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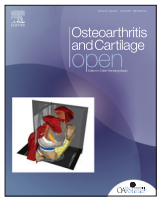

Association between sarcopenic obesity and knee osteoarthritis: A narrative review

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ABSTRACT

Sarcopenia and obesity have been studied independently as risk factors for knee osteoarthritis. However, there is now research interest in investigating whether the co-existence of sarcopenia and obesity (sarcopenic obesity) within the same individual significantly increases the risk of knee osteoarthritis, compared to sarcopenia or obesity alone. This review synthesises current literature to explore the association between sarcopenic obesity and knee osteoarthritis, emphasising both the clinical evidence and existing gaps. We highlight the challenges and progress in defining sarcopenic obesity and discuss the impact that the lack of a consensus definition of sarcopenic obesity has on comparing outcomes of studies investigating the relationship between sarcopenic obesity and knee OA. We offer methodological insights to guide future studies investigating whether sarcopenic obesity increases the risk of knee osteoarthritis above and beyond the risk associated with each condition on its own. The implications for clinical practice are discussed, including the need to incorporate effective resistance exercise into weight loss programs for individuals with sarcopenic obesity. This is critical as a general weight loss program alone among individuals with sarcopenic obesity can include substantial loss of muscle mass, potentially predisposing patients to further functional decline.

1. Introduction

Osteoarthritis (OA) remains a leading cause of disability globally, and it is associated with significant health and economic burdens, including pain, work productivity loss and compromised quality of life [1,2]. OA affects an estimated 654 million individuals worldwide [2], and the prevalence of knee OA, the most commonly reported site for OA, is projected to increase by 75% by 2050 [1]. With no effective disease-modifying therapy, there has been sustained and increasing research interest in identifying modifiable risk factors to reduce the risk and burden associated with knee OA. Changes in body composition, including loss of skeletal muscle mass and function (sarcopenia) and increasing adiposity, have been well-studied as modifiable risk factors for OA. However, both sarcopenia and obesity have generally been studied as independent risk factors [3,4], and there is now research interest in investigating whether the combination of sarcopenia and obesity (sarcopenic obesity) within the same individual significantly increases the risk of musculoskeletal and other health outcomes, compared to sarcopenia or obesity alone. While sarcopenic obesity has been associated with a spectrum of adverse health outcomes, including impaired physical function and metabolic disturbances [5], its potential role as a risk factor for knee OA has garnered limited but growing attention. As the global prevalence of sarcopenia, obesity, and knee OA continues to rise, elucidating the interplay among these conditions becomes crucial for developing holistic, targeted interventions and prevention strategies. Nevertheless, whether sarcopenic obesity should be a distinct disease entity remains an ongoing debate. This review provides a summary of evidence on the relationship between sarcopenic obesity and knee OA. It also offers methodological insights to guide future research endeavours and clinical strategies to mitigate the burden imposed by sarcopenic obesity and knee OA.

2. Defining sarcopenia: progress and challenges

There has been substantial clinical and research interest in sarcopenia since Irwin Rosenberg used the term to describe an age-related decline in

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muscle mass that is associated with detrimental physiological and clinical consequences, including OA. The health impact of sarcopenia is profound, with an estimated yearly cost of £2.5 billion in the UK [6] and $40.4 billion in hospital-related expenditure in the United States [7]. An advancement in the field has been the development of diagnostic criteria to identify individuals with sarcopenia, paving the way for the recognition of sarcopenia as an independent condition with its own ICD-10 code (M62.84) [8]. The earliest definitions of sarcopenia only included low muscle mass, but recent definitions include low muscle strength (e.g., handgrip strength) and/or performance measures (e.g., gait speed). Nevertheless, some challenges remain. For example, multiple diagnostic criteria for sarcopenia have been proposed, and there is no international consensus on the gold standard definition [9]. Hence, the prevalence of sarcopenia among individuals aged 60 years and over varies from 8% to 36%, depending on the diagnostic criteria considered [10].

