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SYSTEMATIC REVIEW

Dynapenic obesity and all-Cause mortality: A systematic review and Meta-analysis of prospective cohort studies

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Abstract

Background Dynapenia and obesity have been independently shown to be associated with an increased risk of all-cause mortality. However, the association between dynapenic obesity [defined by waist circumference (WC) or body mass index (BMI)] and all-cause mortality is not yet fully elucidated.

Methods We systematically searched databases, including PubMed, Web of Science, and Scopus, to explore the relationship between dynapenic obesity and all-cause mortality up to February 2024. Pooled hazard ratios (HRs) for all-cause mortality were calculated for individuals with dynapenic abdominal obesity (DAO) and dynapenic obesity defined by BMI relative to a healthy reference group.

Results Six studies examining DAO and six assessing dynapenic obesity defined by BMI were included. Individuals with DAO had a significantly higher risk of all-cause mortality compared to those without dynapenia and with normal WC. The pooled HR for DAO versus non-dynapenic, non-abdominal obese individuals was 1.73 (95% CI = 1.38–2.16), with substantial heterogeneity across studies (I2 = 77%, $p < 0.01$). Similarly, individuals with dynapenic obesity, as defined by BMI, showed an elevated mortality risk compared to those with normal BMI, with an HR of 1.33 (95% CI = 1.16–1.53). High heterogeneity was observed across these studies (I2 = 76%, $p < 0.01$).

Conclusion This meta-analysis reveals a significant association between dynapenic obesity, whether defined by WC or BMI, with an increased risk of all-cause mortality. Further studies are needed to explore the underlying mechanisms driving this relationship.

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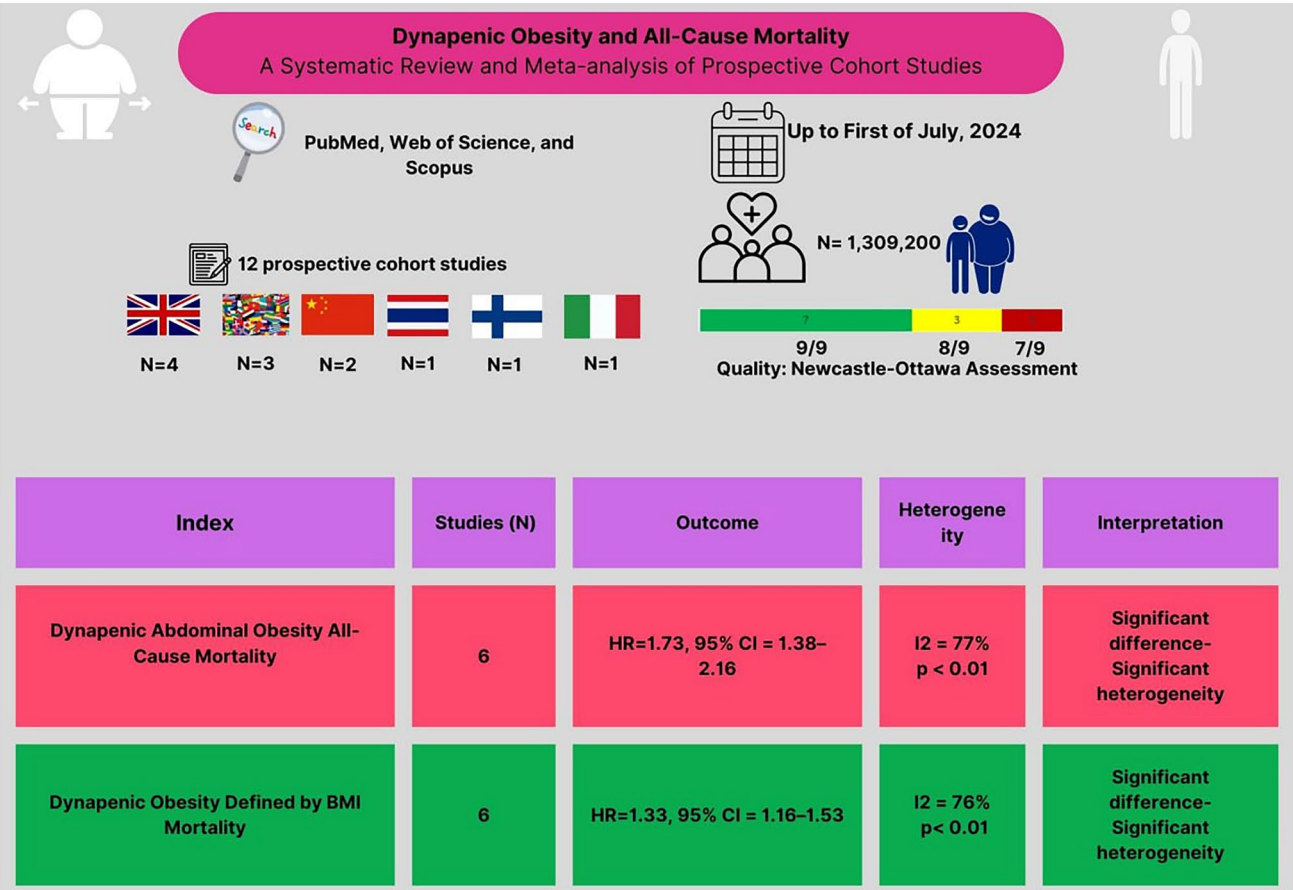
Graphical Abstract



