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Predictors of sarcopenia in individuals with diabetes: a cross-sectional analysis

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Abstract

Background and Purpose—Excess lower extremity intermuscular adipose tissue (IMAT), reduced strength, and functional limitations are common in obese individuals with and without diabetes (the former termed diabetes). Individuals with diabetes are particularly susceptible to accelerated sarcopenia, which may be under-diagnosed. The purpose of this study was to determine critical values for leg IMAT volume, plantar flexor muscle strength, and physical performance that help identify individuals with diabetes who have sarcopenia.

Methods—43 age- and sex-matched obese adults were studied; 12 with type 2 diabetes, 21 with diabetes and peripheral neuropathy, and 10 non-diabetic controls. Dual-energy x-ray absorptiometry (DXA)-derived skeletal muscle index determined classification of sarcopenia. Leg fat (%IMAT), ankle plantar flexor (PF) peak torque and power while ascending 10 steps were used as explanators of sarcopenia. Receiver operating curves (ROC) identified critical values for each explainer individually. Logistic regression models using all 3 explanators, and only PF torque and stair power, were also created. ROC analyses identified the predicted probability that maximized each model's sensitivity and specificity. A leave one out cross validation was used to simulate the models' performance in an independent sample.

Results & Discussion—32 participants were sarcopenic, 11 were not. Critical values for individual explanators were: 21% IMAT, 68 Nm PF torque, and 441 watts of stair power. Predicted probabilities of .76 and .67 were chosen as the optimal cutoff probabilities for the model combining all 3 explanators, and the model combining PF torque and stair power respectively. The cross validation analysis produced an accuracy of 82.4%, using the cutoff probability of .5, and an

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Conflicts of Interest:

The authors have no conflicts of interest or significant financial support for this work that could have influenced its outcome.

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accuracy of 76.5%, using the cutoff of .76. The area under the curve (AUC) for the cross validation ROC analysis was .82. Critical values of leg %IMAT, PF torque, and stair power can classify individuals with diabetes as sarcopenic. The results of the cross validation give us confidence that the sample used in this study was representative of the target population, and suggests models created from this sample may perform well in externally derived datasets

Conclusion—Clinicians may be able to use these critical values to select interventions that specifically target sarcopenia. Measures of %IMAT, PF torque, and stair power may offer a customized alternative to traditional sarcopenic classification systems, which may not be optimally suited to the common impairments among individuals with diabetes.

Keywords

Sarcopenia; Diabetes; Adipose Tissue; Muscle; Neuropathy

INTRODUCTION

Sarcopenia is an age-related loss of skeletal muscle mass that occurs at a rate of 1-2% per year beginning, typically, after age 50 and progressing more rapidly and severely between late middle age and senescence.¹ In addition to age, previous research has shown that the rate of sarcopenic decline can be accelerated by concurrent co-morbid conditions, lifestyle factors, and individual characteristics including sex, genetic background, and hormone balance.² Sedentary lifestyles and infrequent aerobic or resistance training are particularly common contributors to sarcopenic decline in older adults.² For example, in 2010, only 11% of adults 65 years of age or older participated in regular aerobic or muscle-strengthening exercise, which precludes these individuals from the protective effects of these activities.³ Moreover, 45% of women and 43% of men 65 to 74 years of age are classified as obese, with the onset of type 2 diabetes mellitus increasing in prevalence by 21% since 1998.^{3,4} The combination of these 2 common conditions has been referred to as diabetes – the specific form of type 2 diabetes mellitus that typically develops with aging and is associated with obesity.⁵

Diabetes is defined by several etiological characteristics that may contribute to the development of sarcopenia, including insulin resistance -- which interferes with muscle anabolism and lowers the rate of muscle protein synthesis.⁶ The synergistic pathophysiology of these 2 conditions may accelerate the onset and progression of sarcopenia and merits further study.⁷

