was present in 22.5% of patients, including 10% with severe and 12.5% with mild-to-moderate insufficiency Low muscle mass was observed in 15% of participants, while confirmed sarcopenia was identified in 10%. Patients with reduced hand grip strength exhibited significantly lower Mini Nutritional Assessment – Short Form (MNA-SF) scores and serum vitamin D levels; however, in male patients, only MNA-SF was significantly lower. The prevalence of PEI was significantly higher in males with probable sarcopenia compared to those without (34.8% vs. 10%, $p=0.05$). In multivariate analysis among men, obesity showed a borderline significant association with probable sarcopenia, whereas PEI demonstrated a nonsignificant trend toward association.

Discussion and conclusion PEI may contribute to sarcopenia in older adults males with T2DM and should be considered in the clinical evaluation of sarcopenic patients.

Keywords Type 2 diabetes mellitus · Sarcopenia · Pancreatic exocrine insufficiency · Older adults

Introduction

The incidence of type 2 diabetes mellitus (T2DM) increases with age, affecting more than a quarter of people over the age of 65 [1]. The prevalence of sarcopenia and sarcopenic obesity is significantly higher in older people with T2DM [2].

Sarcopenia is a chronic skeletal muscle disorder characterized by reduced muscle strength, low muscle mass and decreased physical performance, leading to an increased risk of falls, fractures, physical disability and mortality [3]. The underlying mechanisms of sarcopenia are multifactorial and involve dysregulation of the cycle of protein synthesis and degradation in skeletal muscle [2]. Insulin plays a critical role in stimulating protein synthesis. However, insulin

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resistance, which increases with age, has been implicated in the pathogenesis of sarcopenia [4].

In T2DM, progressive pancreatic beta-cell dysfunction leads to impaired endocrine function over time. Studies have also demonstrated a strong association between endocrine dysfunction and pancreatic exocrine insufficiency (PEI) [5–8]. Several mechanisms have been proposed to explain PEI in diabetic patients, including pancreatic atrophy due to vasculopathy, neuropathy-induced impairment of exocrine enzyme secretion, autoimmune responses targeting exocrine cells, and genetic predisposition [9].

Recent studies have highlighted an increased incidence of sarcopenia in patients with chronic pancreatitis and pancreatic cancer [10–12]. These conditions are associated with a severe catabolic state, which further increases the risk of sarcopenia. Furthermore, recent evidence suggests an association between sarcopenia and PEI due to benign disorders of the pancreas [13].

In this study, we aimed to investigate the relationship between PEI and sarcopenia in patients with T2DM without known primary or secondary pancreatic disease. We hypothesized that PEI may be involved in the etiology of sarcopenia in T2DM as a secondary complication.

Materials and methods

Patient population

This study included 120 T2DM patients aged ≥ 65 years who were admitted to the internal medicine outpatient clinic of Istanbul University, Faculty of Medicine, between May and December 2021. An informed consent was obtained from all participants prior to enrollment. Exclusion criteria were, advanced dementia, immobility, acute inflammatory disease/medical disorder, presence of a pacemaker, active alcohol use or history of heavy alcohol consumption, active malignancy, pancreatic diseases (including chronic pancreatitis, pancreatic cancer, or prior pancreatic surgery), inflammatory bowel disease, and current use of pancreatic enzyme replacement therapy (PERT) for any reason.

Ethical approval was obtained from the Clinical Research Ethics Committee of Istanbul University, Faculty of Medicine (Approval number: 181035, Date: 26.04.2021). The study was conducted in accordance with the ethical principles of the World Medical Association's Declaration of Helsinki.

