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OPINION PAPER

What's in a name revisited: should osteoporosis and sarcopenia be considered components of "dysmobility syndrome?"

N. Binkley · D. Krueger · B. Buehring

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Abstract Sarcopenia and osteoporosis are age-related declines in the quantity and quality of muscle and bone respectively, with shared pathogeneses and adverse health consequences. Both absolute and relative fat excess, i.e., obesity and sarcopenic obesity, contribute to disability, falls, and fractures. Rather than focusing on a single component, i.e., osteoporosis, sarcopenia, or obesity, we realized that an opportunity exists to combine clinical factors, thereby potentially allowing improved identification of older adults at risk for disability, falls, and fractures. Such a combination could be termed dysmobility syndrome, analogous to the approach taken with metabolic syndrome. An arbitrary score-based approach to dysmobility syndrome diagnosis is proposed and explored in a small cohort of older adults. Further evaluation of such an approach in large population-based and prospective studies seems warranted.

Keywords Dysmobility · Falls · Fracture · Sarcopenia

Introduction

In a recent Osteoporosis International editorial, Siris et al. called for the field to move beyond simply using bone mineral density (BMD) to diagnose osteoporosis and suggested that elevated fracture risk is the disease in need of intervention [1]. This is certainly correct, but we believe it is appropriate to extend this approach beyond osteoporosis and suggest utilizing risk of impaired mobility, fractures, and falls to diagnose "dysmobility syndrome." In this case, dysmobility, i.e., difficult or impaired mobility, refers to a combination of conditions including sarcopenia, obesity, and mobility impairment that lead to an increased risk of adverse musculoskeletal outcomes such as falls and fractures. A comparable approach has been employed and is clinically widely accepted with metabolic syndrome in which an amalgamation of factors, e.g., obesity, hypertension, diabetes, lipid, and blood pressure status, is recognized as a contributor to adverse cardiovascular outcomes [2, 3]. It seems plausible that such an approach could unify osteoporosis, sarcopenia, and sarcopenic obesity to enhance identification of those most at risk of adverse musculoskeletal consequences. This work overviews the rationale behind considering dysmobility syndrome and explores one example of such an approach.

N. Binkley (✉) · D. Krueger · B. Buehring
Osteoporosis Clinical Research Program, University of Wisconsin, 2870 University Avenue, Suite 100, Madison, WI 53705, USA
e-mail: nbinkley@wisc.edu

Are osteoporosis and sarcopenia the same disease?

Sarcopenia, the age-related decline in muscle mass and function is associated with increased risk of disability, falls, and low bone mineral density [4, 5]. It is therefore not surprising that recent reports find sarcopenia and osteoporosis commonly co-exist in older adults who have sustained a hip fracture [6, 7]. Indeed, the parallels between osteoporosis and sarcopenia are striking [8]. Both are age-related decrements in mass and quality of bone and muscle, respectively [9]. Both cause major personal morbidity, increase healthcare costs, and reduce quantity/quality of life. Moreover, both are multifactorial in origin being caused (at least in part) by inflammation, hormonal and/or nutritional deficits, toxins, and sedentariness [10]. Thus, it could be argued that

they are the same disease manifest in different physiologic systems. However, while osteoporosis is widely recognized, sarcopenia remains largely unknown and undiagnosed in clinical care. In part, this clinical nonrecognition reflects lack of a single consensus definition; clearly, the osteoporosis field advanced coincident with widespread adoption of a diagnostic approach provided by the World Health Organization classification based on BMD [11]. This approach provided a framework to increase disease recognition, allowed clinical application, and facilitated medication development. However, it is apparent that bone loss, and thus low bone mass, is not sufficient to explain the dramatic increase in fracture risk with advancing age. Most simply, there is not an exponential decline in BMD coincident with the near exponential increase in fracture risk in older age. This has been recognized and it is now widely appreciated that a simple mass-based approach is not ideal to identify those at risk for fragility fracture; this appreciation has led to development of fracture risk calculators such as FRAX [12]. Such calculators are a major advance, but remain imperfect as some individuals currently identified as being at low risk do sustain fragility fracture [13]. Perhaps these individuals at "low risk" simply sustained falls to cause their fracture. Thus, while an oversimplification, we believe that much of the increased fracture risk currently attributed to advancing age results from impaired mobility ("dysmobility") leading to falls and resulting in fractures [14]. If this is correct, clinical recognition and resulting treatment of dysmobility syndrome could be a major advance in care of older adults.