Sarcopenia is currently classified based on 3 criteria: 1) low muscle mass (defined using data from young individuals age 18-39 years), when total body muscle mass falls 2 standard deviations below the mean value of a younger population assessed by dual energy x-ray absorptiometry (DXA), or bioelectrical impedance analysis (BIA) measures, 2) reduced gait speed (below 0.8 m/s in 4 m walk test), and 3) grip strength with hand-grip dynamometry relative to normative values based on sex, BMI, and force.^{7,8} These diagnostic criteria are typically used for individuals 65 years of age or older, and therefore do not take into account any accelerated model of sarcopenic diabetes. Previous research has shown that individuals with type 2 diabetes and peripheral neuropathy (PN) may present with signs of sarcopenia

(e.g. loss of muscle strength and power, loss of physical function, and excess intermuscular adipose tissue, or IMAT accumulation) well before 65 years of age, suggesting that sarcopenia may be largely under-diagnosed in this population.^{9,10}

Traditional classification criteria may also be inadequate due to the nonlinear relationship between muscle mass and strength or functional performance. Some authors suggest that the key consequence of sarcopenia is the loss of muscle strength, power or force (dynapenia) rather than mass alone.^{7,8,11} Moreover, the reliance on measures of grip strength fails to characterize muscle function in the lower extremity (particularly calf muscles), which is severely affected by type 2 diabetes + PN, and is more closely associated with physical function than thigh or upper extremity musculature.¹² Measures of lower extremity strength and functional power, therefore, may provide a more accurate basis for sarcopenic classification, particularly in individuals with diabetes. Additionally, because changes in muscle composition are critical to muscle quality, and excess IMAT infiltration reduces muscle quality and performance, we hypothesized that there may be relationships between leg IMAT accumulation and sarcopenic decline, particularly in diabetes – a condition characterized by progressive IMAT accumulation and accelerated sarcopenia.⁷

To our knowledge, no studies have determined critical values of leg composition, muscle strength, power and sarcopenia in individuals with diabetes despite previous research showing that these measures are important clinical impairment indicators reflecting common physical function deficits in these individuals.^{9,13} Based on initial evidence for accelerated sarcopenia, we hypothesize that these outcomes may hold diagnostic value in the identification of sarcopenia and its contribution to functional limitation in diabetes, which will assist the clinician in designing interventions to prevent future adverse outcomes (e.g., impaired mobility, falls, hospitalization, and mortality) associated with this condition.^{7,8,14}

Therefore the purpose of this study is to identify critical values of the amount of leg IMAT content, plantar flexion torque, and stair power that correctly classify obese individuals with and without type 2 diabetes and PN as sarcopenic or non-sarcopenic. This will provide clinicians with reference values of key components and constructs of sarcopenia, which can be used to derive a clearer understanding of the status of the musculoskeletal system in this population.

METHODS

Data were obtained from 43 age- and BMI- matched participants; 12 with type 2 diabetes mellitus only, 21 with type 2 diabetes + PN, and 10 obese controls without type 2 diabetes or PN. Participants were recruited from the Washington University School of Medicine Diabetes Clinic, Washington University's Volunteers for Health, the Center for Community Based Research, and from diabetes clinics in the surrounding St. Louis Community. Inclusion criteria included ambulatory individuals with a body mass index (BMI) greater than 27 kg/m²; with or without a diagnosis of type 2 diabetes and with or without evidence of PN as determined by diminished or absent plantar sensation to light touch or pressure. All participants were tested for the presence of peripheral neuropathy, as detailed below.

Individuals were excluded from the study if they weighed greater than 300 pounds (equipment weight limit), presented with any recent history of illness or hospitalization (within previous 6 months), any active infection or ulceration of either foot, previous botulinum toxin injection, ABI < .45, the presence of non-MRI compatible implants and women who may be pregnant, a history of severe foot deformity or amputation, and the presence of any co-morbidity or medications that would limit participation in physical activity testing (rheumatic disease, peripheral arterial disease, dialysis, current cancer treatment). Each participant read and signed an IRB-approved protocol that was approved by the Human Research Protection Office at Washington University in St. Louis, MO.

Participant Demographics

Age, height, weight, BMI, and duration of diabetes were collected through participant interview, weight balance and stadiometer at the beginning of the visit, prior to the administration of any physical testing.

