CURRENT OPINION / OPINION COURANTE

Evolution of sarcopenia research

Ian Janssen

Abstract: The term "saropenia" was coined by Irwin Rosenberg in 1989 to refer to age-related loss of skeletal muscle mass. The purpose of this current opinion is to provide an evolutionary overview of sarcopenia research since 1989. This includes the creation of an operational definition of sarcopenia; consideration of the impacts of sarcopenia on physical function, chronic disease, and mortality risk; the distinction between the process of sarcopenia and the process of age-related loss of muscle strength, a phenomenon that has recently been termed dynapenia; a comparison of the independent effects of sarcopenia and dynapenia on physical function, chronic disease, and mortality risk; and consideration of the combined influence of sarcopenia and dynapenia with obesity (i.e., sarcopenic-obesity and dynapenic-obesity) on physical function, chronic disease, and mortality risk.

Key words: aging, skeletal muscle, muscle strength, obesity.

Résumé : Irwin Rosenberg fut le premier à introduire en 1989 le terme « sarcopénie » comme étant la perte de la masse musculaire squelettique liée au vieillissement. Ce texte se propose de présenter un aperçu de l'évolution de la recherche sur la sarcopénie depuis 1989. On y lit la présentation d'une définition opérationnelle de la sarcopénie; l'impact de la sarcopénie sur les fonctions physiques, les maladies chroniques et le risque de mortalité; la distinction entre le processus de sarcopénie et la dynapénie, un phénomène défini récemment comme un processus de perte de force musculaire lié au vieillissement; la comparaison des effets indépendants de la sarcopénie et de la dynapénie sur les fonctions physiques, les maladies chroniques et le risque de mortalité; et la présentation des effets combinés de la sarcopénie et de la dynapénie en présence d'obésité (l'obésité sarcopénique et l'obésité dynapénique) sur les fonctions physiques, les maladies chroniques et le risque de mortalité.

Mots-clés : vieillissement, muscle squelettique, force musculaire, obésité.

[Traduit par la Rédaction]

Introduction

One of the most dramatic age-related anatomical changes is that which occurs to skeletal muscle mass. In 1989, Irwin Rosenberg coined the term "sarcopenia" to refer to the process of age-related loss of skeletal muscle mass and size (Rosenberg 1989). The term sarcopenia comes from the Greek words *sarx* (flesh) and *penia* (loss). Rosenberg's reason for creating a medical term for age-related muscle loss was to bring increased awareness and attention to this issue, which he felt was greatly underappreciated and understudied. True to form, research on the process, causes, consequences, and treatment of age-related muscle loss exploded in the 1990s.

The results of several longitudinal studies, with follow-up lengths of up to 12 years, suggest that muscle mass decreases by approximately 6% per decade after mid-life (Janssen and Ross 2005). Thus, a typical 85-year-old will have a muscle mass that is three quarters of what it was when they were 45 years old. Unfortunately, it appears that everybody loses muscle mass as they age (Janssen and Ross 2005). Even older adults who are active and healthy are not immune to the sarcopenia process. Thus, according to the definition proposed by Rosenberg, the prevalence of sarcopenia in the older adult population is 100%. However, it is important to recognize that there are considerable interindividual differences in peak muscle mass (e.g., muscle mass at ~25 years), the age at which muscle loss begins, and the rate at which muscle is lost. Therefore, some older adults have a muscle mass that is comparable to most young adults, whereas others have a muscle mass that is so low their ability to perform simple functional tasks may be compromised.

In light of these issues, in 1998, Rick Baumgartner proposed an alternative strategy for identifying individuals with sarcopenia (Baumgartner et al. 1998). This alternative strategy has proven to be particularly useful for making comparisons in research studies. Essentially, Baumgartner proposed a dichotomous process to determine which older persons have unhealthy (i.e., sarcopenic) or healthy (i.e., normal) muscle mass values. More specifically, sarcopenia was defined as a height-adjusted muscle mass (muscle mass·height^{-2}) of 2 SDs or more below the mean of a young

Received 7 April 2010. Accepted 7 August 2010. Published on the NRC Research Press Web site at apnm.nrc.ca on 29 September 2010.

