Lipids in Health and Disease

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Skeletal muscle alterations in type 2 diabetes mellitus with and without dyslipidemia

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Abstract

Background Diabetic dyslipidemia, a common comorbidity in people with type 2 diabetes, has been reported to be associated with adverse metabolic outcomes. Skeletal muscle is a key organ impacted by metabolic disorders; however, the specific effects of diabetic dyslipidemia on skeletal muscle mass, strength, and performance remain unclear. The aim of this study was to assess the skeletal muscle alterations of people with type 2 diabetes with and without dyslipidemia.

Methods This retrospective study included 144 participants (mean age 51.3 ± 7.1 years; 103 female, 41 male) aged 40–65 years. Body composition was assessed using bioelectrical impedance analysis (BIA), muscle strength via dynamometer, and functional capacity with the 6-minute walk test (6MWT). To minimize the confounding effect of longer diabetes duration in the diabetic dyslipidemia group, propensity score matching (PSM) was performed using a 1:1 nearest-neighbor method. All analyses were performed on matched groups. ROC analysis was conducted for variables showing significant differences.

Results After PSM, people with diabetic dyslipidemia showed significantly lower skeletal muscle mass and skeletal muscle index (SMI), higher body fat percentage, and reduced 6MWD compared to those with diabetes alone ($p < 0.05$). In women with diabetic dyslipidemia, handgrip strength was significantly lower. ROC analysis revealed moderate predictive value for skeletal muscle mass (AUC = 0.682), SMI (AUC = 0.654), and 6MWD (AUC = 0.628).

Conclusion This study demonstrated that people with diabetic dyslipidemia had lower skeletal muscle mass, SMI, and decreased physical performance compared to people with diabetes alone, even after matching for diabetes duration. These findings demonstrate early sarcopenic and dynapenic changes and highlight the need to consider skeletal muscle health and lipid abnormalities together in diabetes management.

Keywords Type 2 diabetes, Dyslipidemia, Skeletal muscle, Sarcopenia

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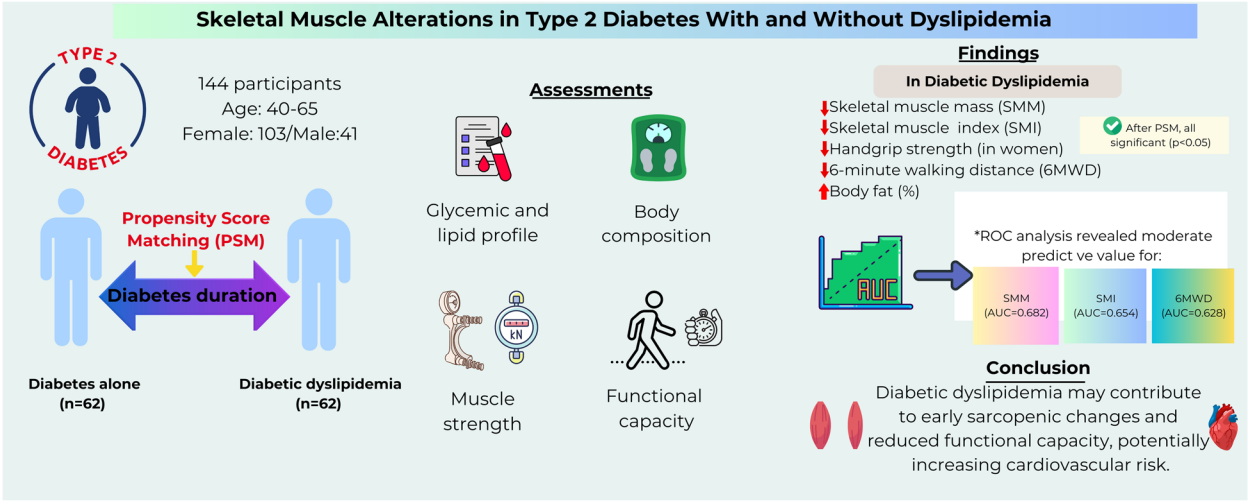
Graphical Abstract



