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Original Research

Inflammation factors mediate association of muscle mass and erectile dysfunction: NHANES 2001–2004

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Abstract

Background: Erectile dysfunction (ED) constitutes a global male health issue. Current evidence indicates that low muscle mass may exacerbate insulin resistance and vascular endothelial damage via inflammatory cascades, both of which are established determinants of ED. The relationship between muscle distribution and its effect on ED remains unclear.
Aim: This study aimed to examine the association between muscle mass and ED prevalence and evaluate potential mediation by inflammatory biomarkers.
Methods: The study analyzed data from 2217 participants in the National Health and Nutrition Examination Survey (NHANES). Appendicular lean mass (ALM) is the total lean mass of the limbs. The Appendicular Skeletal Mass Index (ASMI) is calculated as ALM divided by height in meters squared. The association between ASMI and ED prevalence was evaluated through weighted logistic regression and subgroup analyses. Mediation analyses were conducted to examine the potential mediating roles of inflammatory markers in the relationship between ASMI and ED prevalence.
Outcomes: Compared with the non-ED group, patients with ED exhibited significantly lower ASMI; Monocytes mediated the association between ASMI, vigorous activity, and ED.
Results: Patients diagnosed with ED exhibited significantly lower ALM compared to those in the non-ED group (25.27 ± 4.87 kg vs 27.35 ± 4.52 kg, $P < .001$). Participants in the highest ASMI tertile (Q3) had a 39.6% lower ED risk compared with those in Q1 (OR = 0.606, 95% CI, 0.396-0.925, $P = .033$). Restricted cubic spline analysis showed that there was a nonlinear relationship between ASMI and ED in the fully adjusted model 3 ($P = .047$). Except for drinking status, no statistically significant interactions were observed in any subgroup ($P > .05$). Vigorous activity showed a significant negative correlation with ED prevalence (OR = 0.604, 95% CI, 0.418-0.873, $P = .013$). Monocytes mediated 1.76% and 2.01% of the association between ASMI, vigorous activity, and ED, respectively.
Clinical Implications: Early screening for sarcopenia and ED, followed by resistance training and anti-inflammatory interventions, may provide a comprehensive approach to protecting muscle mass and erectile health.
Strengths and Limitations: Studies utilizing nationally representative databases to investigate the association between muscle mass and ED remain insufficiently explored, a gap that this research aims to fill. The diagnosis of ED relied on participant self-report via questionnaire, which may lead to underreporting or misclassification bias due to psychological factors.
Conclusion: Current research suggests that increased muscle mass is associated with a reduced risk of ED, and that systemic inflammation mediates this relationship to some extent.

Keywords: appendicular muscle mass; sarcopenia; erectile dysfunction; inflammation; National Health and Nutrition Examination Survey.

Introduction

Erectile dysfunction (ED) constitutes a global male health issue, defined as the persistent inability to attain or maintain penile erection sufficient for satisfactory sexual intercourse.[1] Epidemiological studies indicate that approximately 50% of men aged 40-70 years suffer from ED, with its prevalence increasing with age.[2] ED not only severely compromises the quality of life for affected individuals and their partners but is also closely associated with depression, anxiety, and sexual dysfunction in partners, constituting a substantial burden on family stability and public health.[3,4]

Erection is a complex physiological process, and the pathogenesis of ED results from the interaction of multiple systems, including vascular, neural, endothelial, and smooth muscle components.[5] Established independent risk factors for ED encompass aging, obesity, diabetes mellitus (DM), cardiovascular disease, and metabolic syndrome.[6,7] Concurrently, chronic inflammation is recognized as a

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core pathophysiological process, characterized by elevated levels of inflammatory mediators such as C-reactive protein (CRP) and interleukin (IL)-6. These mediators directly impair coordinated vasodilation in penile vessels by inducing endothelial dysfunction, oxidative stress, and neuropathic injury.[8–12] Evidence suggests that systemic inflammatory markers are significantly correlated with the severity of ED,[6] underscoring that inflammation is an independent predictor of ED.

Sarcopenia, characterized by an age-related progressive decline in skeletal muscle mass, strength, and function, has been identified as a significant disease among the elderly.[13] In recent years, increasing attention has been paid to the potential association between sarcopenia, a novel metabolic risk factor, and ED.[14] Current evidence indicates that low muscle mass may exacerbate insulin resistance and vascular endothelial damage via inflammatory cascades, both of which are established determinants of ED.[15] However, the potential mediating role of inflammatory factors in the pathway linking sarcopenia and ED has not yet been empirically validated at the population level.

This study aims to elucidate 2 questions: (1) Is there really a correlation between adult muscle mass (measured as appendicular skeletal muscle index, ASMI) and ED risk? (2) To what extent do inflammatory factors play a role in this association? The findings of this study will provide novel targets for the early prevention of ED, particularly by reducing ED risk through enhancing muscle strength and inhibiting inflammatory pathways. They also offer a theoretical basis for interventions such as anti-inflammatory therapies and resistance training.

Materials and methods

Study population

The National Health and Nutrition Examination Survey (NHANES) is a nationally representative cross-sectional health survey program. The NHANES is a comprehensive health survey that systematically collects information on the health and nutritional status of US adults and children. It combines standardized health interviews, comprehensive physical examinations, and various laboratory tests (including blood analysis and imaging data such as dual X-ray absorptiometry [DXA]). This survey is characterized by its comprehensive coverage of demographic characteristics, physiological indicators, nutritional status, laboratory test results, and health status indicators. The data is collected by professionally trained healthcare personnel and released biennially by the National Center for Health Statistics (NCHS) as a publicly available dataset. All original survey procedures have undergone rigorous review and approval by the NCHS Research Ethics Review Committee, and written informed consent has been obtained from all participants. The NHANES dataset aims to determine disease prevalence, identify risk factors, and establish national health standards. Comprehensive information regarding survey methodology, data content, and ethical review procedures is available on the NCHS official website (http://www.cdc.gov/nchs/nhanes).