I. Janssen. School of Kinesiology and Health Studies, and Department of Community Health and Epidemiology, Queen's University, Kingston, ON K7L 3N6, Canada (e-mail: ian.janssen@queensu.ca).

reference population. Using this strategy, the prevalence of sarcopenia in the New Mexico Elder Health Survey was 14% in those aged 65–69 years, and >50% in those 80 years or older (Baumgartner et al. 1998). As reviewed elsewhere, other researchers have employed a similar threshold approach for classifying sarcopenia (Janssen and Ross 2005). Other strategies have also been used to develop cut-points to distinguish between sarcopenic older adults and older adults with a relatively healthy muscle mass (Janssen and Ross 2005).

Influence of sarcopenia on functional impairment and physical disability

The majority of the pre-2005 scientific literature on the health implications of sarcopenia focused on measures of physical function, such as functional impairment and physical disability. These early studies were also cross-sectional in design (Janssen and Ross 2005). The results from a few of the many cross-sectional studies highlight the findings. Using a cut-off for height-adjusted appendicular muscle mass of 2 SDs or more below the mean of a young adults to define sarcopenia, Baumgartner et al. (1998) reported that the likelihood of having physical disability was approximately 4 times greater in sarcopenic older men and women than in older persons with a normal muscle mass. In the Health Aging and Body Composition study, older adults in the lowest skeletal muscle quintile (adjusted for height and fat mass) were 80% to 90% more likely to have mobility impairment than older adults in the highest quintile (Newman et al. 2003). Finally, in the third National Health and Nutrition Examination Survey, the likelihood of functional impairment and physical disability was 2- to 3-fold higher in older adults with severe sarcopenia, defined as the percent of muscle mass <2 SDs below the mean of young adults, than in older adults with normal muscle mass (Janssen et al. 2002). The strength of the association between sarcopenia and physical function in these cross-sectional studies would be considered moderate to strong by epidemiological standards.

Because of the lack of temporality, these early cross-sectional studies cannot be used to infer causation about the relationship between sarcopenia and physical function. More recent longitudinal findings from cohort studies provide a stronger form of scientific evidence on the cause and effect relationship between sarcopenia and physical function. Two published reports on the Health Aging and Body Composition cohort indicate that sarcopenia, measured by computed tomography in the mid-thigh, was a weak to modest predictor of a loss in physical function over a 2- to 3-year follow-up (Visser et al. 2005; Goodpaster et al. 2006). In an 8-year follow-up of older adults from the Cardiovascular Health Study cohort, the risk of developing physical disability was 27% greater in those with severe sarcopenia than in those with a normal muscle mass (Janssen 2006). In the same study, the likelihood of having physical disability at the start of the study (i.e., baseline exam) was 79% greater in those with severe sarcopenia than in those with normal muscle mass. Thus, the effect of sarcopenia on disability risk was 3 times smaller in the longitudinal analysis than in the cross-sectional analysis, implying that the effects of sarcopenia on functional impairment and physical disability inferred from the cross-sectional studies published in the late 1990s and early 2000s were significantly overestimated.

Influence of sarcopenia on metabolic function, chronic disease, and mortality

Several studies conducted within the past 5 years have considered the potential impact of sarcopenia on metabolic function, chronic disease, and mortality. The metabolic effects of sarcopenia include a modest decrease in resting metabolic rate subsequent to the loss of skeletal muscle mass (Lammes and Akner 2006). While it has been postulated that sarcopenia contributes to metabolic and cardiovascular diseases, such as insulin resistance, type 2 diabetes, dyslipidemia, and hypertension (Karakelides and Nair 2005), the literature is mixed and, in general, does not support this postulation. For instance, a study of 22 obese postmenopausal women found that those with sarcopenia had more favourable lipid and lipoprotein profiles than those without sarcopenia (Aubertin-Leheudre et al. 2006). Additional research on over 3000 members of the Cardiovascular Health Study cohort found that sarcopenia was not a risk factor for the development of cardiovascular disease over an 8-year follow-up period (Stephen and Janssen 2009).

