

Perspective Article

Muscle quality an evolving concept

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Muscle quality concept can be analyzed from a morphological and functional perspectives that include relation between these properties. Morphological muscle quality considers muscle composition, architectural and structural properties. Functional muscle quality has been defined as a ratio between muscle strength or power per unit of muscle mass or area. Biological and adaptative changes to ageing must be considered when interpretation of muscle quality assessment is done in a clinical or research context. One of the conditions that requires an adequate homologation in terminology is sarcopenia, to establish definition and cut-off points.

Keywords: Functional, Morphological, Muscle ageing, Muscle quality, Sarcopenia

Introduction

The assessment of muscle in clinical and research settings is complicated, since it involves both the study of muscle function and the integrity of contractile and non-contractile tissue, and the lack of a consensus to establish definitions in the involved concepts.

Primary muscle function can be described by physiological domains that are involved in clinical muscle assessment, these include force production, power, endurance, flexibility, metabolism, thermoregulation, and production/signaling of myokines that determine an individual's physical capacity, consistent with age, sex, and race¹; different authors have suggested that this evaluation can be through the determination of the "Muscle quality". The term "quality" can have different meanings based on the context it is used, in general it refers to the characteristics or attributes of something; in other words, the "essential character" and its "distinguishing attributes"¹. In this context there is no clearly accepted definition.

One of the biggest problems related to muscle evaluation in clinical practice is sarcopenia. In 1988, Rosenberg proposed the term sarcopenia to refer to muscle wasting in older people². Initially, the operational definition of sarcopenia was based on the quantification of lean mass assessed by densitometry, defining it as more than two standard deviations (SD) below the mean for young adults³. Since there is no instrument that serves as a gold standard, diagnostic integration is carried out through constructs; however, there are different groups that have established

regional consensus^{4,5} (Table 1) without a universal agreement for its definition, diagnosis and evaluation. For the EWGSOP2 consensus (European Working Group on Sarcopenia in Older people 2019), the diagnosis is established through a clinical construct that is based on the initial suspicion of this condition, followed by confirmation through identification of decreased strength, and quantity or muscle quality; subsequently, the functional compromise can be evaluated to establish the severity⁴. In the same way, the AWGS2019 consensus (Asian Working Group for Sarcopenia) proposes the search for cases through surveys and clinimetry, the identification of possible cases through the evaluation of grip strength or physical execution, and diagnostic confirmation through the construct of strength, execution and quantification of muscle mass⁶. Although they do not indicate the method, they state that the diagnosis of sarcopenia requires the measurement of both: muscle quality and quantity.

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| | | EWGSOP2 ⁴ | | AWGS 2019 ⁶ | | FNIH 2014 ⁵ | |
|-----------|--|--|-------|------------------------|-------|------------------------|--------|
| | | Men | Women | Men | Women | Men | Women |
| Strength | Grip (kgf) | <27 | <16 | <28 | <18 | <26 | <16 |
| | Sit-to-stand | >15 s / 5 executions | | ≥12s / 5 executions | | | |
| Quantity | ASM (Kg) | <20 | <15 | | | | |
| | ALM (Kg) | | | | | <19.75 | <15.02 |
| | ASM/height ² † (Kg/m ²) | <7.0 | <5.5 | <7.0 | <5.4 | | |
| | ALM _{BMI} | | | | | <0.789 | <0.512 |
| | ASM‡ (Kg/m ²) | | | <7.0 | <5.7 | | |
| Execution | Gait speed (m/s) | ≤0.8 | | <1.0 | | | |
| | SPPB (points) | ≤ 8 | | ≤ 9 | | | |
| | TUG (s) | ≥ 20 | | | | | |
| | 400 m | Not complete or takes ≥6 min to complete | | | | | |

†through DXA, ‡ through bioelectrical impedance

EWGSOP2: European Working Group in Older People updated in 2019; AWGS2019: Asian Working Group for Sarcopenia 2019 consensus; FNIH 2014: Foundation for the National Institutes of Health published 2014; ALM: appendicular lean mass; ASM: appendicular skeletal muscle mass; DXA: dual-energy X-ray absorciometry; BMI: body mass index; SPPB: Short Physical Performance Battery; TUG: time up and go.

Table 1. Cut points for diagnosis of sarcopenia according to different consensus.

