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Impact of Ethnicity on the Relationship Between Sarcopenia and Diabetes

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Abstract

Objective: Several studies have established a close relationship between sarcopenia and diabetes in aging populations, but to the best of our knowledge, no studies have analyzed if a difference in this relationship exists among different ethnic groups. The main objective of this study was to determine if there is a statistically significant difference in the relationship between sarcopenia and diabetes among different ethnic groups.

Materials and Methods: A literature search was performed via PubMed. After screening, 26 studies were included for a total of 62,070 individuals with diabetes, 39,825 individuals with sarcopenia, and 6,870 with both. A One-Way Analysis of Variance was performed on the sarcopenia-diabetes co-occurrence value for each group.

Results: Our results show that sarcopenia and diabetes appear more prevalent in Asian populations compared to other ethnic groups at a lower body mass index; however, there is no statistically significant difference in the relationship between sarcopenia and diabetes among the Asian, Hispanic, and Caucasian groups analyzed ($F=0.202$, $p=0.819$, at $\alpha<0.05$).

Conclusion: Our meta-analysis supports the previously established relationship between sarcopenia and diabetes in aged populations but does not support the hypothesis that ethnicity alone is a major determining factor for the sarcopenia-diabetes relationship.

Keywords: Sarcopenia, diabetes, metabolic syndrome, Asian

Introduction

A rapidly evolving, fast-paced, and technologically inclined global stage has given rise to an increasingly alarming incidence of chronic, metabolic diseases and associated physiological, economic, and social healthcare burdens. Diabetes is among one of the world's leading causes of morbidity, as well as mortality, and has cost the world an estimated $760 billion in 2019 (1). Depending on the definition used for diagnosis, the global prevalence of sarcopenia ranges from 10-40% of the world population (2,3). Increasing lifespan over the past centuries, coupled with a consequent increase in adults over 65 years of age, has put increasing emphasis on age-related conditions such as sarcopenia and diabetes. In the year 2020, there were 727 million individuals aged 65 years and older, representing approximately 9.3% of the world population (4). Globally, individuals 65 and older is estimated to rise from 9.3% of the world population in 2020 to 16% of the total population in 2050 (roughly 1.5 billion elderly persons) (4).

Several papers have established a reciprocal relationship between diabetes and sarcopenia, with some citing a sarcopenia prevalence two or three times higher in diabetic patients compared to healthy controls, and vice versa (2-12). Several factors have been implicated in contributing to the sarcopenia-diabetes relationship: Insulin resistance, altered metabolism, advanced age, increased adiposity, obesity, inflammation, oxidative stress, advanced glycation end-products (AGEs), mitochondrial dysfunction, vascular complications, muscular atrophy, reduced muscle quality and function, myopathies, and lifestyle (primarily exercise and diet) (Figure 1) (2-4,7,11).

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Of note, Asian populations exhibit higher rates of diabetes at lower body mass indexes (BMIs) compared to other ethnic groups (13). Given the lower initial muscle mass and higher sarcopenia prevalence in Asian populations, as well as higher rates of diabetes at lower BMIs, we hypothesize that the relationship between sarcopenia and diabetes will be stronger compared to other ethnic groups.

To the best of our knowledge, no studies have evaluated the strength of the relationship between sarcopenia and diabetes among different ethnicities. Therefore, in this study, we performed a meta-analysis to determine if a difference exists in the strength of the relationship between sarcopenia and diabetes across different ethnic groups.

Materials and Methods

Data for this meta-analysis was obtained from searching the online, international database PubMed with reference to guidelines from the preferred reporting items for systematic reviews and meta-analyses (PRISMA) (Figure 2) (14). Specific combinations of search strings for each ethnic group were developed using Boolean operators and MeSH terms to further narrow and specify search results.