A 2006 study reported that older sarcopenic patients were twice as likely to contract infection during a hospital stay compared with older patients with a normal muscle mass (Cosquéric et al. 2006). This suggests that sarcopenic individuals may have decreased immunity, which may provide a mechanistic link between sarcopenia and mortality risk, as has been observed in several studies. More specifically, studies of community-dwelling (Prothro and Rosenbloom 1995; Miller et al. 2002) and institutionalized (Mühlethaler et al. 1995) older adults have shown that an upper-arm circumference measure, a crude index of sarcopenia, is predictive of both short-term and long-term mortality risk. Despite the consistency of observations made in studies of upper-arm circumference, a study that relied on more precise measures of muscle mass obtained from computed tomography and duel-energy X-ray absorptiometry suggests that sarcopenia is a poor and clinically irrelevant predictor of mortality risk in older adults (Newman et al. 2006). Thus, it remains unclear whether sarcopenia is a risk factor for mortality.

Sarcopenic-obesity and health

As with sarcopenia, there has been an eruption of research on obesity within the past 2 decades. Most of the body composition research in the elderly has focused on the separate impacts of sarcopenia and obesity. However, in 2000, Baumgartner introduced the idea of sarcopenic-obesity, a condition in which older adults experience both a low muscle mass and a high fat mass (Baumgartner 2000). Although people who gain weight tend to gain both fat mass and muscle mass, there is by no means a perfect correlation or uniform gain of the 2 tissues (Forbes 1987). Thus, it is possible to have both a high fat mass and low muscle mass; the earliest study by Baumgartner (2000) suggested that approximately 15% of those with sarcopenia are also obese.

As with sarcopenia, obesity is a risk factor for the development of functional impairment and physical disability in older adults (Jensen and Friedmann 2002; Janssen 2007). The high prevalence of knee osteoarthritis in obese older adults may contribute to functional impairment and mobility problems (Ling et al. 2006). A number of studies have reported that sarcopenic-obese persons are at particularly high risk of functional impairment and physical disability (Baumgartner 2000; Morley et al. 2001; Baumgartner et al. 2004; Rolland et al. 2009). For instance, in a cross-sectional study of sarcopenic-obesity, Baumgartner (2000) examined participants in the New Mexico Aging Process Study cohort. He reported that the odds ratios for disability in sarcopenic, obese, and sarcopenic-obese groups, relative to the group of seniors with a normal body composition, were 2.07, 2.33, and 4.12, respectively. These findings suggest that sarcopenia and obesity have additive effects when it comes to physical disability risk in elderly persons. More recently, Baumgartner et al. (2004) attempted to replicate these initial cross-sectional findings in a longitudinal study based on the same cohort. In this study, elderly participants with either sarcopenia alone or obesity alone at baseline were not at increased risk of functional decline over 8 years of follow-up, compared with elderly individuals with a normal body composition (Baumgartner et al. 2004). However, individuals with sarcopenic-obesity had a 2.5 times greater risk of functional decline. While the aforementioned findings support the notion that the combination of sarcopenia and obesity has a greater impact on physical function than either body composition abnormality alone, a comparable number of studies do not support the contention that sarcopenic-obesity is a worse condition than obese alone (Davison et al. 2002; Zoico et al. 2004; Bouchard et al. 2009; Choquette et al. 2010). Thus, it is unclear whether sarcopenic-obsese persons are at particularly high risk of functional impairment.

The cardiovascular and metabolic implications of sarcopenic-obesity have not been extensively addressed. A cross-sectional study of 22 postmenopausal women reported that the cardiovascular and metabolic risk factor profile was worse (not better) in obese women with a normal muscle mass than in sarcopenic-obese older women (Aubertin-Leheudre et al. 2006). A longitudinal follow-up study of over 3000 older adults reported that the combination of low muscle mass and abdominal obesity was not associated with an increased risk for the development of cardiovascular disease over an 8-year follow-up period (Stephen and Janssen 2009). In short, sarcopenic-obesity does not appear to have a particularly deleterious impact on cardiovascular and metabolic health.

