Review Article

Ultrasonography for Assessment of Sarcopenia: A Primer

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Abstract

The human skeletal muscle has a pivotal role in preserving health by maintaining mobility, balance, and metabolic homeostasis. Significant muscle loss as a part of aging and accelerated by disease leads to sarcopenia which becomes an important predictor of quality of life in older persons. Therefore, clinical screening for sarcopenia and validation by precise qualitative and quantitative measurement of skeletal muscle mass (MM) and function is at the center-stage of translational research. Many imaging modalities are available, each having their strengths and limitations, either in interpretation, technical processes, time constraints, or expense. B-mode ultrasonography (US) is a relatively novel approach to evaluating muscle. It can measure several parameters such as MM and architecture simultaneously including muscle thickness, cross-sectional area, echogenicity, pennate angle, and fascicle length. It can also evaluate dynamic parameters like muscle contraction force and muscle microcirculation. US has not gained global attention due to a lack of consensus on standardization and diagnostic threshold values to diagnose sarcopenia. However, it is an inexpensive and widely available technique with clinical applicability. The ultrasound-derived parameters correlate well with strength and functional capacity and provide potential prognostic information. Our aim is to present an update on the evidence-based role of this promising technique in sarcopenia, its advantages over the existing modalities, and its limitations in actual practice with the hope that it may emerge as the "stethoscope" for community diagnosis of sarcopenia.

Keywords: *Assessment, imaging, sarcopenia, ultrasonography*

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Introduction

Geriatric health stands on the pillars of memory and function. Brewing in the background of aging is cognitive decline, frailty, osteoporosis, and sarcopenia. While literature is replete with discussions on the former three, there is limited mention of sarcopenia despite its importance in the overall scheme of the aging phenotype. Rosenberg was the first to recognize the rapid decline in lean muscle mass (MM) with age and observed that it was more dramatic and potentially significant than concomitant changes in other body systems.[1] Even though sarcopenia is widespread in older adults, it actually begins before middle age and sometimes progresses rapidly in some individuals, however, it is not a universal occurrence in the elderly.[2,3]

Sarcopenia needs to be differentiated from frailty, a pure geriatric syndrome distinguished by decreased homeostatic reserves and reduced resilience.[4] Physical frailty is identified through various scales which are a mix of self-reported symptoms, and measurement of muscle strength (MS), physical activity, and gait speed. It may be unmasked by the occurrence of an adverse event in the older patient or even before that as prefrail.[5] Sarcopenia predisposes older adults to develop frailty, but all patients with sarcopenia are not frail.[6] Cachexia is an older distinct term characterized by anorexia and a hypermetabolic state often observed with advanced- stage of chronic diseases or cancer and reflects an uncontrolled loss of fat mass or muscle (i.e., myopenia).[7-9]

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While sarcopenia usually amplifies with age, it is also encountered in individuals with additional comorbidities, particularly heart failure, diabetes mellitus, chronic airway disease, and dementia.[10] As the worldwide prevalence of sarcopenia is rising exponentially it is projected that over 200 million individuals may be affected in 2050.[11] However, an accurate figure on the actual burden may not be available as sarcopenia has been underreported in clinical records and has been given short shrift in standard textbooks of medicine. It is understandable as there is a lack of awareness among physicians and uniform international guidelines with validated cut-off values, the complexity of measurements, and the tools available.[12] Whatever definitions are used, in general, its prevalence is lowest in the community-dwelling population and highest in those in long-term care facilities.[13] Globally, the trends in recognizing this entity are improving with a specific diagnosis code M62.84 being allotted to sarcopenia. The research on sarcopenia is evolving with an acceleration in PubMed publications to more than 1800 per annum over the past 5 years.

