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ORIGINAL ARTICLE

High muscle-to-fat ratio predicts slow muscle strength decline in middle-aged and older adults: Longitudinal aging study of Taipei

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Abstract

Background: Handgrip strength is a vital marker of muscle function and predictor of health outcomes in older adults. This study investigated the relationship between the muscle-to-fat ratio and 3-year decrease in handgrip strength in community-dwelling adults aged ≥50 years.

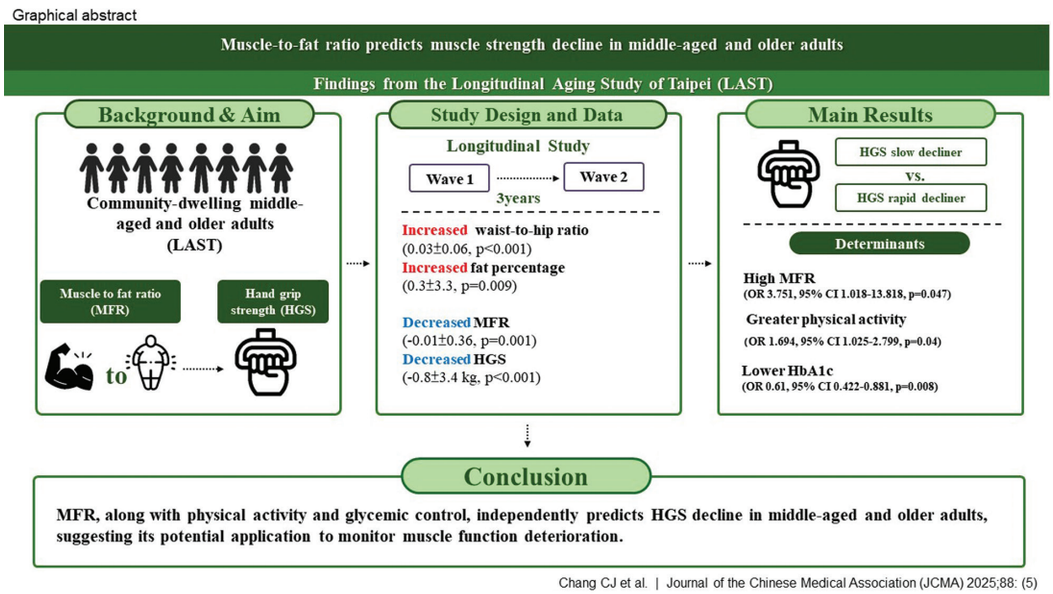
Methods: Data were obtained from the Longitudinal Aging Study of Taipei (LAST), a cohort study of adults aged 50 years and older. Measurements from two waves, 3 years apart, were analyzed. Demographics, laboratory data, and handgrip strength data were collected. Appendicular skeletal muscle mass was assessed using bioimpedance analysis, and the relative appendicular skeletal muscle mass index was calculated by dividing appendicular muscle mass by height squared. The muscle-to-fat ratio was derived by dividing appendicular muscle mass by total body fat. Handgrip strength decrease was divided into quartiles; slow decliners experienced the smallest decrease, whereas rapid decliners had the greatest decrease. Associations between the muscle-to-fat ratio and other risk factors were analyzed.

Results: Over 3 years, the Charlson Comorbidity Index, medication use, waist-to-hip ratio, and fat percentage increased, whereas skeletal muscle mass, the muscle-to-fat ratio, and handgrip strength decreased. Rapid decliners were less likely to be male (21.6% vs 33.3%, $p = 0.008$) or alcohol drinkers (53.8% vs 66.2%, $p = 0.01$) and had lower skeletal muscle mass (6.3 ± 0.9 vs 6.6 ± 1.0, $p = 0.006$) and muscle-to-fat ratios (1.0 ± 0.4 vs 1.1 ± 0.5, $p = 0.004$) but greater fat percentages (30.4 ± 6.6 vs 29.0 ± 7.6, $p = 0.045$). A greater muscle-to-fat ratio (odds ratio [OR] = 3.751, $p = 0.047$), greater physical activity (OR = 1.694, $p = 0.04$), and lower glycated hemoglobin (HbA1c; OR = 0.61, $p = 0.008$) reduced the risk of rapid decline.

Conclusion: The muscle-to-fat ratio, together with physical activity and glycemic control, predicts a decrease in handgrip strength, highlighting its potential as a biomarker of intrinsic capacity and muscle–fat interplay. Further research is needed to explore the underlying biological mechanisms involved.

