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Sarcopenia in Middle-Aged Adults With Type 2 Diabetes Mellitus: Prevalence, Associated Factors and Relationship With Gonadal Hormones

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SARCOPENIA IN MIDDLE-AGED ADULTS WITH TYPE 2 DIABETES MELLITUS: PREVALENCE, ASSOCIATED FACTORS AND RELATIONSHIP WITH GONADAL HORMONES

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ABSTRACT

Background: Sarcopenia is increasingly recognised as a complication of type 2 diabetes mellitus (T2DM), yet data among middle-aged adults with T2DM remain limited, particularly regarding its relationship with gonadal hormones. This study evaluated the prevalence of sarcopenia, its associated factors, and its relationship with gonadal hormones among adults aged 40–60 years with T2DM.

Methods: This cross-sectional study was conducted at a university hospital from February to July 2026. Participants were adults aged 40-60 years with T2DM for at least 12 months (n=100). Sarcopenia was diagnosed according to revised European consensus on the definition and diagnosis of sarcopenia. Demographic, anthropometric, metabolic, body composition and gonadal hormone parameters were assessed. Logistic regression analysis was performed to identify factors associated with sarcopenia.

Results: The prevalence of sarcopenia was 13% (95% CI: 7.8–21.0%) (n=13). Participants with sarcopenia were older and had numerically higher mean glycated haemoglobin (HbA1c) over the preceding year. Hypogonadism was present in 46.2% of participants with sarcopenia and 31.0% of those without, with no significant association (COR 1.905, 95% CI 0.585–6.206; p=0.285). Sex-stratified analyses showed higher sex hormone-binding globulin concentrations in both men and women with sarcopenia, while free androgen index was lower among women with sarcopenia. In multivariable analysis, older age (aOR 1.432, 95% CI: 1.116–1.838; p=0.005) and higher mean HbA1c (aOR 1.567, 95% CI: 1.004–2.445; p=0.048) were associated with greater odds of sarcopenia, whereas insulin use was inversely associated (aOR 0.081, 95% CI: 0.010–0.649; p=0.018).

Conclusions: Sarcopenia was present in approximately one in eight middle-aged adults with T2DM in this single-centre study. Older age and poorer long-term glycaemic control were independently associated with sarcopenia, while hypogonadism was not statistically significant. Larger prospective studies are warranted to clarify the relationships between glycaemic control, gonadal hormones and muscle health in middle-aged adults with T2DM.

Clinical trial number: not applicable

Keywords: Diabetes Mellitus, Middle-aged, Sarcopenia, Prevalence, Risk factors, Gonadal hormones, Testosterone, Oestradiol, SHBG, FAI

BACKGROUND

Sarcopenia is a progressive and generalised skeletal muscle disorder characterised by diminished muscle strength and muscle mass, with impaired physical performance indicating severe disease. It is associated with adverse outcomes including falls, fractures, disability and mortality [1]. Although traditionally regarded as an age-related disorder, sarcopenia is also observed in middle-aged adults, particularly those with chronic metabolic conditions such as type 2 diabetes mellitus (T2DM), suggesting that muscle loss may begin earlier in life [2]. Evidence suggests a bidirectional relationship between T2DM and sarcopenia, with diabetes-related metabolic disturbances contributing to muscle deterioration, while reduced muscle mass may further impair glucose metabolism [3].

Ageing is associated with progressive loss of muscle mass and strength, which becomes more pronounced from midlife onwards, with muscle mass estimated to decline by approximately 1–2% annually after age 50. Muscle strength may decline even more rapidly, by approximately 1.5% annually between 50 and 60 years and 3% annually thereafter [4]. This process may be accelerated by T2DM, as insulin resistance may adversely affect muscle protein metabolism [5], while chronic hyperglycaemia promotes the accumulation of advanced glycation end-products, which may induce oxidative stress and inflammation, contributing to muscle impairment [6]. Consequently, sarcopenia has been reported more frequently among individuals with diabetes, particularly in older populations [2,7-9]. Sarcopenia in individuals with T2DM warrants attention because of its potential cardiovascular consequences, having been associated with an increased risk of cardiovascular disease and cardiovascular events [10]. Early identification and timely management of sarcopenia may therefore help to reduce the burden of cardiovascular risk and functional decline in patients with T2DM.

Studies among older adults with T2DM have reported varying prevalence of sarcopenia, ranging from approximately 15.2% to 28.5% across Asian populations [9,11-13]. A recent systematic review and meta-analysis by Wu et al. (2026) estimated

a pooled sarcopenia prevalence of 13% (95% CI: 8–18%) among middle-aged adults with T2DM in Asia [2]. Despite this pooled estimate, evidence in middle-aged adults remains limited, as only four of the 43 included studies enrolled participants younger than 65 years, and just two specifically focused on middle-aged populations; substantial heterogeneity was also observed [2]. Furthermore, as the included studies were conducted across diverse Asian countries, variation in study populations, age definitions and diagnostic criteria may limit the applicability of the pooled estimate to specific populations. Evidence from Malaysia remains particularly scarce, especially among middle-aged adults with T2DM.

Gonadal hormones may represent an additional link between ageing, T2DM and skeletal muscle health. Testosterone is an anabolic hormone and plays a pivotal role in maintaining muscle mass and strength in men [14-15], and its concentration declines progressively with age, at an average rate of approximately 1.6% per year [16]. T2DM has been associated with hypogonadism and reduced testosterone concentrations in men [17-20] and given the role of testosterone in skeletal muscle maintenance [14-15], lower testosterone availability may therefore be associated with sarcopenia in individuals with T2DM [21].

In women, oestradiol is important in skeletal muscle maintenance, with oestrogen receptors expressed in skeletal muscle and potential effects on muscle regeneration and inflammatory pathways [22]. Oestradiol levels decline substantially during the menopausal transition, coinciding with reductions in muscle mass and strength [22-23]. This decline in oestradiol may be implicated in the development of sarcopenia in women, with Du et al. reporting lower oestradiol concentrations among women with T2DM and sarcopenia, although this association did not remain significant after multivariable adjustment [21].

The bioavailability of both testosterone and oestradiol is influenced by sex hormone-binding globulin (SHBG), which binds circulating sex hormones and regulates their free fractions [24-25]. Oestradiol may also influence SHBG concentrations, suggesting an interplay between oestradiol and SHBG [26]. Higher SHBG concentrations have been associated with lower skeletal muscle mass, suggesting a potential role of SHBG in skeletal muscle health [27]. In this context, the free androgen index (FAI), calculated from total testosterone and SHBG, provides an

indirect estimate of androgen availability [28].

Despite increasing recognition of sarcopenia in T2DM, evidence among middle-aged adults remains limited. The relationships between T2DM and sarcopenia, T2DM and hypogonadism, and gonadal hormones and muscle health have largely been examined separately. Few studies have explored these relationships concurrently, particularly in adults aged 40-60 years with T2DM, which may represent an important period for identifying early muscle changes and potentially modifiable factors.