The definitions of sarcopenia include those proposed by the European Working Group on Sarcopenia in Older People [11], the Sarcopenia Definition and Outcomes Consortium [12], the Foundation for the National Institutes of Health Sarcopenia Project [13], the Society for Sarcopenia, Cachexia, and Wasting Disorders [14] and the International Working Group on Sarcopenia [15]. Ethnic differences in body composition are well established [16], and ethnic-specific definitions of sarcopenia, including the Asian Working Group for Sarcopenia (AWGS) [17] have also been proposed. The various definitions are similar in their assessment of muscle function but somewhat different in how muscle mass is assessed. For example, the Sarcopenia Definition and Outcomes Consortium definition does not assess muscle mass given its weak association with functional outcomes [12].

3. Limitations of measures used to assess muscle mass in the definition of sarcopenia

Most definitions of sarcopenia typically assesses appendicular skeletal muscle mass (ASM) using DXA but is standardised by different anthropometric parameters, including height squared (ASM/ht^2) [11], body mass index (ASM/BMI) [13] and body weight (ASM/weight) [18]. The various measures of muscle mass have implications in defining sarcopenia and characterising an individual as sarcopenic obese. Some of the limitations of these measures of muscle mass are discussed in the following section.

3.1. Limitations of ASM/ht^2

ASM/ht^2 is the first proposed measure of muscle mass and was described by Baumgartner and colleagues [19]. The cut-off used to define sarcopenia is two standard deviations below the value in sex-matched young reference groups [19]. This measure is analogous to those used to define osteoporosis and is widely used in the field. However, because height decreases with advancing age, ASM/ht^2 may not be suitable for determining changes in sarcopenia prevalence over time, as it could result in an artifactual increase in the proportion of individuals with sarcopenia [20,21]. For instance, an artifactual increase of 2.6 kg/m^2 in BMI, a similar measure to ASM/ht^2 (substitutes weight for ASM), has been documented for women aged 80 years [21]. A similar increase of 1.4 kg/m^2 was observed in men of the same age [21]. Furthermore, in the Health Aging and Body Composition (Health ABC) Study, no participant was identified as having sarcopenia using the ASM/ht^2 criteria, and ASM/ht^2 classified fewer obese or overweight individuals as having sarcopenia [22]. Similarly, in a recent Concord Health and Ageing in Men Project study, only 4 of 382 men with obese BMI had sarcopenia using the ASM/ht^2 criteria [23]. ASM/ht^2 was also found to underestimate the prevalence of sarcopenia among obese women in the São Paulo Ageing and Health Study [24]. Obese or overweight individuals with both high lean mass and fat mass may not be classified as having sarcopenia by ASM/ht^2 criteria, even though these individuals have muscle mass that is inadequate for their size and their physical performance [22].

3.2. Limitations of ASM/BMI and ASM/weight

ASM normalised to BMI attempts to account for body size, but it also presents certain limitations. For example, BMI does not distinguish between fat and lean mass; hence, using BMI as a denominator may introduce inaccuracies in assessing muscle mass [5,25]. Also, a low ASM/BMI is closely related to higher adiposity; hence, the association between ASM/BMI and poor health outcomes in older people may be related to obesity rather than low lean mass.

Similar to ALM-to-BMI ratio, ALM normalised to total body weight may underestimate muscle mass in individuals with higher fat mass, particularly in populations with sarcopenic obesity. Furthermore, total body weight can fluctuate due to changes in both muscle and fat mass; hence, considering weight as a denominator may not provide a clear indication of muscle mass changes alone [26]. ALM/weight may also lack sensitivity in detecting changes in muscle mass over time, as alterations in fat mass can confound the interpretation of changes in the ALM/-weight ratio [27]. For instance, due to the increase in fat mass with age, individuals could still maintain or increase their total body weight as they age [27,28]. Nevertheless, ALM normalised to total body weight has been shown to decline with age [18].