Sarcopenia vs. dynapenia

A primary rationale for studying sarcopenia is the belief that the loss of muscle mass is indicative of a loss of muscle strength and function. Thus, in the causal chain of events, sarcopenia was thought to cause a loss in strength, which would ultimately lead to functional impairment and physical disability. In fact, over time, the original definition of sarcopenia as purely a loss of muscle mass (Rosenberg 1989) evolved into one that included a loss of both muscle mass and muscle function. This evolved definition can be seen in several literature reviews that were published around the turn of the century (Morley et al. 2001; Roubenoff 2001; Vandervoot and Symons 2001). The link between muscle mass and strength was supported by early cross-sectional studies, which showed that ~35% of the variability in muscle strength in young adults was predicted by muscle size (Maughan et al. 1983), and that adjusting for muscle mass substantially reduced age-related differences in strength (Frontera et al. 1991). However, several recent longitudinal studies bring into question these cross-sectional observations, as reviewed elsewhere (Clark and Manini 2008). One study in particular demonstrated that, in a sample of 120 adults initially aged 46 to 78 years who were followed over 10 years, less than 5% of the change in strength was attributable to the corresponding change in muscle size (Hughes et al. 2001). Thus, there appears to be a disassociation between age-related changes in muscle mass and strength, and the mechanisms that account for each phenomenon are different (Clark and Manini 2008). Clark and Manini (2008) suggested that distinct terminology be used to refer to age-related muscle loss and age-related strength loss. Specifically, they suggested that the term sarcopenia be reserved for Rosenberg's initial definition of a loss of muscle mass, and that the term dynapenia be used to describe age-related changes in muscle strength (Clark and Manini 2008). The Greek term *dynapenia* translates to "poverty of strength."

There is evidence that dynapenia is a risk factor for functional impairment and physical disability (Carmeli et al. 2000; Visser et al. 2005; Goodpaster et al. 2006). Consider, for example, findings from the Health Aging Body Composition cohort (Visser et al. 2005). The findings in question were based on 3075 well-functioning black and white men and women aged 70–79 years who were followed for 2.5 years. In that study, muscle size in the mid-thigh was measured using computed tomography, and knee extensor strength was measured using a dynamometer. Men and women in the lowest muscle strength quartile had approximately double the risk of developing mobility limitations during the follow-up period than those in the highest muscle strength quartile. There is also some evidence that dynapenia is a risk factor for other health outcomes. A series of published reports from the Aerobics Center Longitudinal Study have demonstrated that, compared with those in the lowest strength group (e.g., bottom quartile), those in the highest strength group are 45% less likely to have the metabolic syndrome (Jurca et al. 2005), 39% less likely to die from cancer (Ruiz et al. 2009), and 20% less likely to die of any cause (FitzGerald et al. 2004). Other studies report that muscle strength is related to insulin resistance (Karelis et al. 2007) and type 2 diabetes (Sayer et al. 2005).

Within the past few years, researchers have started to consider the impact of dyanpenic-obesity on health. Most of this work has focused on physical function. First, a 6-year follow-up of 930 adults aged 65 years or older concluded that obese individuals in the lowest handgrip strength tertile had a greater decline in physical function that the other obese participants (Stenholm et al. 2009). The same research team reported that the prevalence of walking limitations in a cross-sectional study was considerably higher in older adults who had a high body fat percentage and a low handgrip

strength than in those who had a high body fat percentage and high handgrip strength (61% vs. 7%) (Stenholm et al. 2008). In a newly published cross-sectional study of 2039 men and women aged 55 years and older, where leg extension strength was measured with a dynamometer, 12% of the nondynapenic and nonobese group had walking disability, compared with 18% of those with obesity alone, 24% of those with dynapenia, and 36% of those with dynapenic-obesity (Bouchard and Janssen 2010). In that same study, the prevalence of functional impairment based on self-reported measures was 2%, 7%, 5%, and 13% in these 4 groups, respectively.

Finally, a study published in 2010 of 904 men and women aged 67–84 years found that combining handgrip strength and fat mass in an index of relative strength is the best predictor of a low physical function score, compared with any other body composition and strength markers (Choquette et al. 2010).

Collectively, these findings indicate that dynapenia and obesity have independent and additive effects on physical function.

I am aware of 1 study that has considered the impact of dynapenic-obesity on cardiovascular health (Stephen and Janssen 2009). Participants of this study consisted of 3366 community-dwelling adults aged 65 or older. Compared with participants with healthy waist circumference and normal grip strength values, cardiovascular disease risk was not significantly elevated in the obese-alone or dynapenic-alone groups. However, cardiovascular disease risk was 23% higher in the sarcopenic-obese group. These findings suggest that the combination of obesity and poor muscle strength may have relevance for cardiovascular health in older adults.