Lower Extremity Sensation

Semmes Weinstein Monofilament and Biothesiometry testing were used to determine the presence of peripheral neuropathy. We defined PN as the inability to feel the 5.07 (10-gram) monofilament on at least 1 non-callused site on the plantar aspect of either foot or the inability to perceive vibration of < 25 volts on the biothesiometer (Biomedical Instrument, Newbury, OH) applied to the hallux.¹⁵

Body Composition

Each participant received whole-body dual energy x-ray absorptiometry (DXA) scans (Hologic Discovery GDR 1000/W, software version 12.6.2 OD; Waltham, Massachusetts) to assess regional and composite lean and fat mass in grams. Image analysis and subregion (thigh, leg, trunk, upper extremities) composition quantification was carried out following the guidelines provided by Hologic GDR software.

Sarcopenic Index

Sarcopenic indices were calculated as described previously.¹⁶ Appendicular lean mass (ALM) was calculated as the sum of upper and lower extremity lean mass (kg). The skeletal muscle index (SMI) was calculated as shown below. Values denoting the classification for sarcopenia were implemented as outlined by Janssen et al., where scores > 37% for men and > 28% for women indicated classification as sarcopenic.¹⁷

$$SMI = \frac{\text{Total body skeletal muscle mass (kg)}}{\text{Total body mass (kg)}}$$

$$\text{Total body skeletal muscle mass} = [(1.13 \times ALM) \times (.02 \times \text{Age in yrs.})] + (.61 \times \text{sex} \{0=f, 1=m\}) + .97$$

Leg Composition

Leg IMAT, subcutaneous adipose tissue, and muscle volumes (cm³) were quantified using T1-weighted magnetic resonance imaging (MRI) with the ankle in neutral and knee extended. MRI measurement was performed with a 3.0 Tesla superconducting magnet with pulse sequence TE = 12 ms, TR = 1,500 ms, matrix 256×256, collecting both fat-saturated and non-fat saturated images. 30, 7 mm thick transverse slices spanning from the tibial plateau and progressing distally were collected, and 9 slices were analyzed for fat and lean tissue volumes based on voxel brightness.¹⁸ Volumetric assessments were made as described by Tuttle et al., and Hilton et al. for the anterior, lateral, and deep compartments, as well as the gastrocnemius and soleus muscles.^{19,9} Percent IMAT tissue volume (%IMAT) was calculated from the MRI analysis as the ratio of IMAT volume to total fat volume (total = subcutaneous fat volume + IMAT volume). Tuttle et al. reported <1% measurement error in muscle volume quantification, and <2% error in fat volume quantification with these methods, regardless of the individual muscle or compartment analyzed.¹⁹

Stair Vertical Power

Stair vertical power was calculated as a measure of functional performance based on the time it took to climb a standard set of 10 steps. Participants were instructed to ascend the stairs as quickly and safely as possible without the use of the handrail. Data represent the average of 2 trials. Power (watts) was calculated using the equation from Tuttle et al.:¹³

$$\text{Power} = \frac{\text{mass} \times \left(-9.8 \frac{\text{m}}{\text{s}^2}\right) \times \text{Height } 10\text{Steps}}{\text{Time to climb Steps (sec)}}$$

Leg Muscle Strength Assessment

Leg muscle strength was assessed as plantar flexion peak torque measured at 60 deg/sec using a Biodex Isokinetic Dynamometer System 3 (Shirley, NY). The ankle was placed in maximal dorsiflexion (10 degrees or the maximal position achieved actively) and ended in maximal plantar flexion (typically 30-45 degrees). All participants were given 3 submaximal practice trials to familiarize them with the test movements. Plantar flexion was repeated 3 times, with the average of the 3 trials used in the final analysis.