Introduction

Diabetic dyslipidemia is a common condition in individuals with type 2 diabetes mellitus (T2DM), characterized by abnormalities in lipid metabolism. Diabetic dyslipidemia is defined by increased triglyceride (TG) levels, low high-density lipoprotein cholesterol (HDL-C), and the presence of small, dense low-density lipoprotein cholesterol (LDL-C) particles [1]. The combined effects of diabetic dyslipidemia accelerate the development of atherosclerosis, significantly increasing the risk of cardiovascular disease (CVD) [2, 3]. Insulin resistance plays a key role in the pathophysiology of diabetic dyslipidemia. It impairs fat storage in adipose tissue, leading to an increase in free fatty acids and, consequently, an elevation in TG levels. High TG levels further exacerbate insulin resistance and β-cell dysfunction, resulting in a vicious cycle between insulin resistance and lipid metabolism. Additionally, high TG and LDL-C levels aggravate increased inflammation, leading to endothelial dysfunction, an early indicator of atherosclerosis [4, 5].

Skeletal muscle is the main site of glucose disposal in the human body. According to its central role in glucose metabolism, insulin resistance in skeletal muscle is considered an early and critical step in the development of T2DM [6] and may be triggered by anormal lipid metabolism [7, 8]. This insulin resistance has also been linked to changes in muscle composition, specifically an increased ratio of type IIa to type I fibers, which results in reductions in both muscle mass and strength [9]. In addition to these structural changes, an increase in visceral adipose tissue has been shown to induce systemic inflammation and oxidative stress, contributing to endothelial dysfunction and skeletal muscle mass loss [10, 11]. These alterations negatively affect skeletal muscle energy metabolism, leading to decreased functional capacity and exercise intolerance [12]. Additionally, the combination of low skeletal muscle mass and high visceral fat has been strongly associated with reduced physical activity, atherosclerosis, and increased cardiovascular disease risk [13, 14].

Previous studies have demonstrated that reduced skeletal muscle mass or quality is associated with adverse metabolic profiles, including insulin resistance, dyslipidemia, and increased cardiovascular risk [6, 15–17]. While these studies have investigated this relationship between, they have primarily focused on how reduced muscle mass or function contributes to insulin resistance and adverse lipid profiles. However, the reverse relationship, that is, how diabetic dyslipidemia itself may affect skeletal muscle structure and function has not been directly addressed. This gap limits our understanding of the bidirectional interplay between metabolic dysfunction and skeletal muscle health. It also limits the development of targeted strategies aimed at preserving skeletal muscle health and metabolic stability in this high-risk population.

Therefore, considering the bidirectional relationship between T2DM and dyslipidemia, it was important to investigate skeletal muscle in this context. The primary aim of this study was to compare skeletal muscle alterations between individuals with diabetic dyslipidemia and those with type 2 diabetes alone. As a secondary aim, receiver operating characteristic (ROC) curve analysis was performed for the parameters in which significant differences were observed in identifying skeletal muscle alterations associated with diabetic dyslipidemia.

Materials and methods

Study design and participants

The retrospective study was conducted between June 2022 and January 2025 at Istanbul University Medical Faculty Diabetes Outpatient Clinic. It included aged 40–65 years participants, who were evaluated within the scope of our study. This study was approved by the Ethical Committee (approval 2023/85 – 65) and conducted based on the latest version of the Declaration of Helsinki [18]. All participants provided informed consent. The protocol was registered to the "ClinicalTrials.gov" website before the study began (Registration no. NCT06829576). The sample size of our study was calculated with the G*Power 3 program [19]. It was found that 62 participants should be included in each group, with 80% power and 5% margin of error, to obtain a medium effect size (d = 0.50).

The inclusion criteria were as follows: a diagnosis of type 2 diabetes mellitus (T2DM) within the past year; HbA1c values between 6.5% and 11%; a diagnosis of diabetic dyslipidemia confirmed by an endocrinologist [20]; age between 40 and 65 years; to communicate in the national language. The exclusion criteria were as follows: severe peripheral or central neurological disorders, uncontrolled hypertension and arrhythmias, diabetic ulcers, neuropathy, severe proliferative retinopathy, chronic renal failure, chronic liver disease, severe respiratory disease, cardiac pacemaker, history of stroke and myocardial infarction, and the presence of orthopedic defects involving a lower or upper extremity that might limit the assessments, and women who were pregnant or breastfeeding were not included in the study. A total of 149 patients were screened for eligibility based on the inclusion criteria; however, five patients were not included due to missing data.