Keywords: Glycemic level; Handgrip strength; Muscle-to-fat ratio; Physical activity; Sarcopenic obesity

Graphical abstract



1. INTRODUCTION

Aging is a complex process characterized by impaired homeostasis, reduced physiological reserves, increased multimorbidity, and a decrease in physical and cognitive function, which, intertwined with heightened social vulnerability, lead to adverse health outcomes later in life for older adults.[1] At the population level, these adverse health challenges significantly affect individuals, societies, and global communities and are worsened by increases in life expectancy and unhealthy life-years, especially in societies that are rapidly aging.[2] By 2050, approximately 22% of the global population will be 60 years or older, up from 12% in 2015, which poses numerous challenges as health and social infrastructures worldwide struggle to adapt, particularly because the majority of this older population will reside in low- and middle-income countries with comparatively underdeveloped services for older adults.[3]

In 2015, the World Health Organization (WHO) released the World Report on Aging and Health, which defined healthy aging as the process of preserving functional ability to ensure well-being later in life.[4] The WHO subsequently published the Integrated Care for Older People (ICOPE), which introduced the operational definition of intrinsic capacity.[5] This definition includes locomotion, cognition, psychological health, sensory function, and vitality as key assessments of healthy aging. Each element of intrinsic capacity employs distinct operational approaches, with vitality, viewed as homeostasis and reserve in aging, measurable through nutritional status, handgrip strength (HGS), or other aging biomarkers. HGS is a dependable indicator of maximum voluntary muscle strength[6] and is frequently used as a comprehensive muscle strength marker, and its close association with various health outcomes in older adults makes it an important health indicator. Low HGS is linked to adverse health outcomes, underlining its substantial influence on an individual's health trajectory; specifically, reduced HGS is associated with chronic diseases, functional impairments, and increased all-cause mortality, emphasizing the role of HGS in aging populations.[7] In addition, research has shown a robust link between HGS and cognitive function, mental health,[8] health care usage, and functional decline after acute illness.[9] Furthermore, HGS also has a complex relationship with body composition,[10] highlighting the impact of muscular integrity on HGS. The association between HGS and muscle mass is linear, but its relationship with total body fat is nonlinear, indicating intricate interactions.[11,12] Interestingly, adipose tissue might serve a protective function, mitigating negative outcomes such as disability and mortality in older adults, an effect termed the "adipose paradox."[13] An integrative approach encompassing multiple domains is essential for predicting adverse outcomes associated with body composition during the aging process.

The European Society for Clinical Nutrition and Metabolism (ESPEN) and the European Association for the Study of Obesity (EASO) recently released a consensus statement on the diagnosis of sarcopenic obesity, which aims to address the pathological implications of adipose tissue and muscle mass simultaneously, shedding light on the prognostic importance of sarcopenic obesity despite existing controversies in the field.[14] Prior research has established the muscle-to-fat ratio (MFR) as a predictive factor for adverse health outcomes, including mortality and fractures, making it a potential biomarker of sarcopenic obesity.[15] Nonetheless, the interplay between the vitality of intrinsic capacity, represented by HGS, and the biomarker of sarcopenic obesity, MFR, may play a pivotal role in functional ability and healthy aging. This study aims to clarify the complex relationships among HGS, MFR, and sarcopenic obesity over 3 years in the prediction of functional decline. Moreover, we intend to elucidate the various aspects of sarcopenic obesity by comparing muscle mass, adipose tissue, and MFR.

2. METHODS

2.1. Study design and participants

This study used first- and second-wave data, with 3-year intervals (the interval between wave 1 and wave 2 was 3 years), from the Longitudinal Aging Study of Taipei (LAST), which recruited community-dwelling people aged 50 years and older living in Taipei, Taiwan.[16] The entire study was approved by the Institutional Review Board of National Yang Ming University (YM104121F-5). Before enrollment, the research staff offered a comprehensive explanation of the study to all participants, who subsequently provided signed informed consent. The study was planned and conducted in accordance with the principles outlined in the Declaration of Helsinki. The reporting format followed the guidelines set forth by the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE).[17]