This study included 21 161 participants from the NHANES database between 2001 and 2004. We excluded participants with missing ED data ($n = 17\,045$) and missing DXA and covariate data ($n = 1899$). After screening, the final study cohort comprised 2217 subjects (Figure 1), including 752 with ED and 1,455 without ED.

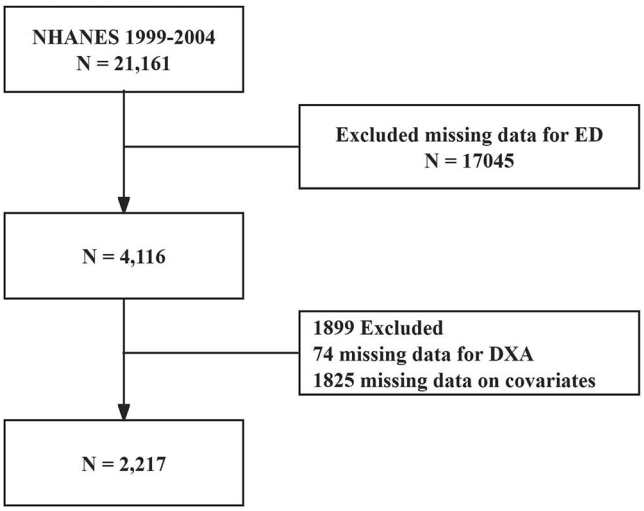


Figure 1 Flow chart of population selection from National Health and Nutrition Examination Survey.

Assessment of ED

The dependent variable in this study was ED. Interviews were conducted in private rooms at MEC using the audio computer-assisted self-interview (ACASI) method. To assess erectile function, researchers asked participants whether they could achieve and maintain an erection sufficient for satisfactory sexual intercourse. The responses to the inquiry were categorized as "always or almost always," "usually," "sometimes," and "never." For this study, "sometimes or never" was defined as having ED, while "always or almost always" and "usually" were defined as not having ED.

Dual-energy X-ray absorptiometry measurement and sarcopenia definitions

Participants underwent whole-body DXA scans using a Hologic QDR 4500A densitometer (Hologic Inc., United States) during NHANES 2001-2004, a validated method for body composition measurement. Participants who weighed over 300 pounds (136 kg) or who were taller than 6 feet 5 inches (198 centimeters) were excluded from the examination.

In DXA measurements, appendicular lean mass (ALM) is defined as the sum of the lean mass of the limbs, excluding bone mineral content. The Appendicular Skeletal Mass Index (ASMI) was defined as the ALM divided by the square of the height (m).[16] According to the European Working Group on Sarcopenia in Older People 2 (EWGSOP2), the threshold for sarcopenia is gender-specific: ASMI values of less than 7 for men and less than 5.4 for women have been documented.[13]

Study covariables

The following variables were incorporated into the study[1]: demographic information, including age, race, education level, smoking status, drinking status, body mass index (BMI), and height[2]; laboratory data, including CRP, white blood cell count (WBC), neutrophil count (NC), and monocyte count (MC)[3]; questionnaire information, including history of comorbidities such as hyperlipidemia and diabetes; and[4] physical activity data. The race was categorized into the

following groups: Mexican Americans, non-Hispanic whites, non-Hispanic blacks, and other ethnic groups. Education level was categorized into three groups: high school diploma, less than high school, and more than high school. Participants who reported having smoked at least 100 cigarettes in their lifetime and were still smoking during the survey period were classified as current smokers. Those who had smoked at least 100 cigarettes in their lifetime but were not smoking during the survey period were defined as former smokers. Non-smokers were defined as those who had never smoked at least 100 cigarettes in their lifetime. Participants who had never consumed at least 12 alcoholic drinks in any one year were classified as non-drinkers; former drinkers were defined as those who had consumed at least 12 alcoholic drinks in any one year but had not consumed alcohol in the past 12 months; and participants who had consumed alcohol in the past 12 months were classified as current drinkers. The inquiry posed to participants, "Has a doctor or other health professional ever informed you/SP that you/SP have a disease?" serves as the basis for the subsequent determination of comorbidities. This determination is made by evaluating the participant's response to the aforementioned inquiry, with "yes" indicating the presence of comorbidities and "no" indicating the absence. The aforementioned comorbidities encompass hyperlipidemia, DM, arthritis, congestive heart failure (CHF), coronary heart disease (CHD), and stroke. The "Physical Activity" section of the NHANES questionnaire is divided into: The term "moderate activity" is defined as the engagement in physical activity for a minimum of 10 minutes within the past 30 days, resulting in mild sweating or mild to moderate increases in breathing or heart rate. Conversely, "vigorous activity" is defined as the engagement in physical activity for more than 10 minutes within the past 30 days, resulting in heavy sweating or a significant increase in breathing or heart rate. Daily physical activity is also categorized into four distinct categories: sitting, standing or walking, light loads, and heavy loads.

Statistical analysis

The data were analyzed using NHANES sampling weights to reflect the complex survey design. Participants were stratified according to whether they had experienced ED. Proportions were used to present categorical data, while means and SDs were used to present continuous variables. Categorical variables were analyzed using chi-square tests, while continuous variables were evaluated using one-way analysis of variance (ANOVA). To ensure the representativeness of the data, all analyses were performed using NHANES data weighting methods. Multivariate logistic regression analysis was performed using three weighting models to examine the relationship between ED and ASMI or activity level. Model 1 was crude; model 2 included age, race, and education; and model 3 included age, race, education, CRP, WBC, MC, drink/smoke status, hyperlipidemia, DM, arthritis, CHF, CHD, and stroke. The results are presented as odds ratios (ORs) and 95% CI, with the lowest tertile designated as the reference value. Subsequent to adjusting for all confounding variables, the restricted cubic spline (RCS) function was employed to describe the existence of a nonlinear relationship between ED and ASMI. In order to assess the stability of the study results, we conducted supplementary interaction and subgroup analyses. These analyses were used to examine the relationship between ED and ASMI in different population characteristics and medical conditions. We also evaluated the robustness of these associations in each subgroup through interaction tests. Through mediation analysis, we investigated the potential mediating role of inflammatory markers (including CRP and monocytes) in the relationship among ASMI, activity level, and ED prevalence. The statistical analysis was executed using DecisionLinc 1.0 software(Statsape Co. Ltd, Hangzhou, China). The statistical significance of the findings was determined by the threshold of $P < .05$.