Age disturbs the delicate balance between muscle anabolism and catabolism and multiple pathophysiologic molecular pathways leading to sarcopenia have been described, but there are no clear answers.[14] The mechanisms include dysregulated protein synthesis and degradation, decrease in size and number of II myofibers, intramuscular and intermuscular fat infiltration, mitochondrial dysfunction, autophagy, and impaired satellite cell activation.[15,16] Like osteoporosis, sarcopenia starts affecting individuals earlier in life, especially in those with the sarcopenia phenotype but the exact age at which the process starts is not clear.[17,18] Newer insights into the genetic and molecular mechanisms may have clinical implications for arresting its progression and interventions that may have a role in reversing it.

A variety of nonimaging and imaging techniques are available for the assessment of sarcopenia. One of the indicators, physical performance can be evaluated in the clinic by using gait speed, chair rise time, and balance testing.[19] Anthropometric measurements including body mass index (BMI), skin-fold thickness, and measurement of the circumference of muscle at different locations can provide an indirect assessment of body composition.[20]

Quantitative MM and qualitative muscle analysis are difficult to estimate accurately.[21] Computed Tomography (CT) imaging at the third lumbar vertebra is considered the gold standard for quantification of MM but is expensive and also exposes patients to high radiation.[22,23] Other diagnostic modalities that are recommended and often used include Dual Energy X-ray Absorptiometry (DXA) and Bio-electrical Impedance Analysis (BIA).[24,25] Magnetic resonance imaging (MRI) and muscle biopsy are used sparingly. Ultrasonography is becoming a popular tool in the community and clinical and experimental laboratory settings due to the obvious advantages of availability, ease of use, lower cost, and no radiation exposure. It has shown accuracy comparable to DXA, CT, and MRI-based measurements.[26-28]

Materials and Methods

Studies were sought through an extensive bibliographic search on PubMed Advanced Search Builder for full-text articles from inception (1995) to October 2022 using the Medical Subject Headings terms "Ultrasonography," AND "Sarcopenia." This search strategy identified 1661 records. Records were screened for eligibility and free full text. Case reports/letter to editor and other studies of animals or cadavers were excluded. Only studies in the English language were retained. This search yielded 161 studies. From these records, the search was confined further to include only the original articles, clinical trials, systematic reviews, review articles as well as meta-analyses pertaining to the last 10 years. Duplicates were removed. Manual cross-referencing for scientifically important older articles was also performed. The final 121 studies were evaluated for their completeness, scientific validity, merit and relevance to the topic in review. The articles were read by all the three authors and data on ultrasonography and sarcopenia extracted to synthesize information discussed in this review. The flow chart of identification, screening and inclusion of the studies is depicted in Figure 1. The main objective of this review is to evaluate the current place of ultrasonography (US) in the diagnostic armamentarium for identification, assessment, and quantification of sarcopenia.

Definitions of Sarcopenia

MS has been highlighted as the principal determinant of sarcopenia by the European Working Group on Sarcopenia in Older People (EWGSOP2) guidelines which define sarcopenia as an unusually low MS coupled with low muscle quantity, quality, and reduced physical performance.[29-31] Muscle quality, indicative of micro- and macro-scopic abnormalities of muscle architecture and composition, is also impaired in sarcopenia.[32]

The EWGSOP2 algorithm includes:

1. Low MS measured by hand grip strength (HGS) and 5 times sit-to-stand
   a. HGS <16 kg (women); <27 kg (men)

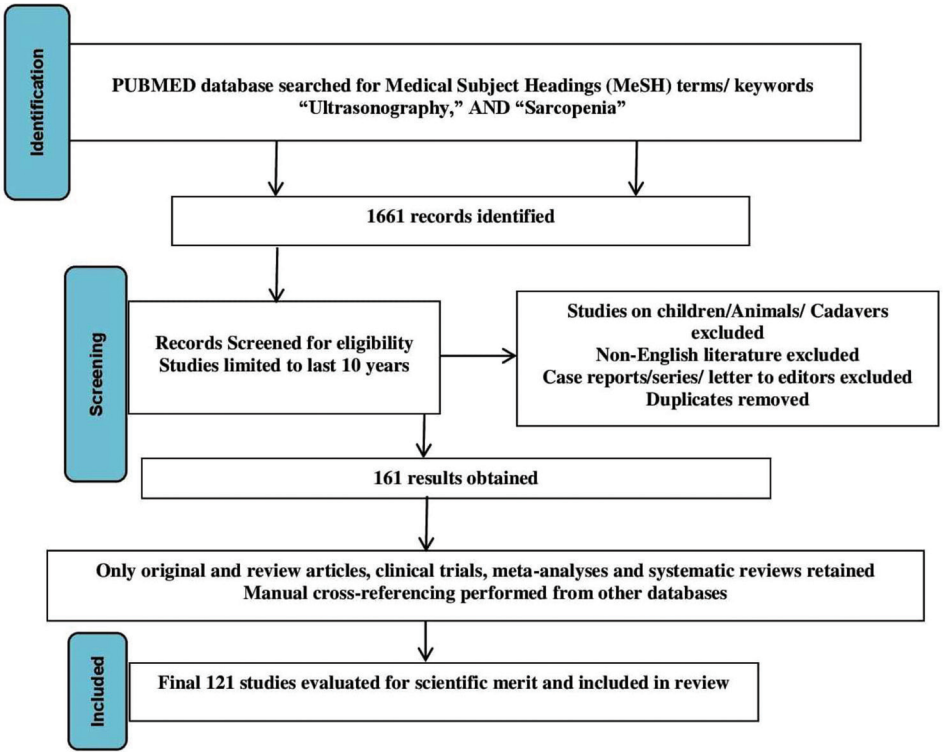

Figure 1: Flowchart of methodology for selection of studies. MeSH: Medical Subject Heading

   b. Five times sit-to-stand >15 s
2. Low MM or muscle quality based on
   a. DXA or
   b. Multifrequency BIA
3. Low physical performance
   a. Gait speed ≤0.8 m/s.

Based on the above, it identifies 4 diagnostic categories:

Presarcopenia: Low MM only; Probable sarcopenia: Low MS alone; Sarcopenia: Both low MS and low muscle quantity or quality; Severe sarcopenia: All 3 criteria, i.e., MS, quantity, and quality are low.

The Asian Working Group for Sarcopenia (AWGS) 2019 identifies sarcopenia using MM measured by DXA and BIA and MS by HGS, 6-min walk test AND Short Physical Performance Battery score (SPPB) OR 5-time chair stand test and the stratification is as follows:

1. Low MM:
   a. DXA <7.0 kg/m^2 (men); <5.4 kg/m^2 (women)
   b. BIA <7.0 kg/m^2 (men); <5.7 kg/m^2 (women)
2. Low MS:
   a. HGS <28.0 kg (men); <18.0 kg (women)
   b. 6-min walk <1.0 m/s
   c. SPPB score ≤9, OR 5-time chair stand test ≥12 s.[33]

The above working group guidelines EWGSOP2 and AWGS do not advocate muscle US for sarcopenia screening or diagnosis. The SWAG-SARCO consensus gives equivalent significance to muscle function, MS, and MM.[34]

Techniques to Measure Muscle Mass

Dual X-ray absorptiometry

DXA has been used as a research tool for the evaluation of fat mass and lean mass.[35-38] DXA is safe, fast, and easy to use.[39] It calculates the appendicular skeletal MM (ASM) which is then adjusted for height (ASM/ht^2), weight (ASM/wt), or BMI (ASM/BMI). ASM/ht^2 is adopted by EWGSOP as Skeletal Muscle Index (SMI).[40] However, DXA-derived measures have been found to correlate poorly with predicting disability and other functional outcomes in the elderly.[41] DXA causes some radiation exposure, the machines are not portable, and not readily available.[42]