The lack of an international consensus on the gold standard definition of sarcopenia has major implications for characterising an individual (and populations) as sarcopenic obese. For example, it is not known which definition of sarcopenia is most clinically important in classifying individuals as sarcopenic obese. A major step towards harmonising the various definitions of sarcopenia is the establishment of the Global Leadership Initiative on Sarcopenia in 2021 [29]. The Global Leadership Initiative on Sarcopenia comprises leading organisations from Europe, Asia, North and South America, Australia, and New Zealand, and it is aiming to provide internationally comparable estimates for sarcopenia and facilitating the assessment of sarcopenia in clinical settings. Its impact is likely to be profound but not yet fully realised as much of the work still underway.

DXA is a reference standard for assessing clinical body composition and identifying low muscle mass in sarcopenia and sarcopenic obesity [30]. However, DXA has some challenges. For example, DXA does not directly measure actual muscle mass, rather it approximates lean mass that includes non-contractile fibrotic and connective tissues [31]. Also, the inability of DXA to distinguish fat infiltration within the skeletal muscle can inflate muscle mass by nearly eight per cent [32]. This measurement error may underestimate the number of individuals classified as sarcopenic [26] and sarcopenic obese. MRI is an advanced imaging technique that can distinguish intramuscular fat infiltration. Nevertheless, MRI is expensive and may not be readily available in some settings [26]. Reassuringly, a strong correlation ($>$0.94) has been reported between MRI and DXA measures of muscle mass, suggesting that the error in the misclassification of an individual as sarcopenic obese is likely to be minimal [26,32,33].

Unlike sarcopenia, there is a widely used internationally recognised indicator (i.e., BMI $\geq$30 kg/m^2) for classifying an individual as obese. However, BMI has major challenges, including the inability to differentiate between fat and lean mass [34] and an artifactual increase due to possible due to height loss with ageing [35]. Also, BMI does not discriminate between visceral and subcutaneous fat, both of which could have a differential impact on OA [25]. For example, compared to subcutaneous fat, visceral fat secretes more pro-inflammatory cytokines, and it is associated with worsening knee pain but not structural changes [36]. Although subcutaneous tissue is associated with osteoarthritic changes, its role in knee OA pathogenesis remains controversial [25]. Indeed, central adiposity increases the risk of mortality even among individuals with normal BMI, highlighting the significance of the pattern of fat distributions within the body. Other measures of adiposity, including waist circumference, fat mass index, and waist to-hip ratio, have been proposed to define excess fat mass in sarcopenic obesity [37]. However, limited studies have investigated the sensitivity of sarcopenic obesity defined

using different measures of adipose tissue to identify individuals at risk of knee OA. This is an important area of research.

4. Defining sarcopenic obesity: progress and challenges

The lack of an internationally accepted definition of sarcopenia and various measures of adiposity poses some challenges in characterising an individual as sarcopenic obese [37]. To establish standardised criteria for identifying and diagnosing sarcopenic obesity, the European Society for Clinical Nutrition and Metabolism (ESPEN) and the European Association for the Study of Obesity (EASO) offer a consensus framework for clinicians and researchers in the field [37]. The proposed criteria provide a basis for consistent identification and study of individuals with sarcopenic obesity.

The ESPEN and EASO diagnostic procedure recommend initial screening for adiposity and sarcopenia (Fig. 1). They proposed screening for sarcopenia using the SARC-F questionnaire and adiposity using ethnic-specific cut-points for BMI or waist circumference [37]. If screening is positive for both high adiposity and probable sarcopenia, then sarcopenic obesity is diagnosed by assessing the individual for altered skeletal muscle function (low handgrip strength or slow chair stands test) and altered body composition (high fat mass and low ASM/W assessed using DXA or bioelectric impedance). The ESPEN and EASO also recommend a two-level staging to describe complications from sarcopenic obesity once the diagnosis is confirmed. Stage one is sarcopenic obesity with no complication and stage two is sarcopenic obesity with complications including metabolic disorders, cardiovascular/respiratory diseases and disability resulting from sarcopenic obesity [37].