Results

Baseline characteristics

The present analysis encompasses a total of 2217 participants. The sample included 752 subjects in the ED group and 1455 subjects in the non-ED group. Table 1 presents a stratified analysis of baseline characteristics according to ED status. Patients diagnosed with ED exhibited significantly lower ALM compared to those in the non-ED group (25.27 ± 4.87 kg vs 27.35 ± 4.52 kg, $P < .001$). Meanwhile, ASMI was found to be considerably lower in the ED group (8.24 ± 1.34 kg/m^2 vs 8.69 ± 1.23 kg/m^2, $P < .001$).

Association between ASMI and ED

Table 2 shows a consistent negative correlation between ASMI and ED risk in the multivariate logistic regression model. In the fully adjusted model (model 3), each unit increase in ASMI was associated with a 17.3% reduction in ED risk (OR = 0.847, 95% CI, 0.750-0.957, $P = .019$). Participants in the highest ASMI tertile (Q3) had a 39.6% lower ED risk compared with those in the lowest ASMI tertile (Q1) (OR = 0.606, 95% CI, 0.396-0.925, $P = .033$).

Restricted cubic spline analysis (Figure 2) showed that there was a nonlinear relationship between ASMI and ED in the fully adjusted model 3 ($P = .047$). Consistent patterns were observed in model 1 (Figure S1) and model 2 (Figure S2).

Subgroup analysis

The subgroup analysis (Figure 3) was stratified by factors such as race, education level, age, smoking status, drinking status, physical activity, and presence of comorbidities. Except for drinking status (interaction $P = .046$), no statistically significant interactions were observed in any subgroup ($P > .05$). Among populations without cardiovascular disease, diabetes, or hyperlipidemia, and among the non-elderly, there was an inverse association between higher ASMI and lower ED risk.

Association between physical activity and ED

Table 3 shows the association between physical activity and ED incidence. In the fully adjusted model 3, vigorous physical activity showed a significant negative correlation with ED prevalence (OR = 0.604, 95% CI, 0.418-0.873, $P = .013$). In contrast, moderate physical activity was not significantly associated with ED (OR = 0.831, 95% CI, 0.634-1.089, $P = .155$). Analysis of daily activities showed that standing/walking and sedentary behavior were associated with a higher risk of ED compared with the heavy load group. However, there was no significant difference in the fully adjusted model (standing/walking group: OR = 1.551, 95% CI, 0.768-3.130, $P = .183$; sedentary group: OR = 1.905,

Table 1 Demographics and characteristics of study participants from National Health and Nutrition Examination Survey 2001-2004.