Bioelectrical impedance analysis

BIA is an economical, noninvasive, and portable technique that utilizes electrical impedance to compute MM, lean mass, or fat-free mass using a prediction formula.[43] However, the reliability of the equations is subject to a variety of factors related to the device itself, the hydration and exercise status of the patient, and the environment.[44-47]

Opportunistic computed tomography

Artificial Intelligence-based tools can evaluate the muscle, bone, and fat during the opportunistic analysis

of CT using automated measurements including three-dimensional volumetric analysis.[48,49] For sarcopenia evaluation, segmented muscle quantity (cross-sectional area [CSA]) and quality can be assessed to calculate SMI. Low muscle attenuation, texture analysis, and high intermuscular adipose tissue are used as surrogates for poor muscle quality. Evidence-based consensus on validated thresholds to diagnose sarcopenia is lacking.[50]

Magnetic resonance imaging

MRI, like CT, evaluates muscle quantity using T1-weighted images and muscle quality by proton density fat fraction to detect myosteatosis. However, a majority of scientific literature has not evaluated the MRI-obtained parameters in relation to clinical outcomes.[51] In addition, there is a lack of agreement about the technical factors and MRI techniques.

Ultrasonography

Although EWGSOP2 and AWGS guidelines advocate validated tools like BIA/DXA/CT/MRI, these are not realistic in certain clinical circumstances and in the presence of co-morbid conditions. US can however be carried out in critically/acutely ill hospitalized patients who are immobile, have dementia or delirium, cannot perform handgrip or perform gait/speed tests, and patients who cannot undergo CT or MRI scans. It is a good tool for screening large populations and when BIA/DXA/CT/MRI is not feasible or available. The US has the advantage that it is rapid, simple to use, noninvasive, and portable. It can be used both in community or hospital-based, bedside, point-of-care settings as it is widely available, comparatively inexpensive, and radiation-free. US, therefore, has the potential to become comparable to CT/MRI at the tissue level, and DXA at the chemical level.

US assesses both muscle quantity and quality with good accuracy and thus has the benefit of repeated measurements.[52-55] Studies have illustrated excellent intra-and inter-rater consistency in the geriatric population with or without comorbidities as well as in the younger population.[56-59] It has the potential for application at the community level as it takes minimal time for evaluation by trained persons.[54,60,61] Skeletal muscle US has a promising role in predicting functional capacity, degree of malnutrition, hospital readmission, length of stay, and survival.[62]

Measuring muscle quantity alone is insufficient to detect age-related muscle degradation as MM in itself has no linear relationship with either strength or function.[63] Therefore, the assessment of the quality of muscle architecture is equally essential. Muscle quality is assessed by the MS or muscle power per unit of MM or muscle echotexture, including the noncontractile tissue.[64] The SARCopenia through Ultrasonography group was the forerunner in providing consensus propositions and standardized techniques for US muscle assessment.[65]

The Basics of Muscle US

Which muscle should be selected?

The best anatomical site that can predict overall skeletal MM is not clear. However, appendicular load-bearing muscles of lower limbs (anterior compartment-quadriceps) are apparently affected earlier in sarcopenia and are easily accessible due to their larger size and location providing ease to both the clinician and patient.[66] The quadriceps muscle provides reproducible measurements with excellent intra-class correlation.[56,67] A list of regional site anatomical landmarks is available in the literature and may be referred to.[68]

Which parameters are to be measured?

These could be qualitative or quantitative measures of skeletal muscle. The quantitative parameters have been widely studied and recorded; however, the complementary qualitative determinants have recently been shown to be more informative and clinically relevant.

Muscle Quantitative Parameters

These parameters are Muscle thickness (MT), Muscle CSA, Muscle Physiologic CSA (PCSA) and Muscle volume (MV).

MT and CSA correlate well with the muscle quantification done with other radiological techniques.[69] MT and CSA are measured generally at the midpoint of the muscle belly.[54] The PCSA is a better parameter that measures CSA perpendicular to muscle fibers and is more directly related to muscle contraction and function. PCSA is more relevant when measured in pennate muscles.