2.2. Demographic data and functional assessment

The study gathered data on many demographic factors, such as age, sex, educational attainment, marital status, living arrangements, smoking and alcohol consumption history, medical history, and the presence of multiple chronic conditions assessed using the Charlson Comorbidity Index (CCI).[18] All participants received comprehensive physical examinations, including blood pressure, body weight, height, waist circumference, and hip circumference measurements. Muscle strength was digitally assessed using the HGS of the dominant hand (Smedley's Dynamometer; TTM, Tokyo, Japan), whereas physical performance was evaluated using the 6-m gait speed and the 5-time chair-rise test. Furthermore, muscle endurance was assessed via the 6-minute walking distance test. Moreover, the average energy expenditure during physical activity was evaluated via the Taiwan version of the International Physical Activity Questionnaire (IPAQ).[19] Nutritional status was assessed using the Mini Nutritional Assessment.[20] Cognitive function was evaluated using the Montreal Cognitive Assessment.[21]

2.3. Body composition

Body composition, encompassing the proportion of overall body fat, lean body mass, and approximated appendicular muscle mass, was assessed via bioimpedance analysis (Inbody S10, Seoul, South Korea). Appendicular skeletal muscle mass was measured by aggregating the lean tissue masses of the upper and lower limbs. The relative appendicular skeletal muscle mass index (RASM) was subsequently determined by dividing the appendicular skeletal muscle mass by the square of the individual's body height, expressed in meters. In this study, the MFR was defined as the appendicular muscle mass divided by the total body fat mass.

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Table 1

Comparison of data between wave 1 and wave 2 at the 3-y follow-up

	Wave 1 (n = 831)	Wave 2 (n = 831)	Difference	*p*
Demographic characteristics				
Age	67.8 ± 6.2	70.0 ± 6.3	3.3 ± 0.5	<0.001*
Male (n, %)	253 (30.4)	253 (30.4)		
Education (y)	13.8 ± 3.4	13.8 ± 3.4		
Current smoker (n, %)	26 (3.1)	24 (2.9)	–0.2%	0.480
Current alcohol drinking (n, %)	491 (59.1)	495 (59.6)	0.50%	0.759
Number of currently used medications	1.6 ± 2.1	2.2 ± 2.6	0.6 ± 1.9	<0.001*
Charlson Comorbidity Index	0.8 ± 1.1	0.9 ± 1.3	0.1 ± 0.8	<0.001*
Anthropometric measurements and body composition				
Body mass index (kg/m^2)	23.4 ± 3.2	23.4 ± 3.1	0.02 ± 1.19	0.114
Waist-to-hip ratio	0.85 ± 0.07	0.89 ± 0.07	0.03 ± 0.06	<0.001*
Total body fat percentage (%)	29.7 ± 7.2	30.0 ± 7.2	0.3 ± 3.3	0.009*
RASM (kg/m^2)	6.52 ± 0.99	6.48 ± 1.20	–0.04 ± 0.74	<0.001*
MFR	1.05 ± 0.46	1.04 ± 0.57	–0.01 ± 0.36	0.001*
Functional assessment				
5-times chair-rise test (s)	9.1 ± 2.7	8.6 ± 3.0	–0.5 ± 2.5	<0.001*
6-m gait speed (m/s)	1.84 ± 0.50	1.77 ± 0.34	–0.07 ± 0.52	0.154
HGS (kg)	26.8 ± 7.8	26.0 ± 8.1	–0.8 ± 3.4	<0.001*
IPAQ (Kcal/week)	1928.1 ± 1565.3	2101.2 ± 1771.9	173.1 ± 1807.6	0.002*
Mini Nutritional Assessment	27.2 ± 2.1	27.4 ± 2.0	0.2 ± 1.7	<0.001*
Montreal Cognitive Assessment	27.02 ± 2.55	26.98 ± 2.85	–0.04 ± 2.10	0.605
Lab data				
Hemoglobin (g/dL)	14.0 ± 1.3	13.9 ± 1.4	–0.9 ± 1.1	0.396
Vitamin D (ng/mL)	23.4 ± 6.7	26.6 ± 9.0	3.3 ± 8.4	<0.001*
Total cholesterol (mg/dL)	202.7 ± 34.8	196.5 ± 37.1	–6.1 ± 35.0	<0.001*
Triglyceride (mg/dL)	110.2 ± 68.2	102.8 ± 51.9	–7.4 ± 60.9	0.001*
HDL-C (mg/dL)	60.2 ± 15.7	61.6 ± 16.6	1.4 ± 10.5	<0.001*
LDL-C (mg/dL)	118.4 ± 30.3	114.6 ± 31.6	–3.8 ± 30.4	0.055
Vitamin B12 (ng/dL)	702.7 ± 655.4	828.8 ± 636.2	126.0 ± 840.0	<0.001*
Fasting plasma glucose (mg/dL)	97.2 ± 20.3	94.7 ± 17.6	–2.5 ± 17.5	<0.001*
HbA1c (%)	5.80 ± 0.62	5.76 ± 0.61	–0.04 ± 0.55	0.165
eGFR (mL/min/1.73 m^2)	90.1 ± 17.4	88.9 ± 17.8	–1.148 ± 14.7	0.073
ALT (U/L)	24.5 ± 11.8	23.4 ± 10.3	–1.1 ± 12.6	0.003*
Homocysteine (mmol/L)	13.3 ± 5.3	13.3 ± 5.5	0.006 ± 3.608	0.767
hs-CRP (mg/dL)	0.15 ± 0.38	0.12 ± 0.35	–0.03 ± 0.43	<0.001*