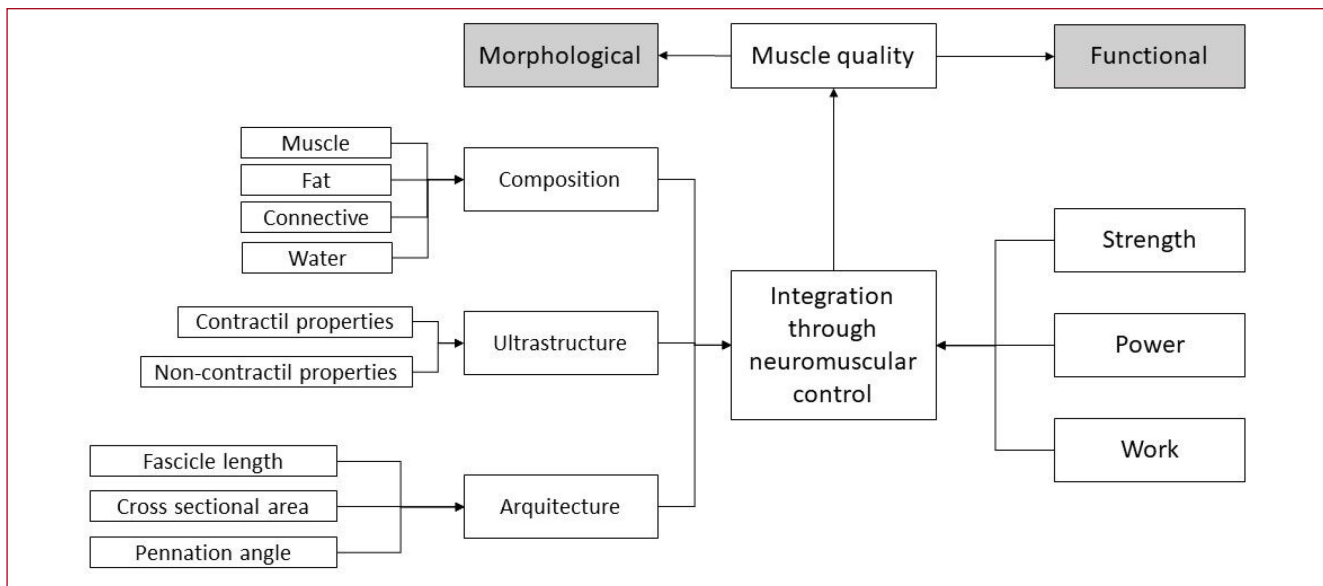


Figure 1. Contractile and non-contractile elements integration with performance to assess muscle quality.

From this perspective, the term muscle quality is ambiguous given the lack of universal definition and the technical difficulty of measuring muscle quantity and quality in a clinical setting, therefore the Global Leadership in Sarcopenia (GLIS)⁷ suggests against using this term due to its imprecision.

What has been described as “muscle quality”?

Since 1995⁸, there has been a growing interest in the term “muscle quality”. Muscle quality is an essential component of human physiology, it refers to the integration of the functional and structural characteristics of the muscle.

| Muscle primary function parameters | |
|------------------------------------|---|
| Force | Influence that can change the movement of an object. It has magnitude and direction. |
| Moment (strength) | Rotational effect of the force generated by a muscle or a muscle group around a joint. |
| Muscle strength | Amount of force a muscle can produce with a single maximal effort. |
| Muscle power | Ability to exert maximum force in the shortest amount of time, such as accelerating, jumping, or throwing. |
| Muscle work | Force exerted by a muscle a muscle or group of muscles to perform a physical task. |
| Muscle contraction type | Two main forms of contraction can be described, when length of the muscle remains without change (isometric) and when length of the muscle changes with contraction (isotonic). Isotonic contraction can be concentric (shortening of muscle length) and eccentric (elongation of muscle length). Isokinetic fixed angular velocity |
| Muscle quantitative parameters | |
| Volume | Tridimensional space of a muscle, considering length and shape (through magnetic resonance, ultrasound) |
| Thickness | Distance between superficial and deep aponeurosis of the muscle (through magnetic resonance, computerized tomography, ultrasound) |
| Cross sectional area | Anatomic: Bidimensional space of a transversal view of an image Physiologic: ratio of muscle volume between the length of its fibers (through magnetic resonance, computerized tomography, ultrasound) |
| Lean mass | Fat-free and bone mineral-free component that includes muscle and other components such as skin, tendons, and connective tissues (through densitometry, bioimpedance, anthropometry or formulas) |
| Appendicular lean mass | Is the sum of lean soft tissue from both arms and legs (through densitometry, bioimpedance, anthropometry or formulas) |
| Skeletal muscle mass | Sum of total muscle mass from the whole body (through magnetic resonance, tomography, indirect by ultrasound and formulas) [20] |
| Appendicular skeletal muscle mass | Sum of muscle mass from arms and legs (magnetic resonance, computerized tomography) |
| Muscle qualitative parameters | |
| Fascicle length | Length of the fascicular path between the insertion of the fascicle to the superficial and deep aponeurosis (magnetic resonance, ultrasound) |
| Stiffness | Change in force divided by the corresponding change in length, when the length change is imposed by an external agent or by a change in the external load in a muscle (myotonometry, ultrasound, magnetic resonance) |
| Muscle contraction | Muscle contraction correlated to cross sectional area at rest and maximal contraction (ultrasound) |
| Microcirculation | Capillary flow in skeletal muscle (ultrasound, magnetic resonance) |
| Pennation angle | Angle of insertion of the fascicles of muscle fibers in the deep aponeurosis (ultrasound) |
| Echogenicity | Brightness of the image acquired by ultrasound in gray scale caused by the reflection of soundwaves and is influenced by sound beam characteristics and tissue density (ultrasound) |