An intriguing question is whether sarcopenia or dynapenia is a stronger predictor of physical function, chronic disease, and mortality risk. The evidence consistently points toward dynapenia. Visser et al. (2005) demonstrated that low muscle mass and low muscle strength were risk factors for mobility decline in older men and women. However, while muscle strength remained an independent predictor of mobility decline after consideration of muscle mass, muscle mass was not a predictor of mobility decline after consideration of muscle strength (Visser et al. 2005). Stephen and Janssen (2009) recently published findings indicating that dynapenic-obesity but not sarcopenic-obesity is a significant predictor of cardiovascular disease risk. Newman et al. (2006) reported that older individuals with dynapenia have a 50% increased all-cause mortality risk independent of sarcopenia, but that individuals with sarcopenia do not have a significantly increased all-cause mortality risk independent of dyanpenia (Newman et al. 2006). These findings, when coupled with the observation that losses of muscle strength are not directly attributable to age-related losses of muscle mass, indicate that research and clinical emphasis should be placed more on dynapenia than on sarcopenia.

Summary and conclusions

The sarcopenia research field has recently entered its third decade. We have learned a tremendous amount about the health consequences of both age-related muscle mass loss (sarcopenia) and age-related muscle strength loss (dynapenia) during the past 20+ years. Given the health consequences of sarcopenia and dynapenia, it is important to note that both of these conditions can be effectively prevented and treated with resistance exercise, as reviewed elsewhere (Paterson et al. 2007; Little and Phillips 2009). Furthermore, there is still much to be learned about the health impacts of these conditions, and consideration should be given to using examples from other research disciplines to move the field forward. For instance, some eloquent studies in obesity research have shown that using a life course approach for obesity assessment provides important information on healthy risk in older persons (Harris et al. 1997; Janssen and Bacon 2008). More specifically, obesity status in mid-life is indicative of chronic disease and mortality risk in older adults, independent of their current obesity status. It is possible that muscle mass and (or) strength throughout the lifespan may also be relevant for the health of older persons. Furthermore, sarcopenia and dynapenia research has been poorly implemented into clinical practice, and examples from the cardiovascular disease literature could be adopted to help solve this problem. For instance, the clinical assessment of cardiovascular risk relies heavily on the Framingham Heart Index (Lloyd-Jones et al. 2004), a simple tool that relies on measures of age, smoking, blood pressure, and cholesterol to predict future risk and to guide prevention and treatment options in the clinical setting. Perhaps the creation and adoption of a clinical risk assessment tool for sarcopenia and dynapenia would help integrate sarcopenia and dynapenia research into clinical practice.

Acknowledgements

The author is supported by a New Investigator Award from the Canadian Institutes of Health Research and an Early Researcher Award from the Ontario Ministry of Research and Innovation.

References

Aubertin-Leheudre, M., Lord, C., Goulet, E.D., Khalil, A., and Dionne, I.J. 2006. Effect of sarcopenia on cardiovascular disease risk factors in obese postmenopausal women. Obesity (Silver Spring), **14**(12): 2277–2283. doi:10.1038/oby.2006.267. PMID: 17189556.

Baumgartner, R.N. 2000. Body composition in healthy aging. Ann. N. Y. Acad. Sci. **904**(1): 437–448. doi:10.1111/j.1749-6632.2000.tb06498.x. PMID:10865787.

Baumgartner, R.N., Koehler, K.M., Gallagher, D., Romero, L., Heymsfield, S.B., Ross, R.R., et al. 1998. Epidemiology of sarcopenia among the elderly in New Mexico. Am. J. Epidemiol. **147**(8): 755–763. PMID:9554417.

Baumgartner, R.N., Wayne, S.J., Waters, D.L., Janssen, I., Gallagher, D., and Morley, J.E. 2004. Sarcopenic obesity predicts instrumental activities of daily living disability in the elderly. Obes. Res. **12**(12): 1995–2004. doi:10.1038/oby.2004.250. PMID:15687401.

Bouchard, D.R., and Janssen, I. 2010. Dynapenic-obesity and physical function in older adults. J. Gerontol. A Biol. Sci. Med. Sci. **65**(1): 71–77. PMID:19887536.

Bouchard, D.R., Dionne, I.J., and Brochu, M. 2009. Sarcopenic/obesity and physical capacity in older men and women: data from the Nutrition as a Determinant of Successful Aging (NuAge)—the Quebec Longitudinal Study. Obesity (Silver

Spring), **17**(11): 2082–2088. doi:10.1038/oby.2009.109. PMID: 19373219.