Is another syndrome needed? Why not just diagnose sarcopenia?

As noted above, it seems likely that sarcopenia, the age-related decline in muscle mass and function, [15] is a major contributor to the increased falls and fracture risk seen with advancing age [5, 16, 17]. However, despite burgeoning interest in and expansion of pathophysiologic knowledge regarding sarcopenia, there has been virtually no translation of this entity to clinical care. In part, this reflects lack of widespread agreement on diagnostic criteria [5]. Two recent consensus definitions recognize that a singular measurement of muscle mass (analogous to the BMD-based approach to osteoporosis) is inadequate [18, 19] and recommend measurement of muscle mass plus function [20, 21]. However, these existing definitions are not identical and do not identify the same individuals as sarcopenic. Clearly, harmonization of diagnostic criteria is needed. Furthermore, both recent consensus definitions require low muscle mass as a prerequisite—in other words, it is not possible to have sarcopenia (and therefore identify an individual as being at risk) if the muscle mass is normal. Such an approach seems too "black and white" in that if this were applied to osteoporosis, it would mean that osteoporosis could not be diagnosed without a T-score below −2.5. Obviously, this is not the case as the majority of fragility fractures occur in people with BMD T-scores better than −2.5.

Importantly, current sarcopenia definitions do not consider fat mass. A relative excess of adipose mass in conjunction with deficient muscle mass is termed "sarcopenic obesity" [22, 23]. Simplistically, a high ratio of fat to lean mass places additional demands on an inadequate locomotor system. Moreover, intramuscular adipose tissue reduces mobility performance [24]. As such, one could expect sarcopenic obesity would lead to adverse outcomes. Consistent with this, some, but not all [25], studies find sarcopenic obesity to be associated with impaired function and to increase disability risk [26–29]. While one could assume that overweight individuals would be at lower fracture risk due to greater mechanical load, recent work finds overweight and obese older adults to be at substantial fracture risk [30, 31]. It is not surprising that there is not a simple relationship between fat and fracture. Indeed, the complex interrelationships of fat, bone, muscle, and fracture are increasingly being recognized [32–35]. It is logical that this risk results from impaired function and higher falls risk; consistent with this, recent work finds obese older adults to have higher falls risk [36]. Clearly, consideration of adipose status must be included in a clinical definition that is linked to adverse health consequences. Singular focus upon muscle mass/function, i.e., sarcopenia, is therefore inadequate. As such, we propose to include consideration of fat mass in the term "dysmobility syndrome" to improve identification of older adults at risk for falls and fractures. We suggest that this syndrome could include low bone mass, low muscle mass, low muscle function, and relatively high fat mass among others. Such an approach is not a new concept; using a combination of factors associated with adverse health consequences to define a syndrome is widely accepted clinically in the case of metabolic syndrome [2, 3]. Recognition of a syndrome complex appropriately returns focus to the entire patient, not simply to his/her bones or muscles. This is certainly not a new concept; to paraphrase William Osler, it is necessary to treat the patient, not the disease. Indeed, comprehensive treatment of bone, muscle, and falls risk has been documented to reduce nursing home readmission and mortality following hip fracture [37].