Table 2. Definition of muscle primary function, quantity and quality components to integrate functional or morphological muscle quality¹²⁻²¹.

It comprises factors such as strength, power, endurance, and flexibility, which determine individual physical capacity. Quality involves various elements that contribute to efficiency and performance, which can be approached from a functional or morphological perspective; without confusing them with the primary functional characteristics of the muscle (Figure 1).

In a recent comprehensive review on muscle quality, whose objective was to identify the current definitions and assessment methods of “muscle quality” in older adults⁹, the authors identified 96 studies (between 2003 and

2022) and found that muscle quality was described in two large domains: functional and morphological. The functional domain is described as assessed muscle function per unit of mass or area; the morphological domain considers changes in architecture, structure, ultrastructure and composition⁹⁻¹¹.

The determination of muscle quality is affected by methodology used to characterize the tissue or measure its performance¹, and the definition used to indicate the results of its evaluation^{1,9}. However, despite identifying two ways of approaching muscle quality, it is important to specify that functional quality would involve the ability to generate

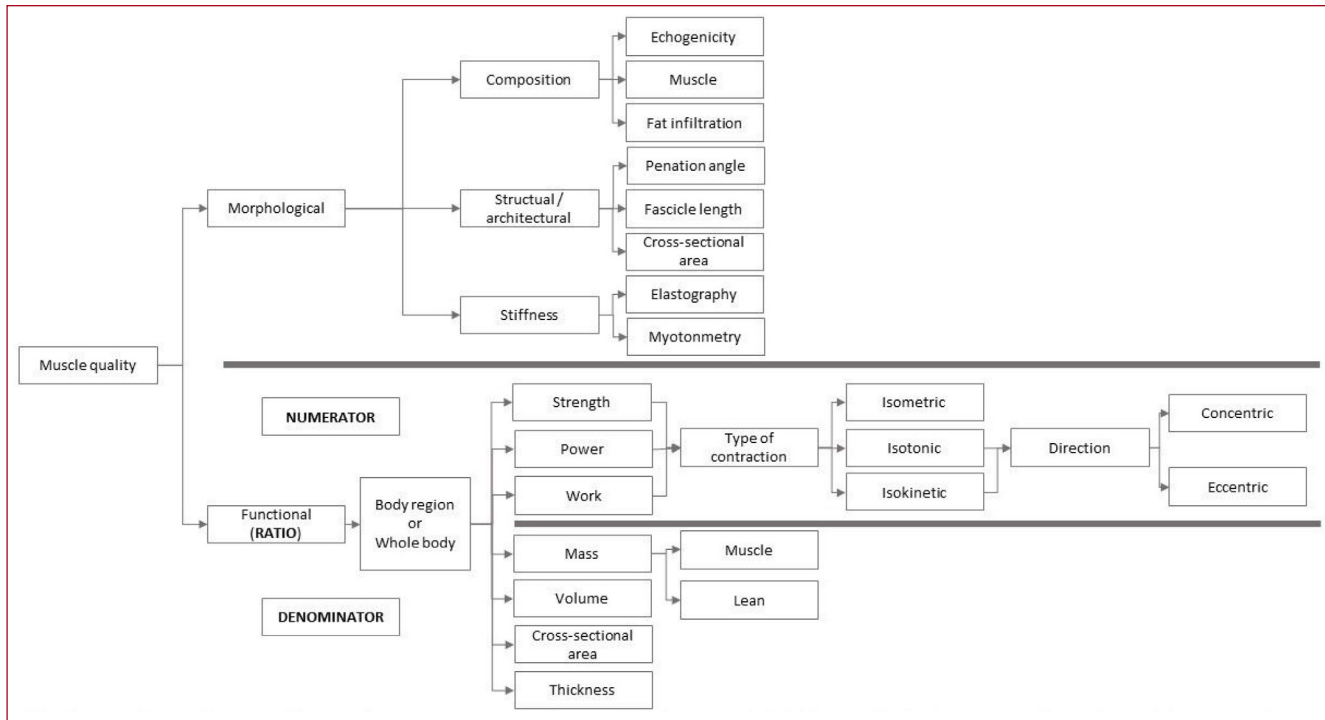


Figure 2. Integration of morphological and functional muscle quality. Muscle composition can be assessed by magnetic resonance or tomography, to establish the amount of fat infiltrate (myosteatorosis) or fibrotic tissue. Echogenicity can indirectly demonstrate fat infiltration and fibrosis in muscle without differentiation. Muscle mass and volume can be measured by magnetic resonance. Volume can indirectly be quantified by ultrasound. Cross-sectional area can be measured by ultrasound, magnetic resonance, and tomography. Lean mass can be measured by body composition with densitometry or bioimpedance.

force and power, dependent on qualitative (morphological) characteristics¹⁰.

Concepts and conditions that must be considered when evaluating skeletal muscle quality

The muscular components that are required to integrate functional and morphological muscle quality can be evaluated from the perspective of function, quantitative or qualitative characteristics. Table 2 integrates the concept and considered definition.

Normalization of parameters that integrate muscle quality

The values obtained from muscle performance (strength, power) and muscle quantity (mass) are strongly correlated to body size, so different ways of normalizing them have been proposed for their adjustment. In 2014 the National Institutes of Health (FNIH) within the sarcopenia project proposed adjusting the value of appendicular skeletal muscle mass by body mass index (ASM/BMI) since they report a strong correlation with weakness and slowness of movement⁷.