Carmeli, E., Reznick, A.Z., Coleman, R., and Carmeli, V. 2000. Muscle strength and mass of lower extremities in relation to functional abilities in elderly adults. Gerontology, **46**(5): 249–257. doi:10.1159/000022168. PMID:10965180.

Choquette, S., Bouchard, D.R., Doyon, C.Y., Sénéchal, M., Brochu, M., and Dionne, I.J. 2010. Relative strength as a determinant of mobility in elders 67–84 years of age. a nuage study: nutrition as a determinant of successful aging. J. Nutr. Health Aging, **14**(3): 190–195. doi:10.1007/s12603-010-0047-4. PMID: 20191251.

Clark, B.C., and Manini, T.M. 2008. Sarcopenia =/= dynapenia. J. Gerontol. A Biol. Sci. Med. Sci. **63**(8): 829–834. PMID: 18772470.

Cosquéric, G., Sebag, A., Ducolombier, C., Thomas, C., Piette, F., and Weill-Engerer, S. 2006. Sarcopenia is predictive of nosocomial infection in care of the elderly. Br. J. Nutr. **96**(5): 895–901. doi:10.1017/BJN20061943. PMID:17092379.

Davison, K.K., Ford, E.S., Cogswell, M.E., and Dietz, W.H. 2002. Percentage of body fat and body mass index are associated with mobility limitations in people aged 70 and older from NHANES III. J. Am. Geriatr. Soc. **50**(11): 1802–1809. doi:10.1046/j.1532-5415.2002.50508.x. PMID:12410898.

FitzGerald, S.J., Barlow, C.E., Kampert, J.B., Morrow, J.R., Jackson, A.W., and Blair, S.N. 2004. Muscular fitness and all-cause mortality: prospective observations. J. Phys. Act. Health, **1**(1): 7–18.

Forbes, G.B. 1987. Lean body mass-body fat interrelationships in humans. Nutr. Rev. **45**(8): 225–231. PMID:3306482.

Frontera, W.R., Hughes, V.A., Lutz, K.J., and Evans, W.J. 1991. A cross-sectional study of muscle strength and mass in 45- to 78-yr-old men and women. J. Appl. Physiol. **71**(2): 644–650. PMID:1938738.

Goodpaster, B.H., Park, S.W., Harris, T.B., Kritchevsky, S.B., Nevitt, M., Schwartz, A.V., et al. 2006. The loss of skeletal muscle strength, mass, and quality in older adults: the health, aging and body composition study. J. Gerontol. A Biol. Sci. Med. Sci. **61**(10): 1059–1064. PMID:17077199.

Harris, T.B., Launer, L.J., Madans, J., and Feldman, J.J. 1997. Cohort study of effect of being overweight and change in weight on risk of coronary heart disease in old age. BMJ, **314**(7097): 1791–1794. PMID:9224080.

Hughes, V.A., Frontera, W.R., Wood, M., Evans, W.J., Dallal, G.E., Roubenoff, R., and Fiatarone Singh, M.A. 2001. Longitudinal muscle strength changes in older adults: influence of muscle mass, physical activity, and health. J. Gerontol. A Biol. Sci. Med. Sci. **56**(5): B209–B217. PMID:11320101.

Janssen, I. 2006. Influence of sarcopenia on the development of physical disability: the Cardiovascular Health Study. J. Am. Geriatr. Soc. **54**(1): 56–62. doi:10.1111/j.1532-5415.2005.00540.x. PMID:16420198.

Janssen, I. 2007. Morbidity and mortality risk associated with an overweight BMI in older men and women. Obesity (Silver Spring), **15**(7): 1827–1840. doi:10.1038/oby.2007.217. PMID: 17636102.

Janssen, I., and Bacon, E. 2008. Effect of current and midlife obesity status on mortality risk in the elderly. Obesity (Silver Spring), **16**(11): 2504–2509. doi:10.1038/oby.2008.400. PMID: 18756264.

Janssen, I., and Ross, R. 2005. Linking age-related changes in skeletal muscle mass and composition with metabolism and disease. J. Nutr. Health Aging, **9**(6): 408–419. PMID:16395513.