Keywords Muscle strength · Obesity · Body mass index · Waist circumference · Mortality · Meta-analysis

Abbreviations

BMI	Body Mass Index
CI	Confidence Interval
DAO	Dynapenic Abdominal Obesity
HDL	High-Density Lipoprotein
HR	Hazard Ratio
NOS	Newcastle-Ottawa Assessment Scale
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-analyses
SO	Sarcopenic Obesity
WC	Waist Circumference
WHO	World Health Organization

Introduction

The global prevalence of overweight and obesity has been on the rise over the past decades [1]. According to the World Health Organization (WHO), the number of overweight adults has surpassed 2.5 billion globally, while over 890 million of these are living with obesity, defined as having a body mass index (BMI) greater than or equal to 30 kg/m2 [2]. Obesity stands as a substantial public health concern since it amplifies the susceptibility to conditions such as type 2 diabetes mellitus [3], various forms of malignancy [4, 5], dyslipidemia [6], and coronary heart disease [7], which poses an elevated risk of all-cause mortality [8].

Current studies suggest that waist circumference (WC), the indicator of abdominal fat, may surpass BMI in significance when determining adverse health implications linked to obesity in older adults [9]. As individuals age, a notable shift in body composition occurs, characterized by increased abdominal and intramuscular fat and a concurrent decline in lean mass [10]. In addition, aging is associated with loss of muscle strength, known as dynapenia, which occurs at a more accelerated rate than the loss of muscle mass [11]. The decline in muscle strength is more pronounced associated with adverse health outcomes, such as physical disability and mortality, than the loss of muscle mass [12]. The interplay between increased visceral adiposity and reduced

muscle strength results in the phenotype termed dynapenic abdominal obesity (DAO) [13]. Visceral fat elevates pro-inflammatory cytokines, potentially playing a role in the onset and advancement of dynapenia [14, 15]. Similarly, dynapenia reduces physical activity levels, potentially raising the likelihood of abdominal obesity [16].

Both dynapenia and obesity have been independently associated with an increased risk of mortality [17, 18]. The metabolic risks Linked to obesity include insulin resistance, type 2 diabetes mellitus, and dyslipidemia [19–21]. Likewise, individuals with dynapenia face an increased risk of low HDL cholesterol [22], hypertriglyceridemia [22], and diabetes mellitus [23], proposing dynapenia and obesity as potential predictors of mortality.

When these two factors converge as dynapenic obesity, a significant risk factor emerges. This combination is associated with a range of adverse health consequences, including falls, reduced walking speed, metabolic changes, elevated cardiovascular risk, hospitalization, and multimorbidity [24]. The presence of multiple risk factors for mortality in these individuals may predict a potential elevation in their overall risk of mortality.

While both dynapenia and obesity have been independently linked to increased risk of mortality, the association between dynapenic obesity and all-cause mortality is not yet fully elucidated. Hence, a comprehensive systematic review and meta-analysis explored the association between dynapenic obesity and all-cause mortality.

Methods

Search strategy

A systematic search was conducted across PubMed, Web of Science, and Scopus to identify all relevant articles examining the association between low muscle strength and obesity and all-cause mortality up to February 2024. The details of the search strategies are provided in **Supplementary File 1** . Furthermore, we manually searched the reference lists of the retrieved studies to identify any additional potentially relevant articles.