METHODS

This cross-sectional study was conducted between February and July 2026 among adults aged 40–60 years with T2DM attending the Endocrine Clinic, Hospital Al-Sultan Abdullah, UiTM. This study aimed to determine the prevalence and factors associated with sarcopenia and to examine its relationship with gonadal hormones in this population. The sample size was calculated using a single population proportion formula with finite population correction, assuming a 15.4% prevalence of sarcopenia among patients with T2DM based on the study by Gorial et al. [29], a 95% confidence level, a 5% absolute precision, and a design effect of 1. Based on an estimated population of 157 patients with T2DM aged 40–60 years attending the Endocrine Outpatient Clinic at Hospital Al-Sultan Abdullah, the calculated sample size was 89 participants. After accounting for an anticipated 10% missing or incomplete data rate, the minimum required sample size was 98 participants.

A total of 100 patients who met the eligibility criteria were recruited via systematic random sampling. Eligible participants included adults aged 40–60 years who had been diagnosed with T2DM for at least 12 months and were able to stand unaided to undergo bioelectrical impedance analysis (BIA). Those with conditions that may hinder the assessment of sarcopenia or hypogonadism, such as chronic kidney disease stage 5, Stage D heart failure, history of stroke assessed using the Modified Rankin Scale (mRS) [30], with a score of three or above considered an exclusion criterion, neuromuscular disorders, spinal cord injuries, myopathies, use of immunosuppressive drugs, corticosteroids or hormonal therapy within the past 3 months, acute illnesses or recent hospital admission within the preceding 3 months, previous diagnosis of hypogonadism due to other causes, malabsorptive disease,

malnutrition (assessed with the Malnutrition Universal Screening Tool, with a score of 2 or more) [31], pregnancy, or known malignancy, were excluded.

Demographic information, diabetes duration, comorbidities, physical activity, and current pharmacological treatments were obtained from medical records and corroborated during medical interviews. Biochemical data for each participant, including renal profile, urinary albumin-to-creatinine ratio (UACR), and lipid profile, were obtained from the most recent available medical records. Mean HbA1c was calculated from HbA1c measurements recorded during the preceding year. The status of diabetes-related complications, including microvascular and macrovascular complications, was assessed and updated at the time of enrolment.

Anthropometric measurements

Anthropometric measurements, including weight, height, waist circumference (WC), and hip circumference (HC), were obtained from all participants. Body weight was measured using a calibrated weighing scale, while height was measured using a stadiometer. Waist circumference was measured at the midpoint between the lowest rib and the iliac crest at the end of normal expiration, while hip circumference was measured horizontally around the maximum circumference of the buttocks with the participant standing upright. Body mass index (BMI) was calculated as body weight in kilograms divided by the square of height in metres (kg/m^2), and waist-to-hip ratio (WHR) was calculated by dividing waist circumference by hip circumference.

Serum gonadal hormone measurements

Serum oestradiol, total testosterone, and sex hormone-binding globulin (SHBG) concentrations were measured as part of the gonadal hormone assessment. A 6-mL venous blood sample was collected between 8:00 am and 10:00 am following an overnight fast. Serum total testosterone and oestradiol concentrations were measured using chemiluminescent immunoassays on the Access 2 Immunoassay System (Beckman Coulter, Inc., USA), while serum SHBG concentration was measured using a chemiluminescent immunoassay on the Atellica Immunoassay Analyzer (Siemens Healthineers, Germany), according to the manufacturers' instructions. The laboratory-specific reference range for total testosterone in men aged 18–66 years was 6.07–27.10 nmol/L, while the reference range for SHBG was 10.84–180.0

nmol/L. The reference ranges for oestradiol in women varied according to reproductive status, with ranges of 82.23–422.17 pmol/L during the early follicular phase, 91.78–422.17 pmol/L during the mid-follicular phase, 117.84–1898.91 pmol/L during the ovulatory peak, 133.99–903.07 pmol/L during the mid-luteal phase, and <92.14 pmol/L in postmenopausal women.

Handgrip strength

Handgrip strength was assessed as a measure of muscle strength using a Jamar hydraulic hand dynamometer (Model 12-0600; Performance Health Supply, LLC, USA). Participants were seated during the assessment, with the shoulders adducted and neutrally rotated, the elbow flexed at 90°, and the forearm and wrist maintained in a neutral position [32]. The device was held in the dominant hand, and the dynamometer handle was adjusted to a comfortable grip. Participants were instructed to squeeze the dynamometer as forcefully as possible and maintain the contraction for as long as possible. Three measurements were performed with a 1-minute rest interval between trials, and the highest value obtained was recorded as the final handgrip strength measurement. Low handgrip strength was defined as less than 27 kg in men and less than 16 kg in women according to the European Working Group on Sarcopenia in Older People 2 (EWGSOP2) criteria [1].

Body composition assessment

Bioelectrical impedance analysis (BIA) was performed to estimate muscle mass and assess body composition using the InBody 380 body composition analyser (InBody Co., Ltd., Seoul, Republic of Korea). Participants underwent measurement barefoot and wearing light clothing, according to the manufacturer's instructions. The device automatically estimated body composition parameters, including appendicular skeletal muscle mass (ASM), skeletal muscle index (SMI), percentage body fat (PBF), and body fat mass (BFM). SMI was calculated as ASM divided by height squared (kg/m²). Low muscle mass was defined as an SMI of less than 7.0 kg/m² in men and less than 5.5 kg/m² in women according to the EWGSOP2 criteria [1].

Physical performance

Physical performance was assessed using the 4-metre gait speed test. Participants

were instructed to walk along a 4-metre marked walkway at their usual walking pace. The time required to complete the 4-metre distance was recorded using a stopwatch. Gait speed was calculated by dividing the distance walked (four metres) by the recorded time and expressed in metres per second (m/s). A gait speed of 0.8 m/s and lower was indicative of poor physical performance according to the EWGSOP2 criteria [1].

Diagnosis of sarcopenia

The dependent variable of this study was sarcopenia, which was determined according to the EWGSOP2 criteria. Confirmed sarcopenia was defined by the presence of both low muscle strength and low muscle mass and was considered severe with the additional presence of poor physical performance [1]. Although the EWGSOP2 criteria were developed primarily for older adults, they were applied in this study to provide a standardised framework for assessing sarcopenia in adults aged 40–60 years.

Hypogonadism

In this study, hypogonadism was defined based on gonadal hormone concentrations below the lower limit of the laboratory-specific reference range, irrespective of the presence or absence of clinical symptoms. As clinical symptoms of hypogonadism were not assessed in this study, the definition was based solely on biochemical measurements. In men, hypogonadism was defined as a serum total testosterone concentration below 6.07 nmol/L, while in women, it was defined as a serum oestradiol concentration below the lower limit of the laboratory-specific reference range according to reproductive status.

