Ministério da Saúde

COORDENAÇÃO DE ENSINO

Programa de Residência Multiprofissional em Oncologia

TAIARA SCOPEL POLTRONIERI

Skeletal muscle quality by computed tomography: integrative review of the methodological perspectives and conceptual evolution

Rio de Janeiro

2019

TAIARA SCOPEL POLTRONIERI

Skeletal muscle quality by computed tomography: integrative review of the methodological perspectives and conceptual evolution

Trabalho de Conclusão de Curso apresentado ao Instituto Nacional de Câncer José Alencar Gomes da Silva como requisito parcial para a conclusão do Programa de Residência Multiprofissional em Oncologia.

Orientadora: Dra. Gabriela Villaça Chaves

Rio de Janeiro
2019

TAIARA SCOPEL POLTRONIERI

Skeletal muscle quality by computed tomography: integrative review of the methodological perspectives and conceptual evolution

Avaliado e aprovado por:

Dra. Gabriela Villaça Chaves

Dra. Lívia Costa de Oliveira

Ms. Mariah Azevedo Aredes

Data: 14/02/2019

Rio de Janeiro – RJ

2019

ABSTRACT

Background & Aims: Low skeletal muscle (SM) quality may be related to the degree of muscle fat infiltration and seems to be associated to worse outcomes. The aim of this study was to summarize the methodologies for indirect evaluation of SM fat infiltration using computed tomography (CT), as well as to describe the evolution of the terms used in the literature to define muscle quality by this method.

Methods: An integrative bibliographic review in four databases included studies published until August 2018 in Portuguese, English or Spanish; performed in humans, adults and/or elderly, of both sex; which investigated SM quality through CT of the region between the third and fifth lumbar vertebrae and evaluated at least two muscular groups.

Results: Sixty-seven studies were selected. A methodological standardization trend was observed in determining the abdominal region and the evaluated muscle groups. However, the most significant methodological variations concern the classification of SM quality, such as, the selection of SM areas, radiodensity ranges delimitation and their cut-off points, as well as the terminologies used.

Conclusions: The methodological differences detected are probably due to the lack of more precise information about the correlation between SM radiodensity by CT and its composition. Therefore, recommendations were made to be followed until new studies considering the mentioned factors correct these gaps.

Key words: Body Composition, Myosteatosis, Radiodensity, Muscle Tissue

SUMMARY

1. INTRODUCTION

Skeletal muscle (SM) quality is determined by several aspects, as its composition, morphology and architecture [1,2]. Among these, muscle composition is highlighted, since it can be affected by fat infiltration, also called myosteatosis, with consequent radiodensity reduction of its tissue [3,4].

Among the available methodologies for muscle composition evaluation, computed tomography (CT) has been increasingly applied to investigate aspects of SM *in vivo*, enabling the identification of body tissue by anatomical characteristics and by radiodensity ranges differences [4–6]. Studies have shown that the muscle radiodensity determined by CT has a direct correlation with the triglyceride content when evaluated by muscle biopsy, that is, the greater the SM fat infiltration, the lower is this tissue radiodensity. Therefore, this imaging method is suggested to be capable of implying, indirectly, SM quality [5,7].

Nevertheless, a methodological plurality can be observed among studies using CT, especially regarding the evaluation of different body regions, muscle groups and methodologies for SM quality classification (selection of SM areas, radiodensity ranges - in Hounsfield Units, HU - and cut-off points) [4]. Similarly, the terminologies used to designate this subject are highly varied. Some authors designate as low quality SM the low radiodensity muscular tissue, while others consider as such the fat infiltrated SM, what leads to a diversity of denominations [8–12]. The lack of standardization impairs an adequate literary search as well as the comparison of scientific findings.

Current studies indicate several health problems related to SM fat accumulation, both in healthy individuals as in those with the most diverse diseases, triggering, for example, functional capacity reduction, damages to glycemic control, lower survival, worse surgical outcomes and toxicity to cancer treatment [3,4,8,9,13–24].

Previous reviews that summarized this issue [4,25,26] did not explore extensively topics related to the methodological approach in different populations. Considering the relevance of this subject, it is necessary to expand the discussion about the theme, corroborating to the alignment among researchers in future studies. Therefore, this integrative literature review aims to summarize the methodologies implemented in different health areas for indirect evaluation of SM fat infiltration by CT, as well as to describe the evolution of the terms used to define muscle quality through this method.

2. METHODS

Search strategies

U.S. National Library of Medicine (PubMed), Scopus, Web of Science and Latin American and Caribbean Health Sciences Literature (LILACS) databases were searched between April and August 2018. Official descriptors consistent with the outcome in focus were selected for the search strategies construction from PubMed's Medical Subject Headings and Descriptors in Health Sciences, in addition to free terms of researchers' previous knowledge, pertinent to the research topic, in order to maximize identification of relevant studies. The process was carried out in English at PubMed, Scopus and Web of Science databases and, in English, Portuguese and Spanish at LILACS database. Moreover, characteristics search methods of each base were also applied.

Aiming a comprehensive literature scan, the search was composed by one conceptual block. Whenever necessary, term truncations and the Boolean operator "OR" for combination of terms were used. Searches comprised title, abstract and keywords, using specific field markers for each database. The complete strategies applied, and the number of studies found in each database are listed in the Supplementary Table.

Eligibility criteria

The eligibility criteria were: studies published until August 2018 in Portuguese, English or Spanish; conducted in humans, addressing adults and/or elderly of both sex, healthy or sick; originals; observational design (transversal or longitudinal); which investigated SM quality by CT of the region between the third and fifth lumbar vertebrae (L3 and L5), since it is the most adequate method according to the literature and because these specific regions present a high correlation with the total body skeletal muscle mass [3,23,27–29]; and studies using at least two muscular groups of this anatomical location, due to the fact that a single SM group is not able to represent the total body musculature [30,31].