Janssen, I., Heymsfield, S.B., and Ross, R. 2002. Low relative skeletal muscle mass (sarcopenia) in older persons is associated with functional impairment and physical disability. J. Am. Geriatr. Soc. **50**(5): 889–896. doi:10.1046/j.1532-5415.2002.50216.x. PMID:12028177.

Jensen, G.L., and Friedmann, J.M. 2002. Obesity is associated with functional decline in community-dwelling rural older persons. J. Am. Geriatr. Soc. **50**(5): 918–923. doi:10.1046/j.1532-5415.2002.50220.x. PMID:12028181.

Jurca, R., Lamonte, M.J., Barlow, C.E., Kampert, J.B., Church, T.S., and Blair, S.N. 2005. Association of muscular strength with incidence of metabolic syndrome in men. Med. Sci. Sports Exerc. **37**(11): 1849–1855. doi:10.1249/01.mss.0000175865.17614.74. PMID:16286852.

Karakelides, H., and Nair, K.S. 2005. Sarcopenia of aging and its metabolic impact. Curr. Top. Dev. Biol. **68**: 123–148. doi:10.1016/S0070-2153(05)68005-2. PMID:16124998.

Karelis, A.D., Tousignant, B., Nantel, J., Proteau-Labelle, M., Malita, F.M., St-Pierre, D.H., et al. 2007. Association of insulin sensitivity and muscle strength in overweight and obese sedentary postmenopausal women. Appl. Physiol. Nutr. Metab. **32**(2): 297–301. doi:10.1139/H07-002. PMID:17486172.

Lammes, E., and Akner, G. 2006. Resting metabolic rate in elderly nursing home patients with multiple diagnoses. J. Nutr. Health Aging, **10**(4): 263–270. PMID:16886096.

Ling, S.M., Xue, Q.L., Simonsick, E.M., Tian, J., Bandeen-Roche, K., Fried, L.P., and Bathon, J.M. 2006. Transitions to mobility difficulty associated with lower extremity osteoarthritis in high functioning older women: longitudinal data from the Women's Health and Aging Study II. Arthritis Rheum. **55**(2): 256–263. doi:10.1002/art.21858. PMID:16583416.

Little, J.P., and Phillips, S.M. 2009. Resistance exercise and nutrition to counteract muscle wasting. Appl. Physiol. Nutr. Metab. **34**(5): 817–828. doi:10.1139/H09-093. PMID:19935843.

Lloyd-Jones, D.M., Wilson, P.W., Larson, M.G., Beiser, A., Leip, E.P., D'Agostino, R.B., and Levy, D. 2004. Framingham risk score and prediction of lifetime risk for coronary heart disease. Am. J. Cardiol. **94**(1): 20–24. doi:10.1016/j.amjcard.2004.03.023. PMID:15219502.

Maughan, R.J., Watson, J.S., and Weir, J. 1983. Strength and cross-sectional area of human skeletal muscle. J. Physiol. **338**(5): 37–49. PMID:6875963.

Miller, M.D., Crotty, M., Giles, L.C., Bannerman, E., Whitehead, C., Cobiac, L., et al. 2002. Corrected arm muscle area: An independent predictor of long-term mortality in community-dwelling older adults? J. Am. Geriatr. Soc. **50**(7): 1272–1277. doi:10.1046/j.1532-5415.2002.50316.x. PMID:12133024.

Morley, J.E., Baumgartner, R.N., Roubenoff, R., Mayer, J., and Nair, K.S. 2001. Sarcopenia. J. Lab. Clin. Med. **137**(4): 231–243. doi:10.1067/mlc.2001.113504. PMID:11283518.

Mühlethaler, R., Stuck, A.E., Minder, C.E., and Frey, B.M. 1995. The prognostic significance of protein-energy malnutrition in geriatric patients. Age Ageing, **24**(3): 193–197. doi:10.1093/ageing/24.3.193. PMID:7645437.

Newman, A.B., Kupelian, V., Visser, M., Simonsick, E., Goodpaster, B., Nevitt, M., et al.; Health ABC Study Investigators. 2003. Sarcopenia: alternative definitions and associations with lower extremity function. J. Am. Geriatr. Soc. **51**(11): 1602–1609. doi:10.1046/j.1532-5415.2003.51534.x. PMID: 14687390.

