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NEUROMUSCULAR COMPONENT OF MUSCLE QUALITY ASSESSMENT IN OLDER ADULTS: NARRATIVE REVIEW

ŽIVČNO-MIŠIČNA KOMPONENTA MIŠIČNE KAKOVOSTI PRI STAREJŠIH ODRASLIH: OPISNI PREGLED

ABSTRACT

The concept of muscle quality encompasses both micro- and macroscopic aspects of muscle architecture and composition and has gained increasing attention with inclusion in the definition of sarcopenia, indicating the significance of muscle quality in evaluating muscle function and strength among older individuals. Muscle quality consists of two main components: neuromuscular and morphological and is often defined as the ratio between the two. The aim of this review is to present currently used methods for assessment of muscle quality with an emphasis on neuromuscular component in older adults. The most used methods for assessing morphological component are imaging techniques, such as magnetic resonance imaging, computed tomography, dual-energy X-ray absorptiometry and non-imaging bioimpedance analysis. In the neuromuscular component upper and lower body strength are assessed with different methods such as hand grip strength, isokinetic lower limb strength and isometric lower limb strength. Currently, there are three proposed muscle quality assessment methods for field or population studies: muscle quality index, ultrasound sarcopenia index and bioimpedance-derived phase angle. Despite the exploration of muscle quality through various assessment methods, a consensus on the most appropriate and universally applicable approach has yet to be established.

Keywords: ageing, skeletal muscle, ultrasound sarcopenia index, muscle quality index, phase angle

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IZVLEČEK

Koncept mišične kakovosti zajema tako mikro- kot makroskopske vidike mišične arhitekture in sestave in je pridobil večjo pozornost z vključitvijo v definicijo sarkopenije, kar kaže na pomen kakovosti mišic pri ocenjevanju mišične funkcije in moči pri starejših posameznikih. Mišična kakovost je sestavljena iz dveh komponent: živno-mišične in morfološke in je najpogosteje definirina kot razmerje med obema komponentama. Namen tega pregleda je predstaviti trenutno uporabljene metode za oceno kakovosti mišic s poudarkom na živčno-mišični komponenti pri starejših odraslih. Najpogosteje uporabljene metode za oceno morfološke komponente so slikovne - magnetna resonanca, računalniška tomografija, dvoenergijska rentgenska absorpciometrija in neslikovna bioimpedančna analiza. Živčno-mišično komponento ocenjujemo z jakostjo zgornjega in spodnjega dela telesa, z metodami kot so stisk pesti, izokinetična jakost spodnjega uda ali izometrična jakost spodnjega uda. Trenutno obstajajo tri predlagane metode ocenjevanja kakovosti mišic za terenske ali populacijske študije: indeks kakovosti mišic, ultrazvočni indeks sarkopenije in fazni kot, pridobljen z bioimpedanco. Kljub raziskovanju mišične kakovosti z različnimi metodami, enoten konsenz o metodi merjenja še ni bil dosežen.

Ključne besede: staranje, skeletna mišica, ultrazvočni sarkopenični indeks, indeks mišične kakovosti, fazni kot

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INTRODUCTION

Muscle quality, a term used to characterize muscle's capacity for contraction, metabolic activity and electrical activity, plays a crucial role in various populations, particularly in low functioning older adults and those with muscle diseases like sarcopenia (Naimo et al., 2021). The concept of muscle quality encompasses both micro- and macroscopic aspects of muscle architecture and composition and has gained increasing attention with inclusion in the definition of sarcopenia, indicating the significance of muscle quality in evaluating muscle function and strength among older individuals (Cruz-Jentoft et al., 2019; Hortobágyi et al., 2023; Radaelli et al., 2021). Additionally, muscle quality is not solely determined by the size and composition of the muscles, but also by the efficiency and effectiveness of the neuromuscular system. Therefore, it is comprised of two major components which describe different components (Hortobágyi et al., 2023): (i) characteristics of morphological component of the non-contractile tissue; and (ii) neuromuscular component defined as the ratio between force or torque and a measure of muscle size (thickness, volume, cross-sectional area or echo intensity) (Fragala et al., 2015; Lynch et al., 1999). So far, muscle quality has been most defined as a ratio between a measure of muscle strength and muscle mass, and in the earlier research it was suggested that muscle quality is an indicator of muscle function rather than muscle strength (Lynch et al., 1999). Later it was found that muscle quality has an inverse association with muscle mass and appendicular skeletal mass index (Barbat-Artigas et al., 2013). To this date, muscle quality does not have a standardised assessment method for diverse population groups. Interestingly, the first study that looked into the muscle quality from a neuromuscular or functional component (ratio between specific strength and muscle volume) was published in 2003 (Newman et al., 2003), and the first one for morphological component (enhanced echointensity measured with ultrasonography) was published ten years later, in 2013 (de Lucena Alves et al., 2023; Watanabe et al., 2013).