Godziuk and colleagues also recommended a systematic approach using relative handgrip strength (grip strength adjusted to BMI) for an initial assessment [30]. This is similar to the EWGSOP-2 case-finding definition for sarcopenia [11]. Low relative handgrip strength (women <0.65 kg/m^2 *vs.* men <1.1 kg/m^2) [30] prompts body composition assessment for further sarcopenic obesity screening [30]. This approach reduces the number of patients subjected to DXA scans. Nevertheless, the cut-points for discriminating low relative handgrip strength were developed among predominantly in a small Caucasian (95%) populations with class II/III obesity (mean BMI: 37.1 kg/m^2 (range: 30 kg/m^2 – 57 kg/m^2). Also, unlike the ESPEN and EASO diagnostic procedure, Godziuk and colleagues' definition were not established by consensus, and the application of their cut-points to other populations warrants further investigation. Indeed, the ESPEN-EASO operational definition appears to provide a valid approach for identifying sarcopenic obesity among obese participants. For example, among 1416 community-dwelling men aged ≥70, only 0.3% were classified as sarcopenic obese when sarcopenic obesity was defined according to the European Working Group on Sarcopenia in Older People criteria and BMI categories [23]. In contrast, 9.6% of the participants were classified sarcopenic obese when the ESPEN-EASO definition was used, and these participants had poorer health outcomes, including muscle function, compared to neither sarcopenia nor obesity [23].

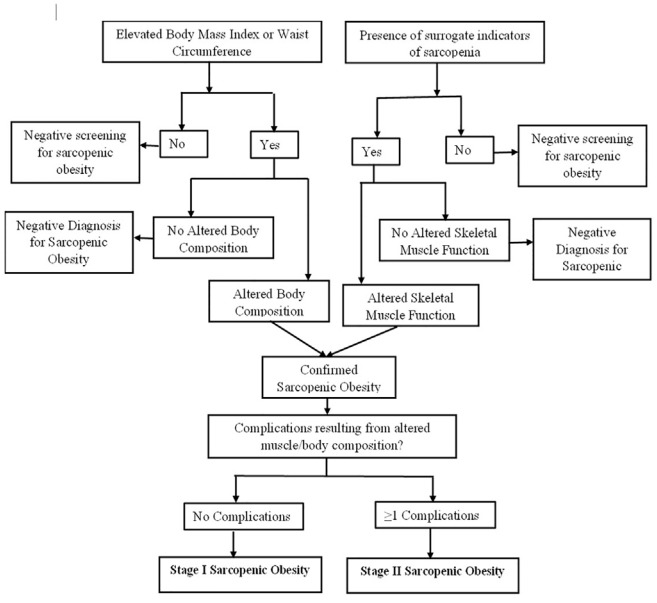

Fig. 1. ESPEN and EASO diagnostic procedure for the assessment of sarcopenic obesity.

5. Sarcopenic obesity and prevalence of knee OA

An increasing number of studies have investigated the relationship between sarcopenic obesity and OA-related outcomes, including prevalence, incidence, and outcomes post-knee/knee joint replacement surgery. The findings from these studies have been mixed, potentially due to inconsistency in the definition of sarcopenia, obesity and sarcopenic obesity. The global prevalence of sarcopenic obesity was estimated to be 11% [38] and its prevalence among people with OA ranges from 0% to 35%, depending on the definition of sarcopenia and measures of adiposity [39–41]. The prevalence of sarcopenic obesity was higher when obesity was defined using either waist circumference or per cent body fat compared to BMI [40,41], suggesting the sensitivity of these indicators to assessing actual adiposity. Also, sarcopenic obesity was more prevalent when sarcopenia was defined as ASM adjusted for weight or BMI, compared to when ASM was adjusted for height squared [40]. Irrespective of the diagnostic criteria considered, the risk and prevalence of sarcopenic obesity increase with age [30,42].