Clinical and laboratory outcomes

Demographic data and the anthropometric measurements of all participants were recorded. T2DM duration, current medications and diabetes-related complications were documented A stool sample was obtained from each participant for the measurement of fecal elastase-1 (FE1). Samples were stored at −80 °C until analysis. FE1 levels were determined using a sandwich enzyme-linked immunosorbent assay (ELISA) kit (Bioserv Diagnostics GmbH), employing two monoclonal antibodies specific to human pancreatic elastase. Based on FE1 levels, participants were categorized as, normal exocrine function (FE1 > 200 µg/g), mild to moderate PEI (FE1: 100–200 µg/g) or severe PEI (FE1 < 100 µg/g) [14].

Assessment of muscle strength, muscle mass and physical performance

Handgrip strength (HGS) was evaluated using a hand-held dynamometer (Jamar, USA). While seated in an upright position with the arms located on both sides and they were flexed through the elbows at 90^0, the patients were instructed to squeeze the hand dynamometer as hard as possible for 2–3 s. The measurements were repeated three times for both hands, and the highest recorded value was obtained [3]. Muscle mass was measured via bioelectrical impedance analysis (BIA) (TANITA MC 780 MA, Japan). BIA was performed under standardized conditions as recommended in previous studies [15]. Patients were instructed to fast for at least 4 h, avoid vigorous physical activity for 12 h, and void their bladder prior to the measurement. All assessments were conducted barefoot, without metal accessories, and in a thermoneutral environment (20–25 °C), in accordance with published guidelines for optimal accuracy [15]. The appendicular skeletal muscle mass index (ASMI) was calculated by dividing the appendicular skeletal muscle mass (ASM) measured via BIA by the square of the patient's height (m^2). ASM was estimated using the Sergi predictive equation, defined as follows: ASM (kg) = −3.964 + (0.227 × resistance index [RI]) + (0.095 × body weight [kg]) + (1.384 × sex) + (0.064 × reactance [Xc]), where sex was coded as 1 for males and 0 for females. This formula demonstrated a high degree of accuracy, with $R^2 = 0.92$ and a standard error of estimate (SEE) of 1.14 kg [16].

The diagnostic criteria established by the European Working Group on Sarcopenia in Older People-2 (EWGSOP2) were applied to diagnose sarcopenia [3]. The following thresholds were used: Muscle strength < 16 kg in females

and <27 kg in males were considered low; ASMI: <5.5 kg/m² in females and <7 kg/m² in males were classified as low [3]. Physical performance was evaluated using the four-meter Usual Gait Speed (UGS) test, which measures walking speed (m/s). Patients with a walking speed≤0.8 m/s in the four-meter walk test were considered to have poor physical performance.

Patients with low muscle strength alone were considered to have probable sarcopenia, whereas patients with both low muscle strength and low muscle mass were considered to have confirmed sarcopenia.

Table 1 Descriptive clinical and demographic characteristics of the older adults patients with T2DM

Variable	Min–Max	Median	Mean±SD *n* (%)	*p*-value*
Age (years)	65.0–82.0	69.0	70.4±4.2	
Female			70.0±4.0	
Male			71.1±4.5	0.18
Sex			No. pts (%)	
Female			77 (64.2%)	
Male			43 (35.8%)	
T2DM Duration			No. pts (%)	
≤10 years			81 (67.5%)	
>10 years			39 (32.5%)	
HbA1C (%)	5.1–13.8	7.25	8.06±2.09	
Female			7.81±1.90	
Male			8.51±2.36	0.10
DM Treatment			No. pts (%)	
No drug			13 (11%)	
OAD			104 (86.7%)	
Insulin			33 (27.5%)	
Insulin+OAD			25 (30%)	
DM Complications			No.pts (%)	
Nephropathy			56 (46.7%)	
Neuropathy			11 (9.2%)	
CaVD			44 (36.7%)	
CVD			13 (10.8%)	
PAD			5 (4.2%)	
Diabetic foot			3 (2.5%)	
Hypertension			100 (83.3%)	
Hyperlipidemia			51 (42.5%)	
BMI (kg/m2)			Mean±SD n (%)	
Female			30.5±4.1	**<0.01**
Male			28.0±4.1	
Obesity			61 (50.8%)	
Female			48 (62.3%)	**<0.01**
Male			13 (30.2%)	