ALT = alanine aminotransferase; eGFR = estimated glomerular filtration rate; HbA1c = glycated hemoglobin; HDL-C = high-density lipoprotein cholesterol; HGS = handgrip strength; hs-CRP = high-sensitivity C-reactive protein; IPAQ = International Physical Activity Questionnaire; LDL-C = low-density lipoprotein cholesterol; MFR = muscle-to-fat ratio; RASM = relative appendicular skeletal muscle.

*$p < 0.01$.

2.4. Laboratory data

In this study, we employed automated analysis (ADVIA Chemistry XPT, Siemens, Erlangen, Germany) to quantify the serum concentrations of albumin, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglycerides, glucose, and high-sensitivity C-reactive protein. The glycated hemoglobin (HbA1c) in whole blood was measured using high-performance liquid chromatography with a Bio-Rad D-100 system manufactured by Bio-Rad in the United States. The serum levels of 25-hydroxyvitamin D were quantified via a chemiluminescent immunoassay (LIAI-SON, DiaSorin, Saluggia VC, Italy).

2.5. Outcome measurements

The primary outcome (dependent variable) of this study was to distinguish between rapid HGS decrease and slow HGS decrease (reference group: rapid HGS decliner). The independent variables, including demographic characteristics, anthropometric measurements and body composition, functional assessments, and laboratory data, are listed in Tables 1 and 2.

According to similar studies, the degree of decrease in HGS is often divided into different levels to compare the two groups with the greatest and least decreases and improve sensitivity.[22] This study also divided the difference in percentile values between the HGS measured in the first wave and the second wave (wave2 – wave1/wave1) into quartiles. The group with the smallest decrease in HGS was defined as the slow HGS decliners, and the group with the most significant decrease was defined as the rapid HGS decliners.

2.6. Statistical analysis

In the current investigation, continuous variables are presented as the mean value accompanied by the SD, whereas categorical variables are presented as numerical values or proportions. Independent *t* tests were conducted to compare continuous data, whereas χ^2 analysis was used to examine categorical variables. Nevertheless, the IPAQ results were divided into tertiles due to considerable variation. Statistical analyses of data that did not follow a normal distribution were performed via nonparametric approaches. Multivariate logistic regression was used to explore