The topic of muscle quality is complex and multifaceted as it can be affected by various factors, such as general adiposity and its distribution, dysfunction of the central nervous system, peripheral nervous system and nutritional and metabolic factors (Moore et al., 2014). While it is known that greater muscle mass can generate greater muscle strength – this relationship is not proportional (Marusic et al., 2021). Muscle strength on its own is affected by many different factors like muscle architecture, muscle composition, neuromuscular components, muscle oxidative capacity and insulin sensitivity (Barbat-Artigas et al., 2013; Kuschel et al., 2022). Studies have shown that improvements in neuromuscular activation precede increases in muscle mass in response to resistance training, suggesting that muscle activation could be considered as a measure of muscle quality (Radaelli et al., 2013; Taaffe et al., 1999). During aging muscle atrophy is accompanied by loss of muscle fibre diameter and loss of motor units (Brown et al., 1988; Doherty & Brown, 1993; McKinnon et al., 2015; Power et al., 2010). Even more, there is also change in muscle composition: infiltration of connective and adipose tissue (McKinnon et al., 2017; Overend et al., 1992; Rice et al., 1989). These changes can result in a decrease of overall force production, ultimately leading to reduced mobility and significant clinical complications for older adults. Another explored component of muscle quality could be muscle fat infiltration which is often defined as an accumulation of intramuscular and intermuscular fat into the skeletal muscle (Hamrick et al., 2016; Jiang et al., 2019). It has been shown that muscle fat infiltration has association with reduced muscle strength, reduced insulin sensitivity and increased mortality among the older population (Hamrick et al., 2016). Furthermore, individuals with pathological conditions, especially stroke (Ryan et al., 2011), muscular dystrophy (Torriani et al., 2012) and diabetes (Hilton et al., 2008), tend to have higher levels of muscle fat infiltration. Recognizing the importance of muscle fat infiltration and its consequences could contribute to better understanding of muscle quality and therefore, overall individual health.

Low muscle quality can have significant impacts on individual's overall health and well-being as literature has shown that it can increase the risks of impairments. Having high muscle quality over higher muscle mass may be preferable, as the Health ABC study found that even increased lean mass did not prevent muscle weakness in older adults (Goodpaster et al., 2006; Hughes et al., 2001). A study by Cooper et al. (2014) suggested that increases of body max index (BMI) could be associated with lower muscle quality. Muscle quality, as a biomarker, goes further than muscle mass alone, as it provides more comprehensive information about muscle function and its metabolic health and in the future it could be a relevant parameter for identification of individuals at risk for developing musculoskeletal disorders.

Assessment of muscle morphological component in laboratory settings relies on established techniques, using magnetic resonance imaging (MRI) and computerized tomography (CT). However, for the population studies muscle morphological component measures rely on less reliable and indirect techniques, such are bioimpedance (BIA) and dual-energy X-ray absorptiometry (DXA). Further, the assessment of neuromuscular component lacks a unified protocol and definition (Cruz-Jentoft et al., 2019). Therefore, the aim of this review is to present currently used methods for assessment of muscle quality with an emphasis on neuromuscular component in older adults.

MORPHOLOGICAL COMPONENT

Morphological component consists of muscle mass measures which are different due to assessment method availability, cost and types of acquired data. The use of acquired data can be adjusted to research needs accordingly.

Magnetic resonance imaging

MRI is a three-dimensional technique that allows determination of muscle mass and volume, mainly for research purposes, and it currently stands as a gold-standard technique for evaluating muscle volume (Pons et al., 2018). Roman et al. (1993) have used MRI on elderly already in 1993 to assess the effects of resistance training on muscle mass in elderly men, where they found that muscle volume increase in elbow flexors by 14 % and they showed that measuring muscle volume eliminated a source of potential intraindividual variation in muscle size determination. MRI has been proposed to be used in sarcopenia diagnosis, however it has yet to be widely applied in clinical practice. This can be attributed to the significant financial investment, lengthy acquisition process, and the absence of clearly defined cut-off values and standardized protocols (Chianca et al., 2022).