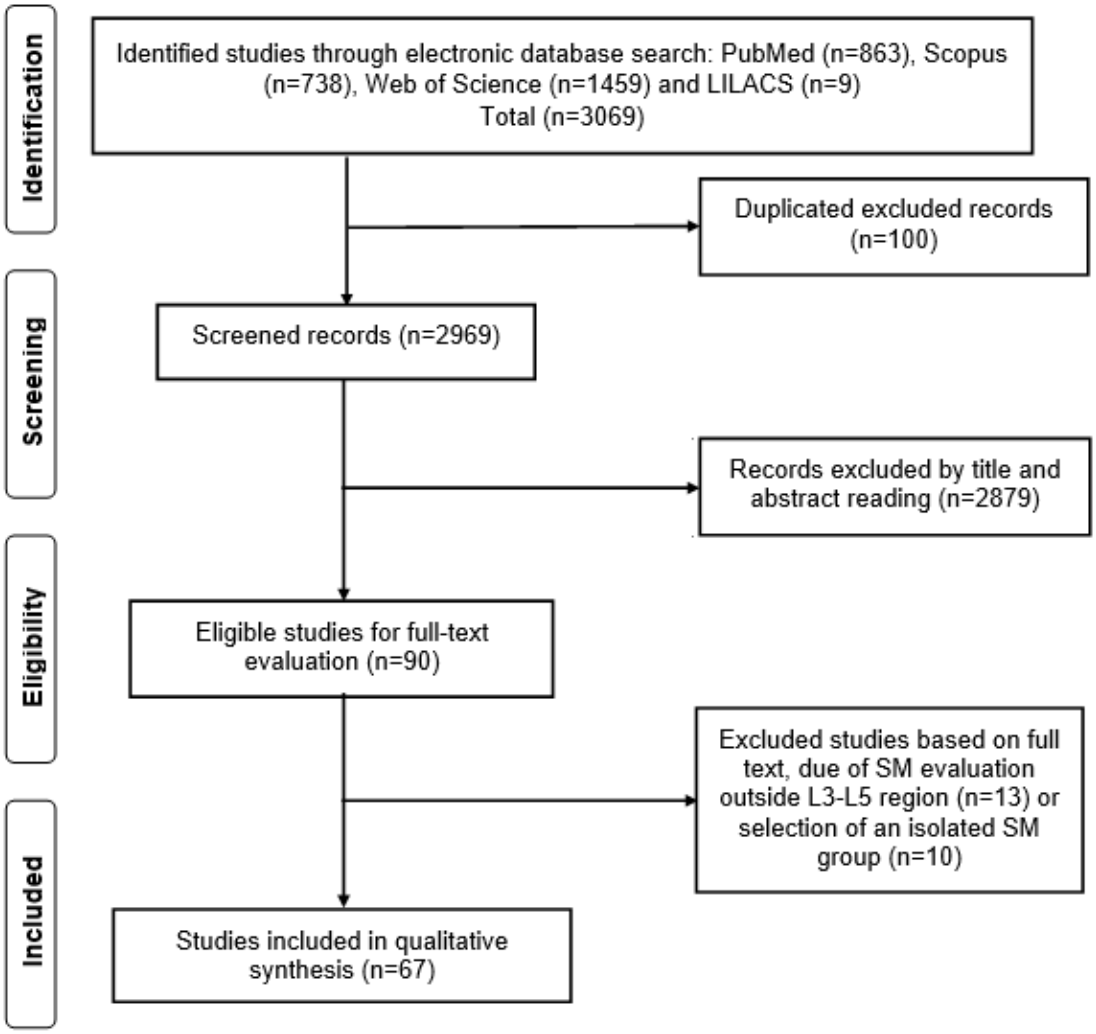
Studies selection

The first researcher systematically assessed the eligibility of each study resulting from database searches based on title and abstract reading. The complete

selected articles were carefully reviewed by another researcher and compared with those of the initial evaluator. When necessary, the articles were discussed with the study group and eligibility was determined by consensus. The selection process is shown in Figure 1.

Data of the included studies were computed and refined during the extraction process. For this, a standard form was developed with the items to be considered during the collection, considering the information contained only in the methodology of the articles. This tool included information about the authors, publication year, population characteristics (age, sex and presence or not of diseases), selected abdominal region, muscle groups and its areas analyzed by CT, radiodensity ranges and methodologies used to set their cut-off points and terms defining muscle quality.

Figure 1. Flow diagram of the studies selection process.



3. RESULTS AND DISCUSSION

Evolution of the imaging tools has allowed more consistent and precise body composition diagnoses and approaches [25,32]. This article reviewed the methodologies and terminologies used to indirectly determine SM quality evaluated by CT in different populations.

Tables 1, 2, 3 and 4 show compiled findings of the sixty-seven included articles [3,5,8,9,11–24,28,33–80]. The high prevalence approach of individuals diagnosed with cancer among the evaluated populations (Table 1) [3,11,16–23,28,33–62] was probably due to previous availability of this exam, performed as routine for diagnosis, staging and clinical follow-up, enabling the convenient use of CT in this population profile [26,81,82].

Usage contextualization of the tool

Besides the mechanical function performed by SM, it is integrally involved in metabolic processes, both in healthy conditions as well as in clinical situations [83]; therefore, the use of tools to evaluate its composition is of major importance. For this purpose, there is an availability of more invasive options, such as biopsy [5,7], however, there is also the possibility of imaging equipment use, such as CT, magnetic resonance [4] and ultrasonography [84,85].

CT was initially applied in order to determine SM composition in different populations – healthy, clinical and/or surgical, but especially elderly – and currently it has been increasingly present in other pathological conditions [4,8,13,86–89]. This technology distinguishes tissues based on their radiodensity that reflects the chemical composition. Radiodensity values are expressed in HU, based on a linear scale, having water as reference (0HU) [5].

The method ability to differentiate SM fat infiltration is given by radiodensity values. Moreover, chemically, CT reading is sensitive to proton content per unit of mass, which is high in adipose tissue [5], providing clear radiological findings, and area, volume and radiodensity precise quantification [26].

This tool was previously validated by Goodpaster et al. [5], who compared it with biopsy in a study demonstrating that muscle radiodensity obtained by CT correlated directly with triglyceride content found in the evaluated tissue. Thus, this imaging method has been suggested to be capable of inferring indirectly SM quality [5,7,26].

However, CT is not able to directly measure the lipid amount and neither differentiate fat deposits location (intra- or extracellular) [90–92]. Another limitation is concerned with the fact that individuals are not usually submitted to this type of exam exclusively for research purposes or body composition assessment, due to the substantial ionization radiation emitted [27]. On the other hand, as mentioned above, this equipment is convenient and easily accessed in health services, since it can integrate therapeutic plans [26,81,82].