CaVD, cardiovascular disease; CVD, cerebrovascular disease; OAD, oral antidiabetic drugs; PAD, peripheral arterial disease Continuous variables are presented as mean±standard deviation (SD) and/or median (min–max), and categorical variables as number (percentage). Comparisons between sexes were performed using the chi-square test for categorical variables and the independent samples t-test or Mann–Whitney U test for continuous variables as appropriate

*p-value: comparison between male and female patients

Nutritional status assessment

Nutritional status was assessed using the Mini Nutritional Assessment-Short Form (MNA-SF). A total score of ≤11 out of 14 indicated a risk of malnutrition [17].

Statistical analysis

Descriptive statistics were expressed as categorical variables (number, percentage, and 95% confidence interval) and continuous variables (mean, standard deviation, median, interquartile range, minimum, maximum, and percentage). The distribution of variables was assessed using the Kolmogorov-Smirnov test.

For quantitative independent data, the Independent Sample Student's t-test and Mann-Whitney U test were used. Categorical independent variables were analyzed using the Chi-square test, while the Fisher's exact test was applied when the assumptions of the Chi-square test were not met. Logistic regression model was used to evaluate relationships between variables. To account for potential differences, analyses were conducted separately for male and female participants.

All statistical analyses were performed using SPSS 26.0 software, and a p-value<0.05 was considered statistically significant.

Results

The mean age of the study population was 70.4±4.2 years, with a median of 69.0 years (range: 65–82 years, females 70.0±4.0 years and males 71.1±4.5 years). 64.2% (n=77) of the participants were female (Table 1). T2DM duration, mean glycated hemoglobin (HbA1c) levels, T2DM complications, medications, and the comorbidities of the patients were given in Table 1.

The mean muscle strength, muscle mass and the gait speed of the patients were given in Table 2. According to EWGSOP2 criteria, 59% of the patients had probable sarcopenia, and 10% had confirmed sarcopenia. Low muscle strength (probable sarcopenia) prevalence was 53.4% in males and 62.3% in females (p=0.34). Low muscle mass was more common in males when compared to females (25.6% vs. 9.1%, p=0.015). Confirmed sarcopenia prevalence was 16.3% in males and 6.5% in females (p=0.08). The mean gait speed of the patients was 0.86±0.19 m/s. It was 0.84±0.21 m/s in females and 0.89±0.16 m/s in males. Malnutrition risk was identified in 15.8% of the patients. The

Table 2 Muscle strength, appendicular muscle mass, and sarcopenia-related indicators in older adults patients with T2DM

Variable	Female (Mean ± SD, *n*%)	Male (Mean ± SD, *n*%)	Total (Mean ± SD, *n*%)	*p*-value*
MS (kg)	14.6 ± 5.4	25.2 ± 6.4	18.4 ± 7.7	**< 0.01**
ASM (kg)	17.0 ± 2.5	21.4 ± 2.4	18.6 ± 3.3	**< 0.01**
ASMI (kg/m²)	6.8 ± 0.7	7.4 ± 0.8	7.0 ± 0.8	**< 0.01**
LMM	7 (9.1%)	11 (25.6%)	18 (15.0%)	**0.015**
PS	48 (62.3%)	23 (53.4%)	71 (59.2%)	0.34
CS	5 (6.5%)	7 (16.3%)	12 (10.0%)	0.08
GS(m/s)	0.84 ± 0.21	0.89 ± 0.16	0.86 ± 0.19	0.12
MNA-SF score	12.6 ± 1.8(6–14)	13.1 ± 1.5 (8–14)	12.8 ± 1.7 (6–14)	0.20
MN Risk	14 (18.2%)	5 (11.6%)	19 (15.8%)	0.34