There are different sequences used in MRI, most commonly MR spectroscopy, chemical-shift based imaging and diffusion tensor imaging which can provide different parameters (Giraudo et al., 2020). These can be split in more groups: fat-related volumes, muscle related volumes (total muscle volume, appendicular skeletal muscle mass), muscle quality related parameters (intramuscular adipose tissue at mid-thigh level, total cross-sectional area of visualized muscles at the L3 level, total cross-sectional area of psoas muscle at the L4 level) and anthropometric measures (circumferences – abdominal, calf, thigh; liver fat fraction) (Huber et al., 2020). Interestingly, muscle MRI parameters of intramuscular adipose tissue and proton density fat fraction showed strong negative association with muscle strength (Chianca et al., 2022).

MRI has been validated to measure body composition reliably and at high accuracy (Lustgarten & Fielding, 2011; Nordez et al., 2009; Selberg et al., 1993). Additionally, MRI has been shown to be excellent for the correlation with pathology in a small cohort (Kuno et al., 1988). However, MRI has limited availability for clinical use and ease of use in terms of data assessment. Data post-processing is time consuming when the data of the whole body is acquired and is currently used for research purposes, not for clinical use (Huber et al., 2020). Therefore, the main challenges are interpretation of image-based results, equipment availability and participant's size limitation.

Computed tomography

CT is also a three-dimensional technique and is also more often used in research trails than in screening protocols, as it is known that reduction of muscle density correlates with fat infiltration (Lenchik & Boutin, 2018). It is possible to assess muscle mass and quality with tracing of cross-sectional area and attenuation values of skeletal muscles (Sergi et al., 2016; Sjostrom et al., 1986). Aging or disuse affect skeletal muscle with increasing intramuscular adipose tissue which can be quantified with this method. CT allows fast acquisition, it is widely available, accurate and reproducible and it has high spatial resolution, however it has non-negligible irradiation, it is expensive and time-consuming segmentation process, there are not yet established cut-off values and it has participant's size limitation (Chianca et al., 2022).

Dual-energy x-ray absorptiometry

DXA is a two-dimensional technique primarily developed for bone density evaluation and osteoporosis diagnosis, but in recent years it has been used as an accurate and reliable method to investigate soft tissue composition in the whole body or regionally (Bazzocchi et al., 2016; Borga et al., 2018; Heymsfield et al., 2015; Minetto et al., 2021). Specifically, DXA provides an estimate of the body compartments: lean mass, fat mass and bone mass, therefore it has also been proposed to be used in sarcopenia classification as a tool to measure muscle quantity in clinical practice (Cruz-Jentoft et al., 2019). It is the most used in non-hospitalized people (Albano et al., 2020). It is accurate, reproducible, fast, relatively inexpensive and has very low radiation dose for the patient and the operator (Bazzocchi et al., 2016). Another advantage of DXA is its ability to instantly yield an estimation of appendicular skeletal muscle mass (ASM), given the use of consistent instrument and designated cut-off points (Cruz-Jentoft et al., 2019).

However, it does not measure muscle quality directly as it does not provide measures of intramuscular fat, solely overall muscle mass or fat. Similar to MRI and CT, also DXA is not portable, which hinders its use in community settings, particularly in countries that favour ageing-in-place. Additionally, accuracy of measurements can also be affected by hydration status of the participant (Cruz-Jentoft et al., 2019). DXA assumes that fat-free tissue hydration is constant at 73%, even though tissue hydration can vary from 67% to 85% (Andreoli et al., 2009; Bazzocchi et al., 2016), therefore affecting the results.

Bioimpedance analysis

BIA is an inexpensive, easy to use and fast, but indirect technique to assess muscle mass which works on the base of electrical properties of the body (Borga et al., 2018) and it has been suggested to be an appropriate alternative for DXA in sarcopenia classification (van den Helder et al., 2022). BIA uses predictive equations to calculate fat free mass, total body water and body cell mass using gender, age, body mass, body height and race and those are generally specific for a certain population (Dehghan & Merchant, 2008). However, the validity of this method has been discussed and it has mostly been validated for certain parameters: fat free mass comparison with DXA (Kyle et al., 2004; Saragat et al., 2014; Tognon et al., 2015), appendicular lean mass comparison with DXA (Sergi et al., 2015; Steihaug et al., 2016; van den Helder et al., 2022). Another interesting parameter acquired with BIA is phase angle, which is the ratio between resistance and reactance and has been proposed to be a convenient index of muscle quality (Akamatsu et al., 2022). BIA has limitations of data interpretation as it is based on participants' hydration status (Dehghan & Merchant, 2008), fluids body distribution, changes in cutaneous and muscle blood flow caused by moderate to intense physical activity 2 to 3 hours before the measurement and medical conditions that impact fluids and electrolytes balance. Overall, BIA can be a useful tool for clinical environment, especially because of its' portability, however caution is needed when used for large studies with diverse population.