Data collection

The demographic characteristics and clinical features of the patients were recorded. The glycemic parameters (Glycosylated hemoglobin; HbA1c, fasting blood glucose; FBG) and lipid profile (total cholesterol, LDL-C, HDL-C, and TG) measured after at least 8 h of fasting were derived from the medical records of the university laboratory. To evaluate skeletal muscle mass, strength, and functional performance, assessments included body composition, upper and lower extremity muscle strength, and functional capacity. All measurements were performed once per participant by the same researcher using standardized protocols and calibrated devices.

Body composition

Body composition was assessed using a Tanita MC-780 Body Composition Analyzer via bioelectrical impedance analysis (BIA) [21]. The device assessed body fat percentage, visceral fat level, and skeletal muscle mass. Patients were briefed about the test protocol and instructed to attend with an empty bladder and to avoid any liquid or food, and vigorous physical activity before this measurement. Measurements were made at room temperature, during the daytime, with indoor clothing but without shoes and socks while standing up [22]. Body mass index (BMI) was calculated by dividing body weight by square meters of height [23], and skeletal muscle mass index (SMI) was calculated by dividing skeletal muscle mass by square meters of height [13]. Waist circumference (WC) was measured at the midpoint between the lower margin of the last palpable rib and the top of the iliac crest, at the mid-axillary line. Hip circumference (HC) was measured at the widest portion of the buttocks. Both measurements were done at exhalation phase using a tape measure while the patient was standing on both feet with equal weight on each (the values of hip and waist measurements were recorded in centimeters) [24, 25]. The waist-to-hip ratios (WHR) were also calculated.

Muscle strength

Muscle strength was assessed using two measurements: quadriceps strength and handgrip strength (HGS).

Quadriceps strength was assessed using a handheld dynamometer (J-Tech CommanderTM Muscle Tester, USA) [26, 27]. Patients sat with arms crossed, hips, and knees at 90° flexion. They extended the knee and performed a 5-sec maximal contraction against resistance near the malleolus. The measurements were repeated three times with 30-second rest intervals for the right and left legs, and the best value was recorded in kilograms (kg) [28, 29]. To standardize this measurement, quadriceps strength was also expressed as a percentage calculated by adding the best effort for each leg and dividing by the participant's body weight [30].

HGS was measured using a "Jamar (NY 10533)" hydraulic-type dynamometer [31]. Participants were seated in a chair without armrests, with their feet flat on the floor, hips and knees flexed at approximately 90°, and their backs upright. The shoulder was in adduction, the elbow was flexed at 90°, the forearm was in a neutral position, and the wrist was positioned in 0°–30° of extension and 0°–15° of ulnar deviation. Three trials were performed for each participant, with a minimum 15-second rest between attempts [32]. The highest value obtained from the three trials was recorded in kg [28, 29].

6-minute walk test (6MWT)

Functional capacity was assessed with the 6-minute walk test (6MWT). The test was performed according to the European Respiratory Society/American Thoracic Society criteria [33]. The patients rested for at least 10 min before the test. They were then asked to walk as fast as possible without running in 6 min in a straight 30-meter

corridor. The oxygen saturation and heart rates of the patients before and after the test were evaluated (Baseline finger pulse oximeter), systolic and diastolic blood pressure (SBP and DBP) (Beurer BM 35 sphygmomanometer), and dyspnea and fatigue levels were evaluated using the modified Borg scale. At the end of the test, the 6-minute walk distance (6MWD) was recorded in meters.

Statistical analysis

Statistical analysis was performed using the IBM Statistical Package for Social Sciences (SPSS) version 30.0. The normality of the variables assessed using the Kolmogorov-Smirnov tests. The descriptive statistics were presented as the mean, standard deviation, and percentage. An independent sample t-test was used to compare the groups according to the normality of the parameter. The Chi-square test was conducted for the analysis of categorical variables.