MS, muscle strength; ASM, appendicular skeletal muscle mass; ASMI, appendicular skeletal muscle mass index; LMM, low muscle mass; PS, probable sarcopenia; CS, confirmed sarcopenia; GS, gait speed; MNA-SF, Mini Nutritional Assessment–Short Form; MN, malnutrition. p-values were calculated using independent samples t-test for continuous variables and Chi-square test for categorical variables. *A p-value < 0.05 was considered statistically significant

Table 3 Evaluation of PEI among patients based on FE1 levels

FE1 Category	Female *n* (%)	Male *n* (%)	Total *n* (%)
Positive	17 (22.1%)	10 (23.3%)	27 (22.5%)
Severe	5 (6.5%)	7 (16.3%)	12 (10.0%)
Mild–Moderate	12 (15.6%)	3 (7.0%)	15 (12.5%)

FE1, fecal elastase-1 level; PEI, pancreatic exocrine insufficiency. Fecal elastase values < 200 µg/g were considered positive for PEI. Values < 100 µg/g indicate severe PEI, while 100–200 µg/g indicate mild-to-moderate PEI

prevalence of malnutrition risk, as assessed by the MNA-SF, was 18.2% in females and 11.6% in males (Table 2).

FE1 levels indicative of PEI were observed in 22.5% of the patients (22.1% of females and 23.3% of males). Mild to moderate PEI was observed in 15.6% of females and 7.0% of males, and severe PEI was diagnosed in 16.3% of males and 6.5% of females. (Table 3).

The association between PEI and probable sarcopenia, confirmed sarcopenia, and malnutrition risk was evaluated in the total cohort and stratified by sex. In the overall population, no statistically significant association was observed between PEI and probable sarcopenia ($p = 0.81$) or confirmed sarcopenia ($p = 0.30$). Similarly, in female patients, PEI was not significantly associated with probable sarcopenia ($p = 0.52$) or confirmed sarcopenia ($p = 0.90$).

However, in male patients, probable sarcopenia was significantly more prevalent among those with PEI compared to those without (80% vs. 45%, $p = 0.05$), suggesting a potential sex-specific relationship. Although the proportions of confirmed sarcopenia and malnutrition risk were also higher among males with PEI, these differences did not reach statistical significance ($p = 0.12$ and p-values not shown, respectively) (Table 4).

In univariate analysis, probable sarcopenia was significantly associated with low serum vitamin D levels in the total population ($p = 0.011$) and among females ($p = 0.015$). In female patients, cerebrovascular disease ($p = 0.01$) and sulfonylurea use ($p = 0.04$) were also associated with probable sarcopenia. In males, the condition was significantly linked to Dipeptidyl Peptidase-4(DPP-4) Inhibitor treatment ($p = 0.03$) and obesity ($p = 0.04$) (Table 5). According to the Mann–Whitney U test, patients with reduced hand grip strength exhibited significantly lower MNA-SF scores and serum vitamin D levels in the overall population and in women. In men, only MNA-SF scores were significantly lower. Albumin levels showed no significant differences across groups (Table 6).

Multivariate logistic regression analysis in the male subgroup revealed that obesity was a borderline significant independent predictor of probable sarcopenia ($p = 0.053$; Exp(B) = 5.324). Although not statistically significant, DPP-4 inhibitor use ($p = 0.082$; Exp(B) = 3.883) and the presence of PEI ($p = 0.142$; Exp(B) = 4.230) demonstrated

Table 4 Association of pancreatic exocrine insufficiency with probable and confirmed sarcopenia: insights from a Sex-Stratified analysis

		Probable Sarcopenia			Confirmed Sarcopenia		
		Yes	**No**	**p***	**Yes**	**No**	**p**
PEI Total	**Yes**	17	10		4	22	
	No	10	39	0.81	8	86	0.3
PEI Female	**Yes**	9	8		1	15	
	No	39	21	0.52	4	56	0.9
PEI Male	**Yes**	8	2		3	7	
	No	15	18	**0.05**	4	29	0.12

PEI, pancreatic exocrine insufficiency. Comparisons were made using the Chi-square test. A p-value < 0.05 was considered statistically significant