NEUROMUSCULAR COMPONENT

As highlighted, muscle quality has multiple neuromuscular assessment techniques, and we will first present the methods that assess neuromuscular component per se, however they are not appropriate to use on its own for assessing muscle quality unless they are normalized to either muscle mass or muscle volume.

Muscle strength is defined as the amount of force a muscle can produce with a single maximal effort (Beaudart et al., 2019). Strength is measured using dynamometry in different contractions, at different muscle lengths and in different muscles: isometric upper limb strength is often determined by handgrip force or strength (HGS) and isometric lower limb strength is measured with knee extension torque. It has been previously reported that in older adults' muscle strength declines between 1 and 2 % per year; however, muscle power is decreasing with the double the rate (Metter et al., 1997; Skelton et al., 1994). Age could solely explain 6 to 44% of the variability in the muscle strength decline (Leblanc et al., 2015).

Handgrip strength

Hand grip strength has been one of the most commonly used assessments for muscle strength as it is easy to use and has good repeatability, however on its own it does not provide the information about muscle quality (Cruz-Jentoft et al., 2019). Compared to other more complicated methods, hand grip is the simplest method to assess strength, even though it has low to fair relationship to lower body strength (Chan et al., 2014; Harris-Love et al., 2018). Hand grip strength is suggested to be a good indicator of general health and all-cause mortality (Buckinx & Aubertin-Leheudre, 2019; Leong et al., 2015). Currently, hydraulic dynamometer is the gold standard for this measurement.

Lower limb muscle strength

Lower limb muscle torque or strength is often taken into the account as it is suggested to be associated with muscle performance and therefore overall mobility (Harris-Love et al., 2018). Most used measures are taken in isokinetic or isometric conditions (Buckinx & Aubertin-Leheudre, 2019). Isometric strength consists of maximal voluntary strength during contraction performed at constant angular position against resistance. This measure reflects static strength as opposed to isokinetic strength. Isometric measurements are often limited by measurement position, measurement site, the type of measurement and the type of muscle contraction. So far, there has been method standardization proposal (Buckinx et al., 2017) for a hand-held dynamometer. Limitation of this method is that the reproducibility is only moderate to good with skills and strength of the evaluator can provide bias in the measurement (Keating & Matyas, 1996). Isokinetic method measures dynamic muscle strength which is done with unidirectional analytical motion, performed at a constant angular velocity and guarantees maximum muscle contraction during the entire range of motion (Buckinx & Aubertin-Leheudre, 2019). This method requires expensive and non-portable isokinetic dynamometer which limits its' use.

While diagnosing sarcopenia, five times sit to stand test has been proposed as a method of lower limb muscle strength measure by the Asian Working Group on Sarcopenia (Chen et al., 2020) and European Working Group on Sarcopenia on Older People (Cruz-Jentoft et al., 2019). The participant needs to stand up and sit down five times as fast as possible and the time of completion is measured. This test has been used on older adults due to its' simplicity, low cost and its' resemblance to everyday activities (Bohannon et al., 2010; De Melo et al., 2019). Multiple factors besides strength affect test result, such as balance and sensation (Lord et al., 2002; Schenkman et al., 1996), however it is a useful test to perform in clinical setting or in population screening as it does not require highly qualified measurer or expensive equipment.

Muscle strength can be expressed in absolute or relative units, where absolute seems to be the simplest to acquire, and relative might be more relevant as muscle strength in daily life is affected by different variables such as body weight, body composition or BMI (Reed et al., 1991). Relative strength can be adjusted to body mass (Ploutz-Snyder et al., 2002) or muscle mass (Lynch et al., 1999; Metter et al., 1997).

PROPOSED MUSCLE QUALITY MEASURES

Muscle quality is an indirect measure, therefore relative strength is important. Sometimes these terms have been used as synonyms, however its interpretation requires caution due to many factors affecting it: type of movement or anatomical location (Fragala et al., 2015). Protocol for sarcopenia diagnosis suggests that muscle quality tool for use in clinical practice needs to be cost-effective, standardised and repeatable across different populations (Cruz-Jentoft et al., 2019). To date, there has been no consensus reached about muscle quality measures but below are presented the ones that have been proposed with respect to neuromuscular component.

