AJR FOCUS ON:

Sarcopenia: Current Concepts and Imaging Implications

Robert D. Boutin[1]
Lawrence Yao[2]
Robert J. Canter[3]
Leon Lenchik[4]

OBJECTIVE. The purpose of this article is to review the nomenclature, clinical impact, and diagnostic techniques characterizing sarcopenia.

CONCLUSION. Sarcopenia—defined as significant loss of muscle—is associated with cachexia and frailty. Specific diagnostic criteria for sarcopenia continue to evolve, but imaging can play a role in the detection and quantification of muscle depletion. Emerging evidence indicates that sarcopenia is a relevant predictor of quality and quantity of life, particularly in patients who are elderly, have cancer, or undergo surgery.

Keywords: body composition, imaging, muscle, sarcopenia

DOI:10.2214/AJR.15.14635

Received February 26, 2015; accepted without revision March 30, 2015.

Based on presentations at the Radiological Society of North America 2013 annual meeting, Chicago, IL, and the International Skeletal Society 2013 annual meeting, Philadelphia, PA.

[1]Department of Radiology, University of California Davis Health System, 4860 Y St, Ste 3100, Sacramento, CA 95817. Address correspondence to R. D. Boutin (rdboutin@ucdmc.ucdavis.edu).

[2]Radiology and Imaging Sciences, National Institutes of Health Clinical Center, Bethesda MD.

[3]Department of Surgery, Division of Surgical Oncology, University of California Davis Health System, Sacramento, CA.

[4]Department of Radiology, Musculoskeletal Imaging Section, Wake Forest School of Medicine, Winston-Salem, NC.

WEB
This is a web exclusive article.

AJR 2015; 205:W255–W266

0361–803X/15/2053–W255

Skeletal muscle is the most abundant tissue in the human body in young adults. In accordance with the Davis law (the corollary to the Wolff law for bone), muscle is normally remarkably plastic, with the ability to gain or lose tissue depending on numerous factors. Muscle depletion commonly occurs with aging, disease, and disuse, but may go unrecognized by clinicians [1].

Sarcopenia—broadly defined as significant loss of muscle mass and function—is recognized increasingly as an important independent risk factor for numerous adverse outcomes [2–4]. These negative outcomes include physical disability [5], osteoporosis [6], falls [7], prolonged hospital stay and readmission [8], major postoperative complications [9], and death [10, 11]. In this review, we discuss key features of the nomenclature, clinical impact, and techniques used to diagnose sarcopenia.

Nomenclature: What Is Sarcopenia?

Definition

Sarcopenia is currently a hot topic for investigation, and the precise definition of the term continues to evolve. Originally defined in 1989 as the progressive reduction in muscle mass in elderly people [12], subsequent operational definitions also incorporate functional criteria (e.g., low muscle strength measured by grip strength and low physical performance measured by gait speed) [3, 4, 13].

The Foundation for the National Institutes of Health Sarcopenia Project [14] recommends specific cutoff points to identify populations with functional limitations associated with sarcopenia. These evidence-based criteria recognize measures of low muscle strength (i.e., grip strength < 26 kg for men and < 16 kg for women) and low lean body mass (i.e., appendicular lean mass adjusted for body mass index [BMI; weight in kilograms divided by the square of height in meters] < 0.789 for men and < 0.512 for women) [14]. These criteria were validated as predictive of future mobility impairment with a 3-year clinical follow-up [14], and this definition of muscle weakness appears to be a treatable symptom of sarcopenia [15].

Related Terminology

Although some experts continue to advocate for a narrow definition of sarcopenia that refers to muscle mass only [13] in elderly patients [1], most now use the term "sarcopenia" broadly to describe clinically significant muscle wasting from any cause. Experts who favor the narrow definition of sarcopenia have proposed other terms to describe clinically relevant muscle depletion that can occur at any age, from any cause, including "myopenia" [1], "muscle wasting" [16], and "skeletal muscle function deficit" [13]. Two particular terms related to sarcopenia warrant mention: "cachexia" and "frailty."

Cachexia—Cachexia is the involuntary loss of muscle mass, fat mass, or both that occurs in patients with chronic diseases [17]. Cachexia can significantly impair survival but often is underrecognized [18] and is a treatable comorbidity of chronic disease [19]. Patients with ca-

chexia have annual mortality rates that range from 10–15% with chronic obstructive pulmonary disease, to 20–30% per year with chronic heart failure and chronic kidney disease, to 80% with advanced cancer [18].

Diagnostic criteria for cancer-related cachexia include sarcopenia or 5% loss of edema-free body weight loss or weight loss greater than 2% in individuals with a BMI less than 20 [20, 21]. The clinical diagnostic indicators have potential pitfalls [22], and the prevalence of cachexia varies widely according to the definition used [20]. As with other forms of sarcopenia, patients with cachexia characteristically have muscle depletion, but cachexia notably involves the prominent overexpression of proinflammatory cytokines (e.g., interleukin 6 or tumor necrosis factor), which can cause proteolysis and lipolysis [17].

Frailty—Frailty is characterized by reduced homeostatic reserves (resilience) [23]. This inability to return to baseline physical status after an insult to the body has multiple causes. Most commonly, frailty is known as a geriatric syndrome that increases nonlinearly with age [24]. Frailty is associated with low muscle mass at the time of diagnosis, as well as further future muscle depletion [25].

Sarcopenia is a major component of frailty [26, 27]. Importantly, although sarcopenia can lead to frailty, not all patients with sarcopenia are frail [28]. In fact, sarcopenia is about twice as common as frailty [28].

Like sarcopenia, frailty may be diagnosed late, and establishing a diagnosis may aid in optimizing treatment and prognosis [29]. The recent consensus definition of frailty from six medical societies specifically identified diminished strength and endurance, as well as reduced physiologic function, as vulnerabilities associated with geriatric dependency or death [30].

Clinically, numerous screening tests for frailty have been evaluated [31], such as the FRAIL (fatigue, resistance, aerobic, illness, and loss of weight) scale [26]. However, existing clinical screening instruments appear to have limited utility in predicting the risk of adverse outcomes in older adults [32].

The Clinical Impact of Sarcopenia

Prevalence

The prevalence of sarcopenia increases with age. For example, the prevalence is 5–13% in the seventh decade of life and increases to 11–50% by the age of 80 years [27].

Importantly, the prevalence of sarcopenia varies widely with variables such as study population, diagnostic technique, and diagnostic criteria [4, 33]. For example, sarcopenia is reported in at least 5% of community-dwelling older adults [33, 34] versus 25% of hospitalized older adults [35]. Overall, the prevalence of sarcopenia is expected to increase worldwide from more than 50 million people in 2010 to more than 200 million people in 2050 [3].

Costs

In the United States, the direct health care cost attributable to sarcopenia in 2000 was estimated at $18.5 billion [36]. A 10% reduction in sarcopenia prevalence in the United States has been estimated to yield a savings of at least $1.1 billion per year [36]. Additional costs are expected when sarcopenia is combined with other body composition abnormalities, such as obesity, because such combinations may result in a higher risk for poor health outcomes than with one condition alone.

Sarcopenic Obesity

Sarcopenic obesity is defined by the simultaneous presence of both sarcopenia and obesity. Many studies have associated sarcopenic obesity with unfavorable health outcomes, including significant disability, metabolic syndrome, lengthened hospital stay, and mortality [37]. Although further study is necessary to better understand when adverse outcomes will or will not occur [38, 39], there can be a vicious cycle between the muscle loss and fat accumulation [40].

In addition to the widely studied muscle-fat interaction, there is increasing interest in muscle-bone, muscle-fat, and muscle-joint interactions as predictors of disability. For this reason, new terms have been introduced, such as "sarcoosteopenia" (describing patients with both sarcopenia and osteopenia) [41] and "osteosarcopenic obesity" (describing concurrent osteoporosis, sarcopenia, and obesity) [42]. For example, women with first-time hip fractures have a high prevalence of sarcopenia (58%) [43], as well as osteoporosis. Sarcopenia, therefore, should be seen in the context of interorgan cross-talk that may be affected by aging, lifestyle, genetics, or disease [44].

Muscle Mass and Strength

Analogous to bone, muscle mass generally peaks in young adults in their 20s, and declines after age 50 by approximately 1% per year [29]. Although muscle mass contributes up to 50% of total body weight in young adults, it may account for only 25% of body weight by age 80 years [45].

Although the loss of muscle mass and muscle strength are interdependent, the loss of muscle strength occurs at least 2–4 times faster than loss of muscle mass and appears to be a more important risk factor for predicting adverse outcomes [46]. For example, in relatively healthy older adults followed for 3 years, the annualized rate of leg strength decline was approximately 3–4%, whereas the annualized rate of loss of lean leg mass was approximately 1% by dual x-ray absorptiometry (DEXA) [47]. Knee immobilization in a cast for 14 days also results in a larger decrease in quadriceps strength (mean, 22.9%) than in cross-section area (CSA) on CT (mean, 8.4%; a rate of 0.5–0.6% per day) [48].

The relative preservation of muscle bulk observed in patients with age-associated decreases in muscle strength may be partially related to the presence of fatty infiltration. There are ongoing debates about the relative importance of muscle mass per se, but there is agreement on the following: Muscle quality, not just quantity, is an essential determinant of strength.

Loss of muscle mass and strength are accelerated in the presence of physical stressors. This can be particularly important in older patients after acute injury (e.g., hip fracture), chronic disease (e.g., stroke), or surgery. In healthy individuals in their 60s, for example, disuse of only 4 days in a knee brace can result in significantly greater loss in quadriceps strength, with impaired recovery, compared with young adults [49]. Thus, in the context of age-related sarcopenia, regional muscle atrophy may become clinically relevant, even if related to only short periods of muscle disuse [48, 49].