Linking a diagnosis of dysmobility syndrome to measureable adverse clinical outcomes is necessary. Such linkage would facilitate disease recognition by healthcare authorities with resultant necessary resource allocation. Potential outcomes include mobility disability, hospitalizations, falls, fractures, and even mortality [6, 38–40]. Consensus would need to develop regarding the choice of outcome(s) most appropriately related to dysmobility, thereby allowing use of these endpoints in clinical trials of pharmacologic agents to mitigate

this syndrome [5, 41]. Subsequently, it is to be expected that these endpoints will be used to document efficacy of pharmacologic interventions. Moreover, it is reasonable that intervention thresholds for such future agents be based on risk of adverse outcomes, analogous to the approach currently recommended for osteoporosis therapy based upon estimation of fracture risk [12, 42–45]. To this end, we suggest the concept that a score-based, i.e., "FRAX®-like," approach, utilizing a combination of factors to estimate risk of future adverse health outcomes, is reasonable and timely for the diagnosis of dysmobility syndrome.

A score-based approach to dysmobility syndrome: proof of concept study

The approach utilized in the development of FRAX is instructive; risk factor(s) chosen for this approach will require robust data documenting their association with adverse outcomes, be intuitive to clinicians and readily available to primary care providers [46]. To begin exploring the feasibility of such an approach, we compared the prevalence of dysmobility syndrome using an arbitrary score-based approach with the prevalence of sarcopenia using published definitions in a small convenience sample of older adults. In this exploratory evaluation, dysmobility was defined arbitrarily using factors associated with adverse outcomes and arbitrarily equally weighted (1 point per risk factor) for a total possible score of six. These factors (specifics noted below) included osteoporosis, low lean mass, history of falls within the past year, slow gait speed, low grip strength, and high fat mass. Dysmobility was considered to be present if the composite score was 3 or higher. We also explored the prevalence of prior falls and fractures in individuals classified as having dysmobility compared with those identified as having sarcopenia.

This evaluation included 97 Caucasian older adults (49 women/48 men). These independently living community dwelling or retirement community research volunteers age 70+ participated in a study of muscle function testing. Volunteer mean (range) age and BMI was 80.7 (70–95)years and 25.6 (15–36)kg/m^2, respectively with no difference between genders. Twenty-four (15 women/9 men) reported a fall within the last year, and prior fragility fracture(s) were present in 30. Total body composition was measured using a dual-energy X-ray absorptiometry (DXA), while self-selected gait speed was determined by a 4-m walk and grip strength with a hand-held dynamometer. Self-reported falls and fracture histories were obtained.

Appendicular lean mass (ALM) ratio is the lean mass of the arms plus legs corrected by height (ALM/height^2). Low ALM/height^2 was defined using published values of 5.45 and 7.26 kg/m^2 for females and males, respectively [15]. These lean mass values defined by DXA were originally described based on comparison with young normal populations [15] and have subsequently been endorsed in sarcopenia consensus definitions [20, 21]. Osteoporosis was defined by the WHO classification, i.e., a T-score of less than or equal to −2.5 at the lumbar spine, femoral neck, or total proximal femur. As no consensus definition of sarcopenic obesity exists [23], obesity was considered to be present simply based on DXA-measured total body percent fat using recently published cutpoints [27]. Slow gait speed was defined as <1.0 m/s [20]. It should be noted that a consensus definition of "slow gait" does not exist and others recommend 0.8 m/s [21]. Low grip strength as measured by hand-held dynamometer was defined as <30 kg (male) and <20 kg (female) [21]. It is recognized that all of these cutpoint values are arbitrary, potentially contentious, and