Table 5 Associations of probable sarcopenia with diabetes-related factors, treatment modalities, comorbidities, and laboratory findings

Clinical Variables		Total (*n*) Probable sarcopenia			Female (*n*) Probable sarcopenia			Male (*n*) Probable sarcopenia		
		Yes	No	p	Yes	No	p	Yes	No	p
DM Duration (years)	>10	31	22	0.86	31	20	0.69	16	14	0.97
	≤10	39	26		17	9		7	6	
HbA1C Goal (<7%)	Yes	31	22	0.86	22	13	0.86	9	9	0.59
	No	39	26		25	16		14	10	
CaVD	Yes	25	19	0.69	12	10	0.37	13	9	0.45
	No	46	30		36	19		10	11	
Diabetic Nephropathy	Yes	32	24	0.67	18	13	0.52	14	11	0.69
	No	39	25		30	16		9	9	
CVD	Yes	5	8	0.10	3	8	**0.01**	2	0	0.17
	No	66	41		45	21		21	20	
PAH	Yes	2	3	0.19	0	1	0.19	2	2	0.88
	No	69	46		48	28		21	18	
Diabetic Neuropathy	Yes	7	4	0.38	4	4	0.44	3	0	0.10
	No	64	45		44	25		20	20	
Diabetic Foot	Yes	3	0	0.14	1	0	0.43	2	0	0.17
	No	68	49		47	29		21	20	
Metformin Use	Yes	49	39	0.20	34	24	0.24	15	15	0.24
	No	22	10		14	5		8	5	
Sulfonylurea Use	Yes	9	13	0.10	7	10	**0.04**	2	3	0.52
	No	62	36		41	19		21	17	
Pioglitazone Use	Yes	5	1	0.21	4	1	0.40	1	0	0.34
	No	66	48		44	28		22	20	
DPP-4 Inhibitor Use	Yes	27	13	0.19	15	9	0.98	12	4	**0.03**
	No	44	36		33	20		11	16	
GLP-1 Analog Use	Yes	2	1	0.79	1	1	0.71	1	0	0.34
	No	69	48		47	28		22	20	
SGLT-2 Inhibitor Use	Yes	8	5	0.85	4	4	0.44	4	1	0.20
	No	63	44		44	25		19	19	
Insulin Use	Yes	21	13	0.71	10	8	0.49	11	5	0.12
	No	50	36		38	21		12	15	
Vitamin D Deficiency	Yes	41	18	**0.01**	27	10	**0.01**	14	8	0.33
	No	10	15		8	12		2	3	
Malnutrition Risk	Yes	14	5	0.16	11	3	0.16	3	2	0.75
	No	57	44		37	26		20	18	
Obesity	Yes	37	24	0.73	27	21	0.15	10	3	**0.04**
	No	34	25		21	8		13	17	

DM, diabetes mellitus; HbA1C, glycated hemoglobin; PAH, peripheral arterial disease; HT, hypertension; CaVD, cardiovascular disease; CVD, cerebrovascular disease; DPP-4, dipeptidyl peptidase-4 inhibitors; GLP-1, glucagon-like peptide-1 agonists; SGLT-2, sodium-glucose co-transporter-2 inhibitors. Comparisons were made using the Chi-square test. Statistically significant values are highlighted in bold. A p-value < 0.05 was considered statistically significant

Table 6 Comparison of clinical and nutritional markers according to hand grip strength using the Mann–Whitney U test in all patients, women, and men

Variable	Total (p)	Female (p)	Men (p)
Albumin	0.466	0.599	0.542
MNA-SF	**<0.001**	**0.013**	**0.032**
Vitamin D	**0.009**	**0.010**	0.342

MNA-SF Mini Nutritional Assessment – Short Form; Mann–Whitney U test, a nonparametric statistical method, was used to compare median values of clinical and nutritional variables. A p-value <0.05 was considered statistically significant

trends toward association with probable sarcopenia. No significant association was found with MNA-SF score ($p = 0.137$) (Table 7).