Nonimaging Diagnostic Techniques

Nonimaging evaluation of individuals with suspected sarcopenia has been used widely in both research and clinical settings.

Questionnaires have been used to screen for impaired physical function. For example, sarcopenia evaluation may include a SARC-F scale, which evaluates for "Slowness, Assistance walking, Rising from chair, Climbing stairs, and Falls" [50]. Like other screening tools, it has only modest predictive power for 4-year physical limitation [51].

Physical performance can be assessed with a variety of tools [26]. For example, the widely validated short physical performance battery takes 10–15 minutes to administer and evaluates lower extremity function using a combination of gait speed, repeated chair

TABLE 1: Imaging Assessment of Sarcopenia

Modality	Commonly Used Parameters	Comments
Whole-body dual x-ray absorptiometry	Whole-body lean mass, appendicular lean mass, appendicular lean mass / height squared	Allows simultaneous measurement of whole-body fat mass and whole-body bone mass
Ultrasound	Muscle size (CSA, volume), muscle echo intensity	Other parameters of interest: muscle stiffness, mobility microvasculature, fascicle length, pennation, belly gearing
MRI	Muscle edema, atrophy, fatty infiltration, muscle size (CSA, volume), muscle adipose tissue content	Although usually used to measure focal muscle groups, has been used to measure whole-body lean mass; MR spectroscopy is promising application
CT	Muscle size (CSA, volume), muscle attenuation	Allows simultaneous measurement of visceral and subcutaneous fat

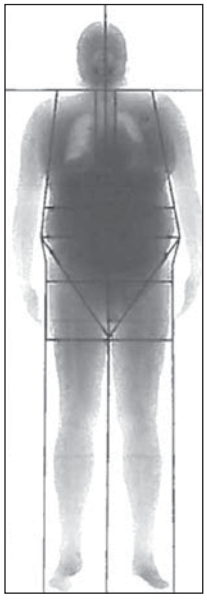
Note—CSA = cross-section area.

rise time, and balance tests. Strength testing with a dynamometer also is used commonly (e.g., grip strength, quadriceps strength).

Anthropometry refers generically to measurements of the body during clinical examination and is the most common approach for recording body composition. Examples of anthropometric techniques include BMI, skinfold thickness (i.e., pinch test), and body circumference (e.g., waist, thigh, and calf) [52].

Bioelectrical impedance analysis is a low-cost portable noninvasive technique that involves the application of an electrical current through the body. Muscle is the largest water-rich tissue in the body, and muscle mass can be estimated on the basis of the conduction of current through water. Measurement errors may be seen with alterations in hydration, soft-tissue edema, exercise status, or food intake [33]. A bioimpedance-based technique referred to as electrical impedance myography (Aim, Skulpt) has been marketed to consumers to measure muscle quality but has not yet received U.S. Food and Drug Administration clearance for medical applications [53].

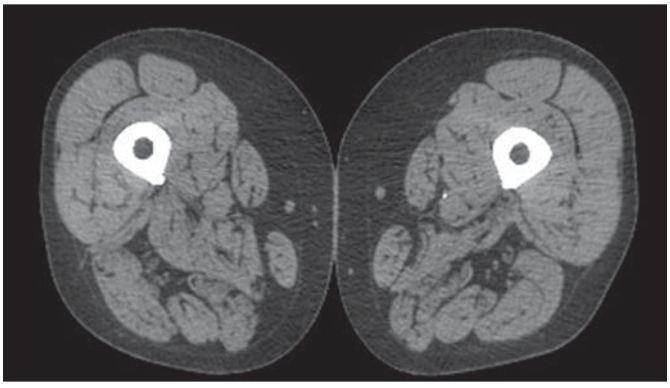
Serum and urinary biomarkers (e.g., C-terminal agrin fragment associated with the neuromuscular junction) are widely used in research but so far appear only weakly associated with clinically relevant outcomes [54].



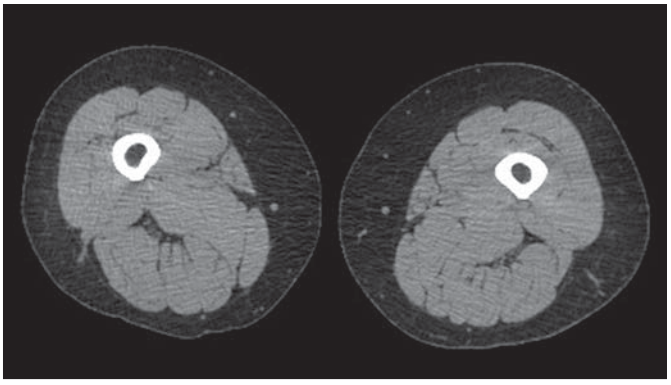
A

Region	Tissue (% Fat)	Region (% Fat)	Tissue (lb)	Fat (lb)	Lean (lb)	BMC (lb)	Total Mass (lb)
Left arm	37.5	35.9	11.11	4.17	6.94	0.50	11.6
Left leg	36.5	35.0	31.93	11.65	20.28	1.34	33.3
Left trunk	52.4	51.4	64.43	33.74	30.69	1.17	65.6
Left total	45.2	43.8	112.34	50.75	61.59	3.62	116.0
Right arm	37.8	36.2	11.29	4.27	7.02	0.50	11.8
Right leg	35.4	34.0	32.08	11.37	20.71	1.32	33.4
Right trunk	53.3	52.2	56.06	29.89	26.17	1.15	57.2
Right total	44.4	42.8	106.16	47.10	59.05	3.93	110.1
Arms	37.7	36.1	22.41	8.44	13.96	1.00	23.4
Legs	36.0	34.5	64.02	23.02	40.99	2.66	66.7
Trunk	52.8	51.8	120.49	63.63	56.86	2.32	122.8
Total	44.8	43.3	218.50	97.85	120.64	7.55	226.0

B



C



D

Fig. 1—Body composition measurements in two different patients.
A–C, 68-year-old man with body mass index (BMI; weight in kilograms divided by square of height in meters) of 34 (obese range). Whole-body dual x-ray absorptiometry scan (**A**) was obtained to measure body composition. Commercial software allows placement of standard ROIs, permitting analysis of whole body and appendicular lean mass, fat mass, and bone mineral content. Lean mass in extremities reflects appendicular muscle mass, circumventing challenges of tissue segmentation and consistent ROI placement inherent to CT and MRI. Body composition analysis (**B**) shows 43.3% whole body fat. Lean mass in arms and legs (13.96 + 40.99), when converted to kilograms and normalized to BMI, yields appendicular lean mass/BMI of 0.735 m^2, indicating relative sarcopenia according to Foundation for National Institutes of Health criteria. BMC = bone mineral content. CT of thighs (**C**) reveals increased intramuscular fat, more notable in posterior compartments.
D, Different 68-year-old man. CT shows normal muscle mass and attenuation, without visible fatty infiltration.

Importantly, nonimaging tests are not always accurate, and findings may be abnormal for reasons unrelated to sarcopenia. For example, orthopedic disorders, neurologic conditions (e.g., depression or altered mental status), and certain medications can contribute to false-positive (or nondiagnostic) results. For this reason, imaging is playing a larger role in the diagnosis of sarcopenia, particularly when screening functional tests are positive.

Imaging Diagnostic Techniques

The most common imaging techniques to evaluate body composition are DEXA, sonography, MRI, and CT (Table 1). Because radiologists are familiar with all these techniques, only recent developments relating to sarcopenia are highlighted here. Discussion here regarding DEXA is particularly limited, given that its role in the evaluation of body composition is well established [55–57].

Dual X-Ray Absorptiometry

For over a decade, DEXA measurements of lean mass and fat mass have been used as endpoints in clinical trials involving diverse populations and a wide variety of disease states [55]. DEXA measurements of lean and fat mass have widely accepted accuracy and precision that have been validated in multiple clinical environments [56] (Fig. 1).

As with any technique, careful attention to technical details and artifacts is essential for accurate body composition measurement. For example, measurement of lean mass with DEXA may be falsely elevated by gastrointestinal or IV contrast material.

Because DEXA is a projectional 2D technique, lean body mass measured by DEXA is not equivalent to muscle mass measured for truncal regions, but appendicular muscle mass can be effectively estimated by DEXA-based measurement of lean mass in the extremities. The definition of appendicular regions and appendicular lean mass is reliable and automated using commercially available DEXA software [56]. However, the use of DEXA for body composition may require specific software packages that incur additional cost, compared with a system used only for bone mineral density measurement.

The most important advantage of DEXA over other imaging modalities is the ability to easily measure whole-body composition. In addition to determining lean mass, DEXA confers the benefit of assessing indexes that combine lean and fat mass measures. For example, ratios of fat-to-lean mass and whole-body fat mass–to–lower extremity lean mass have been suggested as endpoints with particular clinical relevance [57].

Sonography

Well-known attributes of sonography include relatively low cost, ease of use, and accessibility. Sonography has been used in several cross-sectional and longitudinal studies to assess muscle quantity and quality. Specific applications of sonography have included muscle thickness measurements of individuals in epidemiologic studies of sarcopenia, nursing home residents [58], patients with stroke [59], and patients in the ICU [60]. Routine evaluation includes regional assessment of muscle size, as a marker of muscle mass or quantity, and echo intensity, as a marker of muscle quality (Fig. 2).

Size—Sonographic measurements of muscle size have been significantly associated with strength. Changes in these measurements can be seen as early as 6 weeks after beginning resistance training [61]. A study that included both elderly and young subjects (n = 52) concluded that sonography could be used for monitoring sarcopenia by measuring quadriceps muscle thickness, and that muscle thickness was highly correlated with isometric maximum voluntary contraction force [62]. With resistance training, adaptations in muscle architecture also are visualized sonographically [63].