Muscle volume

It is another novel parameter derived from MT and limb length.

Muscle Qualitative Parameters

Assessing muscle architectural qualities is as essential as measuring MM as mass or volume alone is not linearly related to MS or function. Muscle quality can either mean the MS or muscle power per unit of MM or muscle echotexture quality. The latter depends on the degree of myosteatosis and connective tissue infiltration, seen as hyper-echogenicity. Alterations in architecture are crucial parameters that correlate with the muscle force. These parameters are Pennation angle (PA)

and Fascicle length (FL): The PA is associated with maximum force generated and shortening velocity of muscle fibers in sarcopenia.[70] Narici and Maffulli have shown a decreased PA and FL of medial gastrocnemius with age.[71] Structural changes in sarcopenia include reduction of FL that become less pennate, and this is associated with inferior muscle performance.[72]

Muscle echo intensity

Muscle echo intensity (EI) helps identify inflammation, fibrosis, and fat infiltration that is often observed in sarcopenia and cancer cachexia.[73,74] Increased EI correlates with poor MS, Gait speed, lower gait independence and sit-to-stand test scores, and lower scores on activities of daily living.[75,76]

Muscle stiffness

Muscle stiffness measured through US shear-wave elastography, identifies the degree of muscle compression and deformation which are determined by the extracellular matrix specifically collagen). In a study involving 77 participants, the oldest faction had 16.5% lesser stiffness, which paralleled lower MM, poor muscle performance, and strength.[77,78]

Muscle contraction

Measuring the muscle contraction and matching the resting CSA to maximal CSA in contraction is also an interesting tool for evaluation.

Muscle microcirculation

Microvascular damage and nitric oxide deficiency have been identified in the pathogenesis of sarcopenia.[79] Contrast-enhanced US can quantify the defects in microvascular function through alterations in the vascular bed of the muscle. This technique requires expertise and high-end data processing software.[80]

How to Perform US?

Patient positioning

US machine with B-mode with the facility for an extended field of view should be used. A linear transducer probe with 6–10 MHz and a minimum length of 5 cm is recommended. The patient is placed in the recumbent or desired position, preferably 15–30 min before performing the US to help the patient be familiar with the environment and relax the muscles. Identify the correct measuring point by locating the maximal muscle bulk of the selected muscle using anatomical landmarks. Place the transducer perpendicular to the skin with minimal pressure possible between the transducer and the skin [Figure 2].[63] While keeping the transducer longitudinally, in line with the muscle fiber fascicles, measure the MT, PA, and FL [Figures 3 and 4]. Measure the CSA and EI by turning the transducer probe to

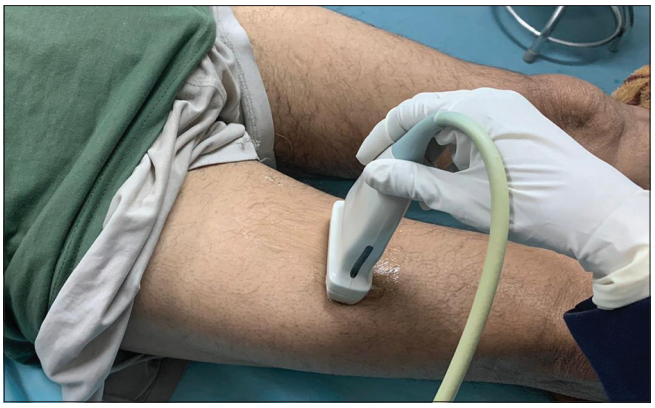

Figure 2: Position of the patient and transducer during ultrasound examination of lower limb muscles