Characteristics	Overall *n* = 2217	Non-ED *n* = 1455	ED *n* = 762	*p*-value
Age	49.80 ± 14.81	45.81 ± 12.72	62.57 ± 13.79	<0.001
Race, *n* (%)				0.020
Mexican American	375.00 (5.07%)	244.00 (5.35%)	131.00 (4.17%)	
Non-Hispanic black	357.00 (7.65%)	254.00 (7.80%)	103.00 (7.17%)	
Non-Hispanic white	1,367.00 (80.44%)	871.00 (79.78%)	496.00 (82.55%)	
Other	118.00 (6.84%)	86.00 (7.06%)	32.00 (6.11%)	
Education, *n* (%)				<0.001
High school diploma	508.00 (24.72%)	348.00 (25.22%)	160.00 (23.13%)	
Less than high school	521.00 (13.16%)	252.00 (9.18%)	269.00 (25.94%)	
More than high school	1,188.00 (62.11%)	855.00 (65.60%)	333.00 (50.93%)	
BMI, kg/m^2	28.50 ± 5.10	28.36 ± 4.94	28.96 ± 5.58	0.100
Height, cm	176.67 ± 7.35	177.23 ± 7.29	174.88 ± 7.24	<0.001
ALM, kg	26.86 ± 4.69	27.35 ± 4.52	25.27 ± 4.87	<0.001
ASMI, kg/m^2	8.58 ± 1.28	8.69 ± 1.23	8.24 ± 1.34	<0.001
CRP, mg/dL	0.34 ± 0.75	0.32 ± 0.73	0.42 ± 0.82	<0.001
WBC	7.10 ± 2.46	7.05 ± 2.13	7.26 ± 3.30	0.217
NEU	4.21 ± 1.58	4.17 ± 1.61	4.34 ± 1.49	0.007
MONO	0.58 ± 0.20	0.57 ± 0.18	0.61 ± 0.23	0.010
Drinking status, *n* (%)				<0.001
Current	1,563.00 (74.99%)	1,116.00 (79.55%)	447.00 (60.37%)	
Former	395.00 (13.68%)	183.00 (10.16%)	212.00 (24.98%)	
Never	259.00 (11.32%)	156.00 (10.29%)	103.00 (14.65%)	
Smoking status, *n* (%)				<0.001
Current	489.00 (22.96%)	347.00 (23.45%)	142.00 (21.39%)	
Former	901.00 (36.12%)	484.00 (31.37%)	417.00 (51.36%)	
Never	827.00 (40.93%)	624.00 (45.19%)	203.00 (27.25%)	
Sarcopenia, *n* (%)				<0.001
No	1,944.00 (91.28%)	1,347.00 (93.77%)	597.00 (83.29%)	
Yes	273.00 (8.72%)	108.00 (6.23%)	165.00 (16.71%)	
Hyperlipidemia, *n* (%)				<0.001
No	1,264.00 (57.86%)	893.00 (61.81%)	371.00 (45.17%)	
Yes	953.00 (42.14%)	562.00 (38.19%)	391.00 (54.83%)	
DM, *n* (%)				<0.001
No	1,890.00 (89.44%)	1,335.00 (93.86%)	555.00 (75.27%)	
Yes	327.00 (10.56%)	120.00 (6.14%)	207.00 (24.73%)	
Arthritis, *n* (%)				<0.001
No	1,591.00 (76.55%)	1,159.00 (82.71%)	432.00 (56.79%)	
Yes	626.00 (23.45%)	296.00 (17.29%)	330.00 (43.21%)	
CHF, *n* (%)				<0.001
No	2,116.00 (96.87%)	1,424.00 (98.57%)	692.00 (91.40%)	
Yes	101.00 (3.13%)	31.00 (1.43%)	70.00 (8.60%)	
CHD, *n* (%)				<0.001
No	2,020.00 (93.16%)	1,391.00 (96.25%)	629.00 (83.23%)	
Yes	197.00 (6.84%)	64.00 (3.75%)	133.00 (16.77%)	
Stroke, *n* (%)				<0.001
No	2,130.00 (97.77%)	1,435.00 (99.12%)	695.00 (93.44%)	
Yes	87.00 (2.23%)	20.00 (0.88%)	67.00 (6.56%)	
Daily activity, *n* (%)				<0.001
Heavy loads	181.00 (9.05%)	152.00 (10.34%)	29.00 (4.91%)	
Light loads	343.00 (17.88%)	251.00 (19.15%)	92.00 (13.82%)	
Sitting	557.00 (24.38%)	323.00 (22.82%)	234.00 (29.40%)	
Standing or walking	1,136.00 (48.68%)	729.00 (47.69%)	407.00 (51.87%)	
Vigorous activity, *n* (%)				<0.001
No	1,512.00 (62.13%)	881.00 (56.69%)	631.00 (79.61%)	
Yes	705.00 (37.87%)	574.00 (43.31%)	131.00 (20.39%)	
Moderate activity, *n* (%)				<0.001
No	993.00 (38.14%)	597.00 (35.50%)	396.00 (46.60%)	
Yes	1,224.00 (61.86%)	858.00 (64.50%)	366.00 (53.40%)	

Values are mean ± SD or *n* (%). For categorical variables, *P* values were analyzed by chi-square tests. For continuous variables, *P* values were analyzed by *t* test. All of the continuous variables were exhibited by mean and SD. Abbreviations: ALM, appendicular lean mass; ASMI, appendicular skeletal muscle index; BMI, body mass index; CHD, coronary heart disease; CHF, congestive heart failure; CRP, C-reactive protein; DM, diabetes mellitus; MONO, monocyte; NEU, neutrophil; WBC, white blood cell.

Table 2 Association between appendicular skeletal muscle index and odds of erectile dysfunction.

	Model 1 OR (95% CI)	*p*-value	Model 2 OR (95% CI)	*p*-value	Model 3 OR (95% CI)	*p*-value
ASMI	0.734 (0.661, 0.815)	<0.001	0.893 (0.815, 0.978)	0.017	0.847 (0.750, 0.957)	0.019
ASMI (quartile)						
Q1	Reference		Reference		Reference	
Q2	0.616 (0.439, 0.863)	0.006	0.789 (0.520, 1.199)	0.254	0.824 (0.446, 1.523)	0.389
Q3	0.413 (0.317, 0.538)	<0.001	0.682 (0.519, 0.895)	0.008	0.606 (0.396, 0.925)	0.033
p for trend	<0.001		0.009		0.021	

Model 1 was crude. Model 2 included age, race, and education; and Model 3 included age, race, education, C-reactive protein, white blood cell, monocyte count, drink/smoke status, hyperlipidemia, diabetes mellitus, arthritis, congestive heart failure, coronary heart disease, and stroke.

Table 3 Association between physical activity and odds of erectile dysfunction.

	Model 1 OR (95% CI)	*p*-value	Model 2 OR (95% CI)	*p*-value	Model 3 OR (95% CI)	*p*-value
Vigorous activity	0.335 (0.252, 0.447)	<0.001	0.501 (0.364, 0.689)	<0.001	0.604 (0.418, 0.873)	0.013
Moderate activity	0.631 (0.507, 0.786)	<0.001	0.750 (0.579, 0.971)	0.031	0.831 (0.634, 1.089)	0.155
Daily activity						
Heavy loads	Reference		Reference		Reference	
Light loads	1.521 (0.852, 2.714)	0.149	1.297 (0.622, 2.702)	0.470	1.361 (0.582, 3.183)	0.419
Stand and walk	2.292 (1.435, 3.662)	0.001	1.650 (0.913, 2.982)	0.092	1.551 (0.768, 3.130)	0.183
Sitting	2.715 (1.707, 4.318)	<0.001	2.280 (1.326, 3.920)	0.005	1.905 (0.944, 3.847)	0.067
p for trend	<0.001		<0.001		0.019	

Model 1 was crude. Model 2 included age, race, and education; and Model 3 included age, race, education, C-reactive protein, white blood cell, monocyte count, drink/smoke status, hyperlipidemia, diabetes mellitus, arthritis, congestive heart failure, coronary heart disease, and stroke.