Propensity score matching (PSM) analysis was used to minimize the effect of potential confounding variables between groups, particularly the significant difference observed in duration of diabetes. A 1:1 nearest neighbor matching algorithm was applied, and analyses were conducted both before and after matching. After matching, the equivalence of the groups in terms of diabetes duration and other baseline variables was statistically re-evaluated. In addition, ROC curve analysis [34] was performed to evaluate the classifier performance of the variables that could potentially be effective in distinguishing individuals with diabetic dyslipidemia from individuals with diabetes. In this analysis, area under the curve (AUC), sensitivity, specificity, positive and negative predictive values were calculated; optimal cut-off points were determined for each variable using the Youden index. Statistical significance was defined as a value of $p < 0.05$.

Results

A total of 144 participants who met the criteria were included in the study. The majority were female ($n = 103$, 71.5%), while 41 participants were male (28.5%). Of these, 82 participants (56.9%) were diagnosed with diabetic dyslipidemia, while 62 participants (43.1%) had diabetes without dyslipidemia. The mean age of all participants was 51.34 ± 7.06 years.

At baseline, a significant difference was observed in the duration of diabetes between the groups ($p < 0.001$), which suggested a potential confounding effect. The duration of diabetes was significantly longer in the diabetic dyslipidemia group compared to the diabetes group (10.60 ± 6.23 vs. 6.58 ± 3.67 years). To minimize the effect of this confounding factor, PSM was performed using a 1:1 nearest-neighbor method. After matching, statistical balance was achieved for the duration of diabetes (7.76 ± 4.10 vs. 6.58 ± 3.67 years, $p = 0.095$), and two well-balanced groups of 62 individuals were formed. The mean age of the matched participants was 50.32 ± 6.77 years, and the majority were female ($n = 87$, 70.2%). The demographic and clinical characteristics of the participants before and after PSM are presented in Table 1.

After PSM, individuals with diabetic dyslipidemia had significantly lower skeletal muscle mass (40.71 ± 16.12

Table 1 Comparison of demographic and clinical characteristics of the people with diabetic dyslipidemia and those with type 2 diabetes mellitus alone before and after PSM

	Before PSM				After PSM			
Variable	**With DD (*n* = 82)**	**With T2DM (*n* = 62)**	**Test**	***P*-value**	**With DD (*n* = 62)**	**With T2DM (*n* = 62)**	**Test**	***P*-value**
Age (year)	52.20 ± 7.11	50.23 ± 6.91	1.666[a]	0.098	50.42 ± 6.70	50.23 ± 6.91	0.158[a]	0.874
Duration of diabetes (year)	10.60 ± 6.23	6.58 ± 3.67	**4.834[a]**	**< 0.001**	7.76 ± 4.10	6.58 ± 3.67	1.685[a]	0.095
Gender n(%)								
Female	58(70.7)	45(72.6)	0.059[b]	0.808	42(67.7)	45(72.6)	0.347[b]	0.556
Male	24(29.3)	17(27.4)			20(32.3)	17(27.4)		
BMI	32.40 ± 5.62	30.93 ± 5.49	1.576[a]	0.117	32.34 ± 5.66	30.93 ± 5.49	1.409[a]	0.161
HbA1c (%)	8.11 ± 1.31	7.88 ± 1.43	0.977[a]	0.330	8.04 ± 1.22	7.88 ± 1.43	0.648[a]	0.518
FBG (mg/dL)	172.21 ± 61.41	161.27 ± 60.33	1.066[a]	0.288	167.70 ± 53.52	161.27 ± 60.33	0.627[a]	0.532
Lipid profile								
HDL-C (mg/dL)	45.11 ± 9.77	49.88 ± 12.44	**2.576[a]**	**0.011**	45.97 ± 9.36	49.88 ± 12.44	1.977[a]	0.050
LDL-C (mg/dL)	134.55 ± 24.22	85.77 ± 12.09	**15.815[a]**	**< 0.001**	136.74 ± 25.11	85.77 ± 12.09	**14.401[a]**	**< 0.001**
TG (mg/dL)	185.21 ± 67.18	146.87 ± 71.03	**3.308[a]**	**0.001**	183.34 ± 64.93	146.87 ± 71.03	**2.984[a]**	**0.003**
Total-C (mg/dL)	200.41 ± 33.76	173.07 ± 32.67	**4.879[a]**	**< 0.001**	205.09 ± 31.66	173.07 ± 32.67	**5.542[a]**	**< 0.001**