Newman, A.B., Kupelian, V., Visser, M., Simonsick, E.M., Goodpaster, B.H., Kritchevsky, S.B., et al. 2006. Strength, but not muscle mass, is associated with mortality in the health, aging and body composition study cohort. J. Gerontol. A Biol. Sci. Med. Sci. **61**(1): 72–77. PMID:16456196.

Paterson, D.H., Jones, G.R., and Rice, C.L. 2007. Ageing and physical activity: exercise recommendations for older adults. Appl. Physiol. Nutr. Metab. **32**(Suppl 2E): S69–S108. doi:10.1139/H07-111. [French translation in Appl. Physiol. Nutr. Metab. **32**(Suppl 2F): S75–S171. PMID:19377547.]

Prothro, J.W., and Rosenbloom, C.A. 1995. Body measurements of black and white elderly persons with emphasis on body composition. Gerontology, **41**(1): 22–38. doi:10.1159/000213659. PMID:7737531.

Rolland, Y., Lauwers-Cances, V., Cristini, C., Abellan van Kan, G., Janssen, I., Morley, J.E., and Vellas, B. 2009. Difficulties with physical function associated with obesity, sarcopenia, and sarcopenic-obesity in community-dwelling elderly women: the EPIDOS (EPIDemiologie de l'OSteoporose) Study. Am. J. Clin. Nutr. **89**(6): 1895–1900. doi:10.3945/ajcn.2008.26950. PMID:19369381.

Rosenberg, I.R. 1989. Summary comments. Am. J. Clin. Nutr. **50**: 1231–1233.

Roubenoff, R. 2001. Origins and clinical relevance of sarcopenia. Can. J. Appl. Physiol. **26**(1): 78–89. PMID:11291626.

Ruiz, J.R., Sui, X., Lobelo, F., Lee, D.C., Morrow, J.R., Jr., Jackson, A.W., et al. 2009. Muscular strength and adiposity as predictors of adulthood cancer mortality in men. Cancer Epidemiol. Biomarkers Prev. **18**(5): 1468–1476. doi:10.1158/1055-9965.EPI-08-1075. PMID:19366909.

Sayer, A.A., Dennison, E.M., Syddall, H.E., Gilbody, H.J., Phillips, D.I., and Cooper, C. 2005. Type 2 diabetes, muscle strength, and impaired physical function: the tip of the iceberg? Diabetes Care, **28**(10): 2541–2542. doi:10.2337/diacare.28.10.2541. PMID:16186295.

Stenholm, S., Rantanen, T., Heliövaara, M., and Koskinen, S. 2008. The mediating role of C-reactive protein and handgrip strength between obesity and walking limitation. J. Am. Geriatr. Soc. **56**(3): 462–469. doi:10.1111/j.1532-5415.2007.01567.x. PMID:18179481.

Stenholm, S., Alley, D., Bandinelli, S., Griswold, M.E., Koskinen, S., Rantanen, T., et al. 2009. The effect of obesity combined with low muscle strength on decline in mobility in older persons: results from the InCHIANTI study. Int J Obes (Lond), **33**(6): 635–644. doi:10.1038/ijo.2009.62. PMID:19381155.

Stephen, W.C., and Janssen, I. 2009. Sarcopenic-obesity and cardiovascular disease risk in the elderly. J. Nutr. Health Aging, **13**(5): 460–466. doi:10.1007/s12603-009-0084-z. PMID:19390754.

Vandervoot, A.A., and Symons, T.B. 2001. Functional and metabolic consequences of sarcopenia. Can. J. Appl. Physiol. **26**(1): 90–101. PMID:11173671.

Visser, M., Goodpaster, B.H., Kritchevsky, S.B., Newman, A.B., Nevitt, M., Rubin, S.M., et al. 2005. Muscle mass, muscle strength, and muscle fat infiltration as predictors of incident mobility limitations in well-functioning older persons. J. Gerontol. A Biol. Sci. Med. Sci. **60**(3): 324–333. PMID:15860469.

Zoico, E., Di Francesco, V., Guralnik, J.M., Mazzali, G., Bortolani, A., Guariento, S., et al. 2004. Physical disability and muscular strength in relation to obesity and different body composition indexes in a sample of healthy elderly women. Int. J. Obes. Relat. Metab. Disord. **28**(2): 234–241. PMID:14708033.