Eligibility criteria and selection of studies

Two independent researchers screened articles based on the most relevant titles and abstracts. Subsequently, they reviewed the full text of retrieved publications, and pertinent studies were selected according to inclusion and exclusion criteria. The inclusion criteria comprised: [1] prospective cohort studies [2], studies reporting relative risk ratios (RRs) or hazard ratios (HRs) along with corresponding 95% confidence intervals (CIs) [3], exposure was dynapenic obese adults and dynapenic obese older adults, and [4] the outcome was all-cause mortality. Exclusion criteria encompassed [1] irrelevant types of studies, including review articles, editorials, commentaries, or studies lacking original data [2], studies lacking a clear definition of low muscle strength [3], studies investigating specific causes of mortality, and [4] studies written in languages other than English.

The meta-analysis was conducted and reported following the guidelines specified in the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) [25]. The PRISMA flow diagram illustrates the study selection process Fig. 1

Data extraction

Two authors independently conducted data extraction. Discrepancies were resolved through discussion until a consensus was reached. Information extracted from the full-text articles included the first author's surname, publication date, country of origin, participant characteristics (such as sample size, age, and sex distribution), duration of follow-up, the definition of low muscle strength and obesity, adjustments made, and outcomes of interest.

Risk of bias assessment

Two investigators evaluated the quality of eligible studies using the Newcastle-Ottawa Assessment Scale (NOS) [26]. Each study was assessed based on three main perspectives: selection (0–4 points), comparability (0–2 points), and outcome (0–3 points), resulting in a score ranging from 0 to 9 points.

Statistical analysis

In this meta-analysis, we applied pooled HRs with their respective 95% CIs to assess the association between dynapenic obesity and all-cause mortality. When studies provided separate data for men and women, we calculated a within-study summary estimate using fixed-effect meta-analysis. Similarly, a summary estimate was computed for studies that reported associations categorized by age or BMI. In cases where studies provided multiple multivariable-adjusted HRs, we selected the most fully adjusted estimate to reduce confounding effects. The random-effects model was employed to compute the pooled HR, considering the heterogeneity among studies and their corresponding effect sizes [27]. We assessed heterogeneity among included studies using the Cochrane Q test and the I2 statistics [28, 29]. A P-value <0.10 for the Q statistics indicated statistically significant heterogeneity, and I2 values of 0%, 25%, 50%, and