Statistical Analysis

Data analysis was performed using the Statistical Package for the Social Sciences (SPSS) software (Version 30.0; IBM Corp., Armonk, NY, USA). The distribution of continuous variables was assessed using the Shapiro–Wilk test and visual inspection of histograms. Normally distributed continuous variables were presented as mean ± standard deviation (SD), while non-normally distributed continuous variables were presented as median and interquartile range (IQR). Categorical variables were

presented as frequencies and percentages. For comparisons between participants with and without sarcopenia, an independent-samples t-test was used for normally distributed continuous variables, while the Mann–Whitney U test was used for non-normally distributed continuous variables. Associations between categorical variables were assessed using Pearson's chi-square test or Fisher's exact test when expected cell frequencies were low and the assumptions for the chi-square test were not met. Univariable and multivariable logistic regression analyses were performed to evaluate factors associated with sarcopenia. Given the limited number of sarcopenia cases, the multivariable model was restricted to a small number of clinically relevant predictors to maintain parsimony. Age, mean HbA1c over the preceding year, and insulin use were included in the multivariable model based on their clinical relevance and potential associations with sarcopenia. Odds ratios (OR), adjusted odds ratios (aOR), 95% confidence intervals (CI), and p-values were reported. A p-value <0.05 was considered statistically significant.

Use of generative AI and AI-assisted technologies

During the preparation of this work, the authors used Gemini (Google) solely for language editing and to improve readability of the manuscript. Following the use of this tool, the authors carefully reviewed and edited the manuscript as needed and take full responsibility for the content of the published article. All scientific content and interpretations are original.

RESULTS

The prevalence of sarcopenia among individuals with T2DM aged 40–60 years was 13% (95% CI: 7.8–21.0%) (n=13). All 13 participants classified as having sarcopenia had both low handgrip strength and low skeletal muscle index (SMI) according to the study definitions. Among participants without sarcopenia, 29 (33.3%) had low handgrip strength despite having normal SMI. All participants had normal gait speed. The median gait speed was 0.96 m/s (IQR 0.89–1.00) among participants with sarcopenia and 1.03 m/s (IQR 0.93–1.12) among those without sarcopenia.

A total of 100 participants were included in this study. Table 1 shows the demographic and clinical characteristics of study participants according to sarcopenia status**.** The median age of the participants was 51.5 years (IQR 44.25–56.00).

Participants were equally distributed by sex, with 50 (50.0%) men and 50 (50.0%) women. Most participants were Malay, comprising 93 (93.0%) participants, while 7 (7.0%) were of other ethnicities. The median duration of diabetes was 8 years (IQR 4.25-12.00). Metformin was the most prescribed glucose-lowering agent (93.0%), followed by sodium-glucose cotransporter-2 inhibitors (SGLT2i) (69.0%), insulin (44.0%), and glucagon-like peptide-1 receptor agonist (GLP-1 RA) (23.0%). A total of 69 (69.0%) participants had microvascular complications, while 29 (29.0%) had macrovascular complications.

Table 1. Demographic and clinical characteristics of study participants

Variables	**All (n=100)**	**Sarcopenia Status**		**P value**
		Yes (n=13)	**No (n=87)**	
Age (years); median (IQR)	51.50 (44.25-56.00)	57.00 (54.00-60.00)	50.00 (44.00-55.00)	**<0.001***
Sex; n (%)				
● Male	50 (50.0)	5 (38.5)	45 (51.7)	0.372
● Female	50 (50.0)	8 (61.5)	42 (48.3)	
Ethnicity; n (%)				
● Malay	93 (93.0)	12 (92.3)	81 (93.1)	
● Chinese	4 (4.0)	1 (7.7)	3 (3.4)	0.640
● Indian	2 (2.0)	0 (0.0)	2 (2.3)	
● Others	1 (1.0)	0 (0.0)	1 (1.1)	
Exercise (min/week); n (%)				
● <60 minutes	92 (92.0)	13 (100.0)	79 (90.8)	0.592
● ≥60 minutes	8 (8.0)	0 (0.0)	8 (9.2)	
T2DM duration (years); median (IQR)	8.00 (4.25-12.00)	8.00 (5.50-17.50)	8.00 (4.00-12.00)	0.207
Glucose-lowering agents				
● Metformin; n (%)	93 (93.0)	12 (92.3)	81 (93.1)	1.000
● Sulfonylurea; n (%)	24 (24.0)	6 (46.2)	18 (20.7)	0.076
● DPP-4 inhibitor; n (%)	47 (47.0)	8 (61.5)	39 (44.8)	0.260
● SGLT2i; n (%)	69 (69.0)	12 (92.3)	57 (65.5)	0.059
● GLP-1 RA; n (%)	23 (23.0)	0 (0.0)	23 (26.4)	**0.036***
● Insulin; n (%)	44 (44.0)	2 (15.4)	42 (48.3)	**0.026***
Microvascular complication; n (%)	69 (69.0)	9 (69.2)	60 (68.9)	1.000

Macrovascular complication; n (%)	29 (29.0)	4 (30.8)	25 (28.7)	0.880

*Data are presented as mean ± standard deviation (SD), median (IQR), or n (%). P values were calculated using the t-test, Mann-Whitney U test, chi-square test, or Fisher's exact test, as appropriate. *P<0.05 was considered statistically significant. T2DM (type 2 diabetes mellitus), DPP-4 (dipeptidyl peptidase-4), SGLT2i (sodium-glucose cotransporter-2 inhibitor), GLP-1 RA (glucagon-like peptide-1 receptor agonist).*

Participants with sarcopenia were significantly older than those without sarcopenia, with median ages of 57.0 years (IQR 54.00–60.00) and 50.0 years (IQR 44.00–55.00), respectively (p<0.001). However, there were no significant differences in sex distribution (p=0.372) or ethnicity (p=0.640) between the two groups. The median duration of diabetes was 8 years in both groups, with no significant difference between the groups (p=0.207).

The use of glucose-lowering agents differed between the two groups. None of the participants with sarcopenia received a GLP-1 RA compared with 26.4% of participants without sarcopenia (p=0.036). Insulin use was also significantly lower among participants with sarcopenia than those without sarcopenia (15.4% vs. 48.3%, p=0.026). Metformin was the most commonly used glucose-lowering agent, with similar use among participants with and without sarcopenia (92.3% vs. 93.1%, p=1.000). SGLT2 inhibitor use was higher among participants with sarcopenia than those without sarcopenia (92.3% vs. 65.5%); however, this difference was not statistically significant (p=0.059). All 13 participants with sarcopenia (100%) reported less than 60 minutes of exercise per week, compared with 79 (90.8%) of the 87 participants without sarcopenia (p=0.592).