Methodologies used for computed tomography application

A methodological standardization trend was identified among the evaluated studies in determining L3 as abdominal region and all muscle groups investigated (Table 2). In contrast, methodologies for SM quality classification, such as the selection of SM areas, radiodensity ranges delimitation, as well as the cut-off points for these ranges, were characterized by inconsistent criteria (Table 3), as reported in other review studies [4,25].

Abdominal region

Similarly to a previous review [25], CT cross-sectional image at L3 level was the most frequent among the included articles (Table 2) [3,8,11,12,15–23,28,33–39,41–53,55–67]. The predominance of this vertebral level evaluation is related to its linear correlation with total body skeletal muscle mass, demonstrated in a validation study [26]. Two references reported the use of images at the umbilical level [9,80], however, this is a non-static reference point, which could result in a measurement error [32].

Muscle groups

Analysis of all muscle groups in the cross-sectional area of the chosen region was done by the majority (76.1%) of the studies (Table 2) [3,11,15–23,28,33–53,55–62,64–67,71–75,77,80]. Assessment of the total cross-sectional muscle area is more sensitive to define total SM and has a strong interobserver agreement [30,31]. Paraspinals (erector spinae - including iliocostalis, longissimus and multifidus - and quadratus lumborum), psoas and abdominal wall muscles (transversus abdominus, internal and external obliques and rectus abdominus) are the SM considered as components of the muscle set at the abdominal region [26,82,93]. Analysis of only one

abdominal muscle group is not indicated, since isolated changes are not representative of the whole and relevant information about remaining tissues can be ignored by the visualization of only one group [30,31].

Other studies have selected, as a measurement of muscular composition, only *psoas*, as representative of the abdominal muscle groups [89,94]. However, this methodology has not been validated and presents a significant bias risk. This muscle, specifically, demonstrates a high measurement error, weak correlation with the total lumbar muscle area and can suffer atrophy due to diseases of the spine [30,32,82,95].

Methodologies for skeletal muscle quality classification

Selection of the skeletal muscle areas

There was a predominance of studies using mean attenuation of the total abdominal muscles area in the cross-sectional images (Table 3) [5,8,9,11–13,15–24,33–48,50–53,55,57–60,64–68,71,73,75,79]. Other authors determined the muscle radiodensity using only a SM specific region, denominated “region of interest” [4,14,54,69,70,72,76–78,80]. However, this may be considered a limiting methodology because it considers only one region as representative of the whole, when, in fact, total muscle composition is heterogeneous between the different groups [96]. Furthermore, small measurement errors of an isolated tissue portion could mathematically generate higher errors when this region is extrapolated to total body skeletal muscle tissue [30].

The use of a mathematical index generated by Weinberg et al. [97], called “skeletal muscle gauge”, that multiplies SM index (SM normalized area multiplied by the square height) by mean muscle radiodensity was justified by the authors since it integrates both SM quantity as well as its quality in the same variable. This new indicator showed a stronger correlation with age, in addition to a greater power to predict toxicity and hospitalizations in patients undergoing chemotherapy [61,62,97], when compared to the isolated indexes. However, it was not associated with overall survival in patients with metastatic breast cancer [62]. The results of this indicator were presented in Arbitrary Units (AU), since the SM index and radiodensity hold different measure units [49,56,61,62,97].

Articles dividing total SM range into two sub-ranges, denominated as "low or high radiodensity SM", were also found. The researchers calculated the representative muscle area of these two ranges [3,28]. This methodology allows the identification of

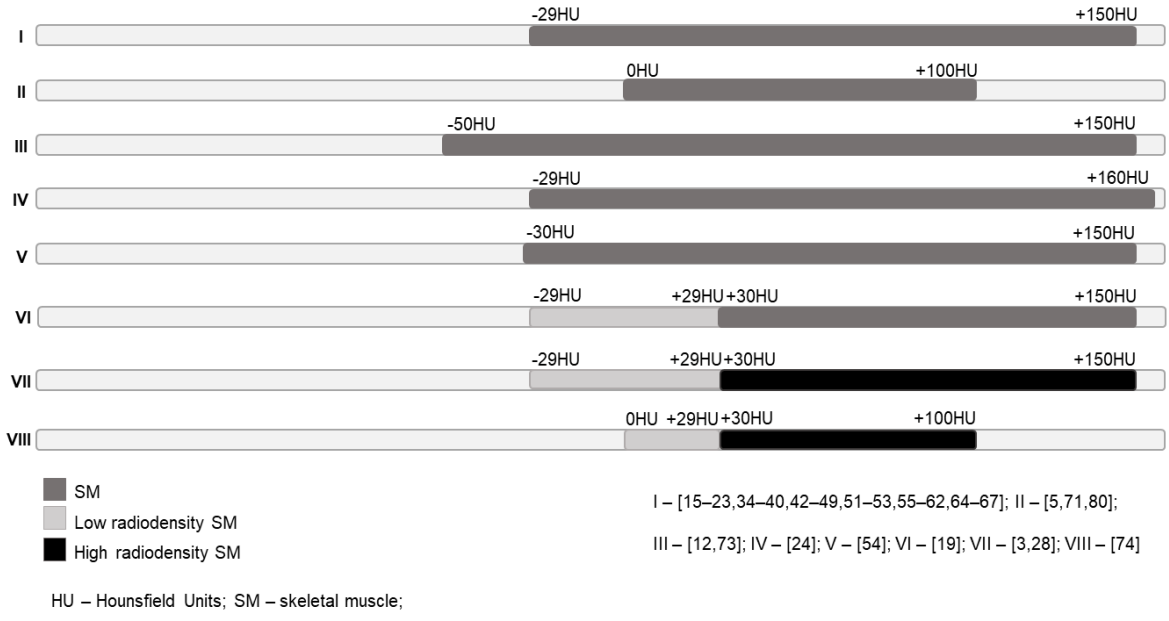
the extension of the SM area with presumed more or less fat infiltration, instead of only classifying it based on mean radiodensity and is considered by the authors as a promising methodology [3].

Radiodensity ranges

Our findings reported some standardization in radiodensity ranges for SM demarcation (Table 3), what corroborates previous reviews [4,25]. It was observed, with only few variations, a predominance of the range from -29HU to +150HU [15–23,34–40,42–49,51–53,55–62,64–67]. Intervals from -29HU to +160HU [24] and from 0HU to +100HU were also found [5,80]. These ranges evaluated SM as a whole, without classifying it in low or high radiodensity [4,5,19,25,33].