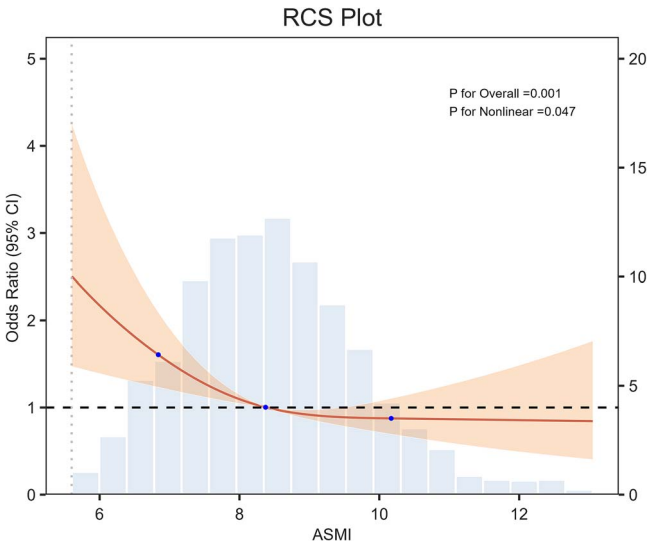


Figure 2 Results of restricted cubic spline. Associations between appendicular skeletal muscle index and erectile dysfunction were evaluated by restricted cubic spline after adjustment for age, race, education, C-reactive protein, white blood cell, monocyte count, drink/smoke status, hyperlipidemia, diabetes mellitus, arthritis, congestive heart failure, coronary heart disease, and stroke.

95% CI, 0.944-3.847, $P = .067$). Meanwhile, there was no significant difference in ED risk in the low-load group ($P > .05$).

Mediation effect of inflammatory markers on ASMI-ED associations

Mediation analysis revealed the proportion of the association between ASMI/physical activity and ED mediated by inflammatory markers (Table 4). Monocytes mediated 1.76% and 2.01% of the association between ASMI, vigorous activity, and ED, respectively. In addition, CRP showed mediating effects on vigorous activity-ED association (mediating effect = 1.36%), while leukocytes and neutrophils did not show significant mediating effects (mediating effect <1%, $P > .05$).

Discussion

This study investigated the relationship between muscle mass, physical activity, and ED in adult male patients, with a particular focus on the mediating role of systemic inflammation. Our results demonstrate that after adjusting for confounding variables, significant correlations exist between the ASMI, vigorous physical activity, and the incidence of ED. Mediation analysis revealed that systemic inflammatory markers—including CRP and MC—partially account for the association between ASMI and ED. These findings suggest that increasing muscle mass and physical activity may reduce the risk of ED, partly through mitigating systemic inflammation. It is noteworthy that this is the first study to utilize a large-scale, nationally representative database to examine the relationship between muscle mass and ED, highlighting the clinical significance of our results.

Our study found that the non-ED group had significantly higher ALM than the ED group, which may stem from the higher comorbidity burden in the ED group (diabetes: 24.73% vs 6.14%; hyperlipidemia: 54.83% vs 38.19%; CHD: 16.77% vs 3.75%; all $P < .001$). Previous studies have confirmed a significantly increased risk of sarcopenia in patients with type 2 diabetes, cardiovascular disease, and hyperlipidemia.[17–19] Concurrently, the ED group also exhibited significantly lower ASMI (8.24 ± 1.34 kg/m^2 vs 8.69 ± 1.23 kg/m^2) and lower rates of vigorous physical activity (20.39% vs 43.41%; $P < .001$). Erection involves

Variable	Count	Percent	P_value	P_for_interaction	OR(95%CI)
Race				0.195	
Mexican American	375	16.9	0.005		0.560 (0.410, 0.760)
Non−Hispanic black	357	16.1	0.072		0.790 (0.620, 1.010)
Non−Hispanic white	1367	61.7	<0.001		0.730 (0.650, 0.820)
Other	118	5.3	0.145		0.770 (0.560, 1.070)
Education				0.341	
High school diploma	508	22.9	0.011		0.730 (0.590, 0.910)
Less than high school	521	23.5	<0.001		0.620 (0.530, 0.730)
More than high school	1188	53.6	0.005		0.810 (0.710, 0.930)
Age				0.789	
<60	1290	58.2	0.014		0.870 (0.780, 0.960)
>=60	927	41.8	0.205		0.910 (0.790, 1.050)
Drink status				0.046	
Current	1563	70.5	<0.001		0.790 (0.700, 0.880)
Former	395	17.8	0.001		0.730 (0.620, 0.860)
Never	259	11.7	<0.001		0.580 (0.460, 0.740)
Smoking status				0.799	
Current	489	22.1	0.038		0.840 (0.720, 0.980)
Former	901	40.6	<0.001		0.640 (0.550, 0.760)
Never	827	37.3	0.085		0.820 (0.660, 1.020)
Hyperlipidemia				0.059	
No	1264	57	<0.001		0.670 (0.590, 0.770)
Yes	953	43	0.006		0.810 (0.700, 0.930)
DM				0.095	
No	1890	85.3	<0.001		0.660 (0.590, 0.740)
Yes	327	14.7	0.19		0.860 (0.700, 1.070)
Arthritis				0.99	
No	1591	71.8	<0.001		0.750 (0.660, 0.860)
Yes	626	28.2	<0.001		0.740 (0.640, 0.850)
CHF				0.073	
No	2116	95.4	<0.001		0.730 (0.660, 0.800)
Yes	101	4.6	0.886		1.020 (0.770, 1.360)
CHD				0.292	
No	2020	91.1	<0.001		0.740 (0.670, 0.810)
Yes	197	8.9	0.197		0.840 (0.650, 1.090)
Stroke				0.622	
No	2130	96.1	<0.001		0.750 (0.680, 0.820)
Yes	87	3.9	0.122		0.620 (0.360, 1.070)
Daily activity				0.999	
Heavy loads	181	8.2	0.352		0.750 (0.410, 1.360)
Light loads	343	15.5	0.09		0.730 (0.520, 1.030)
Sitting	557	25.1	0.041		0.830 (0.710, 0.980)
Standing or walking	1136	51.2	<0.001		0.710 (0.630, 0.790)
Vigorous activity				0.899	
No	1512	68.2	<0.001		0.760 (0.680, 0.840)
Yes	705	31.8	0.016		0.770 (0.630, 0.940)
Moderate activity				0.409	
No	993	44.8	<0.001		0.710 (0.610, 0.830)
Yes	1224	55.2	0.002		0.770 (0.660, 0.890)