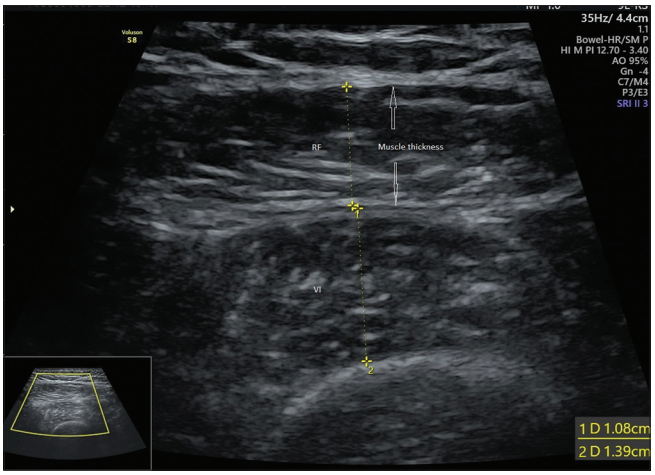

Figure 3: MT of the RF; below the belly of VI can be seen. MT: Muscle thickness, RF: Rectus femoris, VI: Vastus intermedius

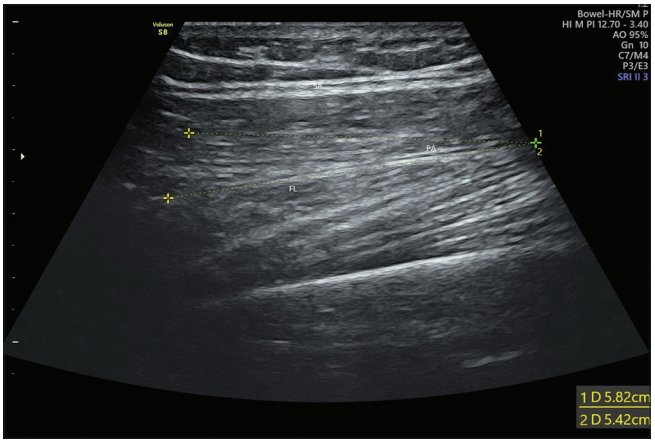

Figure 4: PA and the FL of the rectus femoris muscle. PA: Pennation angle, FL: Fascicle length

90° [Figures 5 and 6]. Use the mean value of three consecutive measurements.[63]

Concept of regional or "site-specific" sarcopenia

Conspicuous loss of overall MM of the body develops late in the natural history of sarcopenia and different