Studies were screened for data on the prevalence of sarcopenia and diabetes. Studies that did not include data on participants with coexisting sarcopenia and diabetes were excluded from this study. Studies with the following characteristics were excluded: (i) not written in English, (ii) published over 10 years ago (before 2011), (iii) included individuals under 18 (child and adolescent studies), (iv) conducted on only one gender, (v) conducted on animals, and (vi) individual case studies. This meta-analysis focused on type II diabetes (T2DM); individuals with type I diabetes were not included. Individual study exclusion criteria were evaluated such that participants included in this meta-analysis were considered relatively healthy without outstanding, potentially confounding health conditions. The studies selected excluded participants with difficulties communicating, outstanding disabilities that impaired study participation, severe cognitive impairment, notable conditions that impaired adequate nutrition, serious heart, kidney, or liver disease, history of stroke, individuals with type 1 diabetes, difficulty ambulating, and incomplete information. In location-specific studies, those who were not registered residents were excluded.

Further, all studies used the Asian Working Group for Sarcopenia or European Working Group for Sarcopenia in Older People criteria for sarcopenia diagnosis; one study used the decrease in the ratio of appendicular lean mass/BMI along with handgrip strength. Diabetes diagnosis was determined via blood sample, patient self-reporting, or physician assessment during the clinic visit.

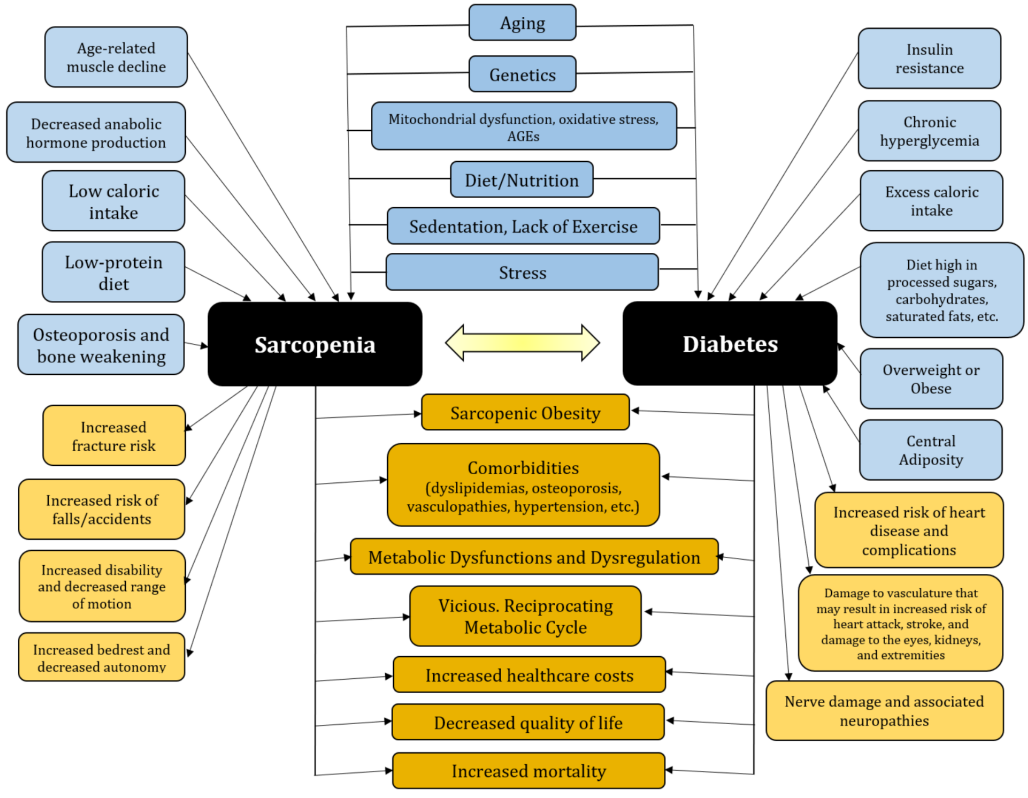

Figure 1. Graphical representation of the reciprocal relationship between sarcopenia and diabetes. The relationship between sarcopenia and diabetes may result in sarcopenic obesity, metabolic dysfunction and dysregulation, and a vicious cycle in which factors influence and are influenced by other factors in the metabolic network. Both conditions have contributed to increasing healthcare costs, decreased quality of life, and increased morbidity and mortality