Statistical Analysis

A chi square test for equality of proportions was used to determine the homogeneity of sex distribution in the 3 groups for disease status (diabetes only, diabetes and PN, and obese controls). One-way analyses of variance (ANOVAs) were performed to determine group differences for age, weight, BMI, and duration of diabetes. One-way ANOVAs were also used to determine group differences in leg %IMAT, plantar flexion peak torque, and stair power. Independent t-tests were used to assess group differences between those classified as sarcopenic and non-sarcopenic. An alpha level = .05 was used for significance. A Games-Howell post-hoc test was used in cases violating the assumption of homogeneity of variance.

To identify values of %IMAT, PF torque, and stair power that identify the presence or absence of sarcopenia, we constructed receiver operator (ROC) curves, which were used to

determine the critical value that maximized each explanator's sensitivity + specificity. Next, we condensed these explanators into a logistic regression model to determine if their linear combination provided a greater sensitivity + specificity than any single explanator alone. 2 separate regression models were created. The first combined leg %IMAT, PF torque, and stair power in the model, while the second only combined PF torque and stair power to provide an alternative for clinicians who cannot measure all 3 variables in their patients. Predicted probabilities from each model were used to create new ROCs. The predicted probability associated with the highest sensitivity + specificity was selected as the cutoff probability for each model. The positive predictive value, negative predictive value, likelihood ratios for positive and negative test results, accuracy, and the diagnostic odds ratio (DOR) were also calculated for the model with the highest sensitivity + specificity as described by Glas et al.²⁰ Briefly, we also ran these models using diabetes status (diabetes only, diabetes + PN, and controls) as an explanator. The addition did not add to the explanatory power of these models (see results). For simplicity, therefore, we are reporting, in detail, the analyses using %IMAT, PF peak torque, and stair power.

To simulate classification in an independent sample, a leave one out cross validation was performed. For each subject, the remaining participants were used to fit the logistic regression model using %IMAT, PF torque, and stair power as explanators, which was subsequently used to classify the left out subject as sarcopenic or non-sarcopenic. The cross-validation accuracy, sensitivity, and specificity were calculated using the cutoff probability of .5 (which makes no assumption about the sample being representative of the population) and the optimal cutoff probability from the ROC analysis outlined above.

Overall regression model fit was assessed using the Hosmer-Lemeshow Goodness of Fit Test and the potency of the model was determined using Nagelkerke's Pseudo R^2 . Area under the ROC curve was analyzed using the c-statistic and Akaike Information Criterion (AIC). Multi-collinearity was checked using the tolerance and variance inflation factor statistics. The leverage statistic was used to identify outliers in the data. Some participants were missing data for %IMAT, PF torque, and stair power at random: 4 were missing all 3, 2 were missing %IMAT, 2 were missing PF torque, and 1 was missing stair power. List-wise deletion was used to maximize all available data. All statistical analyses were performed in IBM SPSS Version 21 (Armonk, NY: IBM Corp) and the statistical computing software R.

RESULTS

Group Demographics

As shown in Table 1, there were no group differences in sex, BMI, weight, or duration (years) of diabetes. The type 2 diabetes groups were younger than individuals in the control group. Monofilament and vibration perception threshold (VPT) testing confirmed that participants in the diabetes + PN group had PN, while the other participants did not. There were no group differences on leg % IMAT, plantar flexion torque and stair power.

Sarcopenic Classification and Group Differences

As shown in Table 2, 32 participants were classified as sarcopenic (SP+), and 11 were not (SP-). 10 of 12 (83%) of the type 2 diabetes group, 16 of 21 (76%) participants in the diabetes + PN group, and 6 of 10 participants (60%) of the control group were classified as sarcopenic. The SP+ group displayed greater leg % IMAT than SP- and reduced stair power compared to SP-. There was no difference between SP+ and SP- in plantar flexion peak torque at 60 deg/sec.

Explanatory Values of Sarcopenia

The results from preliminary ROC analyses for each single explanator are shown in table 3. The values providing the greatest combined sensitivity and specificity were: 21% for leg IMAT, 68 Nm for plantarflexion torque, and 441 watts for stair power (table 3).

The logistic regression model created from the linear combination of all 3 explanators is also shown in table 3. The predicted probability providing the greatest sensitivity + specificity in this model was 0.76, which had an 80% sensitivity, and 89% specificity. This value was used as the cutoff probability. Importantly, the sensitivity + specificity produced by the combination of all 3 explanators was greater than the sum produced by any single explanator.