When delimited the low radiodensity SM ranges, these were not consistent among studies [4,19,25]. Some articles established as low attenuation the ranges from -29HU to +29HU [19] and from 0HU to +29HU [74]. Others, not included in the results, used the interval from 0HU to +34HU [98,99]. Researchers in our group named the interval from -29HU to +29HU as “low radiodensity SM” [3,28], while the interval from +30HU to +150HU was determined as “high radiodensity SM” [3,28]. The variation from +30HU to +100HU for high density SM was also identified [74].

Figure 2. Ranges used by the studies to delimit SM areas according its radiodensity.



This diversity in the radiodensity ranges used (Figure 2), mainly in relation to the lower point of what is considered as SM interval, and specifically, the low radiodensity SM, may be related to technological limitations experienced by the pioneers in determining the real tissue constitution of this "transition" site. This can result in an empirical institution of some parameters and/or based on authors previous knowledge, what made the standardization difficult [99–103]. The wide range of new information persisted and suffered punctual alterations, although heterogeneous over time. This matter has been continuously studied by different groups in isolation, fact that resulted in an arbitrary determination of different methodologies [100–107].

In 1979, even without full knowledge of how tissue biochemistry relates to muscle radiodensity, it was already supposed that the concentration of main contractile proteins and enzymes – myoglobin, hemoglobin, collagen – in addition to fat concentration, were important factors to define muscle radiodensity [101]. In the following years, some authors have stated that portions of SM radiodensity range could also be composed by other lean tissues, muscular components and connective tissue elements. However, it is not clear yet what determines this lower muscle density [99,105,108–111].

In 2000, a CT validation study through biopsy identified that reduction of the muscle radiodensity, determined by this imaging instrument, reflected lipid concentration contained therein [5]. Notwithstanding, the same authors, corroborating previous assumptions, pointed that it would be unlikely that lipid content was the only contributor to the alterations in muscle radiodensity. Other factors or changes in SM properties, such as muscle protein, perfusion or extracellular water content could also affect it [5,112]. Exact histological and biochemical knowledge of the tissues that compose this “transition” region is still scarce. Currently, the most widely accepted molecular constituent likely to cause the marked reduction in SM radiodensity is the infiltrated and accumulated fat [113]. Nevertheless, other possible molecular participations need to be considered in future studies.

In turn, the range from -29HU to -1HU is even less reported by articles. This range was recently used to define the interval classifying low radiodensity muscle [3,19,28], and it was included in the radiodensity interval lower or equal to +30HU to discriminate intermuscular fat [75]. An article not included in our results, treated this range as solely fat [99]. Most of the papers included in the present review inserted it in

a larger range considered as muscle, from -29HU to +150HU [15–23,34–40,42–49,51–53,55–62,64–67]. Other studies have used it in a range from -50HU to +150HU [12,73] or from -30HU to +150HU [54] for SM differentiation.

As discussed above, these variations are, probably, in the same way related to the lack of information about tissue constitution of these specific intervals. Consequently, they are eventually disregarded by researchers or addressed in random ways. Given current disparities, and until more adequate and reliable information are reached, Aubrey et al. [4] suggested as a possibility, the incorporation of the total range from -29HU to +29HU to define low radiodensity SM.

Likewise, variations in the tissue determination of the range equal or lower than -30HU are observed, what is already considered by the literature as fat *per se.* Most of the authors use such range to classify infiltrated muscle fat, and this area, when located within the muscle groups analyzed, is applied to estimate individuals' body fat [107].

Some articles have considered not only muscle tissue radiodensity, but also this range as consistent with fat infiltrated in muscle as a parameter for SM quality. Thus, some authors designate as intermuscular fat [44,48,57,65,66,71] and intramuscular [20,21,28,38,43,45,55,59] the ranges covering tissues presenting radiodensity between -190HU and –30HU. The interval -190HU until –90HU was also named as intramuscular fat [53]. These terms define lipid infiltration both outside and inside the myocyte, respectively, but CT is not capable of differentiating it, as previously mentioned [90].

CT methodological limitations, approach disagreements and determination of the described tissue radiodensity spectrum, result, therefore, in variations for the proposed nomenclatures, which will be discussed later. This scenario and even intervals omission can lead to failures at the evaluation of a significant and clinically representative body area [4].

Cut-off points

Most of the included studies analyzed their findings using the variables in a continuous way [representative tissue area of radiodensity, in cm^2/m^2, or mean muscle attenuation (MA), in HU] for mean or median comparison with dependent variables of the studies interest, without establishing cut-off points for the radiodensity ranges used

(Table 3) [5,8,9,11–13,15,24,33,40,45,47,49,53,55,56,61,62,66,68,69,75,78–80]. Despite the continuous nature of the variable and its capability of predicting outcomes, some authors consider the interpretation of continuous prognostic covariates complex, therefore, they normally prefer to categorize them based on a cut-off point to stratify different risk groups for decision-making [26].

Thereby, another significant portion of studies [16,18,20,23,35,37,39,41,44,46,50,51,57,64,65] used as a parameter the set of cut-off points for low radiodensity muscle determined by Martin et al. [19] (using optimal stratification) in cancer patients [26]. There were also those who stipulated cut-off points for their own population [3,17,19,21,22,28,34,36,38,43,52,54,58,59,67,70–72,74,77]. Two articles [42,60] used pre-established cut-off points of other studies [4,5,114,115], among which, one evaluated visceral, subcutaneous and total fat [114] and another assessed sarcopenia, reporting only the mean MA for its population, stratified by the presence of sarcopenia [115].

Since the range of low radiodensity are not standardized and adequately defined, inconsistencies at data collection and analysis are expected, making the comparison of results difficult [32]. The standardization process must consider specific characteristics of factors such as age, sex, ethnicity and diseases [25].

Conceptual evolution

Another relevant point is the terminology inconsistency to designate SM quality through its composition (Table 4), which is a consequence of the methodological problems discussed previously [4,113]. Among the nomenclatures observed in the evaluated articles, the ones that stood out were those referring to SM, such as "attenuation or radiological attenuation, radiodensity and density" [3,5,8,9,11–24,28,33–39,41–62,64–70,72–80].