DD Diabetic dyslipidemia, *T2DM* Type 2 diabetes mellitus, *PSM* Propensity score matching, PSM ratio: 1:1 nearest neighbor matching method was used. *BMI* Body mass index, *HbA1c* Glycated hemoglobin, *FBG* Fasting blood glucose, *HDL-C* High-density lipoprotein cholesterol, *LDL-C* Low-density lipoprotein cholesterol, *C* Cholesterol, *TG* Triglyceride

$p < 0.05$

[#]Data were presented as Mean ± standard deviation or number (%)

[a]Independent sample t-test; [b]Pearson chi-square test

Table 2 Comparison of body composition, muscle strength, and functional capacity of the people with diabetic dyslipidemia and those with type 2 diabetes mellitus alone before and after PSM

	Before PSM				After PSM			
Variable	**With DD (*n* = 82)**	**With T2DM (*n* = 62)**	**Test**	***P*-value**	**With DD (*n* = 62)**	**With T2DM (*n* = 62)**	**Test**	***P*-value**
Body composition								
WC (cm)	105.88 ± 11.85	101.90 ± 12.46	1.952[a]	0.053	105.36 ± 12.10	101.90 ± 12.46	1.565[a]	0.120
Waist/hip	0.94 ± 0.08	0.93 ± 0.07	0.826[a]	0.410	0.93 ± 0.08	0.93 ± 0.07	0.345[a]	0.730
Muscle mass(kg)	40.96 ± 15.76	50.72 ± 10.17	**4.503[a]**	**< 0.001**	40.71 ± 16.12	50.72 ± 10.17	**4.137[a]**	**< 0.001**
SMI (kg/m^2)	15.45 ± 5.63	18.77 ± 2.95	**4.563[a]**	**< 0.001**	15.27 ± 5.68	18.77 ± 2.95	**4.306[a]**	**< 0.001**
Body fat (%)	38.21 ± 8.88	34.98 ± 9.69	**2.076[a]**	**0.040**	38.59 ± 8.73	34.98 ± 9.69	**2.183[a]**	**0.031**
Visceral fat level	11.38 ± 3.90	10.01 ± 4.45	1.963[a]	0.052	11.42 ± 3.94	10.01 ± 4.45	1.869[a]	0.064
Muscle strength								
Right Q (kg)	7.83 ± 2.11	8.56 ± 1.84	**2.191[a]**	**0.030**	7.98 ± 2.26	8.56 ± 1.84	1.583[a]	0.116
Left Q (kg)	7.33 ± 2.14	7.91 ± 1.96	1.682[a]	0.095	7.55 ± 2.27	7.91 ± 1.96	0.939[a]	0.349
Quadriceps (%)	17.98 ± 5.39	20.44 ± 5.73	**2.637[a]**	**0.009**	18.47 ± 5.91	20.44 ± 5.73	1.889[a]	0.061
HGS (kg)								
Female	22.49 ± 5.35	25.90 ± 7.26	**2.739[a]**	**0.007**	22.48 ± 5.38	25.90 ± 7.26	**2.481[a]**	**0.015**
Male	34.58 ± 10.66	35.80 ± 8.08	0.397[a]	0.693	35.38 ± 10.84	35.80 ± 8.08	0.134[a]	0.894
6MWD (m)	456.49 ± 57.86	488.55 ± 61.98	**3.193[a]**	**0.002**	458.19 ± 57.75	488.55 ± 61.98	**2.821[a]**	**0.006**

DD Diabetic dyslipidemia, *T2DM* Type 2 diabetes mellitus, *PSM* Propensity score matching, PSM ratio: 1:1 nearest neighbor matching method was used. *cm* Centimeter, *kg* Kilogram, *WC* Waist circumference, *SMI* Skeletal mass index, *Q* Quadriceps, *6MWD* 6-minute walking distance, *m* Meter, Visceral fat level (unitless index, range: 1–59, measured by TANITA MC-780)

$p < 0.05$

[a]Independent sample t-test; [cc]Pearson chi-square test

[#]Data were presented as Mean ± standard deviation or number (%)