Comparing the relationship between sarcopenic obesity and the prevalence of radiographic knee osteoarthritis or knee pain among studies is challenging. This is because studies use different categories to define sarcopenic obesity and also differ in the comparison groups used for statistical analysis. (Table 1). Most studies reported an elevated risk of OA among individuals who are sarcopenic obese [40,43–45], compared to those with neither sarcopenia nor obesity. Others reported an elevated risk of OA in sarcopenic obese men [40] or women [46] only, compared to those without sarcopenia or obesity. Sarcopenic obese individuals had a higher risk of OA compared to those who were obese non-sarcopenic (i.e., obese only), whereas there was no significant difference in OA risk between sarcopenic obese participants compared to those who were sarcopenic non-obese (i.e., sarcopenic only) [47]. Sarcopenic obesity was also more prevalent among patients with bilateral knee OA compared to those with unilateral radiographic OA, which may be suggestive of cumulative disease burden [40]. Also, individuals with sarcopenic obesity reported a higher risk of pain compared to those with neither sarcopenia nor obesity in most [47,48], but not all studies [39]. Furthermore, individuals with sarcopenic obesity reported higher pain compared to those who are sarcopenic non-obese [48], but there was no difference in pain between sarcopenic obese and obese non-sarcopenic (i.e., obese only) [47].

The pathways through which sarcopenic obesity increases the risk of OA and its complications are unclear, but several mechanisms have been proposed. The possible interconnection between sarcopenic obesity and knee OA involves a complex interplay of biomechanical, inflammatory, and metabolic factors [49]. For example, excess fat accumulation within and around the skeletal muscle may result in a higher concentration of pro-inflammatory cytokines, and these cytokines accelerate the loss of muscle mass and function, leading to joint instability, pain and increasing the risk of OA [48]. Also, excess adiposity contributes to increased mechanical stress on the knee joints, and sarcopenia contributes to muscle imbalance and altered joint loading, particularly in weight-bearing joints such as the knees [49,50]. Hence, the presence of sarcopenia and obesity

Table 1
Studies reporting an association between sarcopenic obesity and knee osteoarthritis.