Table 2

Comparison of rapid and slow HGS decliners within 3 y

	Fast HGS decliner n=208	Slow HGS decliner n=207	*p*
Demographic characteristics			
Age	67.0 ± 6.6	66.8 ± 6.3	0.792
Male (n, %)	45 (21.6)	69 (33.3)	0.008**
Education (y)	13.5 ± 3.2	14.0 ± 3.6	0.161
Current smoker (n, %)	3 (1.4)	5 (2.4)	0.471
Current alcohol drinking (n, %)	112 (53.8)	137 (66.2)	0.01*
Number of currently used medications	1.7 ± 2.2	1.5 ± 2.2	0.283
Charlson Comorbidity Index	0.9 ± 1.2	0.7 ± 1.1	0.202
Anthropometric measurements and body composition			
Body mass index (kg/m^2)	23.2 ± 3.1	23.4 ± 3.3	0.552
Waist-to-hip ratio	0.84 ± 0.07	0.85 ± 0.08	0.186
Total body fat percentage (%)	30.4 ± 6.6	29.0 ± 7.6	0.045*
RASM (kg/m^2)	6.3 ± 0.9	6.6 ± 1.0	0.006**
MFR	1.0 ± 0.4	1.1 ± 0.5	0.004**
Functional assessment			
5-times chair-rise test (s)	9.2 ± 3.3	9.3 ± 2.8	0.932
6-m gait speed (m/s)	1.77 ± 0.50	1.83 ± 0.46	0.181
IPAQ (Kcal/week)			0.041*
Low tertile	84 (40.4)	65 (31.4)	
Medium tertile	72 (34.6)	68 (32.9)	
High tertile	52 (25.0)	74 (35.7)	
Mini Nutritional Assessment	27.0 ± 2.0	27.1 ± 2.0	0.828
Montreal Cognitive Assessment	26.8 ± 2.6	27.1 ± 2.4	0.159
Laboratory data			
Hemoglobin (g/dL)	13.9 ± 1.3	14.0 ± 1.4	0.446
Vitamin D (ng/mL)	22.9 ± 6.6	23.6 ± 6.9	0.27
Total cholesterol (mg/dL)	203.1 ± 37.1	203.7 ± 32.5	0.871
Triglyceride (mg/dL)	110.1 ± 77.3	105.1 ± 45.9	0.427
HDL-C (mg/dL)	61.3 ± 15.8	60.4 ± 16.1	0.577
LDL-C (mg/dL)	118.6 ± 30.9	119.3 ± 29.7	0.807
Vitamin B12 (ng/dL)	709.7 ± 388.5	674.6 ± 438.6	0.389
Fasting plasma glucose (mg/dL)	99.9 ± 27.9	95.2 ± 16.1	0.036*
HbA1c (%)	5.9 ± 0.8	5.7 ± 0.5	0.006**
eGFR (mL/min/1.73 m^2)	90.2 ± 18.4	90.3 ± 18.0	0.773
ALT (U/L)	25.1 ± 12.5	23.4 ± 8.9	0.122
Homocysteine (mmol/L)	12.8 ± 5.9	13.6 ± 6.9	0.353
hs-CRP (mg/dL)	0.136 ± 0.260	0.138 ± 0.305	0.959

ALT = alanine aminotransferase; eGFR = estimated glomerular filtration rate; HbA1c = glycated hemoglobin; HDL-C = high-density lipoprotein cholesterol; HSG = handgrip strength; hs-CRP = high-sensitivity C-reactive protein; IPAQ = International Physical Activity Questionnaire; LDL-C = low-density lipoprotein cholesterol; MFR = muscle-to-fat ratio; RASM = relative appendicular skeletal muscle.
*$p < 0.05$, **$p < 0.01$.

the independent associations of the MFR with other variables, including demographic characteristics, functional assessment, and laboratory data, among slow HGS decliners and rapid HGS decliners in a stepwise selection of confounders model. Potential confounders reached significance in univariate analyses before selection for multivariate analyses. A two-sided *p* value of <0.1 was considered indicative of significance. The statistical analyses were conducted using SPSS 26.0 software (SPSS Inc., Chicago, IL).

3. RESULTS

Among the 911 community-dwelling adults aged 50 years and older included in this study, 80 with incomplete data were excluded, and 831 participants (mean age: 67.8 ± 6.2 years) remained in the analysis (Fig. 1); males accounted for 30.4% of the sample. Table 1 shows the differences in demographic characteristics, anthropometric measurements, body composition, functional status, and laboratory data between wave 1 and wave 2 among all participants. Within the 3-year interval, the CCI (0.1 ± 0.8, $p < 0.001$) and number of medications used (0.6 ± 1.9, $p < 0.001$) significantly increased over time. Although both the waist-to-hip ratio (0.03 ± 0.06, $p < 0.001$) and the total body fat percentage (0.3 ± 3.3, $p = 0.009$) significantly increased, the in RASM (–0.04 ± 0.74 kg/m^2, $p < 0.001$), MFR (–0.01 ± 0.36, $p = 0.001$), and HGS (–0.8 ± 3.4 kg, $p < 0.001$) notably decreased.

Table 2 shows the comparison of variables associated with rapid and slow decreases in HGS over 3 years. A total of 831 people were used for analysis (Table 1), but to increase sensitivity,[22] we used the quartile with the largest decrease in HGS (rapid decliner, n = 208, HGS change –4.9 ± 2.3 kg) and the quartile with the smallest decrease (slow decliner, n = 207, where grip strength actually increased, HGS change +3.3 ± 2.0 kg) for analysis (Table 2). Compared with slow HGS decliners, rapid HGS decliners were less likely to be male (21.6% vs 33.3%, $p = 0.008$) or currently consume alcohol (53.8% vs 66.2%, $p = 0.01$). In addition, a lower RASM (6.3 ± 0.9 vs 6.6 ± 1.0, $p = 0.006$) and MFR (1.0 ± 0.4 vs 1.1 ± 0.5, $p = 0.004$) and a greater