The logistic regression model created from the combination of PF torque, and stair power is shown in table 3. The predicted probability providing the greatest sensitivity + specificity was 0.67, which had an 80% sensitivity, and 73% specificity. The sensitivity + specificity of this model was higher than PF torque or stair power alone, but was less than % leg IMAT alone or the linear regression using all 3 explanators (table 3).

The linear regression model combining all 3 explanators produced a likelihood ratio of a positive test of 7.92 (indicating a predicted probability >0.76 is ~8 times more likely if the individual has sarcopenia), a likelihood ratio of a negative test of 0.23, a positive predictive value of 95% (the probability of an individual with a predicted probability >0.76 having sarcopenia), and a negative predictive value of 64% (the probability of an individual with a predicted probability <0.76 not having sarcopenia). The model accurately diagnosed 80% of participants, and had a diagnostic odds ratio of 34.2, indicating that the odds of a correct classification of sarcopenia are 34.2 times higher than the odds of an incorrect classification when using this explanatory model. The addition of diabetes status to the models changed the R^2 value by only .9%, and did not affect the model significance, optimal cutoff value from ROC analyses, or explanatory ability.

The cross validation analysis produced an accuracy of 82.4%, a sensitivity of 92%, and a specificity of 60% using the cutoff probability of .5. Using the cutoff probability of .76, the cross validation had an accuracy of 76.5%, a sensitivity of 75%, and a specificity of 80%. The AUC for the cross validation ROC analysis was .82 ($p<.05$).

DISCUSSION

This study is the first to report critical values of leg fat, plantar flexor muscle strength, and physical function as potential explanators of sarcopenia in individuals with diabetes. We demonstrated that all 3 explanators can be used to delineate the presence of sarcopenia, but the regression model using all 3 explanators produced the highest sensitivity (80%) + specificity (89%), suggesting that these measures are most effective when used together. The DOR (34.2) of this model, and the difference between sarcopenic and non-sarcopenic individuals on these measures, lends further support for their diagnostic utility.

When implementing the logistic regression equations clinically, there are many combinations of individual explanatory values that produce the cutoff probability (.76 for the model using all 3 explanators, or .67 for the model using PF torque and stair power). Our results indicate that having a predicted probability of sarcopenia above the cutoff means the individual likely has sarcopenia, which may guide the clinician's plan of care (i.e. to select interventions targeting sarcopenia).

The leave one out cross validation simulated the performance of the regression model combining all 3 explanators when applied to a new sample from the same population. At cutoff probabilities of .5 and .76, the cross validation correctly classified 82% and 76.5% of subjects respectively, and produced a sensitivity + specificity >150, which is very close to model's performance in the derivation dataset. This gives us confidence that the sample used in this study was representative of the target population, and suggests models created from this sample may perform well in externally derived datasets.

Obese individuals with type 2 diabetes are particularly susceptible to the acceleration of sarcopenia due to the coincident impairments in metabolism underlying these conditions. Sarcopenia and diabetes are both associated with mitochondrial dysfunction, low-grade systemic inflammation, insulin resistance, growth hormone and IGF-1 decrements, immobility, reduced physical activity, and sensorimotor neuron loss in the case of diabetes + PN.^{19,21,22,23,24} Baumgartner et al. reported that it took less time for obese, sarcopenic individuals to develop impairments in IADLs than individuals with sarcopenia or obesity alone.²⁵ Our results support this idea, with individuals with type 2 diabetes as young as 38 classified as sarcopenic on the SMI.