Author, Year	Study design	Study purpose	Population	Diagnostic criteria for sarcopenia	Definition of obesity	Classification of sarcopenic obesity	Reference group for analysis	Relevant findings
Lee et al., 2012	Cross-sectional	To investigate the relationship between knee OA and four categories of body composition (normal, sarcopenic non-obesity, non-sarcopenic obesity, and sarcopenic obesity)	N = 2893, age≥50 years with bilateral knee OA	ASM/weight, 2SD below the mean of sex-matched young reference group	BMI ≥27.5 kg/m^2	• Normal body composition, • Sarcopenic non-obesity, • Nonsarcopenic obesity, and • Sarcopenic obesity	Normal body composition	Sarcopenic obesity was more closely associated with ROA than nonsarcopenic obesity.
Misra et al., 2019	Longitudinal	To investigate prospective associations between body composition categories and incident knee OA.	N = 1653, mean age 62 years.	Sex-specific lowest quintile of the residuals of ASM adjusted for age, height, and total body fat mass.	The sex-specific highest quintile of total body fat mass. Sensitivity analysis using BMI≥30 kg/m^2	• Non-sarcopenic non-obese, • Obese non-sarcopenic, • Sarcopenic non-obese, and • Sarcopenic obesity	Non-sarcopenic non-obese	Incident ROA was significantly higher among obese women, obese men, and sarcopenic obese women but not among sarcopenic obese men.
Godziuk et al., 2019	Cross-sectional	To identify the prevalence of sarcopenic obesity (using different criteria for sarcopenia) among individuals with end-stage knee OA.	N = 151, mean age 65.1 ± 7.9 years	Assessed and compared three diagnostic criteria for sarcopenia: (1) ASM/height^2 <5.45 for women & <7.26 for men. (2) ASM/weight × 100, <19.43% for women & <25.72% for men. (3) ASM/BMI, <0.512 for women & <0.789 for men.	BMI≥30 kg/m^2, confirmed by sex-specific WC and %FM assessment.	• Non-sarcopenic obese • Sarcopenic obese	Non-sarcopenic obese	- The prevalence of sarcopenic obesity varied from 1.3% to 27.2%, depending on diagnostic criteria for sarcopenia. - No difference in WOMAC scores between Sarcopenic obese and non-sarcopenic obese individuals.
Jin et al., 2017	Cross-sectional	To describe the relationship between sarcopenia, obesity, and knee OA.	N = 1865, age≥65 years	ASM/weight × 100, 2SD below the mean of sex-matched young reference group	BMI ≥25 kg/m^2	• Normal body composition, • Sarcopenic non-obesity, • Nonsarcopenic obesity, and • Sarcopenic obesity	Normal body composition	Women but not men with sarcopenic obesity had an elevated risk of knee OA.
Razaq et al., 2023	Cross-sectional	To investigate the relationship between sarcopenic obesity and knee OA.	N = 140, age ≥45 years	ISarcoPRM algorithm [15], which assesses regional measurements and functional evaluation of anterior thigh muscle.	BMI ≥30 kg/m^2	• Non-sarcopenic non-obese, • Sarcopenic only, • Obese only, and • Sarcopenic obesity	Non-sarcopenic non-obese	Knee OA risk was significantly elevated among those who were sarcopenic obese but not among those with sarcopenia or obesity alone.
Manoy et al., 2017	Cross-sectional	To investigate the relationships between vitamin D, leptin, muscle strength and performance in knee OA patients.	N = 208, mean age ≥65 ± 7 years.	ASM/weight × 100; cut-off was <30.44% in men and <25.81% in women.	BMI ≥25 kg/m^2	• Normal weight • Obese • Sarcopenic obese	• Normal weight • Obese • Normal weight and obesity combined.	Sarcopenic obese had higher WOMAC total and higher pain and disability subscale, but not stiffness, compared to non-sarcopenic non-obese. There is no difference in WOMAC scores between sarcopenic obese and obese only.
Liao et al., 2023	Cross-sectional	Identify the prevalence and association of sarcopenic obesity with end-stage knee OA.	Adults with unilateral (n = 67, mean age 68.7 ± 9.62) and bilateral knee OA (n = 71, mean age 68.07 ± 9.88 years)	Assessed and compared three diagnostic criteria for sarcopenia: (1) ASM/height^2 <5.7 for women & <7.0 for men. (2) ASM/weight × 100,	Assessed and compared three definitions of obesity BMI ≥30 kg/m^2 and sex-specific	• Sarcopenia • Obesity • Sarcopenic obesity	Not applicable. The study compared the prevalence of sarcopenic obesity among individuals with unilateral and bilateral knee OA, using	Sarcopenic obesity was more prevalent among individuals with bilateral knee OA compared to those with unilateral knee OA.

(*continued on next page*)

Table 1 (*continued*)

Author, Year	Study design	Study purpose	Population	Diagnostic criteria for sarcopenia	Definition of obesity	Classification of sarcopenic obesity	Reference group for analysis	Relevant findings
				<19.43 for women & <25.72 for men. (3) ASM/BMI, <0.512 for women & <0.789 for men.	WC and %FM assessment.		different diagnostic criteria for sarcopenia and obesity.	
Kim et al., 2022	Cross-sectional study	To investigate the prevalence of sarcopenia, obesity, and sarcopenic obesity and their relationship with knee pain and ROA in postmenopausal women.	N = 4150, mean age 62.41 ± 0.25 years	ASM/weight, 2SD below the mean of sex-matched young reference group	BMI ≥25 kg/m^2	• Non-sarcopenic non-obese, • Sarcopenic only, • Obese only, and • Sarcopenic obesity	• non-sarcopenic non-obese, • sarcopenic obese, • obese non-sarcopenic	- Knee pain and ROA were more prevalent among sarcopenic obese individuals compared to those with neither sarcopenia nor obesity. - Sarcopenic obese individuals also had higher knee pain and ROA compared to sarcopenic non-obese. - There is no significant difference in pain and ROA between sarcopenic obese and obese only.