However, the use of "MA" as a synonym for terms such "SM radiodensity or density" needs to be better evaluated. According to Oxford and Cambridge dictionaries, respectively, "attenuation" means reducing the force, effect, or value of something, and "attenuating" means making something smaller, thinner or weaker [116,117]. Its use in the context of SM quality seems to arise from the fact that, when analyzed by CT, the presence of fat attenuates SM radiodensity, because, as previously stated, this tool reads tissue radiodensity, generated by its chemical

composition [5]. Thus, we reinforce that perhaps the term "SM radiodensity" is the most appropriate to be applied, considering the perspectives of interpretation presented here. In addition, since CT is an indirect measure of tissue composition, and therefore, it is not possible to accurately state what tissue is present, in the absence of a direct measure [5].

Terms referring to adipose tissue in muscles were found in a smaller amount [11,13,15,33,36,39,40,46–49,53,55,56,62–66,68–70,72,74–76,80], just as others more specific when designating the fat location in muscle, such as "intramuscular or intramyocellular" [3,9,17,20,21,28,34,38,43,45,50,53,55,67,70,72,78] and "intermuscular" [5,13,45,48,50,57,65,66,71,75]. The presence of two cellular pathways of fat origin in SM enables these nomenclatures variations. The first pathway is direct and is due to lipid accumulation within the myocytes [118]. Whereas, "intermuscular" variation is due to accumulation of satellite cells (stem cell population) and mesenchymal interstitial cells below the basal lamina of muscle fibers [119–121]. The first ones contribute to myogenesis during muscle regeneration, and are more resistant to adipogenic differentiation, while the others differ rapidly in fat under muscle injury or administration of glucocorticoids [119,121,122]. Therefore, it is understood that the authors considered for evaluation lipids as such, infiltrated and accumulated in muscle tissue. Consequently, the term "myosteatosis", which means fat in SM has the same origin [8–12].

This context is related to impaired energetic homeostasis, insulin insensitivity, inflammation and functional muscular deficits [121,123], generating "SM quality or muscular quality” nominal variations [3,17,34,40,47,56,58,64,66,67,74,76,80], due to tissue damage. A vicious cycle can be constituted with the presence of insulin resistance and obesity, since both foster SM fat accumulation by impairment of local fatty acids metabolism [121,124,125].

4. CONCLUSION

This review indicates a methodological standardization trend to determine the abdominal region and muscle groups evaluated, while topics for classification of SM quality, such as the selection of SM areas, radiodensity ranges delimitation and their cut-off points, were characterized by methodological multiplicity, as well as the terms used for its nomenclature.

The continuity of L3 use and evaluation of all muscle groups at this vertebral level is highly recommended as well as the preference for total muscle area selection. Methodology definition to classify fat infiltrated muscle tissue, according to its radiodensity, should be preferably validated with studies comparing CT radiological findings and direct methods of muscle composition evaluation. Specificities consideration of each studied population, which may impact radiodensity cut-off points is also recommended. Nomenclature uniformization can be facilitated by the elucidation of these topics.

Methodological adjustment of this scenario and greater exploration are essential to avoid suboptimal screening and support scientific discussion, allowing a comprehensive understanding about its clinical relevance.

5. BIBLIOGRAPHIC REFERENCES

[1] Correa-de-Araujo R, Harris-Love MO, Miljkovic I, Fragala MS, Anthony BW, Manini TM. The need for standardized assessment of muscle quality in skeletal muscle function deficit and other aging-related muscle dysfunctions: a symposium report. Front Physiol 2017;8:1–19. doi:10.3389/fphys.2017.00087.

[2] Fragala MS, Kenny AM, Kuchel GA. Muscle quality in aging: a multi-dimensional approach to muscle functioning with applications for treatment. Sports Med 2015;45:641–58. doi:10.1007/s40279-015-0305-z.

[3] Silva de Paula N, de Aguiar Bruno K, Azevedo Aredes M, Villaça Chaves G. Sarcopenia and skeletal muscle quality as predictors of postoperative complication and early mortality in gynecologic cancer. Int J Gynecol Cancer 2018;28:412–20. doi:10.1097/IGC.0000000000001157.

[4] Aubrey J, Esfandiari N, Baracos VE, Buteau FA, Frenette J, Putman CT, et al. Measurement of skeletal muscle radiation attenuation and basis of its biological variation. Acta Physiol 2014;210:489–97. doi:10.1111/apha.12224.

[5] Goodpaster BH, Kelley DE, Thaete FL, He J, Ross R. Skeletal muscle attenuation determined by computed tomography is associated with skeletal muscle lipid content. J Appl Physiol 2000;89:104–10. doi:10.1152/jappl.2000.89.1.104.

[6] Brandberg J, Lonn L, Bergelin E, Sjostrom L, Forssell-Aronsson E, Starck G. Accurate tissue area measurements with considerably reduced radiation dose achieved by patient-specific CT scan parameters. Br J Radiol 2008;81:801–8. doi:10.1259/bjr/44384066.

[7] Miljkovic I, Zmuda JM. Epidemiology of myosteatosis. Curr Opin Clin Nutr Metab Care 2010;13:260–4. doi:10.1097/MCO.0b013e328337d826.

[8] Mayer TG, Vanharanta H, Gatchel RJ, Mooney V, Barnes D, Judge L, et al. Comparison of CT scan muscle measurements and isokinetic trunk strength in postoperative patients. Spine 1989;14:33–6.

[9] Komiya H, Mori Y, Yokose T, Kurokawa N, Horie N, Tajima N. Effect of intramuscular fat difference on glucose and insulin reaction in oral glucose tolerance test. J Atheroscler Thromb 2006;13:136–42.

[10] DeAndrade J, Pedersen M, Garcia L, Nau P. Sarcopenia is a risk factor for complications and an independent predictor of hospital length of stay in trauma patients. J Surg Res 2018;221:161–6. doi:10.1016/j.jss.2017.08.018.

[11] Atlan P, Bayar MA, Lanoy E, Besse B, Planchard D, Ramon J, et al. Factors which modulate the rates of skeletal muscle mass loss in non-small cell lung cancer patients: a pilot study. Support Care Cancer 2017;25:3365–73. doi:10.1007/s00520-017-3755-z.

[12] Anderson DE, D'Agostino JM, Bruno AG, Demissie S, Kiel DP, Bouxsein ML. Variations of CT-based trunk muscle attenuation by age, sex, and specific muscle. J Gerontol A Biol Sci Med Sci 2013;68:317–23. doi:10.1093/gerona/gls168.