Panoramic images have been used to measure both CSA and volume, with inter- and intrareader reliability similar to those for MRI [64]. MRI, however, systematically produces larger absolute values of CSA [64, 65]. Of note, total skeletal muscle mass may be estimated using sonographically measured muscle thickness, with a strong correlation with both MRI (R^2 = 0.94) and DEXA (R^2 = 0.95) [66].

Some studies suggest that manifestations of sarcopenia appear first in the thigh, particularly involving the quadriceps, before whole-body sarcopenia can be diagnosed. If these studies are confirmed, sonography

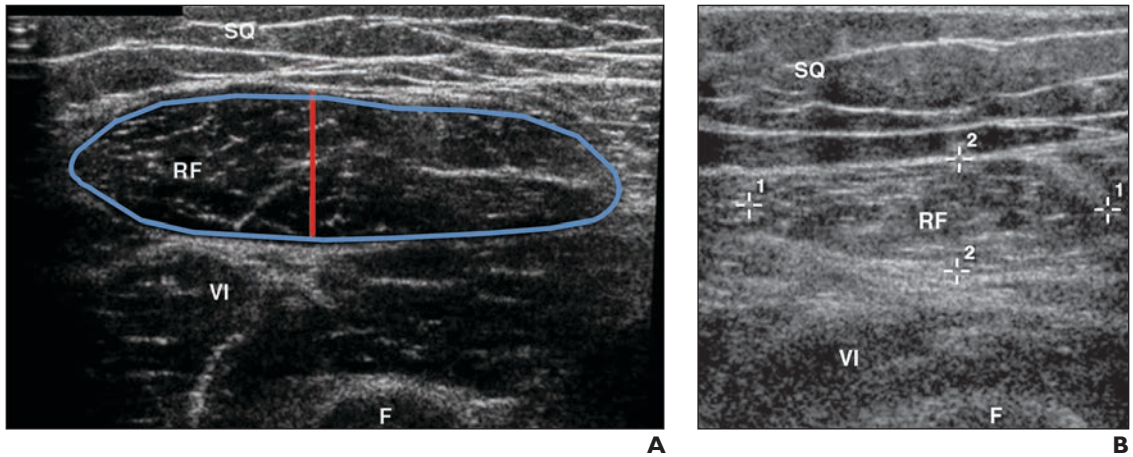


Fig. 2—Ultrasound measurements of muscle size used as regional markers of sarcopenia in two different subjects. (Courtesy of Rider L)
A, Healthy 21-year-old woman. Ultrasound was used to measure rectus femoris (RF) muscle thickness (*red line*) and cross-sectional area (*blue line*). Area muscle measurements can be performed reliably, even for muscles larger than transducer head, using widely available panoramic imaging capability. SQ = subcutaneous fat, VI = vastus intermedius, F = femoral shaft.
B, 46-year-old man with dermatomyositis, who showed no evidence of thigh muscle atrophy or inflammation on MRI. Ultrasound revealed increased echogenicity of RF muscle. Echo intensity may confer information about muscle quality for superficially located muscles, when transducer gain is standardized and transducer orientation and pressure are consistent. Lower muscle echo intensity is associated with greater muscle strength, independent of muscle size or thickness. Calipers labeled 1 and 2 mark the transverse and anteroposterior dimensions of the RF, respectively.

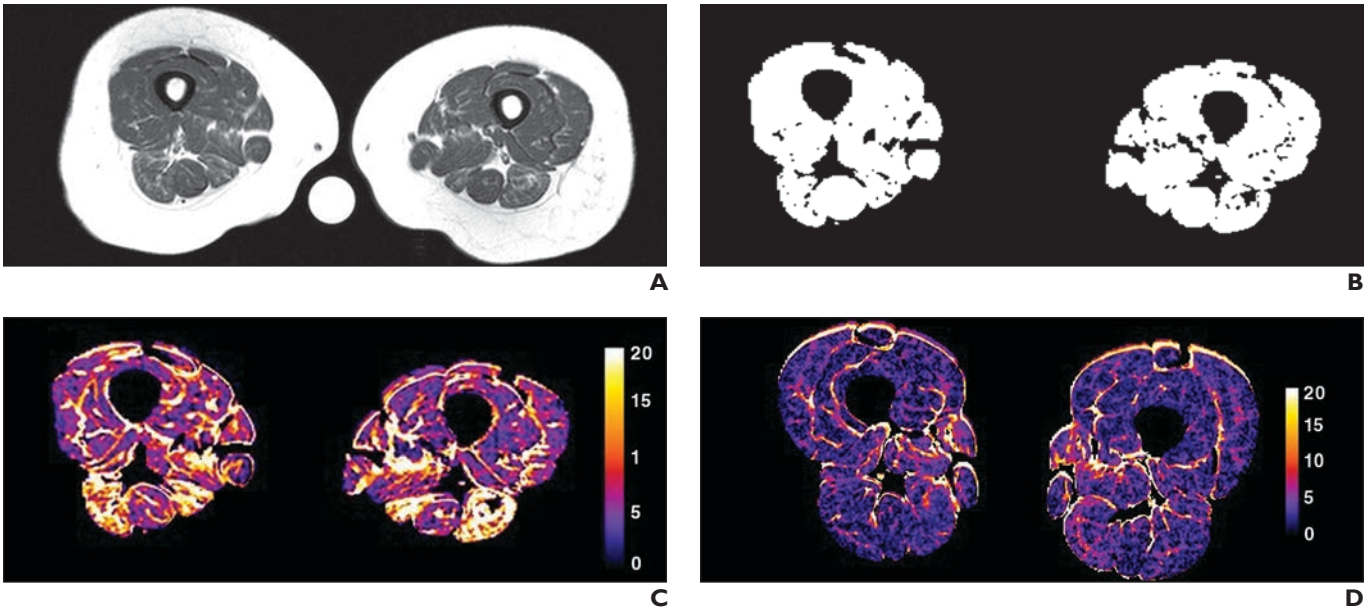


Fig. 3—Use of MRI to measure muscle and fat-water separation in two different patients. (Courtesy of Rider L)
A–C, 78-year-old woman. Axial T1-weighted spin-echo image (**A**) shows diminished muscle mass relative to subcutaneous fat and mild fatty infiltration of muscles. Adaptive thresholding techniques (**B**) can effectively segment muscle according to T1-weighted spin-echo imaging alone. Calculated fat fraction image (**C**) based on 2-point Dixon gradient-echo acquisition (not shown), shows heterogeneity in intramuscular fat, with more pronounced fat content in biceps and semimembranosus muscles (numbers on color scale are percentage of fat).
D, 42-year-old muscular man. Comparative calculated fat fraction image uses same color scale as in panel **C**. MRI fat fraction provides quantitative marker of muscle fat content. Systematic variances in fat fraction may occur because of T1 weighting bias between muscle and fat and based on how calculated images incorporate multispectral characteristics of lipid protons.

may have a role in screening patients before the use of a whole-body technique such as DEXA [66, 67].

Echo intensity—Echo intensity values are related to tissue composition, particularly fat or connective tissue within muscle, and therefore are considered an indicator of muscle quality [68, 69]. For example, muscle echo intensity (e.g., mean pixel intensity in the rectus femoris muscle) is associated with muscle strength, independent of age or muscle thickness [70].

Additional techniques—Additional sonographic parameters are under investigation to further characterize muscle quantity and quality, including mechanical properties (e.g., stiffness with elastography) [71] [72], muscle mobility [73], muscle microvasculature [74], and muscle fascicle length, pennation, and belly gearing evaluation [75, 76].

Potential pitfalls—Drawbacks of sonography in the evaluation of muscle may include factors involving the technique (e.g., reproducibility of transducer positioning or compression of muscle), the patient (e.g., body habitus), and the muscle itself (e.g., resting vs contraction) [37]. However, to date, sonographic measurements of muscle have shown acceptable reliability [77].

MRI

Like ultrasound and CT, MRI can quantify the CSA and volume of muscle, as well as display its morphologic features and distribution. However, MRI is regarded as the most sophisticated imaging technique for characterizing the loss of muscle quality, as manifested by abnormal edema, adipose tissue (myosteatosis), and fibrous connective tissue (myofibrosis) (Fig. 3).

Both fat and fibrosis are noncontractile tissues that increase within muscle during aging [78, 79] (Fig. 4). Muscle lipid content can account for up to one third of the total variance in strength [80, 81] and is a strong pre-

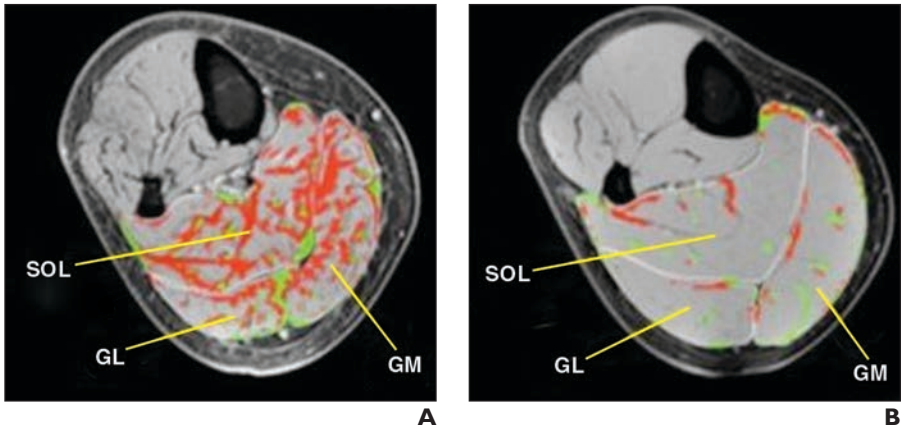


Fig. 4—Although fat-water separation techniques may aid detection of intramuscular fat, ultrashort-TE MRI can help quantify intramuscular connective tissue. Accumulation of these noncontractile muscle elements may partially explain age-related losses in muscle strength that are out of proportion with losses in muscle size. (Reprinted under terms of the Creative Commons Attribution License [79])
A, 83-year-old woman. Postprocessing of multiparametric imaging estimates connective (*red*) and adipose (*green*) tissue components within muscle, shown as color overlays on superficial posterior compartment in older adult. SOL = soleus muscle, GL = lateral gastrocnemius muscle, GM = medial gastrocnemius muscle.
B, 32-year-old woman. Corresponding noncontractile tissue map in posterior calf musculature are much less prominent in younger individual.