Muscle quality index

Muscle quality index was introduced as a predictor of functional capacity and is defined as the ratio between combined hand grip strength and appendicular skeletal mass (Barbat-Artigas et al., 2012). Combined hand grip strength is calculated as a sum of both hand grip strength results and appendicular skeletal mass is calculated as a sum of upper and lower limb skeletal mass. Literature also reports different approaches for this parameter such as ratio of one leg one-repetition maximum and leg muscle mass (Distefano et al., 2018), combination of knee extensor and flexor torque per unit of muscle mass (Francis et al., 2017) or ratio between knee extension strength and thigh muscle cross-sectional area (Moore et al., 2014). Due to the broad definition of this index, it has been used on different populations: patients with obesity (de Sousa Neto et al., 2023), haemodialysis (Nowicka et al., 2022), hip osteoarthritis (Jerez-Mayorga et al., 2019), elderly (Ribeiro et al., 2022) and adolescents (Barahona-Fuentes et al., 2023).

The index has mostly been used in laboratory setting, however the need for the equivalent field test was recognized and the parameter was also tested in the field setting using certain different parameters – DXA (to assess entire arm muscle mass) was replaced by body mass index and hand grip strength was used to assess muscle strength in both settings. Field assessment of muscle quality was defined as the ratio of the highest result of grip strength to body mass index, while laboratory muscle quality index was calculated as the ratio of hand grip strength to entire arm muscle mass in kilograms (de Sousa Neto et al., 2023).

Importance of this parameter has been indicated as muscle quality index can better predict lower extremity function than aerobic fitness and fat mass (Misic et al., 2007). Knowing that the absolute strength values can be significantly affected by body mass or body mass index, it is more appropriate to use normalized values for adequate muscle quality assessment.

Ultrasound sarcopenia index

Ultrasound muscle quality index was proposed as sarcopenia index by Narici et al. and is defined as the ratio between muscle thickness and fascicle length measured with ultrasonography (Narici et al., 2021). As individuals age, both muscle thickness and fascicle length tend to decrease: decrease in fascicle length precedes a loss of sarcomere in series. The authors found that with the increasing degree of sarcopenia, the decrease of muscle thickness exceeds the shortening of fascicle length. The ultrasound sarcopenia index is considered useful for clinical practice due to the widespread availability of ultrasound in clinical settings, as well as its simplicity and affordability. Additionally, using ultrasound for this measurement eliminates the need for exposure to ionizing radiation. This measurement is relatively new, therefore more research needs to be done on larger cohorts. However, it is important to note that while this method shows promise in assessing sarcopenia and muscle quality, it does not evaluate the neuromuscular function of the muscle *per se*.

BIA-derived phase angle

Phase angle has been suggested to assess muscle function and quality and is calculated as the ratio between reactance and resistance, using the arctan value and measured with BIA (Sardinha, 2018). This parameter has been directly related to muscle strength (Norman et al., 2015) and has been found to decline with age (Yamada et al., 2016). In the older population, phase angle predicts adverse outcomes like frailty (Kilic et al., 2017), falls (Uemura et al., 2019) and mortality (Wirth et al., 2010). Sarcopenic population has been shown to have lower values of phase angle (Di Vincenzo et al., 2021). Phase angle has been compared with muscle quality calculated from hand grip strength divided by upper limbs muscle mass and found that skeletal muscle index strongly correlated with phase angle (Akamatsu et al., 2022). The same study reported cut-off values for predicting sarcopenia in young and elderly for both sexes. Limitations of this method can be subtle differences regarding equipment from different manufacturers, and the parameter has not been validated in large cohorts.

FUTURE DIRECTIONS

The concept of muscle quality has emerged as a crucial factor in assessing muscle function and overall health, particularly in older adults. It encompasses both, microscopic and macroscopic aspects, including morphological and neuromuscular component. As the research field of muscle aging progresses, it is evident that standardized and universally accepted assessment method of muscle quality is lacking. The future research should focus on refining and validating the proposed measures, considering their applicability in diverse population and in different settings. Establishing a consensus on muscle quality will contribute to more comprehensive understanding of musculoskeletal health and paving the way for targeted interventions for certain diseases and disorders. In terms of assessment methods, a portable, standardized and cost-effective method should be proposed for muscle quality assessment.

In this regard, we need to mention Slovenian method tensiomyography, a non-invasive and simple method that is closely linked to muscle fibre composition (Šimunič et al., 2011, 2019) and muscle architecture (Pišot et al., 2008; Šimunič et al., 2018), which was pointed out as a promising tool for investigating contractile properties in ageing muscle (Pus et al., 2023). Tensiomyography was not validated for muscle quality assessment, however we believe that it is out the outmost future directions in this field of research.

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