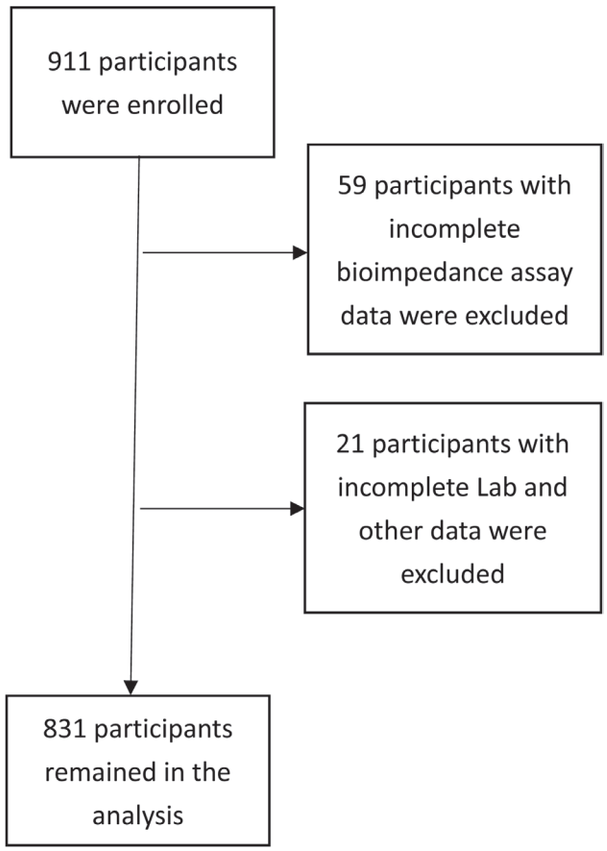

Fig. 1 The flowchart of the study process.

total body fat percentage (30.4 ± 6.6 vs 29.0 ± 7.6, p = 0.045) were also noted in rapid HGS decliners. Age (67.0 ± 6.6 vs 66.8 ± 6.6 years, p = 0.792), education years (13.5 ± 3.2 vs 14.0 ± 3.6, p = 0.161), CCI (0.9 ± 1.2 vs 0.7 ± 1.1, p = 0.202), number of medications used (1.7 ± 2.2 vs 1.5 ± 2.2, p = 0.283), 6-m gait speed (1.77 ± 0.50 vs 1.83 ± 0.46, p = 0.181), five-times chair-rise time (9.2 ± 3.3 vs 9.3 ± 2.8, p = 0.932), Mini Nutritional Assessment (27.0 ± 2.0 vs 27.1 ± 2.0, p = 0.828) or Montreal Cognitive Assessment (26.8 ± 2.6 vs 27.1 ± 2.4, p = 0.159) did not significantly differ between the two groups. According to the laboratory data, fasting plasma glucose (99.9 ± 27.9 vs 95.2 ± 16.1, p = 0.036) and HbA1c (5.9 ± 0.8 vs 5.7 ± 0.5, p = 0.006) levels were significantly greater among participants whose HGS rapidly decreased.

Table 3 shows the independent factors that protect against decreases in HGS at the 3-year follow-up. The number of participants used in the logistic regression model shown in Table 3 was 415 (rapid decliner 208 + slow decliner 207 = 415). After adjusting for potential confounders, including age, sex (male), and those that reached borderline statistical significance (two-sided p value <0.1 shown in Table 2), including current alcohol consumption (p = 0.01), total body fat percentage (p = 0.045), RASM (p = 0.006), MFR (p = 0.004), IPAQ (p = 0.041), fasting plasma glucose (p = 0.036), and HbA1c (p = 0.006), the final model fit through stepwise confounder selection multivariate logistic regression analysis revealed that the MFR was a significant protective factor against decreases in HGS at the 3-year follow-up (OR = 3.751, p = 0.047). In addition, both a lower HbA1c level (OR = 0.61, p = 0.008) and a greater tertile IPAQ score (OR = 1.694, p = 0.04) protected against a decrease in HGS within the 3-year follow-up (Table 3).