Anthropometric, metabolic and body composition parameters according to sarcopenia status are presented in Table 2.

Table 2. Comparison of anthropometric, metabolic and body composition parameters according to sarcopenia status

Variables	**All (n=100)**	**Sarcopenia Status**		**P value**
		Yes (n=13)	**No (n=87)**	
Weight (kg); median (IQR)	82.00 (68.27-101.07)	61.80 (52.35-64.30)	84.10 (73.90-102.0)	**<0.001***
BMI (kg/m²); median (IQR)	31.05 (26.47-37.00)	23.20 (22.80-25.30)	32.00 (28.00-38.00)	**<0.001***

Waist circumference (cm); mean (SD)	103.84 (16.464)	87.62 (6.462)	106.26 (16.140)	**<0.001***
Hip circumference (cm); median (IQR)	106.00 (96.25-119.00)	94.00 (89.50-96.00)	109.00 (100.00-120.00)	**<0.001***
WHR; mean (SD)	0.950 (0.073)	0.945 (0.068)	0.948 (0.074)	0.887
Triglycerides (mmol/L); median (IQR)	1.40 (1.00-2.00)	1.00 (0.90-1.45)	1.50 (1.10-2.00)	0.051
LDL-C (mmol/L); median (IQR)	2.20 (1.60-3.17)	2.30 (1.65-2.90)	2.20 (1.60-3.20)	0.984
FBS (mmol/L); median (IQR)	7.00 (6.00-8.88)	6.70 (5.70-9.25)	7.00 (6.00-8.80)	0.826
Mean HbA1c (1-year) (%); mean (SD)	8.02 (1.646)	8.54 (1.772)	7.94 (1.621)	0.221
Creatinine (µmol/L); median (IQR)	78.00 (61.00-95.75)	63.00 (57.50-95.50)	80.00 (62.00-96.00)	0.412
eGFR (mL/min/1.73 m^2); median (IQR)	90.00 (74.00-90.00)	90.00 (74.50-90.00)	90.00 (73.00-90.00)	0.942
UACR; median (IQR)	4.30 (1.20-15.32)	1.20 (0.55-6.25)	5.20 (1.40-16.30)	0.690
PBF (%); mean (SD)	38.69 (7.865)	33.59 (6.935)	39.45 (7.744)	**0.011***
BFM (kg); median (IQR)	30.70 (24.00-41.27)	18.70 (13.00-27.10)	33.50 (26.70-44.50)	**<0.001***
BFMI (kg/m^2); median (IQR)	11.70 (9.10-16.67)	7.90 (5.10-10.80)	12.80 (9.50-17.50)	**<0.001***

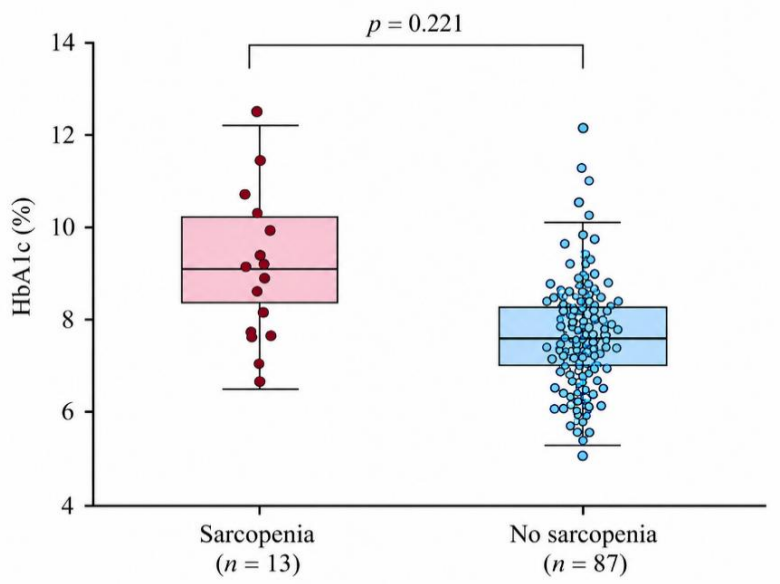
*Data are presented as mean ± standard deviation (SD), median (IQR), or n (%). P values were calculated using the t-test, Mann-Whitney U test, chi-square test, or Fisher's exact test, as appropriate. *P<0.05 was considered statistically significant. BMI (body mass index), WHR (waist-to-hip ratio), LDL (low-density lipoprotein cholesterol) FBS (fasting blood sugar), HbA1c (glycated haemoglobin), eGFR (estimated glomerular filtration rate), UACR (urine albumin-to-creatinine ratio), PBF (percentage body fat), BFM (body fat mass), BFMI (body fat mass index).*

Participants with sarcopenia had lower measures of body size and adiposity than those without sarcopenia. The median BMI was 23.2 kg/m^2 (IQR 22.80–25.30) in the sarcopenia group compared with 32.0 kg/m^2 (IQR 28.00–38.00) in the non-sarcopenia group ($p<0.001$). Waist circumference was significantly lower among participants with sarcopenia (87.62 ± 6.46 cm vs. 106.26 ± 16.14 cm, $p<0.001$), as was median hip circumference (94.0 cm [IQR 89.50–96.00] vs. 109.0 cm [IQR 100.00–120.00], $p<0.001$), while waist-to-hip ratio (WHR) was comparable between the two groups

(0.945 ± 0.068 vs. 0.948 ± 0.074, p=0.887).

Figure 1 shows the distribution of mean HbA1c over the preceding year according to sarcopenia status. Mean HbA1c over the preceding year was higher among participants with sarcopenia than among those without sarcopenia (8.54 ± 1.77% vs. 7.94 ± 1.62%, respectively); however, the difference was not statistically significant (p=0.221). The remaining metabolic and renal parameters did not differ significantly between the two groups.

Figure 1. Distribution of mean HbA1c over the preceding year according to sarcopenia status.



Participants with sarcopenia also had lower measures of body fat compared with those without sarcopenia. Percentage body fat was significantly lower in the sarcopenia group than in the non-sarcopenia group (33.59 ± 6.94% vs. 39.45 ± 7.74%, p=0.011). Median body fat mass was also lower among participants with sarcopenia (18.70 kg [IQR 13.00–27.10] vs. 33.50 kg [IQR 26.70–44.50], p<0.001), as was body fat mass index (7.90 kg/m² [IQR 5.10–10.80] vs. 12.80 kg/m² [IQR 9.50–17.50], p<0.001).

Table 3 shows the sex-stratified body composition according to sarcopenia status. Among males, participants with sarcopenia had significantly lower percentage body fat (PBF), body fat mass (BFM), and body fat mass index (BFMI) compared with those without sarcopenia (p=0.004, <0.001, and <0.001, respectively). A similar pattern was observed among females, where participants with sarcopenia had significantly

lower PBF, BFM, and BFMI than those without sarcopenia (p=0.038, 0.002, and 0.003, respectively). Overall, participants with sarcopenia demonstrated consistently lower measures of adiposity in both sexes.