The incipient impairment of these explanators may be leg intermuscular adipose tissue deposition, which is thought to accumulate in response to a diabetes-related reduction in muscle oxidative capacity.⁷ Mitochondrial dysfunction from IMAT accumulation may lead to myocyte apoptosis, which could be exacerbated by impairments in skeletal muscle autophagy in type 2 diabetes.^{26,27} Diabetic denervation may further accelerate the rate of apoptosis and the loss of lean muscle volume, with IMAT accumulating in space previously occupied by healthy muscle fibers.¹⁴ IMAT accumulation is also inversely correlated with growth hormone secretion and insulin sensitivity and may impart lipotoxic effects and release pro-inflammatory cytokines that contribute to declining force production, muscle quality, and reduced mobility.^{26,28}

Our cutoff analysis suggests that when IMAT comprises 21% of an individual's total leg fat, they likely have sarcopenia. We speculate this value represents a threshold of muscle structural resilience, suggesting IMAT accumulation of equal or greater than 21% may disrupt muscle structure (fascicle arrangement, pennation angle, sarcomeres in-series) and elicit sarcopenic impairment.^{15,23} Bittel et al. showed that for every 1% increase in leg % IMAT, there is an accompanying 0.1-point reduction in the physical performance test (PPT) score (consisting of 9 functional tasks scored 0-36, with lower scores meaning worse performance).²⁹ King et al. found that a 2.4-point reduction in PPT score constituted a clinically meaningful change in physical function.³⁰ Therefore, accumulation of 24% IMAT corresponds to a 2.4-point reduction in PPT score, which coincides closely with our 21% IMAT threshold (i.e. 21% IMAT = 2.1 point reduction in PPT scores).

We acknowledge that the use of MRI to quantify leg IMAT is not (yet) a diagnostic tool that is readily available for most clinicians. However, based on the results of this study, and previous investigations,^{9,13,19} IMAT represents a significant structural impairment that appears in multiple musculoskeletal, neurologic, and pulmonary conditions and affects all levels of physical function.^{24, 31} Leg %IMAT, alone, produced a higher sensitivity + specificity than the linear combination of PF torque and stair power. Furthermore, the regression model combining all 3 explantors, including leg %IMAT, had the highest sensitivity + specificity -- confirming its importance in the identification of sarcopenia.

In addition to leg IMAT, we also determined explanatory values for physical function (stair power) to give clinicians a more readily useful means of assessing and determining progression to sarcopenia. The ability to climb stairs strongly correlates with other measures of functional disability and decline in medical status.³² Our stair power threshold value indicates that along the continuum of progressive metabolic and morphological impairments in diabetes, individuals who produce less than 441 watts of power while ascending a flight of stairs are very likely to have sarcopenia. While this is the first study to provide a threshold value for stair power in this population, similar research coincides with these findings.

Shimada et al. found that among elderly (average age of 80 years) community dwelling adults, leg extensor power of 484 watts differentiated men who reported difficulty with ascending stairs, from those who did not (<484 watts equated with self-reported difficulty).³³ This critical value may represent individuals more affected by sarcopenia, and has notable similarity to our own threshold value.

Ankle plantar flexor strength (a measure of muscle performance), in addition to its role in climbing stairs, is a central component in the successful completion of many functional activities, including ambulation and rising from a chair.^{32,34,35} We found that PF torque of 68 Nm helps differentiate sarcopenic from non-sarcopenic diabetes -- a population that expresses a litany of metabolic and physiological impairments of the leg.^{3,19} Specifically, this cutoff may indicate an increased risk of abnormal gait (including declines in gait speed and step length) or falls.^{36,37,38} Reduced torque from the gastrocnemius and soleus may diminish one's ability to slow the forward progression of the body about the ankle when recovering from a perturbation.³⁸ Indeed, Landi et al. reported that individuals who are sarcopenic are at 3.23 times higher risk for falls than individuals without sarcopenia

regardless of age, gender, BMI, or secondary impairments (e.g., diabetes, stroke).³⁹ We acknowledge that not all clinics will have access to isokinetic dynamometry. Like MRI, we encourage clinicians to work with the patient's physician and the care center to obtain these measurements prior to creating the treatment plan.

These results suggest that clinicians should assess for sarcopenia in individuals with diabetes and consider treatment plans that mitigate its progression. Resistance training may be a cornerstone of these plans, as it improves muscle quality and function, enhances motor recruitment, increases lean body mass, and is the most effective treatment for sarcopenia.⁴⁰ It has been reported that only 12% of North Americans with type 2 diabetes perform regular resistance-exercise.⁴¹ This disengagement potentially contributes to sarcopenia, and mandates further investigation into alternative means of resistance training.