WC: Waist circumference, FM: Fat mass, BMI: Body mass index, OA: Osteoarthritis, WOMAC: Western Ontario and McMaster Universities Arthritis Index; ROA: Radiographic knee OA.

within the same individual could potentially accelerate OA disease progression because sarcopenia confers additional risks besides the consequences of excess adiposity. Furthermore, obesity alters gait parameters, including stride length and stance, leading to reduced gait speeds [51]. Muscle weakness also alters gait kinematics [3] and the compounded influence of sarcopenia and obesity could impact joint biomechanics. It is worth noting that individuals who are nonsarcopenic nonobese were used as the reference category for most analyses. The implication of this is discussed below.

While obesity and sarcopenia often coexist, they can also occur independently, suggesting that these conditions may have distinct underlying mechanisms [52]. The pathophysiological process underlying the independence of obesity and sarcopenia in sarcopenic obesity is unclear. However, several biological connections have been speculated. For example, the decline in physical activity with ageing reduces the trophic effect on muscle and increases energy imbalance and fat mass [53]. The increasing excess adiposity promotes the production of interleukin-6 and other adipocytes that may have a potential direct catabolic effect on muscle [53]. This may create a vicious cycle such that the accumulation of fat reinforces the loss of more muscle [52,53].

6. Sarcopenic obesity and incident knee OA

There appear to be sex differences in the relationship between sarcopenic obesity and incident radiographic knee OA. For example, among participants from the Multicentre OA Study, obesity, with or without sarcopenia, was associated with an increased risk of incident radiographic knee OA in women only [45]. In contrast, an elevated risk of incident radiographic knee OA was found among men with obesity alone but not among those who were sarcopenic obese [45]. Notably, sarcopenic non-obesity was not associated with an elevated risk of incident OA in either men or women. This may suggest that the additional risk of OA among individuals with sarcopenic obesity may be largely due to excess adiposity, while muscle mass has a lesser independent effect.

7. Sarcopenic obesity and total knee arthroplasty

Sarcopenic obesity was associated with end-stage radiographic knee OA [40], and an increased risk of knee joint arthroplasty, post-operative recovery and complications after the procedure have been reported among individuals who are sarcopenic obese [51,54], although the reference category used for analysis in these studies differs. For instance, among community-dwelling older adults followed prospectively over 13 years, knee arthroplasty was more prevalent among older adults who had both obesity and muscle weakness, compared to those with obesity or muscle weakness alone [54]. Nonetheless, obesity combined with low muscle strength did not lead to a significantly greater risk of knee arthroplasty compared to those with low muscle strength or obesity alone [54].

Obesity is an established risk factor for post-operative complications [55], and sarcopenia is associated with an elevated risk of infection post-total knee arthroplasty [56]. Hence, sarcopenic obesity could worsen patients' recovery post knee arthroplasty and potentially contribute to dissatisfaction after the procedure. For example, functional limitation is one of the two leading reasons for patients' dissatisfaction after total knee arthroplasty [57], and sarcopenic obesity has been shown to contribute to functional impairment post-knee joint replacement surgery [51,58].

Among patients who underwent primary unilateral total knee arthroplasty, those who were sarcopenic obese, sarcopenic nonobese and nonsarcopenic obese had a higher risk of mobility impairment compared to those with neither sarcopenia nor obesity [58]. Nevertheless, participants with sarcopenic obesity had the highest risk of mobility impairment, even after adjusting for pre-operative gait speed. Poor knee flexion range of motion post knee replacement surgery has also been reported among OA patients with sarcopenic obesity compared to those who were

non-obese [51]. Similarly, among patients who underwent total hip arthroplasty, obesity was associated with prolonged length of hospital stay and recovery only in patients with muscle weakness [59], further highlighting the potential additive effect of sarcopenic obesity.