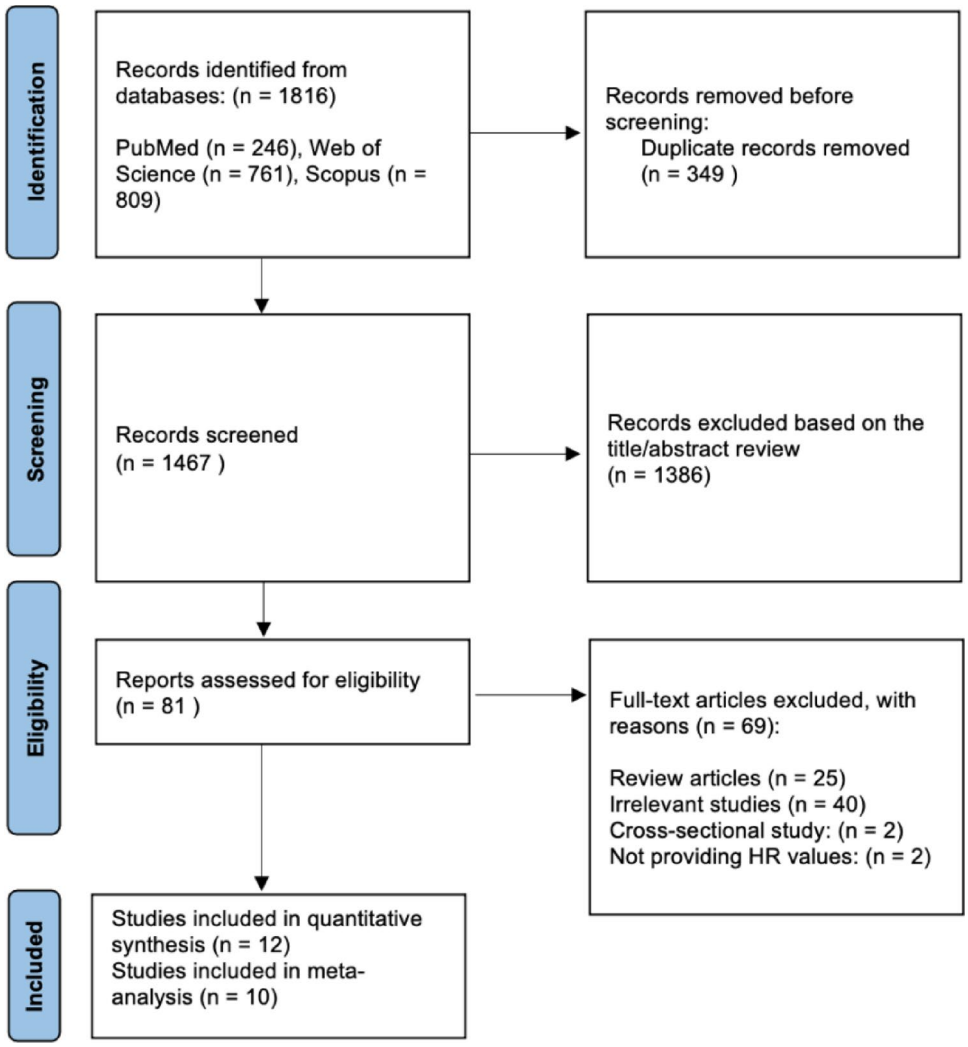


Fig. 1 Flow Diagram of the Study Search and Selection Process

75% represented no, low, moderate, and high heterogeneity, respectively [29]. Two authors independently used STATA version 14.0 (Stata Corp, College Station, Texas, USA) and R for data analysis. A two-sided P-value of <0.05 was considered statistically significant (except for the heterogeneity and Egger's regression tests).

Results

Study selection

A search of online databases resulted in a total of 1816 articles. After eliminating duplicate entries, a total of 1467 distinct records were retained. Following a review of titles and abstracts, 1386 records were excluded. Subsequently, 81 full-text articles were assessed for eligibility, leading to the exclusion of 69 articles. Reasons for exclusion included 25 review articles, 40 studies irrelevant to the topic of sarcopenia, two cross-sectional studies, and studies for not providing HR values. Ultimately, 12 prospective cohort studies were included in the meta-analysis from 10 articles [30–39]. Two articles [34, 37] used both definitions of obesity (BMI and WC). Figure 1 depicts the process of selecting articles included in this meta-analysis.

Characteristics of included studies

Our meta-analysis incorporated twelve prospective cohort studies, encompassing a combined participant pool of 1,309,200 individuals. Among the 12 studies, four were conducted in the UK [32–34], three were multinational [37, 39], two were in Italy [35, 36], one was in China [31], one was in Thailand [30], and one was in Finland [38]. The mean duration of follow-up ranged from 5.1 to 33 years (Table 1). Six studies employed WC as the criterion for defining obesity [31, 34–37, 39], whereas six studies used BMI to define obese individuals [30, 32–34, 37, 38]. Eleven studies utilized low hand grip strength to identify dynapenic

Table 1 Characteristics of 12 prospective cohort studies included in the meta-analysis

Author	Year	Setting	Duration of follow-up	Sample size	Sex	Age range (at baseline)	Dynapenia criteria	Obesity criteria	Adjustments	Outcome
Chen et al. [31]	2023	China	7	3704	Mixed	≥60	Handgrip strength (<28 kg for men and <18 kg for women)	WC (≥90 cm for men and ≥80 cm for women)	Not available	All-cause mortality
Sääksjärvi et al. I [37]	2023	Finland, USA, and Netherland	9.1 for H200, 12.4 for HABC, 10.4 for LASA	4612	Mixed	≥70	Handgrip strength (<27 kg for men and <16 kg for women)	BMI≥30 kg/m2	Age, sex, marital status, education, race, physical activity, alcohol consumption, smoking, and baseline diseases	All-cause mortality
Sääksjärvi et al. II [37]	2023	Finland, USA, and Netherland	9.1 for H200, 12.4 for HABC, 10.4 for LASA	4612	Mixed	≥70	Handgrip strength (<27 kg for men and <16 kg for women)	WC (≥ 102 cm for men and ≥ 88 cm for women)	Age, sex, marital status, education, race, physical activity, alcohol consumption, smoking, and baseline diseases	All-cause mortality
Charatcharoenwitthaya et al. [30]	2022	Thailand	8.5	19,818	Mixed	≥18	Handgrip strength (<28 kg for men and <18 kg for women)	BMI≥25 kg/m2	Age, current smoking, alcohol intake, regular exercise, Charlson comorbidity index, and hyperglycemia/diabetes	All-cause mortality
Farmer et al. [32]	2019	United Kingdom	5.1	452,931	Mixed	40–69	Handgrip strength (<30 kg for men and <20 kg for women)	BMI≥30 kg/m2	Not available	All-cause mortality
Rossi et al. [35]	2017	Italy	11	846	Mixed	65–95	Handgrip strength (<33 kg for men and <19 kg for women)	WC (>99 cm for men and >95 cm for women)	Age, sex, smoking habit, education, medications, diabetes, congestive heart failure, stroke, chronic obstructive pulmonary disease, and coronary heart disease	All-cause mortality
da Silva Alexandre et al. [39]	2017	United Kingdom and Brazil	10	6173	Mixed	≥60	Handgrip strength (<26 kg for men and <16 kg for women)	WC (>102 cm for men and >88 cm for women)	All socioeconomic and behavioral characteristics, clinical conditions, disability, and BMI	All-cause mortality
Hamer et al. [33]	2017	United Kingdom	8	6864	Mixed	66.2±9.5	Handgrip strength (<35.3 kg for men and <19.6 kg for women)	BMI≥30 kg/m2	Age, sex, physical activity, smoking, wealth, depressive symptoms, and chronic illnesses	All-cause mortality