In the same way, since the muscular performance parameters (strength, power and work) are linked to body mass, when comparing a subject against the same subject at two different moments, the absolute value of the implemented test must be considered. And when comparing the results of these variables between subjects, normalization by weight should be considered^{5,21}.

Cut-off points

There are no cut-off points that can be applied to the values of morphological and functional muscle quality. For sarcopenia, some groups^{4,22} recommend the standardization of values with young adults, that is, converting the absolute values in terms of Z score and comparing the number of standard deviations from the mean of the control group. They suggested to consider positive when these values exceed -2 SD⁴; similar to the way that WHO defined osteoporosis²³. For this, it is necessary to take in account that the behavior of muscle mass is different at distinct ages, as well as among men and women. Total appendicular mass increases until the age of 30 years in men and 40 in women, after which it slowly decreases until 60 years in men and between 50-60 years in women; from this moment it accelerates progressively with increasing age²⁴. Therefore, the population of healthy

young adults selected to serve as controls to standardize the values should be around 30 and 40 years of age according to sex and considering a normal body mass index.

Considerations for integration in clinical research

The determination of muscle quality is affected by the function evaluated and by the methodology or technology used to characterize the tissue or measure its performance¹. In sarcopenia, muscle strength is compromised leading to functional impairment and disability. However, it has been observed that strength and muscle mass are not necessarily linked, since there are conditions in which muscle strength can be diminished without decreasing of muscle mass. As associated to ageing there is a relative increase of non-contractile tissue in relation to contractile tissue of the muscle, this can mislead to overestimate the value of muscle lean mass, when evaluation of skeletal muscle mass is not available²⁵. On the other hand, muscle power is strongly associated with gait speed, balance, and functional status^{22,26-27}. It has been observed that muscle strength declines by 1 to 2% per year after the age of 50²⁸, muscle mass is lost by 1 to 2% per year after the age of 50^{3,29} but begins to decline since the age of 30 when a loss of 3 to 8% per decade is observed³⁰; and muscle power is lost from 3 to 4% per year after age of 60³¹. For this reason, some authors proposed to consider muscle power as the main value to assess muscle performance in older adults²².