JASP open-source software was used to analyze data collected from selected articles. A One-Way Analysis of Variance (ANOVA) was performed to obtain an F-statistic and p-statistic to determine significance, as well as an η^2 value to conceptualize effect size. The group means that were compared through ANOVA consisted of each group's average of the following measurement for each study, which we call the co-occurrence value:

$$\text{co-occurrence value for study x} = \frac{\text{individuals with both SC+T2DM}}{\text{total study individuals with T2DM}}$$

In this project, the co-occurrence value will serve as a numerical measure of the strength of the relationship between sarcopenia and diabetes. The co-occurrence value was calculated for each study and the co-occurrence values for all studies within the Hispanic, Caucasian, and Asian groups were averaged to produce the group mean. Moreover, the number of individuals with both sarcopenia and T2DM was divided by the total number of individuals with T2DM. Using ANOVA, the difference in means was compared within groups, as well as between groups to determine if a statistically significant difference in means exists among different ethnic groups.

For this meta-analysis, the null and alternative hypotheses were as follows:

H_0: No difference in means exists among the Hispanic, Caucasian, and Asian groups

H_a: A difference in means exists among the Hispanic, Caucasian, and Asian groups

Results were considered statistically significant at an alpha level of $p<0.05$.

Results

After searching and screening PubMed, 26 studies out of the initial 333 were selected for statistical analysis (Figure 2). The combinations of search terms produced a total of 333 results: Five studies for the African group; 12 studies for the Hispanic group; 89 results for the Caucasian group; and 227 studies for the Asian group. After removal of duplicates, of the 322 studies screened for eligibility, reports were excluded for the following reasons: (i) did not contain relevant data (unrelated topic, extraneous data, etc.), (ii) contained study individuals with outstanding, confounding health conditions, (iii) provided data on either sarcopenia or diabetes, but not on their co-occurrence, (iv) conducted only one gender, (v) child study or study including children (persons younger than 18 years of age), (vi) animal studies, (vii) did not include breakdown for each ethnicity, (viii) study not written in English, and (IX) case study following a single patient. After removing duplicates and conducting initial screening, 38 studies were selected for in-depth evaluation and 26 studies were selected for inclusion in the meta-analysis (6,8,15-38). Twenty-two studies had a cross-sectional design;