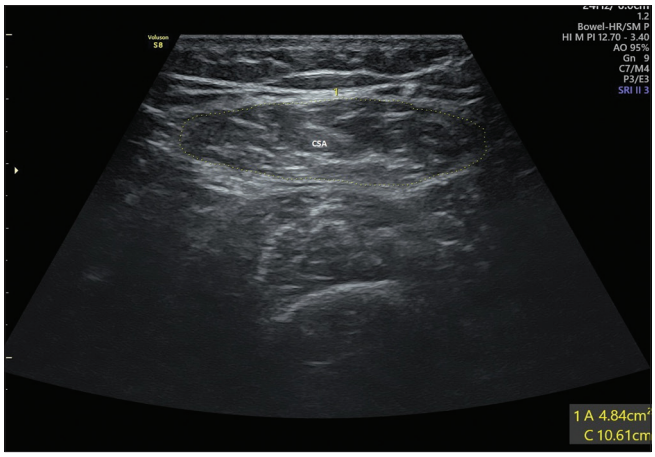

Figure 5: CSA of the rectus femoris muscle. CSA: Cross-sectional area

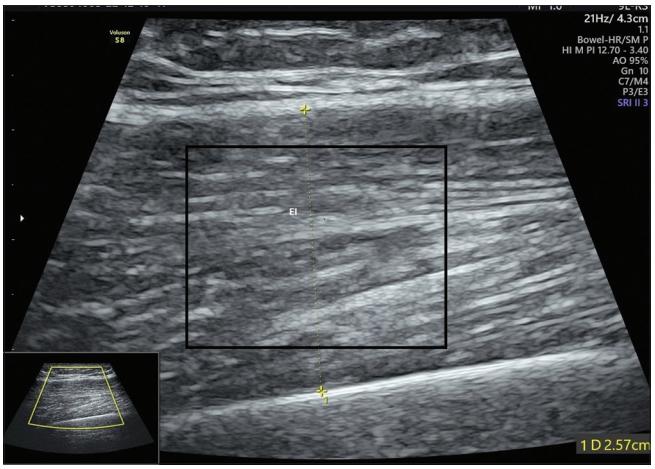

Figure 6: EI of the rectus femoris muscle. EI: Echo intensity

anatomical regions of the body undergo these changes at different rates. The lower limb muscles, especially the anterior thigh muscles have a higher predisposition for loss than upper limb.[71] This phenomenon of "regional" or "site-specific" sarcopenia is evident in studies involving Japanese and healthy Caucasian adults.[81,82] The rectus femoris is the ideal muscle that reflects the MM and parallels the reduced physical performance.[68] Sanz-Paris *et al*. have documented that a significant reduction in MM was associated with a functional deficit corresponding to the specific muscle.[83] Studies using rectus femoris MT showed a good correlation with lean body mass judged against DXA.[84] Rustani *et al*. from Italy established a RF thickness cut-off point of <0.9 cm for males and <0.7 cm for females, whereas in the Thai population, the corresponding cut-off points were ≤1.1 cm and ≤1 cm.[85,86]

US based prediction equations

US measurement of MT has been documented to be valid and reliable in all populations and may be used in equations to predict sarcopenia.[87,88] These equations calculate MM/volume through multiple regression analyses that include MT, CSA, and limb length, adjusted for additional anthropometric parameters. Zhao *et al*. established that these prediction equations have moderate diagnostic performance for sarcopenia.[89] The US-derived equation compared well with MM obtained from DXA or BIA-based equations and the agreement with MRI was moderate. In another systematic review, the authors observed these equations to be valid and applicable, using MRI and DXA as reference methods.[90] However, Liegnell *et al*. concluded that the validity of these was specific to the population groups studied.[91] For a Caucasian population the equation of Abe *et al*., 2015 is recommended while for Asians the equation of Abe *et al*., 2018 is suggested.[37,59]

Limitations of US

Although most US-based studies confirm its scientific validity and its diagnostic predictive power and also report its applicability in the context of functional and clinical outcomes, there are some limitations. There is gross heterogeneity regarding the technical settings, anatomical locations, measurement cut-offs, protocol or reference methods used and regional differences across all the studies. In addition, the reported sensitivities need to be higher to accurately and meaningfully use US in a clinical setting.[92] Although US shows a potential role in the evaluation of sarcopenia in clinical practice, the lack of standardized reference values stalls its routine use unless gender and ethnicity-specific normative data is available.[93] Studies from different regions are inconsistent; with significant gender differences as well as community and clinical practice settings. As a technique, it has considerable operator dependency. Extensive supervised and certified training may be required.

Conclusions

Muscle quantity, quality, and strength vary between individuals. These are under the influence of a complex interplay of nutrition, training, hormones, age, and diseases. US is a potentially promising method to diagnose sarcopenia. At the moment, there is significant heterogeneity in terms of ultrasonography technique and measurements, lack of globally relevant normative data, and the cutoff points are arbitrary. Experts from various countries had dissimilar views on the characterization and assessment of sarcopenia. However, with scientific data pouring in from different nations, US is gaining momentum as a potential tool for muscle assessment and predicting clinically relevant outcomes. US has several advantages over previous techniques. Moreover, newer innovative ultrasonic technologies, for instance,

elastosonography and artificial intelligence might set the scene as better modalities for gauging sarcopenia. Protocols and hard end-points need to be validated across larger populations with diverse physical conditions and functional statuses.

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Conflicts of interest

There are no conflicts of interest.

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