There are limitations to this study. While the diagnostic linear regression model produced high diagnostic utility during cross validation, these models require external validation in a separate sample from the same target population. We did not obtain serum or tissue (muscle, adipose) samples to determine inflammatory status, protein composition, presence of proteolysis, hormone levels, insulin sensitivity, muscle structural status, or mitochondrial content and oxidative function in relation to our selected explanatory values. Thus, our deductions are merely empirical and warrant further investigation. A larger sample size would provide more definitive sarcopenic classification with these explanatory values.

Conclusion

Based on the results of this study, the explanatory values for IMAT, PF peak torque, and stair power can help physical therapists and rehabilitation specialists identify sarcopenia's contribution to muscle and physical dysfunction in diabetes. These measures reflect the pattern of impairment commonly associated with this condition, offering a customized alternative to traditional sarcopenic classification systems, which may not be optimally suited for this clinical population.

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Fig. 1.

Results from the individual and combined ROC analyses. a. Scatterplot of leg intermuscular adipose tissue volume (% IMAT; y-axis) and skeletal muscle index (% SMI; x-axis) for all participants. Triangles represent males. Circles represent females. Filled shapes denote participants who were sarcopenic. Open circles denote participants who were not sarcopenic. The dotted line shows the 21% IMAT cutoff determined through ROC analysis. b. Scatterplot of stair power (y-axis) and skeletal muscle index (%SMI; x-axis) for all participants. Symbols are the same as A. The dotted line shows the 441 watts of stair power cutoff determined through ROC analysis. c. Scatterplot of PF peak torque (y-axis) and skeletal muscle index (%SMI; x-axis) for all participants. The dotted line shows the 68 Nm cutoff determined through ROC analysis. d. ROC curves for each logistic regression model. The (- • -) line represents the ROC curve for the linear combination of %IMAT, PF peak torque, and stair power. The black dot on the curve denotes the cutoff probability of .76, and its sensitivity and 1-specificity. The (- - -) line represents the ROC curve for the linear combination of PF peak torque and stair power. The black dot on the curve denotes the cutoff probability of .67, and its sensitivity and 1-specificity. The (____) line represents chance. The area under the curve (AUC), and its significance, for each model is reported

($p < .05$ indicates classification by the model is significantly better than chance). *Note: 4 participants missing data for all 3 variables, 2 missing %IMAT, 2 missing PF torque, and 1 missing stair power.

Table 1

Demographic Characteristics of Participants

Variable	Controls	T2DM	T2DMPN	P-value	Post-hoc
Gender (Female, Male)	5,5	6,6	6,15	p=.36	
Body Mass Index	33.5 (4.7)	34 (6.1)	32.6 (5.3)	p=.69	
Weight (kg)	100 (20)	100 (16)	102 (21)	p=.99	
Years of Diabetes	NA	8 (7)	14 (11)	p=.115	
Age	67 (6)	55 (11)	64 (13)	p=.03 * [▽]	[#] (p=.01)
Percent Body Fat	40 (6)	36 (10)	34 (7)	p=.09	
Percent Lean Tissue	57 (6)	61 (9)	63 (6)	p=.08	
Biothesiometry Vibration Perception Threshold Left Hallux (volts)	24.4 (13)	18 (12.1)	40.5 (10.4)	p<.001 *	[^] (p<.001)
Semmes Weinstein Monofilament (Avg. Score)	L = 1 (0)	L = 2.1 (.6)	L = 3.3 (.7)	p<.001 * [▽]	[^] (p<.001), ⁺ (p<.001), [#] (p<.001)
Percent IMAT	20 ± 19	20 ± 7	32 ± 22	p=.18	
Stair Power	484 ± 196	395 ± 105	379 ± 131	p=.19	
Plantar Flexion Torque (Nm) At 60 deg/sec	L 44 ± 15 R 59 ± 20	L 35 ± 10 R 48 ± 14	L 40 ± 13 R 54 ± 18	Both L and R p=.33	

Not shown: biothesiometry and semmes weinstein monofilament testing was also performed on the right foot at the same locations identified in the table above. Monofilament testing was identical between feet and VPT differed by less than 3 volts for all locations examined. ANOVA and post-hoc results identical for both feet.