[13] Hicks GE, Simonsick EM, Harris TB, Newman AB, Weiner DK, Nevitt MA, et al. Trunk muscle composition as a predictor of reduced functional capacity in the health, aging and body composition study: the moderating role of back pain. J Gerontol A Biol Sci Med Sci 2005;60:1420–4.

[14] Sebro R. Obesity, hepatic steatosis, and their impact on fat infiltration of the trunk musculature using unenhanced computed tomography. J Comput Assist Tomogr 2017;41:298–301. doi:10.1097/RCT.0000000000000507.

[15] Matsumoto T, Tanizawa K, Tachikawa R, Murase K, Minami T, Inouchi M, et al. Associations of obstructive sleep apnea with truncal skeletal muscle mass and density. Sci Rep 2018;8:6550. doi:10.1038/s41598-018-24750-z.

[16] Chu MP, Lieffers J, Ghosh S, Belch A, Chua NS, Fontaine A, et al. Skeletal muscle density is an independent predictor of diffuse large B-cell lymphoma outcomes treated with rituximab-based chemoimmunotherapy. J Cachexia Sarcopenia Muscle 2017;8:298–304. doi:10.1002/jcsm.12161.

[17] Okumura S, Kaido T, Hamaguchi Y, Kobayashi A, Shirai H, Fujimoto Y, et al. Impact of skeletal muscle mass, muscle quality, and visceral adiposity on outcomes following resection of intrahepatic cholangiocarcinoma. Ann Surg Oncol 2017;24:1037–45. doi:10.1245/s10434-016-5668-3.

[18] Rier HN, Jager A, Sleijfer S, van Rosmalen J, Kock MCJM, Levin M-D. Low muscle attenuation is a prognostic factor for survival in metastatic breast cancer patients treated with first line palliative chemotherapy. Breast 2017;31:9–15. doi:10.1016/j.breast.2016.10.014.

[19] Martin L, Birdsell L, Macdonald N, Reiman T, Clandinin MT, McCargar LJ, 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;31:1539–47. doi:10.1200/JCO.2012.45.2722.

[20] Rollins KE, Tewari N, Ackner A, Awwad A, Madhusudan S, Macdonald IA, et al. The impact of sarcopenia and myosteatosis on outcomes of unresectable pancreatic cancer or distal cholangiocarcinoma. Clin Nutr 2016;35:1103–9. doi:10.1016/j.clnu.2015.08.005.

[21] Van Rijssen LB, van Huijgevoort NCM, Coelen RJS, Tol JA, Haverkort EB, Nio CY, et al. Skeletal muscle quality is associated with worse survival after

pancreatoduodenectomy for periampullary, nonpancreatic cancer. Ann Surg Oncol 2017;24:272–80. doi:10.1245/s10434-016-5495-6.

[22] Akahori T, Sho M, Kinoshita S, Nagai M, Nishiwada S, Tanaka T, et al. Prognostic significance of muscle attenuation in pancreatic cancer patients treated with neoadjuvant chemoradiotherapy. World J Surg 2015;39:2975–82. doi:10.1007/s00268-015-3205-3.

[23] Daly LE, Power DG, O'Reilly Á, Donnellan P, Cushen SJ, O'Sullivan K, et al. The impact of body composition parameters on ipilimumab toxicity and survival in patients with metastatic melanoma. Br J Cancer 2017;116:310–7. doi:10.1038/bjc.2016.431.

[24] Locke JE, Carr JJ, Nair S, Terry JG, Reed RD, Smith GD, et al. Abdominal lean muscle is associated with lower mortality among kidney waitlist candidates. Clin Transplant 2017;31. doi:10.1111/ctr.12911.

[25] Kazemi-Bajestani SMR, Mazurak VC, Baracos V. Computed tomography-defined muscle and fat wasting are associated with cancer clinical outcomes. Semin Cell Dev Biol 2016;54:2–10. doi:10.1016/j.semcdb.2015.09.001.

[26] Daly LE, Prado CM, Ryan AM. A window beneath the skin: how computed tomography assessment of body composition can assist in the identification of hidden wasting conditions in oncology that profoundly impact outcomes. Proc Nutr Soc 2018;77:135–51. doi:10.1017/S0029665118000046.

[27] MacDonald AJ, Greig CA, Baracos V. The advantages and limitations of cross-sectional body composition analysis. Curr Opin Support Palliat Care 2011;5:342–9. doi:10.1097/SPC.0b013e32834c49eb.

[28] Rodrigues CS, Chaves GV. Skeletal muscle quality beyond average muscle attenuation: a proposal of skeletal muscle phenotypes to predict short-term survival

in patients with endometrial cancer. J Natl Compr Canc Netw 2018;16:153–60. doi:10.6004/jnccn.2017.7028.

[29] Shen W, Punyanitya M, Wang Z, Gallagher D, St-Onge M-P, Albu J, et al. Total body skeletal muscle and adipose tissue volumes: estimation from a single abdominal cross-sectional image. J Appl Physiol 2004;97:2333–8. doi:10.1152/japplphysiol.00744.2004.

[30] Rutten IJG, Ubachs J, Kruitwagen RFPM, Beets-Tan RGH, Olde Damink SWM, Van Gorp T. Psoas muscle area is not representative of total skeletal muscle area in the assessment of sarcopenia in ovarian cancer. J Cachexia Sarcopenia Muscle 2017;8:630–8. doi:10.1002/jcsm.12180.

[31] van Dijk DPJ, Bakens MJAM, Coolsen MME, Rensen SS, van Dam RM, Bours MJL, et al. Low skeletal muscle radiation attenuation and visceral adiposity are associated with overall survival and surgical site infections in patients with pancreatic cancer. J Cachexia Sarcopenia Muscle 2017;8:317–26. doi:10.1002/jcsm.12155.

[32] Hopkins JJ, Skubleny D, Bigam DL, Baracos VE, Eurich DT, Sawyer MB. Barriers to the interpretation of body composition in colorectal cancer: a review of the methodological inconsistency and complexity of the CT-defined body habitus. Ann Surg Oncol 2018;25:1381–94. doi:10.1245/s10434-018-6395-8.

[33] Antoun S, Lanoy E, Iacovelli R, Albiges-Sauvin L, Loriot Y, Merad-Taoufik M, et al. Skeletal muscle density predicts prognosis in patients with metastatic renal cell carcinoma treated with targeted therapies. Cancer 2013;119:3377–84. doi:10.1002/cncr.28218.