Table 3 ROC curve analysis

Variable	AUC (95% CI)	Cut-off points[a]	Sensitivity	Specificity	PPV	NPV	Accuracy
Muscle mass(kg)	0.682(0.587–0.778)	38.4	40.3%	93.6%	86.2%	61.1%	66.9%
SMI (kg/m)^2	0.654(0.555–0.754)	15.28	43.6%	93.6%	87.1%	62.4%	68.5%
HGS[b] (kg)	0.632(0.514–0.750)	26.08	74.1%	67.6%	61.5%	76.2%	70.1%
6MWD (m)	0.628(0.530–0.726)	514	91.9%	32.3%	57.6%	80.0%	62.1%

NPV Negative predictive value, *PPV* Positive predictive value, *CI* Confidence interval, *AUC* Area under curve, *SMI* Skeletal mass index, *HGS* Handgrip strength, *6MWD* 6-minute walking distance, *m* Meter, *kg* Kilogram

p<0.05

[a]Cut-off values were determined by the Youden index; [b]HGS for female

vs. 50.72 ± 10.17 kg, $p < 0.001$), lower SMI (15.27 ± 5.68 vs. 18.77 ± 2.95 kg/m², $p < 0.001$), and higher body fat percentage (38.59 ± 8.73 vs. 34.98 ± 9.69%, $p = 0.031$) compared to that diabetes. Although quadriceps and handgrip strength values were lower in the diabetic dyslipidemia group, these differences were not statistically significant after PSM ($p > 0.05$). 6MWD was significantly lower in people with diabetic dyslipidemia (458.19 ± 57.75 vs. 488.55 ± 61.98 m, $p = 0.006$). The body composition, muscle strength, and functional capacity of the participants, both before and after PSM, are presented in Table 2.

ROC curve analysis showed that skeletal muscle mass, SMI, HGS for female and 6MWD were moderate predictors of diabetic dyslipidemia. Skeletal muscle mass had an AUC of 0.682 (95% CI: 0.587–0.778, $p < 0.001$) with an optimal cut-off of 38.4 kg (sensitivity: 40.3%, specificity: 93.6%). The SMI had an AUC of 0.654 (95% CI: 0.555–0.754, $p < 0.01$) with a cut-off of 15.28 kg/m² (sensitivity: 43.6%, specificity: 93.6%). The HGS for female had an AUC of 0.632 (95% CI: 0.514–0.750, $p = 0.060$) with an optimal cut-off of 26.8 kg (sensitivity: 74.1%, specificity: 67.6%). The 6MWD had an AUC of 0.628 (95% CI: 0.530–0.726, $p < 0.05$) with an optimal cut-off of 514 m (sensitivity: 91.9%, specificity: 32.3%) (Table 3).

The post-hoc power of the study was calculated based on the comparison of SMI and muscle mass values in the groups using G*power sample size calculation. According to this analysis, the observed power of the study was found to be 98% for SMI (d = 0.773, type 2 error probability = 0.05, two-tailed) and 98% for skeletal muscle mass (d = 0.742, type 2 error probability = 0.05, two-tailed).

Discussion

The results of this study showed that diabetic dyslipidemia has negative effects on skeletal muscle mass and skeletal muscle index and imposes an additional burden on muscle health beyond the effects of diabetes alone.

In females with diabetic dyslipidemia, handgrip strength was found to be significantly lower. These findings suggest that diabetic dyslipidemia play a role in the deterioration of skeletal muscle health irrespective of the diabetes duration.

Previous research has associated longer diabetes duration with regional muscle loss, particularly in the lower limbs [35]. In our study, diabetes duration was initially longer in the diabetic dyslipidemia group, which may have influenced muscle-related outcomes. To minimize this potential confounding effect, propensity score matching was performed to achieve comparable diabetes duration between groups. In line with earlier studies that identified diabetes duration as a confounding factor in metabolic outcomes [36], our use of PSM strengthens the interpretation that the observed differences in skeletal muscle composition and function are more likely attributable to diabetic dyslipidemia. Even after balancing diabetes duration, our findings suggest a more widespread decrease in muscle mass throughout the body in individuals with diabetic dyslipidemia, indicating a broader and potentially more severe impact on skeletal muscle health.