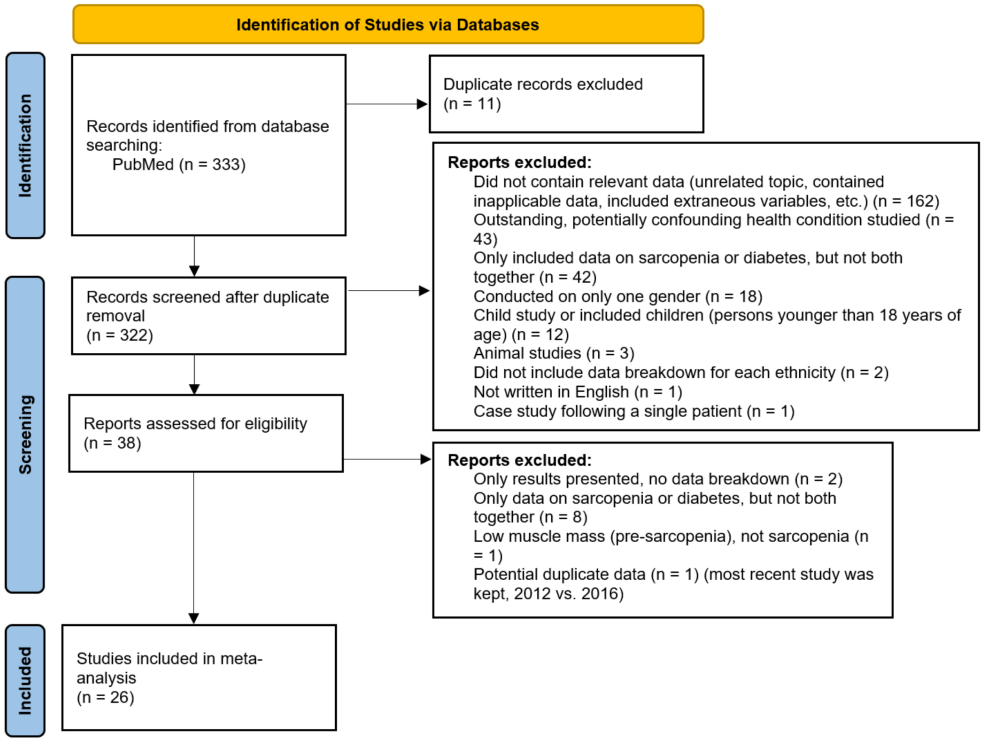

Figure 2. Preferred Reporting Items for Systematic Reviews (PRISMA) for identification of studies via databases. Chart adapted from Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71. (14) Licensed under the Creative Commons Attribution License

3 studies had mixed study designs (a combination of cross-sectional and cohort); 1 study had a cohort design. There were 5 studies for the Hispanic group (6,8,18-20), 3 studies for the Caucasian group (15-17), and 18 studies for the Asian group (21-38). Due to lack of eligible study data, the African group was not able to be included in the final analysis. A scarcity of study data may be due to lack of access to medical care and documentation in these regions. Out of the 26 selected studies, 18 were chosen for the Asian group. Patients were drawn from the following countries: China (5 studies), Korea (2), Japan (7), Malaysia (1), North India (1), Singapore (1), and Thailand (1). Of the 26 selected studies, 5 were from the Hispanic group and were drawn from the following countries: Brazil (4) and Mexico (1). Furthermore, 3 of the 26 studies were included in the Caucasian group, with 1 study conducted in Australia, 1 in Italy, and 1 in the UK (encompassing England, Scotland, and Wales).

Author names, number of individuals with sarcopenia, diabetes, and both, and BMI were collected from each study (Table 1). The study population consisted of 531,023 individuals (62,070 total patients with T2DM and 39,825 total patients with sarcopenia; 6,870 patients had both sarcopenia and T2DM) with an average age of 68.27 years; 45.44% of participating individuals (241,313) were male. For all studies, the co-occurrence value (SC + T2DM/total T2DM) ranged from 7-82%. For the Asian group, the co-occurrence value ranged from 7-82%. The co-occurrence values ranged from 9-37% for the Caucasian group and 14-30% for the Hispanic group. The Asian group exhibited the greatest variation in co-occurrence values, whereas the Hispanic group displayed the least variation. Among the Asian studies, the means of the co-occurrence values for China, Korea, and Japan are as follows: 0.39, 0.27, and 0.16, respectively. The mean co-occurrence value for the studies conducted in Brazil was 0.22.

The Asian group had the highest of the group means (highest average of co-occurrence values) when the selected studies were averaged. The group means for co-occurrence value in the Caucasian, Hispanic, and Asian groups were 0.23, 0.22, and 0.27, respectively. For all studies taken together, the average for the co-occurrence value was 0.26.

ANOVA produced an F-statistic of 0.202 and a p-statistic of 0.819 with an η^2 value of 0.017. Using an alpha level of p=0.05, the p-statistic obtained is greater than the stated alpha level; therefore, the results are not statistically significant, and we fail to reject the null hypothesis. The available data therefore does not support the hypothesis that Asian groups have a stronger relationship between sarcopenia and diabetes compared to the Hispanic and Caucasian groups analyzed.

Discussion

Several published studies have established a reciprocal relationship between sarcopenia and diabetes in which the presence or onset of one influences or is influenced by, the presence or onset of the other. This meta-analysis explored if ethnicity plays a significant role in the relationship between sarcopenia and diabetes. Given the higher prevalence of sarcopenia and diabetes at lower BMIs in Asian populations, we hypothesized that this relationship would be significantly stronger in Asian groups.

The p-value obtained from ANOVA was greater than the accepted alpha level of $p<0.05$. Thus, the results do not support ethnicity as a major impacting factor in the relationship between sarcopenia and diabetes. Furthermore, based on currently available data, the Asian group did not demonstrate a stronger relationship between sarcopenia and diabetes. These findings pose additional questions for future sarcopenia and diabetes research.