[34] Fujiwara N, Nakagawa H, Kudo Y, Tateishi R, Taguri M, Watadani T, et al. Sarcopenia, intramuscular fat deposition, and visceral adiposity independently

predict the outcomes of hepatocellular carcinoma. J Hepatol 2015;63:131–40. doi:10.1016/j.jhep.2015.02.031.

[35] Malietzis G, Lee GH, Bernardo D, Blakemore AIF, Knight SC, Moorghen M, et al. The prognostic significance and relationship with body composition of CCR7-positive cells in colorectal cancer. J Surg Oncol 2015;112:86–92. doi:10.1002/jso.23959.

[36] Aust S, Knogler T, Pils D, Obermayr E, Reinthaller A, Zahn L, et al. Skeletal muscle depletion and markers for cancer cachexia are strong prognostic factors in epithelial ovarian cancer. PloS One 2015;10:e0140403. doi:10.1371/journal.pone.0140403.

[37] Malietzis G, Johns N, Al-Hassi HO, Knight SC, Kennedy RH, Fearon KCH, et al. Low muscularity and myosteatosis is related to the host systemic inflammatory response in patients undergoing surgery for colorectal cancer. Ann Surg 2016;263:320–5. doi:10.1097/SLA.0000000000001113.

[38] Tamandl D, Paireder M, Asari R, Baltzer PA, Schoppmann SF, Ba-Ssalamah A. Markers of sarcopenia quantified by computed tomography predict adverse long-term outcome in patients with resected oesophageal or gastro-oesophageal junction cancer. Eur Radiol 2016;26:1359–67. doi:10.1007/s00330-015-3963-1.

[39] Hayashi N, Ando Y, Gyawali B, Shimokata T, Maeda O, Fukaya M, et al. Low skeletal muscle density is associated with poor survival in patients who receive chemotherapy for metastatic gastric cancer. Oncol Rep 2016;35:1727–31. doi:10.3892/or.2015.4475.

[40] Boer BC, de Graaff F, Brusse-Keizer M, Bouman DE, Slump CH, Slee-Valentijn M, et al. Skeletal muscle mass and quality as risk factors for postoperative outcome

after open colon resection for cancer. Int J Colorectal Dis 2016;31:1117–24. doi:10.1007/s00384-016-2538-1.

[41] Malietzis G, Lee GH, Al-Hassi HO, Bernardo D, Blakemore AIF, Kennedy RH, et al. Body composition of the host influences dendritic cell phenotype in patients treated for colorectal cancer. Tumour Biol 2016;37:11359–64. doi:10.1007/s13277-016-5009-y.

[42] Malietzis G, Currie AC, Athanasiou T, Johns N, Anyamene N, Glynne-Jones R, et al. Influence of body composition profile on outcomes following colorectal cancer surgery. Br J Surg 2016;103:572–80. doi:10.1002/bjs.10075.

[43] Sjøblom B, Grønberg BH, Wentzel-Larsen T, Baracos VE, Hjermstad MJ, Aass N, et al. Skeletal muscle radiodensity is prognostic for survival in patients with advanced non-small cell lung cancer. Clin Nutr 2016;35:1386–93. doi:10.1016/j.clnu.2016.03.010.

[44] Pędziwiatr M, Pisarska M, Major P, Grochowska A, Matłok M, Przęczek K, et al. Laparoscopic colorectal cancer surgery combined with enhanced recovery after surgery protocol (ERAS) reduces the negative impact of sarcopenia on short-term outcomes. Eur J Surg Oncol 2016;42:779–87. doi:10.1016/j.ejso.2016.03.037.

[45] Kumar A, Moynagh MR, Multinu F, Cliby WA, McGree ME, Weaver AL, et al. Muscle composition measured by CT scan is a measurable predictor of overall survival in advanced ovarian cancer. Gynecol Oncol 2016;142:311–6. doi:10.1016/j.ygyno.2016.05.027.

[46] Cushen SJ, Power DG, Murphy KP, McDermott R, Griffin BT, Lim M, et al. Impact of body composition parameters on clinical outcomes in patients with metastatic castrate-resistant prostate cancer treated with docetaxel. Clin Nutr ESPEN 2016;13:e39–45. doi:10.1016/j.clnesp.2016.04.001.

[47] Kubo Y, Naito T, Mori K, Osawa G, Aruga E. Skeletal muscle loss and prognosis of breast cancer patients. Support Care Cancer 2017;25:2221–7. doi:10.1007/s00520-017-3628-5.

[48] van Roekel EH, Bours MJL, Te Molder MEM, Breedveld-Peters JJL, Olde Damink SWM, Schouten LJ, et al. Associations of adipose and muscle tissue parameters at colorectal cancer diagnosis with long-term health-related quality of life. Qual Life Res 2017;26:1745–59. doi:10.1007/s11136-017-1539-z.

[49] Williams GR, Deal AM, Muss HB, Weinberg MS, Sanoff HK, Nyrop KA, et al. Skeletal muscle measures and physical function in older adults with cancer: sarcopenia or myopenia? Oncotarget 2017;8:33658–65. doi:10.18632/oncotarget.16866.

[50] Ní Bhuachalla ÉB, Daly LE, Power DG, Cushen SJ, MacEneaney P, Ryan AM. Computed tomography diagnosed cachexia and sarcopenia in 725 oncology patients: is nutritional screening capturing hidden malnutrition? J Cachexia Sarcopenia Muscle 2018;9:295–305. doi:10.1002/jcsm.12258.

[51] Daly LE, Ní Bhuachalla ÉB, Power DG, Cushen SJ, James K, Ryan AM. Loss of skeletal muscle during systemic chemotherapy is prognostic of poor survival in patients with foregut cancer. J Cachexia Sarcopenia Muscle 2018;9:315–25. doi:10.1002/jcsm.12267.

[52] Choi MH, Yoon SB, Lee K, Song M, Lee IS, Lee MA, et al. Preoperative sarcopenia and post-operative accelerated muscle loss negatively impact survival after resection of pancreatic cancer. J Cachexia Sarcopenia Muscle 2018;9:326–34. doi:10.1002/jcsm.12274.

[53] Rier HN, Jager A, Sleijfer S, van Rosmalen J, Kock MCJM, Levin M-D. Changes in body composition and muscle attenuation during taxane-based chemotherapy in

patients with metastatic breast cancer. Breast Cancer Res Treat 2018;168:95–105. doi:10.1007/s10549-017-4574-0.