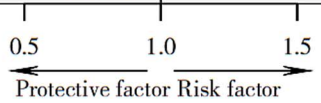


Figure 3 Subgroup analysis (forest plots). Abbreviations: CHF, congestive heart failure; CHD, coronary heart disease; DM, diabetes mellitus.

penile vasodilation mediated by endothelial nitric oxide (NO) release and the NO-cGMP-cGK signaling pathway, ultimately leading to corpus cavernosum congestion.[20,21] Elevated oxidative stress, insulin resistance, and inflammation disrupt this pathway, resulting in endothelial dysfunction and tissue remodeling within the penile vasculature—key mechanisms in vasculogenic ED.[20,22] Studies have shown that, besides age, established independent risk factors for ED (such as diabetes, dyslipidemia, metabolic syndrome, atherosclerosis, and smoking) directly reduce NO synthase activity in endothelial and smooth muscle cells while also inducing apoptosis.[23,24] Further analysis indicated a negative

Table 4 Mediation effects of inflammatory markers on the associations of appendicular skeletal muscle index, vigorous activity, and erectile dysfunction.

	Variables	Mediation effect	*P*-value	Proportion mediated	Direct effect	*P*-value
ASMI-ED	CRP	0.0014	<0.001	−0.0264	−0.0539	0.255
	WBC	−0.0001	0.454	0.0004	−0.0523	<0.001
	NEU	−0.0002	<0.001	0.0039	−0.0522	<0.001
	MONO	−0.0009	<0.001	0.0174	−0.0516	<0.001
Vigorous Act-ED	CRP	−0.0024	<0.001	0.0136	−0.1739	<0.001
	WBC	−0.0012	<0.001	0.0065	−0.1752	<0.001
	NEU	−0.0018	<0.001	0.0104	−0.1746	<0.001
	MONO	−0.0035	<0.001	0.0201	−0.1729	<0.001

correlation between ASMI and ED risk in the multivariate logistic regression model, and RCS analysis suggested that this negative association is nonlinear. Subgroup analyses also observed that this negative correlation was more pronounced, particularly among individuals without diabetes, cardiovascular disease, or hyperlipidemia. Considering previous evidence demonstrating a protective effect of muscle mass against type 2 diabetes and cardiovascular disease,[20] these results suggest that the potential protective role of muscle mass in ED warrants further investigation.

Current research posits that obesity-induced chronic low-grade inflammation is a key mediator of obesity-related metabolic disorders. Our mediation analysis found that MC mediated the correlations between ASMI (mediating effect = 1.76%, $P < .001$), vigorous exercise (mediating effect = 2.01%, $P < .001$), and ED. Sarcopenia primarily stems from age-related changes, including alterations in sex hormones, accelerated apoptosis, and mitochondrial dysfunction. Skeletal muscle, accounting for approximately 40% of total body weight, is a key site for NO metabolism.[21] Insulin, muscle contraction, and exercise stimulate glucose uptake in skeletal muscle via GLUT4 transporters, thereby reducing serum glucose levels and enhancing insulin sensitivity.[25] Insulin also promotes endothelial NO production.[26] Therefore, increasing skeletal muscle mass can elevate basal insulin levels and improve insulin sensitivity. Simultaneously, as the primary site for fatty acid oxidation, skeletal muscle can reduce circulating triglycerides and increase high-density lipoprotein (HDL) levels, thereby protecting vascular endothelial function[21,27] and mitigating vasculogenic ED. Male diabetic patients exhibit reduced muscle mass, increased adiposity, and a higher prevalence of sarcopenia. Adipose tissue releases cytokines and inflammatory mediators (eg, TNF-α, IL-6, CRP), exacerbating insulin resistance.[20,28] This forms a multidirectional interaction network wherein obesity, diabetes, and sarcopenia mutually exacerbate adverse effects, with inflammation playing a central role. Furthermore, an inflammatory state suppresses testosterone production by impairing gonadotropin-releasing hormone (GnRH) secretion,[22,29] while insulin resistance and inflammation create a vicious cycle, further promoting obesity. Overall, these conditions significantly exacerbate sexual dysfunction by concurrently impairing skeletal muscle function and erectile function.

Crucially, exercise is vital for muscle development and maintenance. After analyzing the association between physical activity and ED incidence, we found that vigorous activity has a protective effect against ED (OR = 0.604, 95% CI, 0.418-0.873, $P = .013$). Regular physical activity maintains mobility and muscle mass while improving mitochondrial function and reducing oxidative stress.[21,23,30] High-intensity resistance training can upregulate androgen receptor expression in skeletal muscle and stimulate testosterone release,[31,32] thereby improving erectile function through metabolic and endocrine regulation.

Previous research on the relationship between sarcopenia and ED remains limited.[33] Demirdağ et al. reported a high prevalence of sexual dysfunction in older adults but found no significant association between sarcopenia and sexual dysfunction.[34] However, several cross-sectional studies focusing on older men have demonstrated significant associations between sarcopenia and ED.[14,30,35–37]

Studies utilizing nationally representative databases to explore the relationship between muscle mass and ED in the adult population are scarce and insufficiently explored. Our work addresses this gap by specifically investigating the protective role of muscle mass against ED. Furthermore, we highlight vigorous exercise as a promising non-pharmacological intervention associated with a 39.6% reduction in ED incidence.