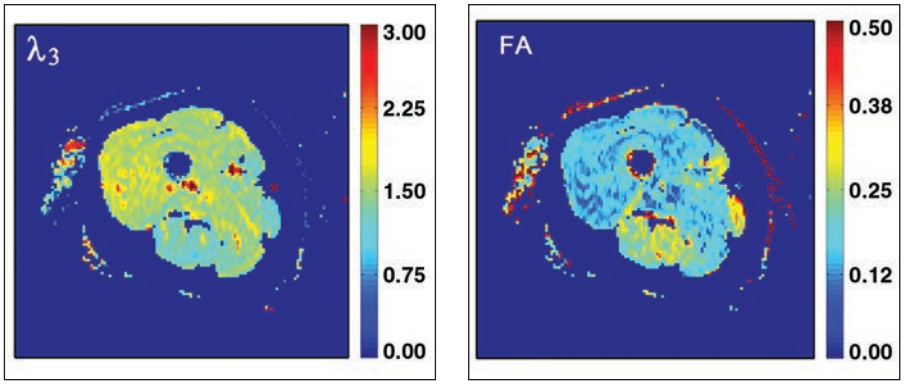


Fig. 5—30-year-old woman. DWI may yield information about diffusion anisotropy, and, indirectly, about structural features of muscle that may help determine muscle quality. (Reprinted with permission from Wiley [90])
A, Diffusion-tensor MRI of thigh yielded third eigenvalue (λ_3) image, which revealed generally higher values in anterior compartment [90]. Third eigenvector reflects average muscle fiber diameter but may also be influenced by variances in proportion of noncontractile muscle elements. Units for color scale are $10^{-3}mm^2s^{-1}$.
B, Pseudocolor image derived from diffusion-tensor imaging reflects fractional anisotropy (FA) of proton diffusion [90]. FA, as seen in hamstrings, gracilis, and sartorius muscles, may correlate with relative type I muscle fiber predominance.

dictor of loss of mobility in well-functioning older persons [82]. Similarly, muscle fibrosis is thought to be associated with decreased strength, as well as decreased elasticity, reduced blood supply, and increased atrophy in muscle [78]. MRI using tensor strain rate tensor imaging can be used to show changes in muscle contractility and elasticity that may accompany the accumulation of extracellular matrix in muscle [83].

With conventional MRI, qualitative grading of regional muscle edema, atrophy, and fatty infiltration is commonly performed. Although less common, several additional quantitative MRI techniques have been applied in clinical settings. For example, a 2-point Dixon-based technique has been used to quantify muscle-fat content in the leg of patients with achillodynia [84]. In addition, chemical shift–based water-fat separation techniques have been applied to quantify fat infiltration in the leg muscles of postmenopausal women [85], the paravertebral musculature in patients with low back pain [86], and the rotator cuff musculature of patients with symptoms of cuff tears [87].

Recently, multiparametric MRI has shown value in automated quantification of intramuscular adipose tissue depots [88], which may exert a paracrine-mediated myocyte

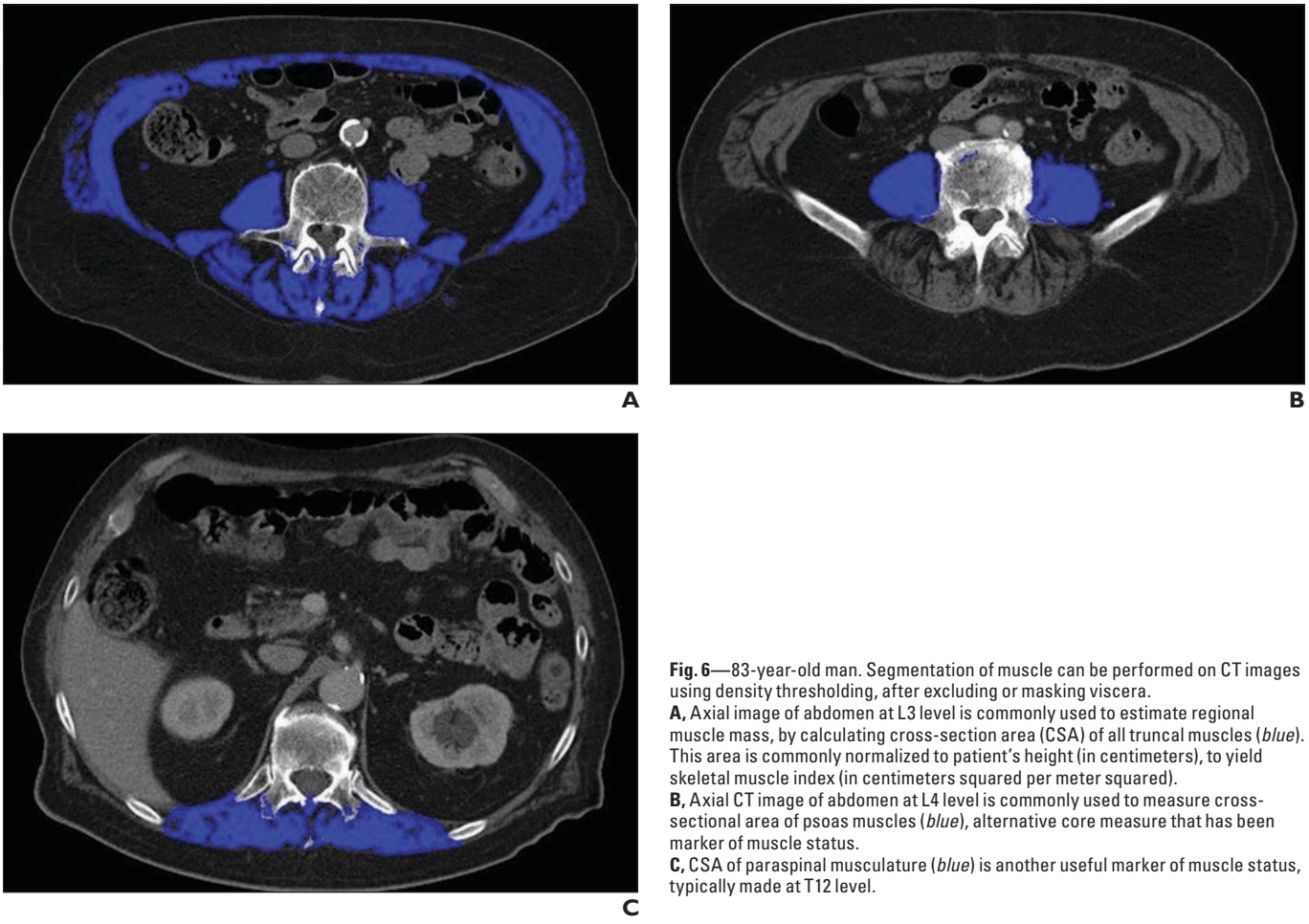


Fig. 6—83-year-old man. Segmentation of muscle can be performed on CT images using density thresholding, after excluding or masking viscera.
A, Axial image of abdomen at L3 level is commonly used to estimate regional muscle mass, by calculating cross-section area (CSA) of all truncal muscles (*blue*). This area is commonly normalized to patient's height (in centimeters), to yield skeletal muscle index (in centimeters squared per meter squared).
B, Axial CT image of abdomen at L4 level is commonly used to measure cross-sectional area of psoas muscles (*blue*), alternative core measure that has been marker of muscle status.
C, CSA of paraspinal musculature (*blue*) is another useful marker of muscle status, typically made at T12 level.

toxicity [89]. A combination of quantitative MRI methods (fat-water imaging, lipid-suppressed T2 mapping, selective inversion recovery for lipid-suppressed quantitative magnetization transfer imaging, and diffusion-tensor imaging) holds promise for elucidating issues of muscle quality [90] (Fig. 5).

Finally, MR spectroscopy can be used to specifically quantify intramyocellular lipid, which cannot be accomplished with other MRI techniques [91, 92]. Intramyocellular lipids, although associated with insulin resistance, also may be increased in the presence of cancer because of impaired mitochondrial function and, paradoxically, increase further with cancer-related weight loss [93].

CT

CT has become a routine diagnostic tool. Indeed, over 81 million CT examinations were performed in the United States in 2014, a 7% increase from 2013 [94]. When interpreting routine CT scans of patients with cancer, for example, the emphasis is appropriately on lesion detection, regional staging, and assessment for adverse outcomes after treatment. There is accumulating evidence, however, that CT body composition data, which are routinely collected but not analyzed, may be objective consequential biologic markers that can help personalize patient care.

Why mine myopenia metrics—Given that muscle is the largest protein reservoir in the body, it is not surprising that muscle mass and quality might be biomarkers of a patient's physiologic reserves. Using imaging to assess for morphometric aging biomarkers may be important for several reasons, including for evaluation of frailty, which is not consistently assessed by clinicians because of limited resources (e.g., time and expertise); for evaluation of any cause of sarcopenia, which is an independent risk factor for adverse health outcomes; for detection of sarcopenia in obese patients, because obesity can mask the clinical detection of muscle depletion; and for monitoring muscle metrics on serial examinations to better understand an individual patient's disease trajectory.