Discussion

In this study, we evaluated the association between PEI and sarcopenia in older adults patients with T2DM. While no significant relationship was observed between PEI and sarcopenia in the total population or in females, a significant association between PEI and probable sarcopenia was identified in male patients. This finding suggests a potential

Table 7 Independent predictors of probable sarcopenia in older adults male patients with T2DM: Results of multivariate logistic regression analysis

Variable	B	SE	Wald	p-value	Exp(B)	95% CI Lower	95% CI Upper
MNA-SF	-0.416	0.274	2.209	0.137	0.660	0.386	1.129
DPP-4 Inhibitor	1.357	0.779	3.032	0.082	3.883	0.843	17.879
PEI	1.442	0.982	2.157	0.142	4.230	0.617	28.995
Obesity	1.672	0.864	3.750	**0.053**	5.324	0.980	28.924

MNA-SF, Mini Nutritional Assessment – Short Form; DPP-4 Inhibitor, Dipeptidyl Peptidase-4 Inhibitor; PEI, Pancreatic Exocrine Insufficiency. Results are expressed as regression coefficients (B), standard error (SE), Wald statistics, p-values, odds ratios (Exp(B)), and 95% confidence intervals (CI)

sex-specific interaction, possibly reflecting differences in body composition, hormonal profiles, or the clinical manifestations of PEI between men and women. In the study by Shintakuya et al., which investigated the association between PEI and sarcopenia in patients with chronic pancreatitis, sarcopenia was also found to be more prevalent among male patients [10].

The link between sarcopenia and PEI has been previously hypothesized based on shared mechanisms such as malnutrition, fat-soluble vitamin deficiencies, and systemic inflammation. However, evidence from human studies remains limited. Our findings add to the existing literature by highlighting that even in the absence of overt malnutrition, PEI may contribute to the decline in muscle function in certain subgroups, particularly older adults men with T2DM.

Sarcopenia was defined as primary and secondary, in which the former is related with ageing, and the latter is associated with many clinical and metabolic disorders, such as malnutrition, inflammation, cancer, multimorbidity, immobility, osteomalasia, neurological denervation, drugs, etc [2]. PEI was recently related with sarcopenia. PEI results in malabsorption and subsequent nutritional deficiencies that can accelerate muscle loss [10, 11]. While PEI is classically linked to chronic pancreatitis, pancreatic cancer, or pancreatic surgery, its occurrence in diabetes appears to follow a distinct pathophysiological profile and may develop in the absence of overt pancreatic pathology [12, 13]. Importantly, the Catalan Pancreas Society has recently recognized sarcopenia as a clinical manifestation of PEI in its diagnostic guidelines [18].

Protein malabsorption resulting from PEI is a potential mechanistic link to muscle wasting and sarcopenia. While fat malabsorption is a well-established consequence of PEI, experimental animal studies have also demonstrated significant protein malabsorption [19–21]. In a porcine model of PEI, a marked reduction in the incorporation of labeled nitrogen into plasma proteins was observed, indicating impaired protein metabolism [22]. Despite these findings, direct human studies evaluating the impact of PEI-induced protein malabsorption on muscle mass and function remain scarce. Future research is warranted to explore whether PERT could attenuate muscle loss in patients with coexisting PEI and sarcopenia.

The univariate associations between probable sarcopenia and low vitamin D levels, cerebrovascular disease, sulfonylurea use (in females), and DPP-4 inhibitor use and obesity (in males) are consistent with previous reports. Vitamin D deficiency has been widely recognized as a contributor to muscle weakness and frailty, especially in older adults [23]. Sulfonylureas have also been associated with increased risk of hypoglycemia and subsequent muscle loss, particularly in frail older adults patients [24].