A significant amount of variability was found within each study group, especially in the Asian group. A primary contributor to significant in-group variation is the inherent variability (physical, behavioral, genetic, demographic, cultural, etc.) of different study populations. The Asian group, as with Hispanic and Caucasian groups, consists of heterogenous populations of individuals from many different countries, regions, and environments. The classifications of "Hispanic", "Caucasian", and "Asian" are far from homogenous, and some individuals who fall under one category geographically may qualify for multiple categories or share more similarities with another individual from a different category compared to an individual from their own category. Data for this meta-analysis was drawn from several Asian countries (China, Japan, Korea, Malaysia, Singapore, North India, Singapore, and Thailand) with multifactorial differences that cannot be understated when examining the great degree of within-group variability obtained in this study. Further studies may explore if or how particular differences (genetic markers, diet, culture, etc.) within ethnic groups contribute to the co-occurrence of sarcopenia and diabetes. Moreover, future studies may benefit from exploring different levels and guidelines for evaluation that can more fully address the variability within ethnic groups.

Of note, a general trend observed in the study population was a general increase in sarcopenia and diabetes with age. Older study populations exhibited higher rates of sarcopenia, diabetes, and sarcopenia with diabetes. Additionally, there appeared to be an increased prevalence of sarcopenia in those populations that had diabetes. These trends further confirm previously established relationships between sarcopenia and diabetes.

Certain diseases such as diabetes, hypertension, and osteoporosis demonstrate ethnic trends in presentation, prevalence, and severity. Though this may be true when observing a certain condition by itself, analyzing multiple conditions together does not translate to statistically significant differences in the

Table 1. Study and patient characteristics from selected studies

First Author	Year	Category	Country	Study Design	# of patients	Mean Age (years)	% Men	SC Definition	T2DM Definition	Total SC	Total T2DM	SC + T2DM	(SC+T2DM)/Total T2DM percentage	Average BMI
Asian														
Xiu, Shuangling	2021	Asia	China	Cross-sectional	582	70.54	50%	AWGS, 2019 criteria	Blood samples after overnight fast (>10h), FPG	52	582	52	**8.93%**	24.33
Yuenyongchaiwat, Kornanong	2021	Asia	Thailand	Cross-sectional	330	66.85	24%	AWGS	Insulin-resistant	21	82	21	**25.61%**	**T2DM** = 26.39 **No T2DM** =25.27
Yin, Ting	2021	Asia	China	Cross-sectional	14,926	56.75	39.8%	AWGS	2010 ADA guidelines: FPG > 7.0 mmol/L	9721	744	539	**72.45%**	**Mean for all** = 24.94 **SO** = 26.54 **No SO** = 21.95
Su, Ya	2019	Asia	Japan	Cross-sectional	310	76	29%	EWGS OP2	Self-reported	25	26	6	**23%**	**Overall** =22.7 **SC** = 20.5
Kaur, Parjett	2021	Asia	North India	Cross-sectional	194	43.23	52%	EWGS OP2	Outpatient check-up; FPG and HbA1c levels measured	62	95	45	**47.37%**	**T2DM** = 28.15 **No T2DM** = 27.45
Mori, Hiroyasu	2021	Asia	Japan	Cross-sectional	1328	67.53	61.8%	AWGS 2019 criteria	Physician's diagnosis, medical chart review	102	645	76	**11.78%**	**T2DM** = 26.6 **T2DM + SC** = 21.3
Kang, Sunyoung	2021	Asia	Korea	Cross-sectional (nationwide cohort study)	2403	76	47.2%	AWGS	Self-report or current antidiabetic medication; newly diagnosed diabetes determined via ADA guidelines	284	670	88	**13.13%**	Not reported
Sazlina, Shariff-Ghazali	2020	Asia	Malaysia	Longitudinal study	506	67.6	40.0%	AWGS	FPG of ≥7.0mmol/L or ≥11.1mmol/L, respectively; or HbA1c of ≥6.3%, in accordance with Malaysian guidelines on Management of T2DM, 2015	144	506	144	**28.46%**	27.5
Sugimoto, Ken	2019	Asia	Japan	Cross-sectional	746	69.9	60.3%	AWGS	Not reported	52	746	52	**6.97%**	**SC** = 20.7 **Non-SC** = 25.0