A homologation of definitions to describe muscle quality is necessary since, as GLIS points out, the use of the term without establishing its components can be imprecise or ambiguous⁷. An example of this is relative strength and specific strength, that refer to the same concept, functional muscle quality:

- Relative strength¹: Ratio of peak force and a measure of body size, regional lean mass or cross-sectional area.
- Specific strength: Strength standardized to muscle size⁷.

Another example is that for the integration of the diagnosis of sarcopenia, the assessment of “muscle quantity” cut-off points proposed by EWGSOP2⁴ and by AWGS2019⁶ refer to “appendicular skeletal muscle mass” (ASM), which gold standard to evaluate would be magnetic resonance. However, they suggest as a more accessible option the use of body composition through dual-energy X-ray absorciometry (DXA), which actually reports lean mass (integrating contractile and non-contractile tissues). It is important to be cautious when applying cut-off points since ASM values are lower than ALM values, as they are different concepts (Table 2). Thus, the recommended cut-off points should consider ALM as it is more available and at a lower cost.

From a morphological point of view, assessment of muscle quality may include assessment of fascicle length, assessment of muscle and tendon stiffness, assessment of

muscle contraction, microcirculation, angle of pennation and echogenicity (Figure 2)^{1,10,19,22}.

From a functional perspective, the assessment of muscle quality should include the quantification of aspects of muscle performance (considering the type and direction of movement), such as power, strength and work, in relation to quantitative parameters of muscle mass, such as muscle mass, lean mass, muscle thickness and physiological or functional cross-sectional area (CSA). These values can be studied from a body region or whole body (Figure 2)^{22,32}.

Biological and adaptative changes that impact on muscle quality

Muscular ageing involves changes and adaptations of muscular composition of non-contractile and contractile elements, and neuromotor control³³⁻³⁴. With ageing, intramuscular and intermuscular fat infiltration increases (myosteatosis)^{1,9,35}, as well as architectural and structural changes that alter the mechanical and elastic properties of muscle connective tissue³⁶. In the same way, the contractile component is affected by changes and adaptations in muscle fibers, with a decrease in the fascicle length, pennation angle, decreased cross-sectional area, predominance of fibers I over II, and a decrease in satellite cells^{34,37}. Motor control is affected by changes in the peripheral nervous system, spinal and supraspinal central nervous system, such changes are caused by connective tissue infiltration, decreased myelin and myelination, decreased motor neurons, loss of motor units, generation of large motor units and changes in central motor coordination³⁴. These changes and adaptations of the contractile and non-contractile elements and in neuromotor control generally translate into decreased strength (~2% per year)²⁸, power (~3 a 4% per year)³¹, mass (~1 a 2% per year)^{3,29} and functional muscle quality (~2.5% per year)³⁸.

It has been observed during isokinetic tests that comparing young adults (23 to 32 years of age) and older adults (60 to 75 years of age) testing at low speeds, force values (peak torque) were significative lower in older adults³⁹⁻⁴⁰. However, during high velocity evaluation (180° per sec) the eccentric peak torque of older adults tends to be preserved⁴¹.

In the same way, it has been shown that changes in the mobility of elderly population are linked to the force-velocity relationship, eccentric contractions in a stronger way than concentric contractions³⁹. Although the stability of movement control has been shown to be lower in eccentric than in concentric activity, eccentric contraction exhibits stronger activation due to neuromotor control network activation of the primary, secondary, and association cortices.

When compared with young adults, eccentric activity-biased activation shows different patterns. In older adults it was higher in secondary and associations cortices (supplementary, premotor and motor areas) and cingulate cortex; and in young adults in primary motor cortex and sinus sensory cortex⁴⁰.

These changes and adaptations have clinical and research

relevance because they translate into a greater loss of concentric than eccentric strength, linked to velocity with age³⁹. Muscle mass assessment might be biased by relative preservation due to myosteatosis. It should be integrated as a ratio between muscle strength or power unit, considering eccentric and concentric contraction, per unit of mass or ACT or thickness within functional quality. It reflects a relationship between execution, composition and neuromotor control, that will allow a better understanding of muscle functional behavior.

Conclusion

Considering strength and muscle mass independently, in the assessment of age-associated loss of strength could be misleading. Ageing muscular changes and their functional implications should be considered when evaluating sarcopenia, which should include muscle quality measurement as it refers to the morphological and functional characteristics of skeletal muscle.

Morphological and functional muscular qualities should be considered in clinical practice and research, since they are feasible to estimate and there are different options to do so. Determination of these types of muscle quality will lead to a comprehensive assessment of neuromuscular function and a more targeted treatment.

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