Table 1 (continued)

Author	Year	Setting	Duration of follow-up	Sample size	Sex	Age range (at baseline)	Dynapenia criteria	Obesity criteria	Adjustments	Outcome
Kim et al. I [34]	2017	United Kingdom	7	403,199	Mixed	40–69	Handgrip strength < 27.7 kg	BMI ≥ 30 kg/m2	Ethnicity, smoking status, employment, Townsend Deprivation Index, statin use, hormone replacement therapy (women only), alcohol consumption, processed/red meat consumption, resting pulse rate, and moderate-to-vigorous physical activity time	All-cause mortality
Kim et al. II [34]	2017	United Kingdom	7	403,199	Mixed	40–69	Handgrip strength < 27.7 kg	WC (≥ 102 cm for men and ≥ 88 cm for women)	Ethnicity, smoking status, employment, Townsend Deprivation Index, statin use, hormone replacement therapy (women only), alcohol consumption, processed/red meat consumption, resting pulse rate, and moderate-to-vigorous physical activity time	All-cause mortality
Rossi et al. [36]	2015	Italy	10	262	Mixed	66–78	Leg muscle strength (< 15.33 kg for men and < 8.33 kg for women)	WC (> 100 cm for men and > 87 cm for women)	Age, gender, disability at baseline, low income, actual or past smoking, high alcohol intake, fibrinogen, vitamin D3 level, hypertension, diabetes, hypercholesterolemia, COPD, chronic heart failure, myocardial infarction and stroke	All-cause mortality
Stenholm et al. [38]	2014	Finland	33	2980	Mixed	≥5-	Handgrip strength < 42 kp for men 50–69 and < 28 kp for men ≥ 70; Handgrip strength < 23 kp for women 50–69 and < 18 kp for women ≥ 70	BMI ≥ 30 kg/m2	Age, sex, education, smoking, alcohol use, physical activity, hypertension, cardiovascular disease, diabetes and cancer	All-cause mortality

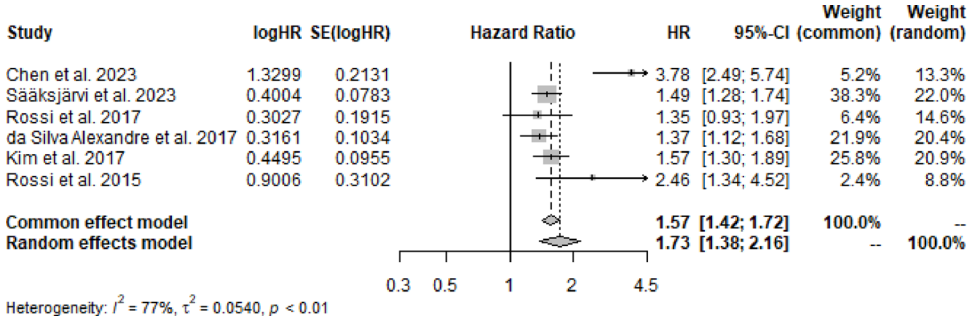


Fig. 2 Forest Plots Demonstrating the Association Between Dynapenic Abdominal Obesity and Increased Risk of All-Cause Mortality