8. Analytical consideration for studies investigating sarcopenic obesity and OA

There is ongoing debate regarding whether sarcopenic obesity should be a distinct disease entity from each component condition. Indeed, there is a pathophysiological overlap between sarcopenia and obesity; nevertheless, a causal relationship has yet to be proven [60]. Limited studies have documented evidence of an additive or multiplicative interaction between sarcopenia and obesity [60], as very few have compared individuals with sarcopenic obesity to those with obesity or sarcopenia alone. For example, many previous studies investigating the relationship between sarcopenic obesity and OA-related outcomes used analytical approaches which did not allow the exploration of whether sarcopenic obesity is clinically worse than having either sarcopenia or obesity alone. Most studies classified their participants into four mutually exclusive categories depending on their sarcopenic or obesity status (non--sarcopenic non-obese, sarcopenia alone, obesity alone and sarcopenic obesity). Thereafter, they performed their statistical analysis comparing those with sarcopenic obesity (and those with sarcopenia or obesity alone) to those who were non-sarcopenic non-obese (i.e. healthy individuals). This approach does not evaluate whether sarcopenic obesity increases the risk of OA compared to either condition on its own. Rather, it assesses whether OA risk is higher among those with sarcopenic obesity relative to the 'healthy' population with no sarcopenia or obesity. Other studies categorised their study populations as having sarcopenic obesity or not, with their reference group including a combination of participants who had sarcopenia or obesity alone and those with neither sarcopenia nor obesity. This approach makes it challenging to ascertain whether OA-related outcomes are higher in sarcopenic obese compared to those with sarcopenia or obesity alone [30].

A cross-sectional analysis of participants from the Korea National Health and Nutrition Examination Survey demonstrates that knee pain and radiographic knee OA were most prevalent among participants with sarcopenic obesity, compared to those with neither sarcopenia nor obesity. There was no difference in pain and OA between sarcopenic obese participants and those with obesity alone. However, sarcopenic obese participants had greater pain and radiographic OA compared to those with sarcopenia alone. Also, among community-dwelling older people followed prospectively for 13 years, obesity combined with low muscle strength did not lead to a significantly greater risk of total knee arthroplasty than having low muscle strength or obesity alone [54]. This may suggest that combining muscle and fat assessments may not provide better predictive ability than each condition on its own for future risk of total knee arthroplasty [54].

9. Clinical considerations for intervention opportunities in OA patients with sarcopenic obesity

Exercise is one of the most effective non-surgical treatments for knee OA and the benefit of weight loss in reducing the burden of OA is relatively well-established [61]. However, general weight loss in individuals with sarcopenic obesity may not be optimal as this can include a substantial loss of muscle mass, potentially predisposing patients to further functional decline and metabolic dysfunction of the muscle tissue [62]. For example, among obese patients with knee OA, a 16-week low-energy diet-induced weight loss intervention was associated with a loss of total body and leg lean mass, in addition to loss of fat mass [62]. This highlights the need to incorporate effective muscle hypertrophy-oriented resistance exercise into weight loss programs to ensure the preservation or improvement in muscle mass and function while reducing adiposity [39,44,63,64]. Protein supplementation may also enhance the beneficial effects of resistive exercises and help mitigate against undesirable muscle loss [65].

10. Conclusion

There is great interest in identifying OA phenotypes to better target prevention and management strategies. Sarcopenic obesity may represent a condition that could be targeted with specific interventions. Sarcopenia, obesity, and knee OA represent prevalent and interconnected health conditions that have garnered increasing attention in both clinical and research settings. However, limited studies to date have examined whether sarcopenic obesity as a condition is associated with worse knee OA prognosis than either condition on their own. Understanding the intricate relationship among these conditions is of paramount importance as it may provide insights into shared pathophysiological mechanisms and inform novel strategies for prevention and management. Weight loss and protein supplementation, combined with resistance training for people with obesity and knee OA, regardless of their sarcopenic obesity status may hold promise as an intervention to improve patients' outcomes. is likely to be beneficial in improving function.

Authors' contribution

SB, DS and DA contributed to the conception and design of the review. SB prepared the first draft of the manuscript and SB, DS, and DA contributed to the critical revision of the manuscript for important intellectual content. SB, DS and DA approved the final version of the manuscript.

Declaration of competing interest

All authors declare that they have no financial and personal relationships with other people or organisations that could inappropriately influence (bias) this manuscript.

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