4. DISCUSSION

In this study of 831 adults aged 50 years and older, the CCI score, number of medications used, waist-to-hip ratio, and total body fat percentage increased over a 3-year period. In contrast, the RASM, MFR, and HGS decreased as the participants aged. Compared with slow HGS decliners, rapid HGS decliners were less likely to be male or currently consume alcohol. In the 3-year follow-up study, the MFR demonstrated a significant role as a protective factor against a decrease in HGS. Concurrently, lower levels of HbA1c and increased physical activity were also observed to exhibit protective effects against the deterioration of HGS within the same period. This study unequivocally demonstrated that a decrease in HGS, an operational proxy for the vitality of intrinsic capacity in healthy aging, is significantly correlated with sex, metabolic health, and physical activity levels after adjustment for nutritional status.

Aging is associated with body composition changes, notably increased fat mass, and decreased lean mass and bone mineral density, independent of weight and body mass index fluctuations.[23] A prior systematic review highlighted the beneficial impact of increased physical reserves and improved survival rates in overweight or obese older adults with chronic diseases.[13] Sarcopenic obesity, the simultaneous occurrence of sarcopenia and obesity in an individual,[24,25] is a significant research focus because of its association with frailty, impairment in daily activities, and a range of health conditions, including metabolic syndrome, cardiovascular disease, fractures, dementia, cancer,

Table 3

Independent factors to protect against decreases in HGS at the 3-y follow-up (n = rapid decrease 208 + slow decrease 207 = 415)

	OR	95% CI	*p*
Age	1.0	0.967-1.034	0.991
Male sex (female as the reference group)	1.24	0.533-2.881	0.618
MFR	3.751	1.018-13.818	0.047*
RASM	1.125	0.799-1.583	0.5
HbA1c	0.61	0.422-0.881	0.008**
Total body fat percentage	1.074	0.990-1.164	0.084
IPAQ			
Medium vs low tertile	1.246	0.773-2.008	0.367
High vs low tertile	1.694	1.025-2.799	0.04*

HbA1c = glycated hemoglobin; HGS = handgrip strength; IPAQ = International Physical Activity Questionnaire; MFR = muscle-to-fat ratio; RASM = relative appendicular skeletal muscle.
* $p < 0.05$, ** $p < 0.01$.

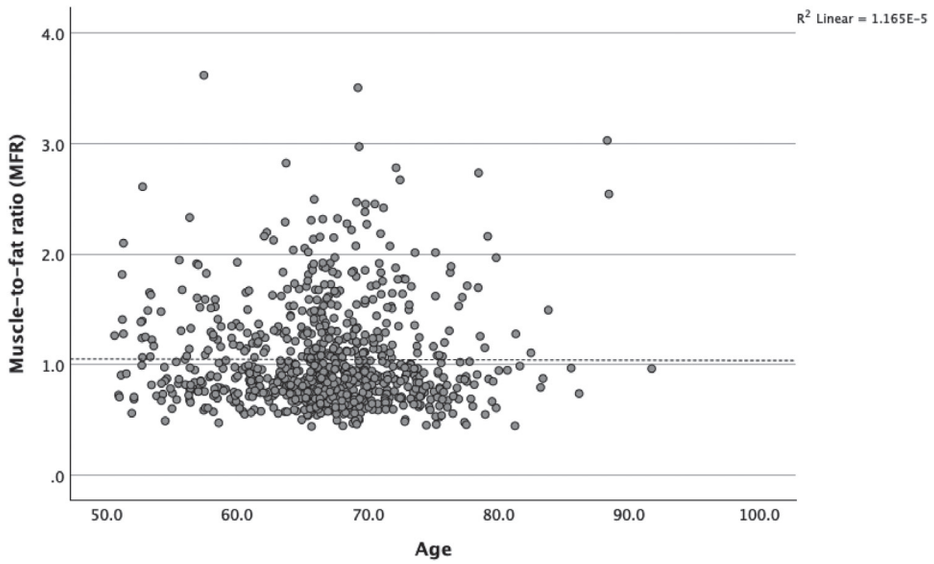

Fig. 2 Scatter plot of the muscle-to-fat ratio as a function of age (R^2 = 1.165 × 10^{-5}, p = 0.922).

and increased overall mortality rates.[26–28] Notwithstanding the proposal of sarcopenic obesity diagnosis by the ESPEN/EASO, debates surrounding the diagnostic criteria for obesity, sarcopenia, and sarcopenic obesity are ongoing, particularly in the older population. In the context of sarcopenia, various research methodologies have been employed. Some studies have used the ratio of appendicular lean mass to weight,[29] others have used the ratio of ALM to the square of height,[29] and yet others have considered muscle strength metrics, such as HGS, to define sarcopenia.[30] The challenge is similar to that of obesity; studies have employed different measures for obesity definition: some have used waist circumference,[31] others have used the waist-to-hip ratio,[32] and yet others have used body mass index,[32,33] which varies significantly across countries.[31–34]