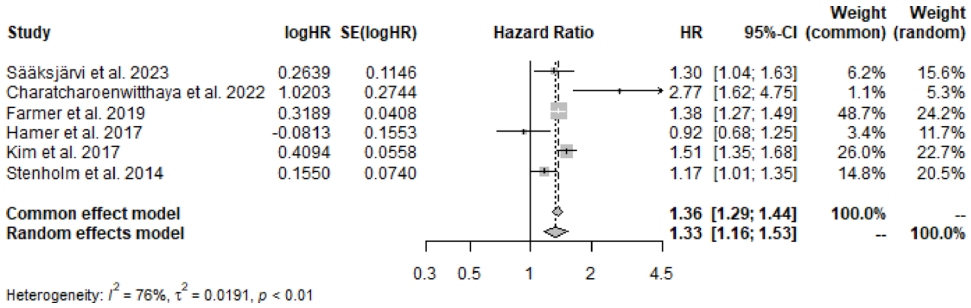


Fig. 3 Forest Plots Demonstrating the Association Between Dynapenic Obesity Defined by BMI and Increased Risk of All-Cause Mortality

individuals [30–35, 37–39], while only one study used low leg muscle strength to characterize dynapenia [36].

Quality assessment

Supplementary File 2 comprehensively describes the methodological quality assessment using NOS. Among the studies, 7 achieved 9 points [30, 33, 35–38], 3 attained 8 points [34, 39], and 2 scored 7 points [31, 32]. The average score is greater than 8 points, indicating high research quality in this meta-analysis.

Dynapenic abdominal obesity mortality

Six prospective cohort studies investigated the correlation between DAO and all-cause mortality in adults [31, 34–37, 39]. We employed a random-effects model to calculate the pooled HR values. As illustrated in Fig. 2, individuals with DAO exhibited a significantly heightened risk of all-cause mortality compared to healthy participants (the reference group). The pooled HR for all-cause mortality in DAO versus non-dynapenic, non-abdominal obese individuals was 1.73 (95% CI = 1.38–2.16), with high heterogeneity observed across these studies (I2 = 77%, p < 0.01).

Dynapenic obesity defined by BMI mortality

We included six prospective cohort studies exploring the relationship between dynapenic obesity (defined by BMI) and all-cause mortality [30, 32–34, 37, 38]. A random-effects model was utilized to calculate the pooled HR values. Figure 3 shows that individuals with dynapenic obesity

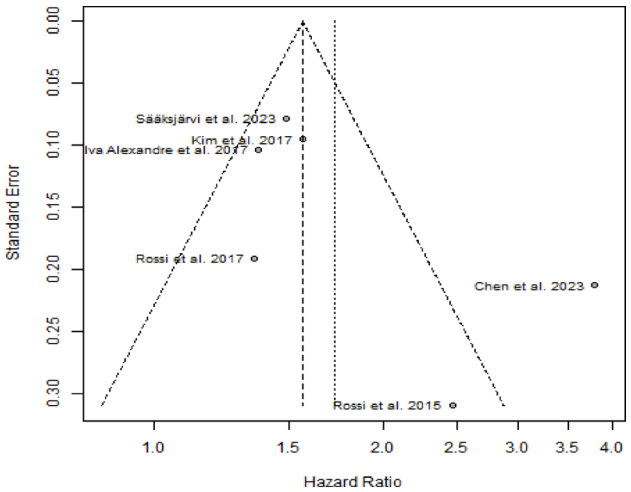


Fig. 4 Funnel Plot Demonstrating the Symmetrical Distribution of Studies Investigating Association Between Dynapenic Obesity Defined by BMI and Increased Risk of All-Cause Mortality

measured by BMI show a significantly increased risk of all-cause mortality compared to healthy individuals. The pooled HR for all-cause mortality in dynapenic obesity measured by BMI versus non-dynapenic non-obese individuals was 1.33 (95% CI = 1.16–1.53), with high heterogeneity observed across these studies (I2 = 76%, p < 0.01).