Table 3. Sex-stratified body composition according to sarcopenia status

MALE				
Variables	**All (n=50)**	**Sarcopenia Status**		**P value**
		Yes (n=5)	**No (n=45)**	
PBF (%); mean (SD)	34.86 (7.426)	26.02 (2.586)	35.83 (7.137)	**0.004***
BFM (kg); median (IQR)	29.90 (23.95-41.96)	17.20 (13.40-18.40)	32.80 (26.50-44.25)	**<0.001***
BFMI (kg/m²); median (IQR)	9.85 (8.73-15.00)	6.20 (5.35-6.80)	11.20 (9.05-16.10)	**<0.001***
SMI (kg/m²); mean (SD)	8.50 (1.111)	6.84 (0.114)	8.69 (1.011)	N/A
FEMALE				
Variables	**All (n=50)**	**Sarcopenia Status**		**P value**
		Yes (n=8)	**No (n=42)**	
PBF (%); mean (SD)	42.53 (6.304)	38.33 (3.477)	43.34 (6.428)	**0.038***
BFM (kg); mean (SD)	34.32 (12.968)	21.61 (3.759)	36.74 (12.692)	**0.002***
BFMI (kg/m²); mean (SD)	14.09 (5.271)	9.20 (1.480)	15.02 (5.222)	**0.003***
SMI (kg/m²); median (IQR)	6.65 (5.80-7.75)	5.30 (5.00-5.47)	6.85 (6.10-7.93)	N/A

*Data are presented as mean ± standard deviation (SD), median (IQR), or n (%). P values were calculated using the t-test, Mann-Whitney U test, chi-square test, or Fisher's exact test, as appropriate. *P<0.05 was considered statistically significant. PBF (percentage body fat), BFM (body fat mass), BFMI (body fat mass index), SMI (skeletal muscle index), N/A (not applicable).*

The prevalence of hypogonadism was 33.0% (95% CI: 24.6–42.8%) (n=33) in the overall study population. Hypogonadism was present in 6 (46.2%) participants with sarcopenia and 27 (31.0%) participants without sarcopenia, with no statistically significant difference between the groups (p=0.346). Sex-stratified analyses of gonadal hormones and hypogonadism are presented in Table 4.

Table 4. Sex-stratified analyses of gonadal hormone parameters and hypogonadism according to sarcopenia status

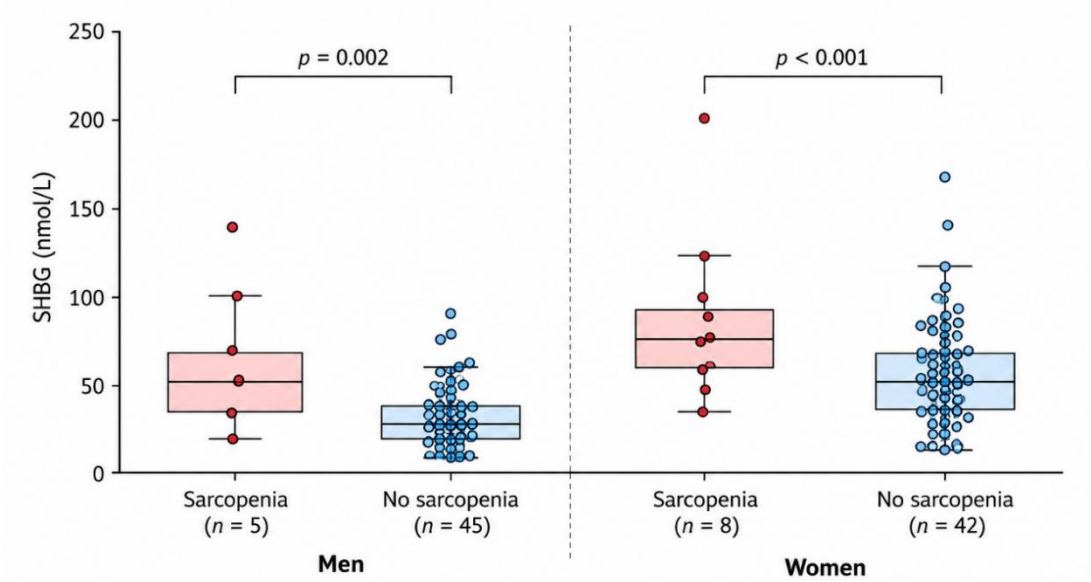
OVERALL				
Variables	**All (n=100)**	**Sarcopenia Status**		**P value**
		Yes (n=13)	**No (n=87)**	
Hypogonadism; n (%)	33 (33.0)	6 (46.2)	27 (31.0)	0.346
MALE				
Variables	**All (n=50)**	**Sarcopenia Status**		**P value**
		Yes (n=5)	**No (n=45)**	
Hypogonadism; n (%)	3 (6.0)	0 (0.0)	3 (6.7)	1.000
Total Testosterone (nmol/L); mean (SD)	11.51 (4.185)	11.71 (5.858)	11.48 (4.047)	0.912
SHBG (nmol/L); mean (SD)	33.54 (19.019)	56.64 (39.649)	30.97 (13.875)	**0.002***
FAI; median (IQR)	36.35 (28.91-50.87)	31.54 (14.12-37.08)	39.24 (29.49-51.84)	0.108
FEMALE				
Variables	**All (n=50)**	**Sarcopenia Status**		**P value**
		Yes (n=8)	**No (n=42)**	
Hypogonadism; n (%)	30 (60.0)	6 (75.0)	24 (57.1)	0.450
Menopausal status; n (%)	27 (54.0)	6 (75.0)	21 (50.0)	0.261
Menopausal age (years); median (IQR)	52.00 (51.00-53.00)	52.00 (51.00-53.25)	51.00 (50.00-53.00)	0.476
Oestradiol (pmol/L); median (IQR)	59.75 (55.10-237.72)	55.10 (55.10-528.72)	72.50 (55.10-237.72)	0.474
SHBG (nmol/L); median (IQR)	40.30 (24.05-56.07)	69.30 (52.62-92.52)	37.20 (22.87-47.32)	**<0.001***
FAI; median (IQR)	2.33 (1.23-4.06)	1.04 (0.43-2.17)	2.72 (1.43-4.12)	**0.031***

*Data are presented as mean ± standard deviation (SD), median (IQR), or n (%). P values were calculated using the t-test, Mann-Whitney U test, chi-square test, or Fisher's exact test, as appropriate. *P<0.05 was considered statistically significant. SHBG (sex hormone-binding globulin), FAI (free androgen index).*

Among men, there was no significant difference in the prevalence of hypogonadism between participants with and without sarcopenia (0.0% vs. 6.7%, p=1.000). Mean total testosterone levels were also comparable between the two groups (11.71 ± 5.858 vs. 11.48 ± 4.047 nmol/L, p=0.912). Mean SHBG concentration was significantly higher among men with sarcopenia than those without sarcopenia (56.64 ± 39.649 vs. 30.97 ± 13.875 nmol/L, p=0.002), while free androgen index (FAI) did not differ significantly (p=0.108).