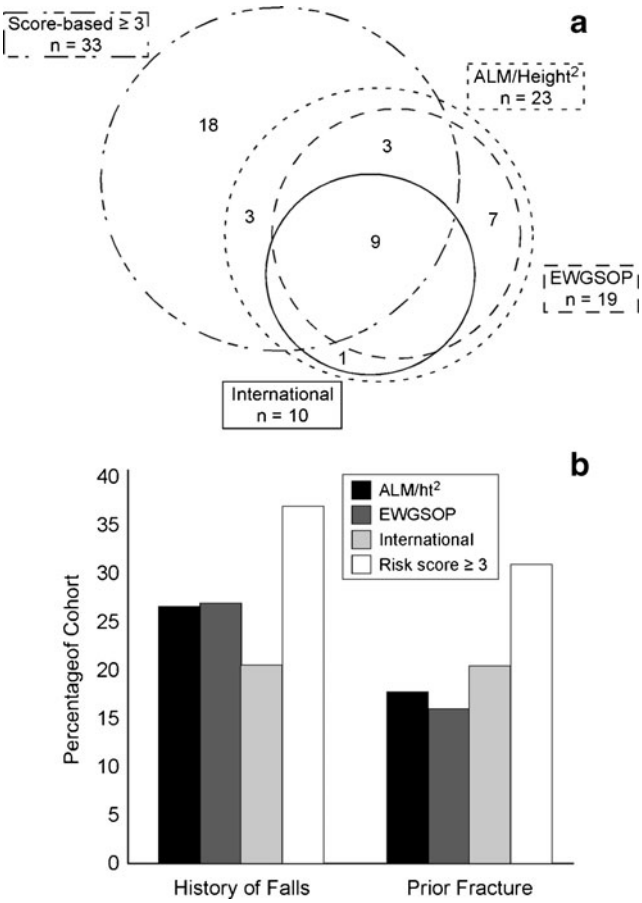

Fig. 1 Comparison of sarcopenia and dysmobility syndrome. In this cohort of 97 older adults, application of three approaches to diagnose sarcopenia, and an arbitrary score-based approach to diagnose dysmobility syndrome, identifies different individuals as being "at risk" (**a**). Self-reported falls and prior fragility fracture were numerically more common in individuals with dysmobility syndrome (36 and 30 %, respectively) than in those diagnosed with sarcopenia by any of the three approaches (**b**). *ALM/ht^2* appendicular lean mass/height^2, *EWGSOP* European Working Group on Sarcopenia in Older People, *International* International Working Group on Sarcopenia

may very well require refinement and alteration if the dysmobility syndrome concept moves forward. Nonetheless, these values were based upon published work and as such seem appropriate to select for this exploratory assessment.

Disease prevalence (i.e., sarcopenia or dysmobility) ranged from 10 to 34 % based on the definition applied, and the various definitions identify somewhat different populations as sarcopenic (Fig. 1a). Of those diagnosed with dysmobility syndrome using this score-based approach, 30 % had prior fragility fracture and 36 % a fall within the last year (Fig. 1b), roughly the expected prevalence of fractures and falls among older adults.

Is dysmobility syndrome an approach worthy of consideration?

The basic tenant underpinning this opinion paper is that improvement in clinical identification of older adults at risk for adverse musculoskeletal outcomes (e.g., mobility disability, falls, and fractures) is needed and timely. We believe that lessons from the osteoporosis field, plus the approach taken with metabolic syndrome, provide a blueprint to further advance care of older adults by providing a risk factor-based approach for diagnosis which is then linked to quantifiable adverse health outcomes.

In this exploratory evaluation, disease prevalence (either dysmobility syndrome or sarcopenia) varied depending on the definition used. This highlights the need to develop widespread agreement regarding any definition if the field is to move forward. Interestingly, this arbitrary score-based approach identified 34 % of this cohort as having dysmobility syndrome and therefore at risk, surprisingly similar to the annual incidence of falls in older adults.

Clearly, suggesting the diagnosis of dysmobility syndrome based upon compilation of risk factors for adverse outcomes is novel and the factors selected arbitrary. An important limitation of the approach proposed is that the factors chosen and cutpoints applied here are almost certainly not ideal. For example, it is logical that neurological disease (e.g., stroke and peripheral neuropathy), joint disease (e.g., osteoarthritis), and vascular disease (e.g., peripheral vascular disease) also contribute to dysmobility. While it is possible that gait speed captures these conditions, further evaluation of the relationship of candidate risk factors with outcomes (along the lines utilized in the development of FRAX) and comparison with currently proposed definitions is certainly necessary. Nonetheless, we believe that this approach has potential clinical utility in that it is intuitive to clinicians and builds upon prior approaches that have widespread clinical acceptance. We are hopeful that a similar approach will be evaluated in larger epidemiologic studies with multiple outcomes such as mobility disability, fractures, falls, and mortality to identify the combination of factors best able to predict adverse musculoskeletal outcomes in older adults.

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