Compared with the abovementioned methods, the MFR provides a more pertinent measure of the muscle–fat interplay and its influence on the prognosis of sarcopenic obesity, offering a broader perspective than the conventional definition that emphasizes the concurrent presence of sarcopenia and obesity. Recent research has indicated that the MFR significantly impacts the progression and prognosis of chronic diseases, with a notable outcome from the Korean Genome and Epidemiology Study suggesting that a lower fat-to-muscle mass ratio could mitigate the occurrence of chronic kidney disease in middle-aged and older individuals.[35] Another noteworthy study revealed that a low MFR is intimately linked with the incidence of metabolic syndrome and insulin resistance.[36] The current study reveals that the MFR, rather than the RASM, has a stronger correlation with decreases in HGS, suggesting its efficacy in capturing reductions in vitality in older adults. In contrast to RASM or HGS, which typically decrease with age, the MFR is age independent (as shown in Fig. 2) and maintains a significant correlation with changes in HGS over time.

An additional noteworthy observation from this study is that participants with the most pronounced HGS decreases presented significantly elevated levels of fasting glucose and HbA1c. Specifically, the fasting glucose and HbA1c levels among individuals with rapid decreases in HGS were significantly greater than those in the group exhibiting slow decreases in HGS. Recent studies have suggested a link between elevated blood sugar levels and decreased muscle strength in older individuals, pointing to a broader connection between metabolic health and muscle health.[37] In nondiabetic older individuals, an increase in blood glucose levels is associated with a decrease in muscle strength and function.[38,39] Furthermore, HGS, a reliable measure of muscle strength, has been demonstrated to decrease as blood glucose levels increase.[40,41] The associations between blood glucose and muscle strength can be attributed to multiple mechanisms, such as the formation of advanced glycation end products due to high blood glucose levels, which accumulate in muscle tissue and impair its function and strength.[42] In addition, persistent hyperglycemia may induce oxidative stress and inflammation, both of which can detrimentally affect muscle health by causing muscle cell damage, muscle wasting, and decreased strength.[43] Furthermore, insulin resistance, which frequently co-occurs with elevated blood glucose levels, can compromise muscle health, resulting in a reduction in strength.[44] To counteract the effects of high blood glucose on muscle strength, adopting strategies such as regular physical activity, particularly resistance training, can be beneficial for improving muscle strength and insulin sensitivity, thus playing a vital role in preserving HGS in older adults.[45] Our findings corroborate that higher levels of physical activity minimize decreases in HGS, emphasizing the importance of promoting exercise as a proactive strategy for preserving muscle strength and healthy aging. HGS decreases, a proxy for the vitality of intrinsic capacity, is influenced by the MFR, physical activity, and glycemic levels, suggesting a potential association between metabolic health and muscle health in healthy aging and indicating that the MFR could serve as a suitable biomarker of intrinsic capacity. Although the WHO proposes that aging biomarkers, particularly inflammatory biomarkers, can serve as indicators of vitality, the findings from our current study suggest that the MFR could also be a suitable candidate.

To the best of our knowledge, this study is the first to use the MFR to explore the association between decreases in vitality and the aging process. Many studies have shown that throughout the aging trajectory, muscle mass and fat mass are closely related to muscle strength. Concurrently, the decrease in muscle mass and increase in adiposity are associated with a deterioration in muscle strength. Despite these research efforts, this study has several limitations. First, the participants in this study exhibited a favorable state of physical well-being, which may

underestimate the effects of the MFR on decreases in HGS. Second, this study is limited by its 3-year follow-up data, which preclude the investigation of associations over a more extended period. Finally, the biological mechanisms underlying our findings remain elusive, but a multifaceted etiology encompassing inflammation, metabolism, and muscle aging is highly likely and warrants further investigation.

In conclusion, the MFR, in conjunction with physical activity and glycemic levels, serves as a significant predictor of deterioration in muscle health and the vitality domain of intrinsic capacity among healthy community-dwelling older adults. This relationship, which is independent of age, suggests that the MFR could be a useful biomarker of intrinsic capacity and muscle–fat interactions, which warrants further research into the underlying biological mechanisms.

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