Among women, the prevalence of hypogonadism was 75.0% in participants with sarcopenia compared with 57.1% in those without sarcopenia, although the difference was not statistically significant (p=0.450). There were also no significant differences in menopausal status (75.0% vs. 50.0%, p=0.261), menopausal age (52.0 vs. 51.0 years, p=0.476), or oestradiol concentration (55.10 pmol/L [IQR 55.10–528.72] vs. 72.50 pmol/L [IQR 55.10–237.72], p=0.474). Figure 2 shows the sex-specific distribution of SHBG according to sarcopenia status.

Figure 2. Sex-specific distribution of SHBG according to sarcopenia status.



The mean SHBG concentration was significantly higher among men with sarcopenia than those without sarcopenia (56.64 ± 39.649 vs. 30.97 ± 13.875 nmol/L, p=0.002), while free androgen index (FAI) did not differ significantly (p=0.108). Among women, SHBG concentration was significantly higher among women with sarcopenia than those without sarcopenia (69.30 nmol/L [IQR 52.62–92.52] vs. 37.20

nmol/L [IQR 22.87–47.32], p<0.001), while FAI was significantly lower (1.04 [IQR 0.43–2.17] vs. 2.72 [IQR 1.43–4.12], p=0.031).

Univariable and multivariable logistic regression analyses were performed to identify factors associated with sarcopenia, as shown in Table 5. In the univariable analysis, older age was associated with higher odds of sarcopenia (COR 1.428, 95% CI: 1.147–1.776, p=0.001), while insulin use was associated with lower odds of sarcopenia (COR 0.195, 95% CI: 0.041–0.931, p=0.040). Neither hypogonadism (COR 1.905, 95% CI: 0.585–6.206, p=0.285) nor mean HbA1c over the preceding year (COR 1.220, 95% CI: 0.884–1.682, p=0.226) showed a significant association with sarcopenia in the univariable analysis. In the multivariable logistic regression analysis, as presented in Figure 3, age, insulin use, and mean HbA1c over the preceding year were independently associated with sarcopenia. Each one-year increase in age was associated with higher odds of sarcopenia (aOR 1.432, 95% CI: 1.116–1.838, p=0.005), while insulin use was associated with lower odds of sarcopenia (aOR 0.081, 95% CI: 0.010–0.649, p=0.018). Although mean HbA1c was not significantly associated with sarcopenia in the univariable analysis, it showed an independent association after adjustment for age and insulin use, with each 1% increase associated with higher odds of sarcopenia (aOR 1.567, 95% CI: 1.004–2.445, p=0.048).

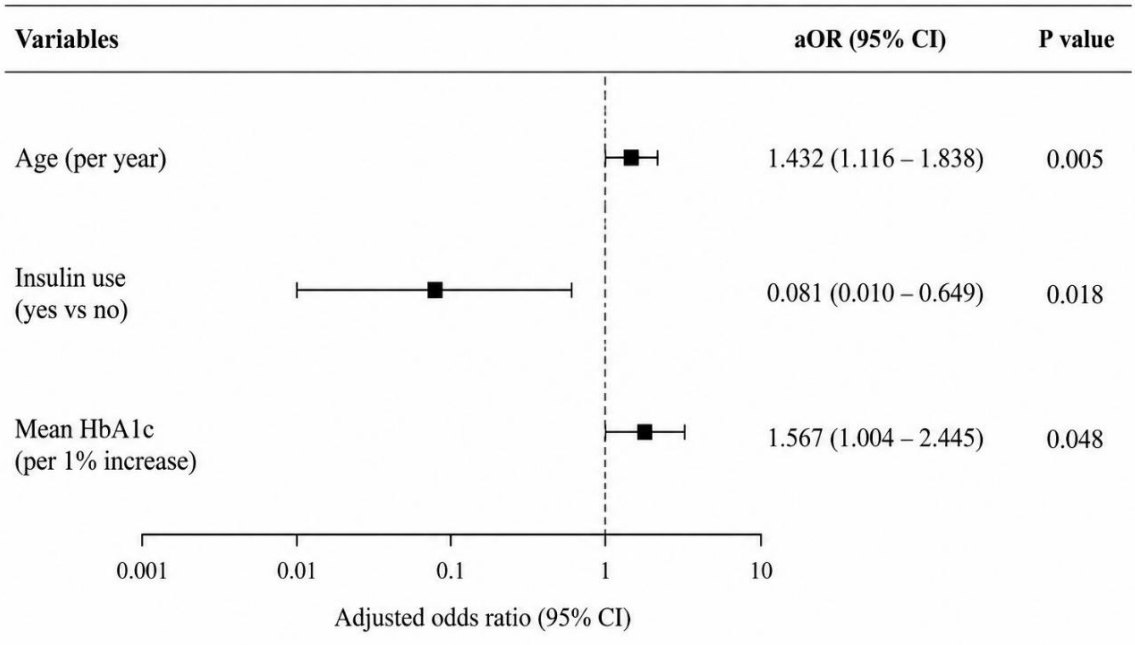
Table 5. Univariable and multivariable logistic regression analysis of factors associated with sarcopenia

Variables	Univariable Logistic Regression		Multivariable Logistic Regression	
	COR (Lower 95% CI - Upper 95% CI)	P value	aOR (Lower 95% CI -Upper 95% CI)	P value
Age (years)	1.428 (1.147-1.776)	**0.001***	1.432 (1.116-1.838)	**0.005***
Gender	1.714 (0.520-5.657)	0.376		
T2DM duration	1.065 (0.974-1.164)	0.165		
Insulin use	0.195 (0.041-0.931)	**0.040***	0.081 (0.010-0.649)	**0.018***
FBS (mmol/L)	0.938 (0.716-1.228)	0.642		
Mean HbA1c (%) [a]	1.220 (0.884-1.682)	0.226	1.567 (1.004-2.445)	**0.048***

Hypogonadism	1.905 (0.585-6.206)	0.285	

*[a] mean HbA1c over the preceding year, COR (crude odds ratio), aOR (adjusted odds ratio), CI (confidence interval), T2DM (type 2 diabetes mellitus), FBS (fasting blood sugar), CORs and aORs were derived from univariable and multivariable logistic regression analyses, respectively. *P<0.05 was considered statistically significant.*

Figure 3. Factors associated with sarcopenia in multivariable logistic regression analysis



DISCUSSION

To the best of our knowledge, this study provides the first country-specific data on the prevalence of sarcopenia and its relationship with gonadal hormones among middle-aged patients with type 2 diabetes mellitus.