Publication bias

We assessed the presence of publication bias in the meta-analysis using the funnel plots presented in Figs. 4 and 5. The plots around the central effect estimate revealed a

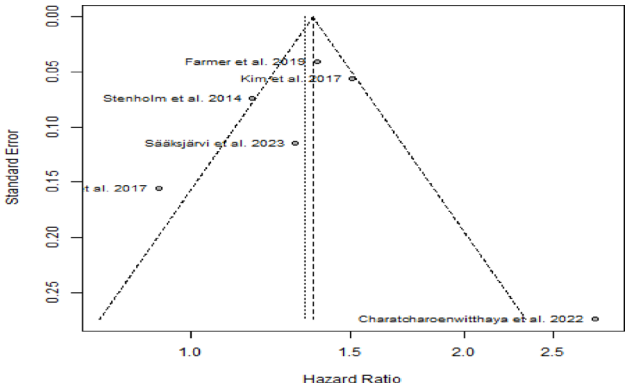


Fig. 5 Funnel Plot Demonstrating the Symmetrical Distribution of Studies Investigating Association Between Dynapenic Obesity Defined by BMI and Increased Risk of All-Cause Mortality

relatively symmetrical distribution of studies, indicating a minimal likelihood of publication bias.

Discussion

The growing prevalence of overweight and obesity has become a global health concern, with substantial consequences for morbidity and mortality [40]. This meta-analysis explored the association between two key factors -low muscle strength and obesity- and their combined impact on all-cause mortality. The results showed a significant association between dynapenic obesity and heightened all-cause mortality risk, with both WC and BMI serving as indicators. The results of this meta-analysis revealed that those with DAO have a significantly increased risk of mortality, 1.73 times greater, compared to those without both conditions. Additionally, our research indicated that dynapenic individuals with obesity (defined as a BMI of ≥25 or 30) have a statistically significant 1.33 times higher risk of mortality compared to those without dynapenia and with a normal BMI. This meta-analysis marks the inaugural investigation into the correlation between dynapenic obesity and the risk of all-cause mortality, drawing upon prospective cohort studies. These studies encompassed diverse geographical locations and varied follow-up durations and employed two distinct definitions of obesity. The observed heterogeneity across studies warrants careful consideration and highlights the need for further research to explore potential contributing factors. Factors such as variations in age, sex, ethnicity, underlying health conditions, measurement techniques for muscle strength and obesity, and differences in follow-up durations may have contributed to the heterogeneity. Subgroup analyses based on gender, setting, and different definitions of low muscle strength and obesity will provide insights into potential sources of heterogeneity. However, additional exploration is warranted to elucidate underlying mechanisms.

The findings of this meta-analysis underscore the significant association between DAO and dynapenic obesity measured by BMI and heightened mortality risk. In line with these findings, previous studies have consistently demonstrated both dynapenia and obesity are independently associated with increased risk for all-cause mortality. For instance, meta-analyses by Flegal et al. [41] and Aune et al. [42] have demonstrated a significant association between obesity, as measured by BMI, and heightened all-cause mortality. Flegal et al. reported an overall summary HR of 1.18, indicating a substantial increase in mortality risk among individuals classified as obese compared to those with normal weight BMI categories. Aune et al. found that for every 5-unit increment in BMI, the relative risk for all-cause mortality increased by 1.05, further emphasizing the detrimental impact of obesity on mortality outcomes. Also, Silva et al. [17] demonstrated that adults with dynapenia had a higher risk for mortality with an HR of 1.29 (95% CI: 0.71–2.34).

Moreover, investigations into specific types of obesity, such as sarcopenic obesity (SO), have also revealed noteworthy associations with increased mortality risk. Studies conducted by Zhang et al. [43] and Tian et al. [44] have reported significant links between SO and elevated all-cause mortality rates. Zhang et al. observed a pooled HR of 1.21 for SO, indicating a substantially higher mortality risk among adult individuals with this condition. Similarly, Tian et al. found a pooled HR of 1.24 for SO, further underscoring the increased mortality risk associated with this phenotype compared to healthy subjects. Our meta-analysis adds to the existing body of evidence by specifically investigating the combined effect of dynapenia and obesity on mortality risk. Our findings support the notion that both DAO and dynapenic obesity measured by BMI presents an even more significant risk factor for mortality compared to obesity alone.