How to measure myopenia—A single axial CT image can be used as a valid, accurate, and precise method to estimate whole-body composition (Fig. 6). Two approaches are generally used for quantifying muscle CSA (squared centimeters) and density (Hounsfield units) on abdominal CT scans (see Appendixes 1 and 2). One method involves segmenting all of the muscle on an axial image at the L3 level, with image analysis software set to include tissue between –29 and 150 HU [95]. Another method measures the psoas muscle CSA at the L3 [96] or L4 level [97, 98]. In a study comparing these two general methods in patients with soft-tissue sarcoma [99], segmentation of the psoas to measure CSA and Hounsfield units was the most predictive of major surgical complications and mortality. There is wide variability among experts concerning the diagnostic cutoff values and protocol optimization (e.g., measurement level, anatomy measured, software used, and normalization for factors such as age, sex, height, and ethnicity).

Who should be measured—CT muscle metrics have been used as a biomarker of sarcopenia in patients already undergoing CT scans, particularly patients who are elderly, have cancer, or are undergoing major surgery. If the results of initial promising studies are corroborated—and imaging examinations can be standardized, measurements automated, cutoff values established, and effective treatments identified—then quantitative muscle imaging will represent a momentous paradigm shift in medicine. Intense research is focused on solving existing technical issues and assessing optimal treatments for individual patients. In patients with cancer cachexia, for example, CT is being used to assess muscle mass longitudinally in a large randomized phase-3 study comparing standard care versus specific interventions (e.g., exercise, nutrition, and antiinflammatory treatment) [37]. Hypothetically, muscle biomarkers will play a role in better understanding medical risks, allowing more informed decisions regarding treatment, prognosis, and allocation of finite resources (e.g., preoperative and postoperative nutrition and physical therapy).

Conclusion

In conclusion, sarcopenia is a condition that becomes more prevalent with advancing age, as well as with many diseases and exercise deficit disorder. Although there is continuing debate about the optimal application of clinical algorithms, diagnostic thresholds, and imaging techniques, sarcopenia is increasingly recognized as an independent risk factor for adverse health outcomes. Muscle is routinely included on radiologic examinations, and imaging analysis of sarcopenia as a potential prognostic biomarker deserves further attention.

Acknowledgment

We thank Lisa Rider for her contribution of case material with images from studies conducted at the National Institute of Environmental Health Sciences, National Institutes of Health.

References

1. Fearon K, Evans WJ, Anker SD. Myopenia: a new universal term for muscle wasting. *J Cachexia Sarcopenia Muscle* 2011; 2:1–3
2. Cruz-Jentoft AJ, Landi F, Schneider SM, et al. Prevalence of and interventions for sarcopenia in ageing adults: a systematic review—report of the International Sarcopenia Initiative (EWGSOP and IWGS). *Age Ageing* 2014; 43:748–759
3. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, et al. Sarcopenia: European consensus on definition and diagnosis—report of the European Working Group on Sarcopenia in Older People. *Age Ageing* 2010; 39:412–423
4. Fielding RA, Vellas B, Evans WJ, et al.; International Working Group on Sarcopenia. Sarcopenia: an undiagnosed condition in older adults—current consensus definition; prevalence, etiology, and consequences. *J Am Med Dir Assoc* 2011; 12:249–256
5. Kim H, Suzuki T, Saito K, et al. Long-term effects of exercise and amino acid supplementation on muscle mass, physical function and falls in community-dwelling elderly Japanese sarcopenic women: a 4-year follow-up study. *Geriatr Gerontol Int* 2015 Feb 5 [Epub ahead of print]
6. Ahedi H, Aitken D, Scott D, Blizzard L, Cicuttini F, Jones G. The association between hip muscle cross-sectional area, muscle strength, and bone mineral density. *Calcif Tissue Int* 2014; 95:64–72
7. Landi F, Liperoti R, Russo A, et al. Sarcopenia as a risk factor for falls in elderly individuals: results from the ilSIRENTE study. *Clin Nutr* 2012; 31:652–658
8. Gariballa S, Alessa A. Sarcopenia: prevalence and prognostic significance in hospitalized patients. *Clin Nutr* 2013; 32:772–776
9. Jones KI, Doleman B, Scott S, Lund JN, Williams JP. Simple psoas cross-sectional area measurement is a quick and easy method to assess sarcopenia and predicts major surgical complications. *Colorectal Dis* 2015; 17:O20–O26
10. Alexandre Tda S, Duarte YA, Santos JL, Wong R, Lebrão ML. Sarcopenia according to the European Working Group on Sarcopenia in Older People (EWGSOP) versus dynapenia as a risk factor for mortality in the elderly. *J Nutr Health Aging* 2014; 18:751–756
11. Vetrano DL, Landi F, Volpato S, et al. Association of sarcopenia with short- and long-term mortality in older adults admitted to acute care wards: results from the CRIME study. *J Gerontol*

A Biol Sci Med Sci 2014; 69:1154–1161

12. Rosenberg IH. Summary comments. *Am J Clin Nutr* 1989; 50:1231–1233 ajcn.nutrition.org/content/50/5/1231.full.pdf
13. Correa-de-Araujo R, Hadley E. Skeletal muscle function deficit: a new terminology to embrace the evolving concepts of sarcopenia and age-related muscle dysfunction. *J Gerontol A Biol Sci Med Sci* 2014; 69:591–594
14. McLean RR, Shardell MD, Alley DE, et al. Criteria for clinically relevant weakness and low lean mass and their longitudinal association with incident mobility impairment and mortality: the Foundation for the National Institutes of Health (FNIH) Sarcopenia Project. *J Gerontol A Biol Sci Med Sci* 2014; 69:576–583
15. Fragala MS, Dam TT, Barber V, et al. Strength and function response to clinical interventions of older women categorized by weakness and low lean mass using classifications from the Foundation for the National Institutes of Health Sarcopenia Project. *J Gerontol A Biol Sci Med Sci* 2015; 70:202–209
16. Anker SD, Coats AJ, Morley JE, et al. Muscle wasting disease: a proposal for a new disease classification. *J Cachexia Sarcopenia Muscle* 2014; 5:1–3
17. von Haehling S, Anker SD. Treatment of cachexia: an overview of recent developments. *J Am Med Dir Assoc* 2014; 15:866–872
18. von Haehling S, Anker SD. Prevalence, incidence and clinical impact of cachexia: facts and numbers—update 2014. *J Cachexia Sarcopenia Muscle* 2014; 5:261–263
19. Muscaritoli M, Molfino A, Lucia S, Rossi Fanelli F. Cachexia: a preventable comorbidity of cancer—a T.A.R.G.E.T. approach. *Crit Rev Oncol Hematol* 2015; 94:251–259
20. Blum D, Stene GB, Solheim TS, et al. Validation of the Consensus-Definition for Cancer Cachexia and evaluation of a classification model: a study based on data from an international multicentre project (EPCRC-CSA). *Ann Oncol* 2014; 25:1635–1642
21. Johns N, Hatakeyama S, Stephens NA, et al. Clinical classification of cancer cachexia: phenotypic correlates in human skeletal muscle. *PLoS ONE* 2014; 9:e83618
22. Baracos VE. Pitfalls in defining and quantifying cachexia. *J Cachexia Sarcopenia Muscle* 2011; 2:71–73
23. Handforth C, Clegg A, Young C, et al. The prevalence and outcomes of frailty in older cancer patients: a systematic review. *Ann Oncol* 2014 Nov 20 [Epub ahead of print]
24. Theou O, Brothers TD, Peña FG, Mitnitski A, Rockwood K. Identifying common characteristics of frailty across seven scales. *J Am Geriatr Soc* 2014; 62:901–906
25. Jung HW, Kim SW, Lim JY, et al. Frailty status can predict further lean body mass decline in older adults. *J Am Geriatr Soc* 2014; 62:2110–2117
26. Mijnarends DM, Schols JM, Meijers JM, et al. Instruments to assess sarcopenia and physical frailty in older people living in a community (care) setting: similarities and discrepancies. *J Am Med Dir Assoc* 2015; 15:301–308
27. Morley JE, Anker SD, von Haehling S. Prevalence, incidence, and clinical impact of sarcopenia: facts, numbers, and epidemiology—update 2014. *J Cachexia Sarcopenia Muscle* 2014; 5:253–259
28. von Haehling S, Morley JE, Anker SD. An overview of sarcopenia: facts and numbers on prevalence and clinical impact. *J Cachexia Sarcopenia Muscle* 2010; 1:129–133
29. von Haehling S, Morley JE, Anker SD. From muscle wasting to sarcopenia and myopenia: update 2012. *J Cachexia Sarcopenia Muscle* 2012; 3:213–217
30. Morley JE, Vellas B, Abellan van Kan G, et al. Frailty consensus: a call to action. *J Am Med Dir Assoc* 2013; 14:392–397
31. Malmstrom TK, Miller DK, Morley JE. A comparison of four frailty models. *J Am Geriatr Soc* 2014; 62:721–726
32. Carpenter CR, Shelton E, Fowler S, et al. Risk factors and screening instruments to predict adverse outcomes for undifferentiated older emergency department patients: a systematic review and meta-analysis. *Acad Emerg Med* 2015; 22:1–21
33. Yoshida D, Suzuki T, Shimada H, et al. Using two different algorithms to determine the prevalence of sarcopenia. *Geriatr Gerontol Int* 2014; 14(suppl 1):46–51
34. Volpato S, Bianchi L, Cherubini A, et al. Prevalence and clinical correlates of sarcopenia in community-dwelling older people: application of the EWGSOP definition and diagnostic algorithm. *J Gerontol A Biol Sci Med Sci* 2014; 69:438–446
35. Smoliner C, Sieber CC, Wirth R. Prevalence of sarcopenia in geriatric hospitalized patients. *J Am Med Dir Assoc* 2014; 15:267–272
36. Janssen I, Shepard DS, Katzmarzyk PT, Roubenoff R. The healthcare costs of sarcopenia in the United States. *J Am Geriatr Soc* 2004; 52:80–85
37. Prado CM, Heymsfield SB. Lean tissue imaging: a new era for nutritional assessment and intervention. *JPEN J Parenter Enter Nutr* 2014; 38:940–953
38. Batsis JA, Mackenzie TA, Barre LK, Lopez-Jimenez F, Bartels SJ. Sarcopenia, sarcopenic obesity and mortality in older adults: results from the National Health and Nutrition Examination Survey III. *Eur J Clin Nutr* 2014; 68:1001–1007
39. Visser M, van Venrooij LM, Vulperhorst L, et al. Sarcopenic obesity is associated with adverse clinical outcome after cardiac surgery. *Nutr Metab Cardiovasc Dis* 2013; 23:511–518
40. Kim TN, Park MS, Ryu JY, et al. Impact of visceral fat on skeletal muscle mass and vice versa in a prospective cohort study: the Korean Sarcopenic Obesity Study (KSOS). *PLoS ONE* 2014; 9:e115407
41. Binkley N, Buehring B. Beyond FRAX: it's time to consider "sarco-osteopenia". *J Clin Densitom* 2009; 12:413–416
42. Ilich JZ, Kelly OJ, Inglis JE, Panton LB, Duque G, Ormsbee MJ. Interrelationship among muscle, fat, and bone: connecting the dots on cellular, hormonal, and whole body levels. *Ageing Res Rev* 2014; 15:51–60
43. Di Monaco M, Castiglioni C, De Toma E, et al. Presarcopenia and sarcopenia in hip-fracture women: prevalence and association with ability to function in activities of daily living. *Aging Clin Exp Res* 2015 Jan 10 [Epub ahead of print]
44. Müller MJ, Geisler C, Pourhassan M, Glüer CC, Bosy-Westphal A. Assessment and definition of lean body mass deficiency in the elderly. *Eur J Clin Nutr* 2014; 68:1220–1227
45. Faulkner JA, Larkin LM, Claflin DR, Brooks SV. Age-related changes in the structure and function of skeletal muscles. *Clin Exp Pharmacol Physiol* 2007; 34:1091–1096
46. Wall BT, Dirks ML, van Loon LJ. Skeletal muscle atrophy during short-term disuse: implications for age-related sarcopenia. *Ageing Res Rev* 2013; 12:898–906
47. Goodpaster BH, Park S, Harris T, et al. 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* 2006; 61:1059–1064
48. Wall BT, Dirks ML, Snijders T, Senden JM, Dolmans J, van Loon LJ. Substantial skeletal muscle loss occurs during only 5 days of disuse. *Acta Physiol (Oxf)* 2014; 210:600–611
49. Hvid LG, Suetta C, Nielsen JH, et al. Aging impairs the recovery in mechanical muscle function following 4 days of disuse. *Exp Gerontol* 2014; 52:1–8
50. Cao L, Chen S, Zou C, et al. A pilot study of the SARC-F scale on screening sarcopenia and physical disability in the Chinese older people. *J Nutr Health Aging* 2014; 18:277–283
51. Woo J, Leung J, Morley JE. Validating the SARC-F: a suitable community screening tool for sarcopenia? *J Am Med Dir Assoc* 2014; 15:630–634
52. Al-Gindan YY, Hankey C, Govan L, Gallagher D, Heymsfield SB, Lean ME. Derivation and validation of simple equations to predict total muscle mass from simple anthropometric and demographic data. *Am J Clin Nutr* 2014; 100:1041–1051
53. Anderson DE, Bean JF, Holt NE, Keel JC, Boux-