This study observed that sarcopenia was present in adults aged 40-60 years with T2DM. It is consistent with meta-analysis by Wu et al. who reported 13.0% pooled prevalence specifically among middle-aged adults with T2DM in Asia [2]. It was also comparable with the 15.4% reported by Gorial et al. [29], but lower than the 18.8% reported by Shahi et al. [33]. Differences in prevalence may reflect variations in study populations, diagnostic criteria and muscle mass assessment. Gorial et al. had an older cohort with a mean age of 57.0 years [29], while the present study had a lower median

age. In addition, Shahi et al. used AWGS 2019 criteria and dual-energy X-ray absorptiometry (DXA) for muscle mass assessment [33-34], whereas Gorial et al. used EWGSOP2 criteria and DXA while present study used EWGSOP2 criteria and BIA, which has different thresholds for muscle strength and muscle mass [1, 29]. Recent meta-analyses by Wu et al. and Ai et al. demonstrated substantial heterogeneity in sarcopenia prevalence among patients with T2DM according to diagnostic criteria and muscle mass assessment methods [2,7]. In particular, Wu et al. reported a higher pooled prevalence in studies using DXA (19%) compared with those using BIA (11%), highlighting the potential influence of assessment modality on prevalence estimates [2].

In the present study, 13% of adults aged 40–60 years with T2DM had sarcopenia despite preserved gait speed. This aligns with the EWGSOP2 framework, which places low muscle strength at the centre of sarcopenia diagnosis and considers impaired physical performance an indicator of severe sarcopenia [1]. Lu et al. reported that among patients with T2DM, gait speed remained relatively preserved until older age, with significant declines occurring mainly after 70 years, whereas declines in muscle mass and strength were observed earlier, particularly among women [35]. This is consistent with the present findings, where gait speed remained preserved despite established sarcopenia, which may partly reflect the relatively younger age of this study population. These observations suggest that abnormalities in muscle mass and strength could be detectable before overt physical performance impairment. Therefore, early assessment of muscle health may facilitate identification of muscle abnormalities before functional decline develops.

Hypogonadism was not significantly associated with sarcopenia in the present study, although a numerically higher proportion of participants with hypogonadism was observed in the sarcopenia group than in the non-sarcopenia group. This finding differs from Du et al. who reported that in patients with T2DM, lower testosterone was independently associated with sarcopenia in men, while women with sarcopenia had lower estradiol concentrations, although estradiol was not independently associated with sarcopenia [21]. The lack of statistical significance should be interpreted in the context of the relatively small sarcopenia group, which may have limited the statistical power to detect an association, as well as differences in age, population characteristics and hormonal assessment between studies.

Similarly, total testosterone in men and oestradiol in women did not differ significantly according to sarcopenia status. Although sex hormones are involved in the regulation of skeletal muscle, circulating hormone concentrations may not fully represent their biological availability, particularly in the presence of variations in SHBG concentrations [25,36]. Of note, SHBG concentrations were significantly higher among participants with sarcopenia in both men and women, which aligns with the findings of Qin et al., who reported that higher SHBG concentrations were independently associated with low muscle mass in both sexes [27]. Higher SHBG concentrations may influence sex hormone bioavailability; however, the mechanisms underlying the association between SHBG and muscle mass remain unclear [25].

In women, FAI was significantly lower among those with sarcopenia, supporting the possibility that reduced androgen availability could be relevant to muscle mass. Hwang et al. also reported positive associations between FAI and skeletal muscle mass and strength in both men and women [37]. In men, however, FAI was not significantly different despite higher SHBG concentrations. These observations suggest that measures of androgen availability, such as FAI, may provide additional information beyond total testosterone when examining the relationship between gonadal hormones and muscle health [25,37]. Nevertheless, given the cross-sectional design and small sarcopenia group, these results should be interpreted as associations rather than evidence of a causal hormonal effect.

Older age was independently associated with higher odds of sarcopenia in the present study. This finding is supported by recent meta-analyses; Wu et al. reported that each additional year of age was associated with higher odds of sarcopenia among Asian adults with T2DM (OR 1.12), while Feng et al. reported similar findings among patients with diabetes (OR 1.10) [2,38]. The higher magnitude of association observed in the present study may be related to differences in study population and age distribution. Wu et al. included Asian adults aged ≥45 years with T2DM, whereas Feng et al. included adults aged ≥18 years with different types of diabetes, therefore representing a broader population [2, 38].

In contrast, the present study focused on patients with T2DM aged 40–60 years, within a relatively narrow age range. The smaller sample size and limited number of participants with sarcopenia may also have contributed to the greater variability in the

estimated association. Increasing age may predispose to a greater risk of sarcopenia due to age-related muscle fibre atrophy, loss of muscle fibres and reduced anabolic responsiveness, while chronic low-grade inflammation may further contribute to impaired muscle protein metabolism [39-40]. In patients with T2DM, insulin resistance, chronic inflammation, oxidative stress and hyperglycaemia may further contribute to muscle deterioration [41].

Mean HbA1c over the preceding year was numerically higher among participants with sarcopenia, although no statistically significant difference was observed in the unadjusted comparison (p=0.221). Following adjustment for age and insulin use, notably, higher mean HbA1c was independently associated with sarcopenia, with each 1% increase associated with 1.57-fold higher odds of sarcopenia (aOR 1.567, p=0.048). Given the relatively small number of sarcopenia cases, this adjusted association should be interpreted cautiously. This finding is consistent with previous evidence, with Ai et al. reporting an aOR of 1.16 and Wu et al. reporting an aOR of 1.11, demonstrating a similar positive association between increasing HbA1c and sarcopenia [2,7]. Chronic hyperglycaemia may contribute to muscle deterioration through insulin resistance, oxidative stress and chronic inflammation, which may impair muscle protein synthesis and promote muscle protein breakdown [42]. The association observed in the present study therefore suggests that suboptimal long term glycaemic control may be associated with adverse effects on muscle health.

Insulin use was independently associated with lower odds of sarcopenia in the present study. This finding is consistent with the Multicentre Study for Clarifying Evidence for Sarcopenia in Patients with Diabetes Mellitus (MUSCLES-DM), longitudinal study by Sugimoto et al., which demonstrated an association between baseline insulin use and subsequent changes in skeletal muscle mass over one year. In their multiple linear regression analysis, insulin use was independently associated with changes in skeletal muscle mass after adjustment for age, sex, BMI and other covariates (standardised β=0.115, p=0.022). The authors observed that skeletal muscle mass was maintained or increased among patients using insulin and proposed that this could partly reflect the anabolic effects of insulin on skeletal muscle [43].