Delving deeper into the underlying mechanisms linking DAO and dynapenic obesity measured by BMI to mortality reveals a complex interplay of factors that merit further investigation. One potential mechanism contributing to the heightened mortality risk observed in individuals with obesity is increased inflammation [45]. WC has been suggested as a proxy measure for regional fat distribution due to its simplicity in measurement and its strong correlation with visceral and total fat, as assessed by computerized tomography [46]. Visceral fat, a characteristic feature of abdominal obesity, releases pro-inflammatory cytokines, which contribute to the development of insulin resistance, hypertriglyceridemia, dyslipidemia, decreased muscle strength, and endothelial dysfunction, all of which are established risk factors for cardiovascular disease [47–50]. This chronic

inflammatory state induced by visceral adiposity likely amplifies the mortality risk through its detrimental effects on cardiovascular health [51, 52]. Similarly, adults with dynapenia are at a higher risk for developing metabolic diseases, such as Lipid disorders, metabolic syndrome, or type 2 diabetes [53]. Individuals with dynapenic obesity exhibit higher levels of low HDL-cholesterol, hypertriglyceridemia, and metabolic syndrome compared to non-dynapenic/non-obese and dynapenic-only groups, underscoring the presence of multiple mortality risk factors in these individuals, thereby heightening their risk of mortality [54]. Moreover, impaired physical function emerges as another critical pathway linking dynapenic obesity to mortality [55]. Reduced muscle strength, a hallmark of dynapenia, not only compromises mobility but also undermines functional independence, predisposing individuals to an elevated risk of falls, accidents, and subsequent hospitalizations [56]. The compromised physical function resulting from dynapenia exacerbates the risk of adverse outcomes, including mortality, highlighting the importance of preserving muscle strength in older adults to mitigate mortality risk [57]. Additionally, poor nutritional status emerges as a significant contributing factor to mortality risk in individuals with dynapenic obesity [58]. Dynapenia may lead to difficulties in maintaining adequate nutritional intake, whether due to challenges in chewing, swallowing, or preparing nutritious meals [59]. This can result in malnutrition, further accelerating the progression of dynapenia and exacerbating the mortality risk associated with dynapenic obesity.

The findings from this meta-analysis have significant implications for clinical practice and public health interventions. Clinicians should recognize the synergistic impact of dynapenia and obesity on mortality risk. Screening for both factors and comprehensive assessments of metabolic health may aid in identifying individuals at heightened risk and facilitate targeted interventions to mitigate adverse outcomes. Public health initiatives to combat obesity should adopt a multifaceted approach that addresses weight management and preserving muscle strength and functionality. Promoting physical activity, particularly resistance training, can help mitigate muscle loss and improve overall strength, reducing the risk of dynapenia. Additionally, strategies to promote healthy dietary habits and reduce central adiposity are essential for mitigating the risk of DAO and its associated complications.

To our knowledge, this is the first meta-analysis of prospective cohort studies investigating the association between dynapenic obesity and risk of all-cause mortality. However, there are several Limitations to acknowledge in this meta-analysis. Firstly, certain articles included in this study did not categorize patients according to the standard WHO BMI classification. Some studies combined normal weight and underweight individuals or overweight and obese individuals, which could impact the reliability of the results. Secondly, we Limited our analysis to Literature published exclusively in English. As a result, we may have unintentionally excluded important studies published in other languages, thus introducing bias into our findings. Furthermore, whereas the HRs for the dynapenic obese group were obtained using the fully adjusted model, the confounding factors exhibited significant variation. Additionally, the duration of the follow-up period showed variation among different research, spanning from 5 to 33 years. It is vital to consider these Limitations when analyzing the findings of the current investigation. However, these Limitations do not diminish the significance of our study, as it boasts several strengths. Firstly, we thoroughly searched multiple databases using a sensitive search strategy. Secondly, all original studies included in the analysis were prospective in design, minimizing potential bias. Thirdly, we employed a rigorous study selection and quality assessment process, which was duplicated. Moreover, due to the substantial sample size, our meta-analysis possessed sufficient statistical power to explore the causal relationship between dynapenic obesity and mortality. Lastly, we utilized adjusted HR with 95% CI from the included studies to derive the pooled estimate, thereby mitigating the influence of confounding factors on the association.

Conclusion

We found that individuals with DAO and dynapenic individuals with obesity (defined by BMI) are associated with a significantly increased risk of all-cause mortality compared to those without dynapenia and with a normal WC or BMI. Further research is warranted to explore potential mechanisms underlying the observed association and to inform targeted interventions to reduce mortality risk in individuals with dynapenic obesity.

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Data availability The datasets analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Conflict of interest The authors declared no potential conflicts of interest regarding this article's research, authorship, and/or publication.

Consent for publication Not applicable.

Ethics Not applicable.

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