sein ML. Computed tomography-based muscle attenuation and electrical impedance myography as indicators of trunk muscle strength independent of muscle size in older adults. *Am J Phys Med Rehabil* 2014; 93:553–561

54. Cesari M, Fielding RA, Pahor M, et al. Biomarkers of sarcopenia in clinical trials: recommendations from the International Working Group on Sarcopenia. *J Cachexia Sarcopenia Muscle* 2012; 3:181–190
55. Kendler DL, Borges JLC, Fielding RA, et al. The official positions of the International Society for Clinical Densitometry: indications of use and reporting of DXA for body composition. *J Clin Densitom* 2013; 16:496–507
56. Hangartner TN, Warner S, Braillon P, Jankowski L, Shepherd J. The official positions of the International Society for Clinical Densitometry: acquisition of dual-energy X-ray absorptiometry body composition and considerations regarding analysis and repeatability of measures. *J Clin Densitom* 2013; 16:520–536
57. Shepherd JA, Baim S, Bilezikian JP, et al. Executive summary of the 2013 International Society for Clinical Densitometry Position Development Conference on Body Composition. *J Clin Densitom* 2013; 16:489–495
58. Takeshima N, Shimada K, Islam MM, Kanehisa H, Ishida Y, Brechue WF. Progressive, site-specific loss of muscle mass in older frail nursing home residents. *J Aging Phys Act* 2014 Nov 11 [Epub ahead of print]
59. Scherbakov N, Sandek A, Doehner W. Stroke-related sarcopenia: specific characteristics. *J Am Med Dir Assoc* 2015; 16:272–276
60. Puthucheary ZA, Rawal J, McPhail M, et al. Acute skeletal muscle wasting in critical illness. *JAMA* 2013; 310:1591–1600
61. Scanlon TC, Fragala MS, Stout JR, et al. Muscle architecture and strength: adaptations to short-term resistance training in older adults. *Muscle Nerve* 2014; 49:584–592
62. Strasser EM, Draskovits T, Praschak M, Quittan M, Graf A. Association between ultrasound measurements of muscle thickness, pennation angle, echogenicity and skeletal muscle strength in the elderly. *Age (Dordr)* 2013; 35:2377–2388
63. Wells AJ, Fukuda DH, Hoffman JR, et al. Vastus lateralis exhibits non-homogenous adaptation to resistance training. *Muscle Nerve* 2014; 50:785–793
64. Scott JM, Martin DS, Ploutz-Snyder R, et al. Reliability and validity of panoramic ultrasound for muscle quantification. *Ultrasound Med Biol* 2012; 38:1656–1661
65. Ahtiainen JP, Hoffren M, Hulmi JJ, et al. Panoramic ultrasonography is a valid method to measure changes in skeletal muscle cross-sectional area. *Eur J Appl Physiol* 2010; 108:273–279
66. Abe T, Thiebaud RS, Loenneke JP, Loftin M, Fukunaga T. Prevalence of site-specific thigh sarcopenia in Japanese men and women. *Age (Dordr)* 2014; 36:417–426
67. Loenneke JP, Thiebaud RS, Abe T. Estimating site-specific muscle loss: a valuable tool for early sarcopenia detection? *Rejuvenation Res* 2014; 17:496–498
68. Nishihara K, Kawai H, Hayashi H, et al. Frequency analysis of ultrasonic echo intensities of the skeletal muscle in elderly and young individuals. *Clin Interv Aging* 2014; 9:1471–1478
69. Rosenberg JG, Ryan ED, Sobolewski EJ, Scharville MJ, Thompson BJ, King GE. Reliability of panoramic ultrasound imaging to simultaneously examine muscle size and quality of the medial gastrocnemius. *Muscle Nerve* 2014; 49:736–740
70. Watanabe Y, Yamada Y, Fukumoto Y, et al. Echo intensity obtained from ultrasonography images reflecting muscle strength in elderly men. *Clin Interv Aging* 2013; 8:993–998
71. Brandenburg JE, Eby SF, Song P, et al. Ultrasound elastography: the new frontier in direct measurement of muscle stiffness. *Arch Phys Med Rehabil* 2014; 95:2207–2219
72. Wang CZ, Li TJ, Zheng YP. Shear modulus estimation on vastus intermedius of elderly and young females over the entire range of isometric contraction. *PLoS ONE* 2014; 9:e101769
73. Souza H, Rocha T, Pessoa M, et al. Effects of inspiratory muscle training in elderly women on respiratory muscle strength, diaphragm thickness and mobility. *J Gerontol A Biol Sci Med Sci* 2014; 69:1545–1553
74. Mitchell WK, Phillips BE, Williams JP, et al. Development of a new Sonovue contrast-enhanced ultrasound approach reveals temporal and age-related features of muscle microvascular responses to feeding. *Physiol Rep* 2013; 1:e00119
75. Randhawa A, Wakeling JM. Associations between muscle structure and contractile performance in seniors. *Clin Biomech (Bristol, Avon)* 2013; 28:705–711
76. Narici MV, Flueck M, Koesters A, et al. Skeletal muscle remodeling in response to alpine skiing training in older individuals. *Scand J Med Sci Sports* 2011; 21(suppl 1):23–28
77. Tillquist M, Kutsogiannis DJ, Wischmeyer PE, et al. Bedside ultrasound is a practical and reliable measurement tool for assessing quadriceps muscle layer thickness. *JPEN J Parenter Enteral Nutr* 2014; 38:886–890
78. Zoico E, Corzato F, Bambace C, et al. Myosteatosis and myofibrosis: relationship with aging, inflammation and insulin resistance. *Arch Gerontol Geriatr* 2013; 57:411–416
79. Csapo R, Malis V, Sinha U, Du J, Sinha S. Age-associated differences in triceps surae muscle composition and strength: an MRI-based cross-sectional comparison of contractile, adipose and connective tissue. *BMC Musculoskelet Disord* 2014; 15:209
80. Goodpaster BH, Carlson CL, Visser M, et al. Attenuation of skeletal muscle and strength in the elderly: the Health ABC Study. *J Appl Physiol* 2001; 90:2157–2165
81. Marcus RL, Addison O, Dibble LE, Foreman KB, Morrell G, Lastayo P. Intramuscular adipose tissue, sarcopenia, and mobility function in older individuals. *J Aging Res* 2012; 2012:629637
82. Murphy RA, Reinders I, Register TC, et al. Associations of BMI and adipose tissue area and density with incident mobility limitation and poor performance in older adults. *Am J Clin Nutr* 2014; 99:1059–1065
83. Sinha U, Malis V, Csapo R, Moghadasi A, Kinugasa R, Sinha S. Age-related differences in strain rate tensor of the medial gastrocnemius muscle during passive plantarflexion and active isometric contraction using velocity encoded MR imaging: potential index of lateral force transmission. *Magn Reson Med* 2015; 73:1852–1862
84. Fischer MA, Pfirrmann CWA, Espinosa N, Raptis DA, Buck FM. Dixon-based MRI for assessment of muscle-fat content in phantoms, healthy volunteers and patients with achillodynia: comparison to visual assessment of calf muscle quality. *Eur Radiol* 2014; 24:1366–1375
85. Alizai H, Nardo L, Karampinos DC, et al. Comparison of clinical semi-quantitative assessment of muscle fat infiltration with quantitative assessment using chemical shift-based water/fat separation in MR studies of the calf of post-menopausal women. *Eur Radiol* 2012; 22:1592–1600
86. Fischer MA, Nanz D, Shimakawa A, et al. Quantification of muscle fat in patients with low back pain: comparison of multi-echo MR imaging with single-voxel MR spectroscopy. *Radiology* 2013; 266:555–563
87. Nardo L, Karampinos DC, Lansdown DA, et al. Quantitative assessment of fat infiltration in the rotator cuff muscles using water-fat MRI. *J Magn Reson Imaging* 2014; 39:1178–1185
88. Valentinitsch A, Karampinos DC, Alizai H, et al. Automated unsupervised multi-parametric classification of adipose tissue depots in skeletal muscle. *J Magn Reson Imaging* 2013; 37:917–927
89. Kob R, Bollheimer LC, Bertsch T, et al. Sarcopenic obesity: molecular clues to a better understanding of its pathogenesis? *Biogerontology* 2015; 16:15–29
90. Li K, Dortch RD, Welch EB, et al. Multi-parametric MRI characterization of healthy human thigh muscles at 3.0 T: relaxation, magnetization transfer, fat/water, and diffusion tensor imaging. *NMR Biomed* 2014; 27:1070–1084