Table 1. Continued

Li, Chun-Wei	2019	Asia	China	Interdisciplinary cross-sectional, cohort, and intervention study	102	68.65	49%	AWGS	Not reported	56	11	9	**81.82%**	**SC** = 21.44 **Non-SC** = 24.69
Okamura, Takuro	2019	Asia	Japan	Cross-sectional	391	72.4	52.4%	AWGS	Not reported	55	391	55	**14.06%**	**SC** = 21.1 **Non-SC** = 24.2
Murata, Yuko	2018	Asia	Japan	Cross-sectional	288	74.2	52.4%	AWGS	Outpatient clinic	88	288	88	**30.56%**	SC = 22.2 Non-SC = 24.2
Han, PeiPei	2017	Asia	China	Cross-sectional	711	**Non-SC** = 66.33 **SC** = 72.71	49%	AWGS	Questionnaire; combination of self-reporting and physician diagnosis	77	80	18	**22.50%**	**SC** = 22.35 **Non-SC** = 25.55
Morikawa, Yoshinobu	2021	Asia	Japan	Cross-sectional	161	65.9	48%	AWGS	Current treatment with oral hypoglycemic agents or insulin or FPG > 126 mg/dL	31	161	31	**19.25%**	**SC** = 21.1 **Non-SC** = 25.8
Sugimoto, Ken	2020	Asia	Japan	Observational longitudinal study	588	70	59%	AWGS	HbA1c, data taken from patient visits	46	588	46	**7.80%**	24.7
Chen, Fenqin	2020	Asia	China	Cross-sectional	1427	> 60	37%	AWGS, 2019 criteria	Clinic visit, questionnaire	148	1427	148	**10.37%**	Not reported
Fung, Foon Yin	2019	Asia	Singapore	Longitudinal	387	68.3	53%	EWGSOP, AWGS	Patient's electronic medical records (EMR)	106	387	106	**27.39%**	Not reported
Lim, Hee-Sook	2018	Asia	Korea	Cross-sectional	3492	68.8	53%	Not reported; data from KNHANES	Data from KNHANES	1373	340	137	**14.70%**	**SO** = 25.1 (male); 26.7 (female) **SC** = 23.4 (M); 21.0 (F) **No-SC** = 22.0 (M); 22.8 (F)

Table 1. Continued

Hispanic													
Souza, Anelza Biene Farias	2019	Hispanic	Brazil, Amazon	Cross-sectional	1078	**Non-SC** = 69 **SC** = 79 (median)	20.8%	EWGSOP	Self-reported or FPG > 126 mg/dl or HbA1c > 6.5%	101	245	35	14.29%	**SC** = 28.7 **Non-SC** = 23.5 (median)
Beretta, Mileni V.	2020	Hispanic	Brazil	Cross-sectional	610	71.35	49%	EWGSOP	Self-reported, hospital check-up	237	306	93	30.39%	Not reported
Freitas, Veronica Porto de	2018	Hispanic	Brazil	Cross-sectional	76	No average listed, all adults > 60 years	42%	EWGSOP	Self-reported, questionnaire	15	16	3	18.75%	Not reported
Trierweiler, Heloisa	2018	Hispanic	Brazil	Cross-sectional	166	**T2DM:** 65.84 **No T2DM:** 65.92	28.92%	ALM/BMI ratio and handgrip strength	Questionnaire or current use of diabetes medication	15	83	13	15.66%	**T2DM** = 28.16 **Non-T2DM** = 25.96
Manrique-Espinoza, Betty	2017	Hispanic	Mexico	Cross-sectional	543	76.1	47.30%	EWGSOP	Not reported	198	66	19	28.79%	N/A
Caucasian														
Dodds, Richard M.	2020	Caucasian	UK (England, Wales, Scotland)	Cross-sectional	499,046	**SC** = 59.9 **No SC** = 56.3	45.55%	EWGSOP2	UK Biobank data	26,671	53,442	4985	10.29%	**SC** = 28.1 **Non-SC** = 27.4
Churilov, Irina	2021	Caucasian	Australia	Cross-sectional	300	63 (median)	51.70%	EWGSOP, 2018	Prior history of T2DM; inpatient hospital visit	44	46	11	23.91%	**SC** = 21.8 **SC + T2DM** = 22.9
Landi, Francesco	2016	Caucasian	Italy	Cohort study	332	86.1	32.30%	EWGSOP	Self-report via MDS-HC form	101	97	36	37.11%	**SC** = 24.3 **Non-SC** = 26.7