In this study, people with diabetic dyslipidemia had significantly lower muscle mass and SMI, despite having similar glycemic profiles to those with diabetes alone. This suggests that lipid abnormalities independently contribute to skeletal muscle deterioration. The observed decrease in muscle mass and SMI may be explained by insulin resistance and chronic inflammation, which, along with increased visceral fat and circulating free fatty acids, lead to lipotoxicity, mitochondrial dysfunction, and impaired muscle protein synthesis and may lead to atrophy in people with obesity and T2DM [10, 11]. While previous studies have primarily focused on low skeletal muscle mass as a contributor to dyslipidemia and atherogenic lipid profiles [17, 37, 38], fewer have explored the reverse relationship the effect of dyslipidemia on skeletal muscle health [16]. Emerging evidence now suggests that dysregulated lipid metabolism may directly impair muscle structure and function, as reflected by decreased muscle mass, increased intramuscular fat accumulation, and reduced strength, independent of overall adiposity and systemic inflammation [10, 15–17]. In line with previous research, our results highlight the potential role of diabetic dyslipidemia in skeletal muscle alterations. Given these findings, diabetic dyslipidemia may provide further clinical insight as a metabolic phenotype with potential implications for skeletal muscle health.

In people with diabetic dyslipidemia, changes in skeletal muscle mass were also reflected in early functional outcomes. Notably, a significant decline in handgrip strength was observed in women, whereas no significant differences were found in men or in quadriceps strength between the groups. The female-specific decrease in muscle strength, when considered alongside decreased muscle mass, may reflect early functional outcomes of skeletal muscle deterioration in this population. The decreased muscle mass and low SMI observed when dyslipidemia accompanies diabetes suggest that it may accelerate sarcopenic processes in people with diabetic dyslipidemia. These findings may represent early indicators of sarcopenia. Sarcopenia, traditionally defined as an age-related decline in muscle mass and function, has been increasingly recognized to also occur secondary to chronic conditions such as metabolic diseases. This concept, known as secondary sarcopenia [39], highlights the impact of metabolic disorders on muscle health.

Furthermore, people with diabetic dyslipidemia had a significantly higher body fat percentage compared to those without dyslipidemia. This increase in adiposity, particularly in visceral fat, is known to promote proinflammatory cytokine activity and metabolic stress, which may exacerbate muscular deterioration [12, 40]. The coexistence of low muscle mass and elevated fat mass supports the potential development of sarcopenic obesity in this population. This condition represents not only the combined burden of muscle loss and fat accumulation but is also closely associated with an elevated risk of cardiovascular disease and all-cause mortality, as demonstrated in previous studies [11, 12, 40].

In people with diabetic dyslipidemia, alterations in muscle mass and body fat percentage were observed, along with reduced physical performance. People with diabetic dyslipidemia had a shorter 6MWD. This reduction in physical performance may be attributed to a combination of decreased muscle mass, increased adiposity, and compromised muscle quality [15–17], reinforcing the early functional consequences of sarcopenic changes. Given the relationship between decreased physical capacity and increased cardiovascular risk, these findings underscore the clinical importance of early detection and intervention in individuals with diabetic dyslipidemia.

ROC analysis showed that skeletal muscle mass, SMI, HGS and 6MWD had limited diagnostic value for detecting diabetic dyslipidemia. While skeletal muscle mass and SMI showed high specificity (93.6%) but low sensitivity, HGS showed a more balanced profile in women. Conversely, 6MWD showed high sensitivity (91.9%) but low specificity, suggesting its potential utility as a screening rather than diagnostic tool. These results are consistent with previous studies that have applied ROC analysis to muscle-related parameters in metabolic conditions. In the literature, investigated optimal cut off values for HGS and SMI to detect osteosarcopenic obesity in obese postmenopausal women, reporting similarly variable diagnostic performance depending on the parameter assessed [41]. These findings suggest that the combined use of

multiple parameters may improve diagnostic accuracy in the assessment of diabetic dyslipidemia.