91. Cao P, Fan SJ, Wang AM, et al. Diffusion magnetic resonance monitors intramyocellular lipid droplet size in vivo. *Magn Reson Med* 2014 Jan 27 [Epub ahead of print]
92. Hu HH, Kan HE. Quantitative proton MR techniques for measuring fat. *NMR Biomed* 2013; 26:1609–1629
93. Stephens NA, Skipworth RJ, MacDonald AJ, Greig CA, Ross JA, Fearon KC. Intramyocellular lipid droplets increase with progression of cachexia in cancer patients. *J Cachexia Sarcopenia Muscle* 2011; 2:111–117
94. IMV Medical Information Division. 2014 CT market outlook report. IMV website. www.imvinfo.com/index.aspx?sec=ct&sub=dis&itemid=200081. Published accessed October 2014. Accessed February 1, 2015
95. Martin L, Birdsell L, MacDonald N, et al. Cancer cachexia in the age of obesity: skeletal muscle depletion is a powerful prognostic factor, independent of body mass index. *J Clin Oncol* 2013; 31:1539–1547
96. Peng PD, van Vledder MG, Tsai S, et al. Sarcopenia negatively impacts short-term outcomes in patients undergoing hepatic resection for colorectal liver metastasis. *HPB (Oxford)* 2011; 13:439–446
97. Miller AL, Min LC, Diehl KM, et al. Analytic morphomics corresponds to functional status in older patients. *J Surg Res* 2014; 192:19–26
98. Zarinsefat A, Terjimanian MN, Sheetz KH, et al. Perioperative changes in trunk musculature and postoperative outcomes. *J Surg Res* 2014; 191:106–112
99. Boutin RD, Katz J, Chaudhari A, et al. Significance of sarcopenia in soft-tissue sarcoma patients: do skeletal muscle and fat measures of body composition on routine CT exams help predict clinical outcomes? (abstract) RSNA 2014. Oak Brook, IL: Radiological Society of North America. archive.rsna.org/2014/14011743.html. Accessed May 7, 2015
100. Lee JS, He K, Harbaugh CM, et al. Frailty, core muscle size, and mortality in patients undergoing open abdominal aortic aneurysm repair. *J Vasc Surg* 2011; 53:912–917
101. Englesbe MJ, Lee JS, He K, et al. Analytic morphomics, core muscle size, and surgical outcomes. *Ann Surg* 2012; 256:255–261
102. Sabel MS, Terjimanian M, Conlon AS, et al. Analytic morphometric assessment of patients undergoing colectomy for colon cancer. *J Surg Oncol* 2013; 108:169–175
103. Krell RW, Kaul DR, Martin AR, et al. Association between sarcopenia and the risk of serious infection among adults undergoing liver transplantation. *Liver Transpl* 2013; 19:1396–1402
104. Sheetz KH, Zhao L, Holcombe SA, et al. Decreased core muscle size is associated with worse patient survival following esophagectomy for cancer. *Dis Esophagus* 2013; 26:716–722
105. Sheetz KH, Waits SA, Terjimanian MN, et al. Cost of major surgery in the sarcopenic patient. *J Am Coll Surg* 2013; 217:813–818
106. Canvasser LD, Mazurek AA, Cron DC, et al. Paraspinous muscle as a predictor of surgical outcome. *J Surg Res* 2014; 192:76–81
107. Lee CS, Cron DC, Terjimanian MN, et al. Dorsal muscle group area and surgical outcomes in liver transplantation. *Clin Transplant* 2014; 28:1092–1098
108. Joglekar S, Asghar A, Mott SL, et al. Sarcopenia is an independent predictor of complications following pancreatectomy for adenocarcinoma. *J Surg Oncol* 2015; 111:771–775
109. Otsuji H, Yokoyama Y, Ebata T, et al. Preoperative sarcopenia negatively impacts postoperative outcomes following major hepatectomy with extrahepatic bile duct resection. *World J Surg* 2015; 39:1494—1500
110. Prado CM, Lieffers JR, McCargar LJ, et al. Prevalence and clinical implications of sarcopenic obesity in patients with solid tumours of the respiratory and gastrointestinal tracts: a population-based study. *Lancet Oncol* 2008; 9:629–635
111. Tan BH, Birdsell LA, Martin L, Baracos VE, Fearon KC. Sarcopenia in an overweight or obese patient is an adverse prognostic factor in pancreatic cancer. *Clin Cancer Res* 2009; 15:6973–6979
112. Antoun S, Baracos VE, Birdsell L, Escudier B, Sawyer MB. Low body mass index and sarcopenia associated with dose-limiting toxicity of sorafenib in patients with renal cell carcinoma. *Ann Oncol* 2010; 21:1594–1598
113. Lieffers JR, Bathe OF, Fassbender K, Winget M, Baracos VE. Sarcopenia is associated with postoperative infection and delayed recovery from colorectal cancer resection surgery. *Br J Cancer* 2012; 107:931–936
114. van Vledder MG, Levolger S, Ayez N, Verhoef C, Tran TC, Ijzermans JN. Body composition and outcome in patients undergoing resection of colorectal liver metastases. *Br J Surg* 2012; 99:550–557
115. Harimoto N, Shirabe K, Yamashita YI, et al. Sarcopenia as a predictor of prognosis in patients following hepatectomy for hepatocellular carcinoma. *Br J Surg* 2013; 100:1523–1530
116. Meza-Junco J, Montano-Loza AJ, Baracos VE, et al. Sarcopenia as a prognostic index of nutritional status in concurrent cirrhosis and hepatocellular carcinoma. *J Clin Gastroenterol* 2013; 47:861–870
117. Lanic H, Kraut-Tauzia J, Modzelewski R, et al. Sarcopenia is an independent prognostic factor in elderly patients with diffuse large B-cell lymphoma treated with immunochemotherapy. *Leuk Lymphoma* 2014; 55:817–823
118. Barret M, Antoun S, Dalban C, et al. Sarcopenia is linked to treatment toxicity in patients with metastatic colorectal cancer. *Nutr Cancer* 2014; 66:583–589
119. Fogelman DR, Holmes H, Mohammed K, et al. Does IGFR1 inhibition result in increased muscle mass loss in patients undergoing treatment for pancreatic cancer? *J Cachexia Sarcopenia Muscle* 2014; 5:307–313
120. Tan BH, Brammer K, Randhawa N, et al. Sarcopenia is associated with toxicity in patients undergoing neo-adjuvant chemotherapy for oesophagogastric cancer. *Eur J Surg Oncol* 2015; 41:333–338
121. Fukushima H, Yokoyama M, Nakanishi Y, Tobisu K, Koga F. Sarcopenia as a prognostic biomarker of advanced urothelial carcinoma. *PLoS ONE* 2015; 10:e0115895
122. Reisinger KW, van Vugt JL, Tegels JJ, et al. Functional compromise reflected by sarcopenia, frailty, and nutritional depletion predicts adverse postoperative outcome after colorectal cancer surgery. *Ann Surg* 2015; 261:345–352
123. van Vugt JL, Braam HJ, van Oudheusden TR, et al. Skeletal muscle depletion is associated with severe postoperative complications in patients undergoing cytoreductive surgery with hyperthermic intraperitoneal chemotherapy for peritoneal carcinomatosis of colorectal cancer. *Ann Surg Oncol* 2015 Feb 12 [Epub ahead of print]
124. Miyamoto Y, Baba Y, Sakamoto Y, et al. Sarcopenia is a negative prognostic factor after curative resection of colorectal cancer. *Ann Surg Oncol* 2015 Jan 7 [Epub ahead of print]