* (significant difference between groups)

[▽] (Games-Howell post-hoc)

[^] (difference between T2DM and T2DMPN)

⁺ (difference between T2DMPN and Controls)

[#] (difference between T2DM and controls).

Table 2

Average values of participants classified as sarcopenic and non-sarcopenic based on skeletal muscle index (SMI)

Variable	Sarcopenic (SP+)	Non-Sarcopenic (SP-)	P-value
N	32	11	
Gender (Male ,Female)	22, 10	4, 7	p=.058
IMAT (%)	30 (20)	13 (7)	p=.01 *
Stair Vertical Power (watts)	363 (104)	528 (178)	p=.001 *
Plantar flexion Peak Torque @ 60 deg/sec. (Nm)	52 (16)	60 (20)	p=.27

*
(p < .05) two-tailed, independent t-test. M=male, F=female.

Table 3

Individual Cutoff and Logistic Regression Model Parameters. The Cutoff Analysis portion of the table shows the results from the individual ROC analyses, including the value of each explanator that maximized its sensitivity and specificity. The sensitivity and specificity associated with the cutoff probabilities for each logistic regression model are also reported. The Logistic Regression Results (1 & 2) portions of the table contain the 2 logistic regression models, their coefficients, standard errors, explanator significance, overall model significance, and variance in the log odds of sarcopenia accounted for by each model (Nagelkerke's R^2). The regression equations, created from the regression coefficients, demonstrates how values for %IMAT, PF Torque, and Stair Power can be used to calculate a predicted probability (p) of having sarcopenia

Cutoff Analysis				
Explanator/Model	Cutoff Value	Sensitivity	Specificity	Sensitivity + Specificity
%IMAT ROC	21%	65%	90%	155
Plantar Flexion Torque ROC	68 Nm	85%	36%	121
Stair Power ROC	441 Watts	78%	73%	151
Logistic Regression 1 (all 3 explanators)	See Below	80%	89%	169
Logistic Regression 2 (Plantar Flexion Torque + Stair Power)	See Below	80%	73%	153

Logistic Regression Results (1)							
Explanator	β	Standard Error	Wald	Degrees of Freedom	Significance	$\exp\beta$	95% CI $\exp\beta$
%IMAT	.127	.074	2.963	1	.085	1.14	.982-1.313
Plantarflexion Torque	.014	.043	.187	1	.665	.99	.979-.999
Stair Power	-.011	.005	4.447	1	.035 *	1.02	.936-1.109
Constant	2.611	2.996	.760	1	.383	13.6	
Regression Equation: $\ln(p/1-p) = .127(\%IMAT) + .014(Nm \text{ Plantarflexion Torque}) - .011(Stair Power) + 2.611$ Model Significance: $X^2(3)=17.954$, $p<.001$ * Nagelkerke's $R^2 = .584$ Cutoff Probability = .76							

Logistic Regression Results (2)							
Explanator	β	Standard Error	Wald	Degrees of Freedom	Significance	$\exp\beta$	95% CI $\exp\beta$
Stair Power	-.011	.005	6.264	1	.012 *	.989	.980-.998
Plantarflexion Torque	-.0089	.035	.122	1	.727	.988	.923-1.058
Constant	6.237	2.632	6.979	1	.008	511.2	
Regression Equation: $\ln(p/1-p) = -.0089(Nm \text{ Plantarflexion Torque}) - .011(Stair Power) + 6.237$ Model Significance: $X^2(2)=12.264$, $p=.002$ * Nagelkerke's $R^2 = .408$ Cutoff Probability = .67							

* denotes significant at $p < .05$. $\exp\beta$ = odds ratio, CI = confidence interval. ROC = receiver operating characteristic curve

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