Strengths and limitations

This study has several strengths. First, it is the first to specifically investigate skeletal muscle alterations in individuals with diabetic dyslipidemia, addressing a notable gap in the literature regarding the reverse effects of lipid abnormalities on skeletal muscle health. Second, the study employed PSM to control for the confounding effect of diabetes duration, thus strengthening the internal validity of the findings. Third, it included both structural (muscle mass, SMI) and functional (grip strength, 6MWT) measures, providing a comprehensive assessment of muscle health. In this study observed a reduction in handgrip strength among women with diabetic dyslipidemia, suggesting a possible early functional impact in this subgroup. While further research is needed to confirm this sex-specific trend, the finding may indicate that women with diabetic dyslipidemia could experience earlier muscle strength decline, underlining the importance of considering sex differences in future assessments and interventions. Additionally, the study evaluated a relatively clinically relevant population within the early to middle age range (40–65 years), enhances the generalizability of the results to a working-age diabetic population. Finally, the integration of ROC curve analysis allowed for preliminary evaluation of diagnostic performance of muscle-related parameters in detecting diabetic dyslipidemia, offering potential utility for future clinical screening strategies. This study has several limitations. First, the temporal relationship between dyslipidemia and diabetes remains unclear, limiting causal interpretations. Second, the single-center design and relatively small sample size may restrict generalizability. Third, skeletal muscle composition was not assessed using imaging techniques such as ultrasound or computed tomography, which offer more detailed insights into structural and qualitative changes. Although these were necessary to reduce confounding factors that independently affect muscle strength and performance, they may also limit the generalizability of our findings to a broader population of people with type 2 diabetes mellitus. Future studies should consider including a more diverse sample and adjusting for comorbidities using statistical methods. Another limitation of our study is that, although a diagnosis of T2DM within the past year was used to identify incident cases, this may lead to misclassification of prevalent cases.

Conclusion

This study highlights the important role of lipid abnormalities in skeletal muscle deterioration and suggests that diabetic dyslipidemia may be a stronger determinant of muscle health than diabetes alone. This condition may contribute to early-onset secondary sarcopenia and increase the risk of sarcopenic obesity, particularly through the coexistence of increased adiposity and reduced muscle mass. The observed decrease in handgrip strength in women with diabetic dyslipidemia may indicate a greater susceptibility to sarcopenic changes, highlighting the need for gender-specific strategies in muscle health assessment and intervention. These findings highlight the need for treatment strategies in type 2 diabetes that go beyond glycemic control to include lipid regulation and muscle-targeted preventive rehabilitation programs. While lipid management is a routine component of diabetes care, its potential role in maintaining muscle health remains underrecognized. Future studies are needed to elucidate to explore the causal relationship and to support the development of preventive and rehabilitation approaches, including individualized exercise prescriptions aimed at preserving muscle mass, strength, and physical function in this high-risk population.

Abbreviations

AUC	Area under the curve
BIA	Bioelectrical impedance analysis
BMI	Body mass index
CVD	Cardiovascular disease
DBP	Diastolic blood pressure
FBG	Fasting blood glucose
HbA1c	Glycosylated hemoglobin
HC	Hip circumference
HDL-C	High-density lipoprotein cholesterol
HGS	Handgrip strength
kg	Kilograms
LDL-C	Low-density lipoprotein cholesterol
PSM	Propensity score matching
ROC	Receiver operating characteristic
6MWD	6-minute walk distance
SBP	Systolic blood pressure
SMI	Skeletal muscle mass index
T2DM	Type 2 diabetes mellitus
TG	Triglyceride
WC	Waist circumference
WHR	Waist-to-hip ratios

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Authors' contributions

S.Y.: Writing– review and editing, writing– original draft, methodology, investigation, formal analysis, data curation, conceptualization. B.U.E. and D.K.D.: Investigation, data curation, writing– review and editing. I.S.: Writing– review and editing, supervision. F.C. and H.R.S.: Investigation. F.P: Writing– review and editing. B.A.: Writing– review and editing, writing– original draft, methodology, investigation, formal analysis, data curation, supervision, conceptualization. All authors read and approved the final manuscript.

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Data availability

The datasets used or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Biruni University (Approval no: 2023/85 – 65). The study was conducted in accordance with the Declaration of Helsinki. Informed consent: All participants provided written informed consent prior to their enrollment in the study. The study was registered on ClinicalTrials.gov prior to initiation (Registration no: NCT06829576).

Competing interests

The authors declare no competing interests.

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