(Appendixes continue on next page)

APPENDIX 1: Studies That Used CT to Evaluate Sarcopenia in Surgical Patients (Psoas or Paravertebral Muscles)

Study (Year)	Operation	No. of Patients	Muscle Measured	Level	Key Findings Among Patients With Sarcopenia
Peng et al. [96] (2011)	Liver resection	259	Psoas	L3	Increased postoperative complications, longer ICU and hospital stays
Lee et al. [100] (2011)	Aortic aneurysm	262	Psoas	L4	Decreased survival
Englesbe et al. [101] (2012)	General or vascular	1453	Psoas	L4	Decreased survival, increased postoperative complications
Sabel et al. [102] (2013)	Colon cancer	302	Psoas	L4	Increased postoperative complications
Krell et al. [103] (2013)	Liver transplant	207	Psoas	L4	Increased postoperative infections, decreased survival
Sheetz et al. [104] (2013)	Esophagectomy	230	Psoas	L4	Decreased survival
Sheetz et al. [105] (2013)	General or vascular	1593	Psoas	L4	Increased medical costs[a]
Zarinsefat et al. [98] (2014)	General	425	Psoas	L4	Decreased survival
Canvasser et al. [106] (2014)	General	1309	Paravertebral	T12	Decreased survival
Lee et al. [107] (2014)	Liver transplant	325	Paravertebral	T12	Increased postoperative complications, decreased survival
Joglekar et al. [108] (2015)	Pancreatectomy	118	Psoas	L3	Increased postoperative complications, longer ICU and hospital stays
Otsuji et al. [109] (2015)	Liver resection	256	Psoas	L3	Increased morbidity, including liver failure

Note—The minimum sample size for inclusion in this table is 100 patients.
[a]Postoperative care of patients with sarcopenia resulted in an average negative margin for the hospital (–$873), in contrast to average positive margin for all patients ($1806) and for patients without sarcopenia ($3170).

APPENDIX 2: Studies That Used CT and the L3 Skeletal Muscle Index to Evaluate Sarcopenia in Patients With Cancer

Study (Year)	Type of Cancer	No. of CT Examinations	L3 Skeletal Muscle Index Cutoff Point for Sarcopenia[a]	Prevalence of Sarcopenia (%)	Key Findings Among Patients With Sarcopenia	Comments
Prado et al. [110] (2008)	Lung, gastrointestinal	250	< 38.5 in women; < 52.4 in men	15	Poor functional status, decreased survival	All patients were obese (BMI ≥ 30)
Tan et al. [111] (2009)	Pancreas	111	< 38.5 in women; < 52.4 in men	56	Decreased survival (for obese or overweight patients)	16% of patients were both sarcopenic and overweight or obese.
Antoun et al. [112] (2010)	Renal	55	< 38.9 in women; < 55.4 in men	55	Increased toxicity from chemotherapy	40% of obese or overweight patients had sarcopenia
Lieffers et al. [113] (2012)	Colorectal	234	< 38.5 in women; < 52.4 in men	39	Increased postoperative infections, increased hospital stays	Infection risk 4.6-fold higher in patients (age ≥ 65 years) with sarcopenia than for patients without sarcopenia
van Vledder et al. [114] (2012)	Colorectal	196	< 41.1 in women; < 43.75 in men	19	Decreased survival	5-year survival: 20% with sarcopenia vs 50% without sarcopenia
Harimoto et al. [115] (2013)	HCC	186	< 41.1 in women; < 43.75 in men	40	Decreased survival	5-year survival: 71% with sarcopenia vs 84% without sarcopenia
Martin et al. [95] (2013)	Lung, gastrointestinal	1473	< 41 for women; < 43 for normal or underweight men; < 53 for overweight or obese men	53 in women; 31 in men	Decreased survival	Muscle attenuation thresholds for lower survival: < 41 HU for normal or underweight; < 33 HU for overweight or obese
Meza-Junco et al. [116] (2013)	HCC	116	< 41 for women; < 43 for normal or underweight men; < 53 for overweight or obese men	30	Decreased survival	Mortality risk > 2-fold higher in patients with sarcopenia than in patients without sarcopenia
Lanic et al. [117] (2014)	Lymphoma	82	< 38.9 in women; < 55.8 in men	55	Decreased survival	2-year overall survival: 46% with sarcopenia vs 84% without sarcopenia
Barret et al. [118] (2014)	Colorectal	51	< 38.9 in women; < 55.4 in men	71	Increased toxicity from chemotherapy	45% of patients were obese or overweight

Appendix 2 continues on next page

APPENDIX 2: Studies That Used CT and the L3 Skeletal Muscle Index to Evaluate Sarcopenia in Patients With Cancer (continued)

Study (Year)	Type of Cancer	No. of CT Examinations	L3 Skeletal Muscle Index Cutoff Point for Sarcopenia[a]	Prevalence of Sarcopenia (%)	Key Findings Among Patients With Sarcopenia	Comments
Fogelman et al. [119] (2014)	Pancreas	53	≥ 6 cm^2 muscle loss after 2 months of treatment	64	Decreased survival	Muscle retention after 2 months of treatment correlated with better survival (hazard ratio 0.51, $p = 0.03$)
Tan et al. [120] (2015)	Esophagogastric	89	< 38.5 in women; < 52.4 in men	49	Increased toxicity from chemotherapy	Median survival: 19 months with sarcopenia vs 34 months without sarcopenia
Fukushima et al. [121] (2015)	Urothelial	88	< 41 for women; < 43 for normal or underweight men; < 53 for overweight or obese men	60	Decreased survival	Median survival: 11 months with sarcopenia vs 31 months without sarcopenia
Reisinger et al. [122] (2015)	Colorectal	310	< 38.5 in women; < 52.4 in men	48	Decreased survival	In-hospital 30-day mortality rate: 8.8% with sarcopenia vs 0.7% without sarcopenia
van Vugt et al. [123] (2015)	Colorectal	206	< 38.5 in women; < 52.4 in men	44	Increased postoperative complications	Repeat surgery in 26% of patients with sarcopenia vs 12% of those without sarcopenia
Miyamoto et al. [124] (2015)	Colorectal	220	< 42.1 in women; < 49.6 in men	25	Decreased survival	Association of sarcopenia with shorter survival strongest in patients age < 65 years

Note—The minimum sample size for inclusion in this table is 50 patients. BMI = body mass index (weight in kilograms divided by the square of height in meters), HCC = hepatocellular carcinoma.

[a]The total cross-sectional area (centimeters squared) of skeletal muscle segmented at the L3 level, normalized for patient height squared (meters squared), yields the skeletal muscle index (centimeters squared divided by meters squared). L3 refers to skeletal muscle evaluated at the third lumbar level; the cross-sectional area segmented in all of these studies contained the psoas, paraspinal muscles (erector spinae and quadratus lumborum), and abdominal wall muscles (transversus abdominis, external and internal obliques, and rectus abdominis).

This article has been cited by:

1. Lohit Garg, Sahil Agrawal, Timothy Pew, George S. Hanzel, Amr E. Abbas, Michael J. Gallagher, Francis L. Shannon, Ivan D. Hanson. 2017. Psoas Muscle Area as a Predictor of Outcomes in Transcatheter Aortic Valve Implantation. *The American Journal of Cardiology* **119**:3, 457-460. [CrossRef]
2. Joyce Veld, Josephina A. Vossen, Karen De Amorim Bernstein, Elkan F. Halpern, Martin Torriani, Miriam A. Bredella. 2016. Adipose tissue and muscle attenuation as novel biomarkers predicting mortality in patients with extremity sarcomas. *European Radiology* **26**:12, 4649-4655. [CrossRef]
3. Robert D. Boutin, Justin M. Kaptuch, Cyrus P. Bateni, James S. Chalfant, Lawrence Yao. 2016. Influence of IV Contrast Administration on CT Measures of Muscle and Bone Attenuation: Implications for Sarcopenia and Osteoporosis Evaluation. *American Journal of Roentgenology* **207**:5, 1046-1054. [Abstract] [Full Text] [PDF] [PDF Plus]
4. Andrey Sinelnikov, Chuanxing Qu, David T. Fetzer, Jean-Sébastien Pelletier, Michael A. Dunn, Allan Tsung, Alessandro Furlan. 2016. Measurement of skeletal muscle area: Comparison of CT and MR imaging. *European Journal of Radiology* **85**:10, 1716-1721. [CrossRef]
5. Takashi Abe, Eiji Fujita, Robert S. Thiebaud, Jeremy P. Loenneke, Takuya Akamine. 2016. Ultrasound-Derived Forearm Muscle Thickness Is a Powerful Predictor for Estimating DXA-Derived Appendicular Lean Mass in Japanese Older Adults. *Ultrasound in Medicine & Biology* **42**:9, 2341-2344. [CrossRef]
6. Ronald M. Summers. 2016. Progress in Fully Automated Abdominal CT Interpretation. *American Journal of Roentgenology* **207**:1, 67-79. [Abstract] [Full Text] [PDF] [PDF Plus]
7. Samuel Mamane, Louis Mullie, Nicolo Piazza, Giuseppe Martucci, José Morais, Antonio Vigano, Mark Levental, Kristoff Nelson, Ruediger Lange, Jonathan Afilalo. 2016. Psoas Muscle Area and All-Cause Mortality After Transcatheter Aortic Valve Replacement: The Montreal-Munich Study. *Canadian Journal of Cardiology* **32**:2, 177-182. [CrossRef]