In male patients, the observed associations between probable sarcopenia and both DPP-4 inhibitor use and obesity may be multifactorial. DPP-4 inhibitors have been hypothesized to affect muscle metabolism via incretin-related pathways, though results are conflicting and mechanistic data remain limited [25]. Obesity, particularly in the context of sarcopenic obesity, is increasingly recognized as a clinical phenotype that combines excess adiposity with diminished muscle function, and is associated with increased risk of functional decline and adverse outcomes [26]– [27].

In the multivariate analysis, although not statistically significant, both PEI and DPP-4 inhibitor use showed trends toward association with probable sarcopenia in men. The limited sample size in this subgroup may have reduced the statistical power to detect significant associations. Nevertheless, the observed trends support the hypothesis that PEI may play a contributory role in the development of sarcopenia in older adults male patients with T2DM, potentially through malabsorption-related mechanisms that impair protein and micronutrient balance [5].

Our study has several limitations that should be considered when interpreting the findings. First, although the total sample size was determined to be adequate based on a priori power analysis, it may have been insufficient for certain subgroup analyses—particularly among male participants, who constituted only 35.8% of the cohort ($n=43$). This limited statistical power may explain the lack of significance in the multivariate analysis examining the relationship between PEI and sarcopenia in men. Similarly, the absence of a significant association between malnutrition risk and

sarcopenia in both the total cohort and in sex-stratified analyses may reflect the same limitation.

Second, the cross-sectional design of the study precludes the ability to infer causal relationships. Therefore, while PEI and sarcopenia may be associated, it remains unclear whether PEI plays a direct etiological role in the development of sarcopenia.

Third, the diagnosis of PEI was based solely on FE1 levels. Although this is a widely used and non-invasive diagnostic method, it may have limited sensitivity in detecting mild to moderate exocrine insufficiency, and it does not differentiate between primary pancreatic insufficiency and secondary causes. Additionally, advanced imaging or functional diagnostic modalities to rule out underlying pancreatic pathology in patients with low FE1 levels were not employed.

To minimize potential confounding, individuals with known conditions that could affect pancreatic function or muscle mass—such as active alcohol use, history of pancreatitis, pancreatic malignancy, hereditary pancreatic disorders, use of PERT, or new-onset diabetes—were excluded from the study.

Despite these limitations, this is, to our knowledge, the first study to investigate the potential association between PEI and sarcopenia specifically in older adults with T2DM. The study design was methodologically robust, incorporating validated tools to assess both muscle mass and function based on EWGSOP2 criteria. All assessments were performed by a trained and experienced clinical nutrition team, consisting of two nurses and one dietitian, using calibrated equipment under standardized procedures. These strengths enhance the reliability and reproducibility of our findings.

Conclusion

In conclusion, this study highlights the high prevalence of both sarcopenia and PEI among older adults with T2DM. Our findings suggest that PEI may be a contributing factor to sarcopenia, particularly in older adults male patients. This observation may add a novel etiological component to the multifactorial pathogenesis of secondary sarcopenia in this population. Future longitudinal and interventional studies are needed to confirm these associations and to evaluate whether targeted strategies—such as nutritional optimization and the management of PEI—can prevent or mitigate sarcopenia in older individuals with T2DM.

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Author contributions All authors meet the criteria of authorship. S.G. led the conceptualization of the study, with contributions from M.A., S.G.U., and B.S. Methodology was developed by S.G., M.A., T.S.A., and B.S. Formal analysis and investigation were conducted by S.G., M.A., and B.S. The original draft of the manuscript was prepared by S.G., T.S.A., S.N.E., and B.S. S.G., M.A., T.S.A., S.N.E., S.G.U., and B.S. reviewed, commented on, and revised the manuscript. Resources were provided by S.G., M.A., T.S.A., S.N.E., S.G.U., and B.S. Supervision was carried out by S.G., S.N.E., S.G.U., and B.S. All authors approved the final version of the manuscript for submission.

Data availability No datasets were generated or analysed during the current study.

Declarations

Competing interests The authors declare no competing interests.

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