A possible physiological explanation is provided by Dimitriadis et al., who described insulin as an anabolic hormone, noting that insulin increases muscle protein

synthesis and decreases muscle protein degradation, thereby favouring protein accumulation in skeletal muscle [44]. However, evidence regarding the effects of insulin on human muscle protein metabolism is complex. A systematic review and meta-analysis by Abdulla et al. found no significant overall increase in muscle protein synthesis with insulin, although insulin significantly reduced muscle protein breakdown and increased net protein acquisition. The authors further suggested that insulin could have a permissive role in muscle protein synthesis when amino acid availability is elevated [45].

Therefore, the lower odds of sarcopenia observed in the present study should not be interpreted as evidence that insulin directly prevents sarcopenia. Insulin use could also reflect differences in diabetes management and glycaemic control, which could partly contribute to the observed association. In addition, the wide confidence interval around the present estimate indicates considerable uncertainty, and the observational nature of both the present study and the MUSCLES-DM study limits causal interpretation.

The group with sarcopenia had significantly lower measures of adiposity and body size, including lower waist and hip circumference, BMI, body fat mass, and BFMI in the unadjusted analysis. These results aligned with evidence from Du et al., who reported that higher BMI was associated with lower odds of sarcopenia among patients with T2DM, whereas higher body fat percentage was associated with greater risk [21]. In the present study, these differences in adiposity should be interpreted in the context of the lower overall body size and reduced skeletal muscle mass among participants with sarcopenia. As adiposity measures were not included in the final multivariable model, their independent associations with sarcopenia could not be determined. The lower body size may partly reflect the reduction in skeletal muscle mass and overall body mass observed among participants with sarcopenia. These findings also highlight the limitation of relying on BMI alone, as BMI does not distinguish between muscle mass and fat mass and therefore may not adequately reflect muscle health.

Although more than 90% of participants reported less than 60 minutes of exercise per week, exercise duration was not significantly associated with sarcopenia in the present study. This lack of association could partly reflect the limited variability in physical activity within the study population, as most participants reported similarly

low levels of exercise, reducing the ability to detect differences between the sarcopenia and non-sarcopenia groups. This is relevant in the Malaysian context, where national data indicate that physical inactivity remains relatively common, with 29.9% of Malaysian adults classified as physically inactive in the NHMS 2023, while inactivity was particularly high in the recreation-related and travel-related domains [46].

In addition, self-reported exercise duration may not adequately capture the type and intensity of physical activity, including resistance training, occupational activity and habitual daily movement. Nevertheless, previous Malaysian evidence among older adults with T2DM found that low and moderate levels of physical activity were independently associated with sarcopenia, with ORs of 2.15 and 2.23 respectively [9]. Therefore, the absence of a significant association in the present study could reflect the relatively homogeneous and generally low activity levels of the cohort, rather than indicating that physical activity is unrelated to sarcopenia.

This is the first Malaysian study to provide data on the prevalence of sarcopenia and its relationship with gonadal hormones among middle-aged patients with type 2 diabetes mellitus. The predominantly Malay and relatively homogeneous study population reduces ethnic heterogeneity and provides context-specific findings for the local population. The use of BIA enabled a comprehensive and non-invasive assessment of body composition, allowing both muscle and adiposity profiles to be evaluated concurrently. In addition, this study concurrently examined the interrelationship between type 2 diabetes mellitus, sarcopenia, and gonadal hormones, which remains relatively understudied.

The cross-sectional design limits the ability to establish causal relationships between sarcopenia and the factors examined. The relatively small number of participants with sarcopenia may have limited the statistical power of subgroup analyses and the precision of the multivariable regression estimates. Although the multivariable model was restricted to a small number of clinically relevant predictors to maintain parsimony, the adjusted estimates should therefore be interpreted cautiously. BIA provided a practical method for assessing body composition; however, its estimates of muscle mass may differ from those obtained using DXA. Furthermore, nutritional status was not assessed, which may have introduced residual confounding.

CONCLUSIONS

Sarcopenia was detected in thirteen percent of middle-aged individuals with T2DM in this cohort. It was independently associated with older age and poorer glycaemic control, while insulin use was associated with lower odds of sarcopenia. Although hypogonadism was not significantly associated with sarcopenia, differences in SHBG and FAI were observed in sex-stratified analyses. The presence of sarcopenia in this relatively younger population highlights the need to consider muscle health in individuals with T2DM, particularly those with suboptimal glycaemic control. Further prospective studies with larger sample sizes are needed to clarify the relationships between glycaemic control, gonadal hormones and sarcopenia, while interventional studies could explore whether targeted strategies help preserve or improve muscle health in this population.

LIST OF ABBREVIATIONS

Abbreviation	Full term
ASM	Appendicular skeletal muscle mass
AWGS	Asian Working Group for Sarcopenia
aOR	Adjusted odds ratio
BFM	Body fat mass
BFMI	Body fat mass index
BIA	Bioelectrical impedance analysis
BMI	Body mass index
CI	Confidence interval
COR	Crude odds ratio
DPP-4	Dipeptidyl peptidase-4
DXA	Dual-energy X-ray absorptiometry
eGFR	Estimated glomerular filtration rate
EWGSOP2	European Working Group on Sarcopenia in Older People 2
FAI	Free androgen index
FBS	Fasting blood sugar
GLP-1 RA	Glucagon-like peptide-1 receptor agonist
HbA1c	Glycated haemoglobin

Abbreviation	Full term
HC	Hip circumference
IQR	Interquartile range
LDL-C	Low-density lipoprotein cholesterol
N/A	Not applicable
OR	Odds ratio
PBF	Percentage body fat
SD	Standard deviation
SHBG	Sex hormone-binding globulin
SGLT2i	Sodium-glucose cotransporter-2 inhibitor
SMI	Skeletal muscle index
SPSS	Statistical Package for the Social Sciences
T2DM	Type 2 diabetes mellitus
UACR	Urine albumin-to-creatinine ratio
UiTM	Universiti Teknologi MARA
WC	Waist circumference
WHR	Waist-to-hip ratio

DECLARATIONS

Ethics approval and consent to participate

Ethics approval was obtained from Research Ethics Committee, Universiti Teknologi MARA (UiTM). Ethics registration number: REC/01/2026 (PG/FB/9). This study was carried out according to the Code of Ethics of the World Medical Association (Declaration of Helsinki). Participation was voluntary. Informed consent was obtained from all participants recruited into this study, prior to their participation.

Consent for publication

Not applicable

Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available due to privacy and ethical restrictions but are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

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Formal Analysis: HNMY, FZMS, RAG, MRI
Investigation: HNMY, FZMS, RAG, MRI
Methodology: HNMY, FZMS, RAG, MRI
Project Administration: HNMY, FZMS
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Software: HNMY, FZMS, RAG, MRI
Supervision: FZMS, RAG, MRI
Validation: FZMS, RAG, MRI
Visualization: HNMY, FZMS, RAG
Writing; Original Draft: HNMY
Writing; Review & Editing: HNMY, FZMS, RAG, MRI

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