This study has several limitations. First, these cross-sectional analyses are based on data from US adults, limiting their generalizability to other racial or geographical populations. Second, the diagnosis of ED relied on participant self-report via questionnaire, which may lead to underreporting or misclassification bias due to psychological factors.

Future research should prioritize prospective cohort studies utilizing more comprehensive datasets to overcome these limitations, thereby clarifying the mechanistic links between ASMI and ED and informing appropriate treatment strategies for ED patients. Randomized controlled trials are also needed to assess whether increasing muscle mass through exercise can reduce the incidence or severity of ED. Furthermore, mechanistic studies are essential to elucidate the role of inflammatory biomarkers in mediating the relationship between muscle and ED.

Conclusion

In summary, current research suggests that increased muscle mass is associated with a reduced risk of ED, and that systemic inflammation mediates this relationship to some extent. In a clinical setting, early screening for sarcopenia and ED, followed by resistance training and anti-inflammatory interventions, may provide a comprehensive approach to protecting musculoskeletal and erection.

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Author contributions

Z.W.: Conceptualization, Methodology, Software, Writing—original draft. X.Z.: Methodology, Software, Writing—original draft. H.W.: Conceptualization, Formal analysis. C.S.: Conceptualization, Writing—review & editing, Supervision. C.L.: Writing—review & editing. M.C.: Supervision. All authors have read and agreed the version of published manuscripts.

Supplementary material

Supplementary material is available at *Sexual Medicine* online

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Conflicts of interest

The authors declare no competing interests.

Data availability

This research examined publically accessible datasets. For additional queries, feel free to reach out to the corresponding author.

Ethics approval and consent to participate

The NHANES study protocol was reviewed and approved by the National Center for Health Statistics institutional review board (NCHSIRB/ERB Protocol No. #98-12). All participants signed informed consent forms at enrollment. Secondary analyses do not require additional Institutional Review Board approval; therefore, this study is exempt from ethical review and approval procedures.

References

1. Shamloul R, Ghanem H. Erectile dysfunction. *Lancet*. 2013;**381**(9861):153–165. https://doi.org/10.1016/S0140-6736(12)60520-0
2. Burnett AL, Nehra A, Breau RH, *et al*. Erectile dysfunction: AUA guideline. *J Urol*. 2018;**200**(3):633–641. https://doi.org/10.1016/j.juro.2018.05.004
3. Chen L, Shi GR, Huang DD, *et al*. Male sexual dysfunction: a review of literature on its pathological mechanisms, potential risk factors, and herbal drug intervention. *Biomed Pharmacother*. 2019;**112**:108585. https://doi.org/10.1016/j.biopha.2019.01.046
4. McMahon CG. Current diagnosis and management of erectile dysfunction. *Med J Aust*. 2019;**210**(10):469–476. https://doi.org/10.5694/mja2.50167
5. Ma J, Chen Y, Si Y, *et al*. The multifaceted nature of diabetic erectile dysfunction: uncovering the intricate mechanisms and treatment strategies. *Front Endocrinol (Lausanne)*. 2024;**15**:1460033. https://doi.org/10.3389/fendo.2024.1460033
6. Nguyen HMT, Gabrielson AT, Hellstrom WJG. Erectile dysfunction in young men-a review of the prevalence and risk factors. *Sex Med Rev*. 2017;**5**(4):508–520. https://doi.org/10.1016/j.sxmr.2017.05.004
7. Liu C, Gao Y, Ji J, Sun C, Chen M. Association between inflammatory indexes and erectile dysfunction in U.S. adults: National Health and Nutrition Examination Survey 2001-2004. *Sex Med*. 2023;**11**(4):qfad045
8. Kaya-Sezginer E, Gur S. The inflammation network in the pathogenesis of erectile dysfunction: attractive potential therapeutic targets. *Curr Pharm Des*. 2020;**26**(32):3955–3972. https://doi.org/10.2174/1381612826666200424161018
9. Giugliano F, Esposito K, Di Palo C, *et al*. Erectile dysfunction associates with endothelial dysfunction and raised proinflammatory cytokine levels in obese men. *J Endocrinol Investig*. 2004;**27**(7):665–669. https://doi.org/10.1007/BF03347500
10. Chiurlia E, D'Amico R, Ratti C, Granata AR, Romagnoli R, Modena MG. Subclinical coronary artery atherosclerosis in patients with erectile dysfunction. *J Am Coll Cardiol*. 2005;**46**(8):1503–1506. https://doi.org/10.1016/j.jacc.2005.06.068
11. Li H, Qi T, Huang ZS, *et al*. Relationship between gut microbiota and type 2 diabetic erectile dysfunction in Sprague-Dawley rats. *J Huazhong Univ Sci Technolog Med Sci*. 2017;**37**(4):523–530. https://doi.org/10.1007/s11596-017-1767-z
12. Hayward MD, Jones BK, Saparov A, *et al*. An extensive phenotypic characterization of the hTNFalpha transgenic mice. *BMC Physiol*. 2007;**7**:13. https://doi.org/10.1186/1472-6793-7-13
13. Cruz-Jentoft AJ, Bahat G, Bauer J, *et al*. Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing*. 2019;**48**(1):16–31. https://doi.org/10.1093/ageing/afy169
14. Surmeli DM, Karpuzcu HC, Atmis V, *et al*. Association between sarcopenia and erectile dysfunction in older males. *Arch Gerontol Geriatr*. 2022;**99**:104619. https://doi.org/10.1016/j.archger.2021.104619
15. Araña Rosaínz Mde J, Ojeda MO, Acosta JR, *et al*. Imbalanced low-grade inflammation and endothelial activation in patients with type 2 diabetes mellitus and erectile dysfunction. *J Sex Med*. 2011;**8**(7):2017–2030. https://doi.org/10.1111/j.1743-6109.2011.02277.x
16. Chen LK, Liu LK, Woo J, *et al*. Sarcopenia in Asia: consensus report of the Asian working Group for Sarcopenia. *J Am Med Dir Assoc*. 2014;**15**(2):95–101. https://doi.org/10.1016/j.jamda.2013.11.025
17. Anagnostis P, Gkekas NK, Achilla C, *et al*. Type 2 diabetes mellitus is associated with increased risk of sarcopenia: a systematic review and meta-analysis. *Calcif Tissue Int*. 2020;**107**(5):453–463. https://doi.org/10.1007/s00223-020-00742-y
18. Fulster S, Tacke M, Sandek A, *et al*. Muscle wasting in patients with chronic heart failure: results from the studies investigating co-morbidities aggravating heart failure (SICA-HF). *Eur Heart J*. 2012;**34**(7):512–519. https://doi.org/10.1093/eurheartj/ehs381
19. Damluji AA, Alfaraidhy M, AlHajri N, *et al*. Sarcopenia and cardiovascular diseases. *Circulation*. 2023;**147**(20):1534–1553. https://doi.org/10.1161/CIRCULATIONAHA.123.064071
20. Viken AF, Siiak SP, Schlünssen V, *et al*. Muscle strength and male sexual function. *J Clin Med*. 2024;**13**(2):426. https://doi.org/10.3390/jcm13020426
21. Levine AB, Punihaole D, Levine TB. Characterization of the role of nitric oxide and its clinical applications. *Cardiology*. 2012;**122**(1):55–68. https://doi.org/10.1159/000338150
22. Jaschke N, Wang A, Hofbauer LC, Rauner M, Rachner TD. Late-onset hypogonadism: clinical evidence, biological aspects and evolutionary considerations. *Ageing Res Rev*. 2021;**67**:101301. https://doi.org/10.1016/j.arr.2021.101301