AWGS—Asian Working Group for Sarcopenia; *EWGSOP*—European Working Group on Sarcopenia in Older People; *T2DM*—type II diabetes mellitus; *SC*—sarcopenia; *SO*—sarcopenic obesity

relationship between the two conditions. Moreover, in this meta-analysis, though sarcopenia and diabetes appeared more prevalent in Asian populations compared with other ethnic groups at a lower BMI, this does not necessarily translate to a stronger sarcopenia-diabetes relationship when the two conditions are analyzed together.

Worldwide, there is increased homogenization in the presentation, trends, and prevalence of comorbid metabolic diseases, a phenomenon we will call the modern-day global metabolic syndrome. This is likely a result of increasing similarities in lifestyle and diet trends, reinforced by an increasingly technological, interconnected modern landscape: More frequent and longer periods of sedentation with less frequent and shorter periods of physical activity, diets high in processed ingredients, sugar, and empty calories, and heightened, chronic feelings of anxiety, pressure, and stress. Though it is possible that genetic variations shared by similar ethnic groups may contribute to altered metabolic patterns (for instance, some increasing metabolic thrift while others decreasing it and thus predisposing some groups to certain diseases over others), these differences are superseded when considering the complex, reciprocal, and inevitable interplay of multiple co-occurring metabolic morbidities in a modern landscape.

Study Limitations

A prominent limitation in this study is the lack of data from the African, as well as Hispanic and Caucasian study groups. Out of the 5 African studies obtained from an initial keyword search, none of the studies met this study's inclusion criteria; consequently, the group had to be removed from the meta-analysis due to lack of available data. The lack of sufficient data may be due to the lack of access to adequate medical care and documentation in these regions. Moreover, some groups had more available data compared to others. Out of the 26 selected studies, 18 of these studies were from Asian countries; 5 studies were included in the Hispanic group and 3 studies were selected for the Caucasian group. Within the 18 Asian studies, 7 of these were conducted in Japan. Further research would greatly benefit from the availability of more sarcopenia and diabetes studies conducted in each of these groups.

Great variability in sample size may have contributed to non-negligible in-group variability. Sample sizes ranged from 76 participants to 499,046 (a national cross-sectional study). Given the current paucity of information, future studies are advised to draw from a larger sample size and should strive to increase the number of studies included, if or when available. Inclusion criteria should be more stringent to address limitations due to non-negligible variations that were observed in this study.

Conclusion

This meta-analysis further supports the previously established relationship between sarcopenia and diabetes. This meta-analysis has shown that, although differences in the prevalence of sarcopenia and diabetes have been demonstrated, ethnicity is not a determining factor in the strength of the sarcopenia-diabetes relationship among aged populations. Both sarcopenia and diabetes affect a substantial portion of the world population and are major contributors to increasing healthcare costs and decreased quality of life. Both sarcopenia and diabetes are becoming increasingly prevalent as populations age and undergo increased homogenization in modern lifestyle and diet transitions (which may be responsible for a phenomenon we call the modern-day global metabolic syndrome).

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Ethics

Ethics Committee Approval: Our article is a review/meta-analyses of previously published research.

Informed Consent: We did not conduct or perform any research involving patients.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: R.W., M.P., Design: R.W., M.P., Data Collection or Processing: R.W., Analysis or Interpretation: R.W., M.P., Literature Search: R.W., M.P., Writing: R.W., M.P.

Conflict of Interest: No conflict of interest was declared by the authors.

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