23. Jensen GL. Inflammation: roles in aging and sarcopenia. *JPEN J Parenter Enteral Nutr*. 2008;**32**(6):656–659. https://doi.org/10.1177/0148607108324585
24. Sun C, Gao Y, Liang Z, Liu C, Chen M. Association of METS-IR index with prevalence of erectile dysfunction in US adults: a cross-sectional study. *Int Urol Nephrol*. 2024;**56**(7):2157–2164. https://doi.org/10.1007/s11255-024-03961-6
25. Jobgen WS, Fried SK, Fu WJ, Meininger CJ, Wu G. Regulatory role for the arginine-nitric oxide pathway in metabolism of energy substrates. *J Nutr Biochem*. 2006;**17**(9):571–588. https://doi.org/10.1016/j.jnutbio.2005.12.001
26. Bhasin S, Krishnan V, Storer TW, Steiner M, Dobs AS. Androgens and selective androgen receptor modulators to treat functional limitations associated with aging and chronic disease. *J Gerontol A Biol Sci Med Sci*. 2023;**78**(Suppl 1):25–31. https://doi.org/10.1093/gerona/glad027
27. Hauck AK, Bernlohr DA. Oxidative stress and lipotoxicity. *J Lipid Res*. 2016;**57**(11):1976–1986. https://doi.org/10.1194/jlr.R066597
28. Lee DM, Tajar A, Ravindrarajah R, *et al*. Frailty and sexual health in older European men. *J Gerontol A Biol Sci Med Sci*. 2013;**68**(7):837–844. https://doi.org/10.1093/gerona/gls217
29. Dorner TE, Berner C, Haider S, *et al*. Sexual health in patients with rheumatoid arthritis and the association between physical fitness and sexual function: a cross-sectional study. *Rheumatol Int*. 2018;**38**(6):1103–1114. https://doi.org/10.1007/s00296-018-4023-3
30. Park H, Jang IY, Han M, *et al*. Sarcopenia is associated with severe erectile dysfunction in older adults: a population-based cohort study. *Korean J Intern Med*. 2020;**35**(5):1245–1253. https://doi.org/10.3904/kjim.2019.148
31. Corona G, Rastrelli G, Morelli A, *et al*. Treatment of functional hypogonadism besides pharmacological substitution. *World J Mens Health*. 2020;**38**(3):256–270. https://doi.org/10.5534/wjmh.190061
32. Willoughby DS, Taylor L. Effects of sequential bouts of resistance exercise on androgen receptor expression. *Med Sci Sports Exerc*. 2004;**36**(9):1499–1506. https://doi.org/10.1249/01.MSS.0000139795.83030.D1
33. Defeudis G, Mazzilli R, Di Vincenzo O, *et al*. Sarcopenia and its impact on sexual health: a systematic review. *Diabetes Metab Res Rev*. 2025;**41**(5):e70067. https://doi.org/10.1002/dmrr.70067
34. Demirdağ F, Kıvrak Güçer B, Kolbaşı EN. Sarcopenic obesity is not associated with sexual dysfunction in older adults: a cross-sectional study. *Aging Male*. 2023;**26**(1):2252502. https://doi.org/10.1080/13685538.2023.2252502
35. Darmadi D, Pakpahan C, Ruslie RH, Amanda B, Ibrahim R. The sex life of male patients with cirrhosis and its organic factors: what we have got so far? *PLoS One*. 2023;**18**(2):e0280915. https://doi.org/10.1371/journal.pone.0280915
36. Uçak S, Sivritepe R, Kara O, *et al*. Association between sarcopenia and erectile dysfunction in males with type II diabetes mellitus. *Aging Male*. 2019;**22**(1):20–27. https://doi.org/10.1080/13685538.2018.1441276
37. Jang IY, Lee CK, Jung HW, *et al*. Urologic symptoms and burden of frailty and geriatric conditions in older men: the aging study of PyeongChang rural area. *Clin Interv Aging*. 2018;**13**:297–304. https://doi.org/10.2147/CIA.S158717

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