[54] Deng C-Y, Lin Y-C, Wu JS, Cheung Y-C, Fan C-W, Yeh K-Y, et al. Progressive sarcopenia in patients with colorectal cancer predicts survival. Am J Roentgenol 2018;210:526–32. doi:10.2214/AJR.17.18020.

[55] Souza BU de, Souza NCS, Martucci RB, Rodrigues VD, Pinho NB de, Gonzalez MC, et al. Factors associated with sarcopenia in patients with colorectal cancer. Nutr Cancer 2018;70:176–83. doi:10.1080/01635581.2018.1412480.

[56] Williams GR, Deal AM, Muss HB, Weinberg MS, Sanoff HK, Guerard EJ, et al. Frailty and skeletal muscle in older adults with cancer. J Geriatr Oncol 2018;9:68–73. doi:10.1016/j.jgo.2017.08.002.

[57] Versteeg KS, Blauwhoff-Buskermolen S, Buffart LM, de van der Schueren MAE, Langius JAE, Verheul HMW, et al. Higher muscle strength is associated with prolonged survival in older patients with advanced cancer. The Oncologist 2018;23:580–5. doi:10.1634/theoncologist.2017-0193.

[58] Okumura S, Kaido T, Hamaguchi Y, Kobayashi A, Shirai H, Yao S, et al. Visceral adiposity and sarcopenic visceral obesity are associated with poor prognosis after resection of pancreatic cancer. Ann Surg Oncol 2017;24:3732–40. doi:10.1245/s10434-017-6077-y.

[59] Bye A, Sjøblom B, Wentzel-Larsen T, Grønberg BH, Baracos VE, Hjermstad MJ, et al. Muscle mass and association to quality of life in non-small cell lung cancer patients. J Cachexia Sarcopenia Muscle 2017;8:759–67. doi:10.1002/jcsm.12206.

[60] Loumaye A, de Barsy M, Nachit M, Lause P, van Maanen A, Trefois P, et al. Circulating Activin A predicts survival in cancer patients. J Cachexia Sarcopenia Muscle 2017;8:768–77. doi:10.1002/jcsm.12209.

[61] Shachar SS, Deal AM, Weinberg M, Williams GR, Nyrop KA, Popuri K, et al. Body composition as a predictor of toxicity in patients receiving anthracycline and taxane-based chemotherapy for early-stage breast cancer. Clin Cancer Res 2017;23:3537–43. doi:10.1158/1078-0432.CCR-16-2266.

[62] Shachar SS, Deal AM, Weinberg M, Nyrop KA, Williams GR, Nishijima TF, et al. Skeletal muscle measures as predictors of toxicity, hospitalization, and survival in patients with metastatic breast cancer receiving taxane-based chemotherapy. Clin Cancer Res 2017;23:658–65. doi:10.1158/1078-0432.CCR-16-0940.

[63] Laroche M, Cintas P. Bent spine syndrome (camptocormia): a retrospective study of 63 patients. Joint Bone Spine 2010;77:593–6. doi:10.1016/j.jbspin.2010.05.012.

[64] Wang CW, Feng S, Covinsky KE, Hayssen H, Zhou L-Q, Yeh BM, et al. A comparison of muscle function, mass, and quality in liver transplant candidates: results from the functional assessment in liver transplantation study. Transplantation 2016;100:1692–8. doi:10.1097/TP.0000000000001232.

[65] Montano-Loza AJ, Angulo P, Meza-Junco J, Prado CMM, Sawyer MB, Beaumont C, et al. Sarcopenic obesity and myosteatosis are associated with higher mortality in patients with cirrhosis. J Cachexia Sarcopenia Muscle 2016;7:126–35. doi:10.1002/jcsm.12039.

[66] Looijaard WGPM, Dekker IM, Stapel SN, Girbes ARJ, Twisk JWR, Oudemans-van Straaten HM, et al. Skeletal muscle quality as assessed by CT-derived skeletal

muscle density is associated with 6-month mortality in mechanically ventilated critically ill patients. Crit Care 2016;20:386. doi:10.1186/s13054-016-1563-3.

[67] van Grinsven J, van Vugt JLA, Gharbharan A, Bollen TL, Besselink MG, van Santvoort HC, et al. The association of computed tomography-assessed body composition with mortality in patients with necrotizing pancreatitis. J Gastrointest Surg 2017;21:1000–8. doi:10.1007/s11605-016-3352-3.

[68] Hicks GE, Simonsick EM, Harris TB, Newman AB, Weiner DK, Nevitt MA, et al. Cross-sectional associations between trunk muscle composition, back pain, and physical function in the health, aging and body composition study. J Gerontol A Biol Sci Med Sci 2005;60:882–7.

[69] Kalichman L, Hodges P, Li L, Guermazi A, Hunter DJ. Changes in paraspinal muscles and their association with low back pain and spinal degeneration: CT study. Eur Spine J 2010;19:1136–44. doi:10.1007/s00586-009-1257-5.

[70] Therkelsen KE, Pedley A, Speliotes EK, Massaro JM, Murabito J, Hoffmann U, et al. Intramuscular fat and associations with metabolic risk factors in the Framingham Heart Study. Arterioscler Thromb Vasc Biol 2013;33:863–70. doi:10.1161/ATVBAHA.112.301009.

[71] Miljkovic I, Cauley JA, Wang PY, Holton KF, Lee CG, Sheu Y, et al. Abdominal myosteatosis is independently associated with hyperinsulinemia and insulin resistance among older men without diabetes. Obes Silver Spring 2013;21:2118–25. doi:10.1002/oby.20346.

[72] Therkelsen KE, Pedley A, Hoffmann U, Fox CS, Murabito JM. Intramuscular fat and physical performance at the Framingham Heart Study. Age 2016;38:31. doi:10.1007/s11357-016-9893-2.

[73] Anderson DE, Bean JF, Holt NE, Keel JC, Bouxsein 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;93:553–61. doi:10.1097/PHM.0000000000000059.

[74] Idoate F, Cadore EL, Casas-Herrero A, Zambom-Ferraresi F, Martínez-Velilla N, Rodriguez-Mañas L, et al. Noncoronary vascular calcification, bone mineral density, and muscle mass in institutionalized frail nonagenarians. Rejuvenation Res 2017;20:298–308. doi:10.1089/rej.2016.1868.

[75] Erlandson KM, Fiorillo S, Masawi F, Scherzinger A, McComsey GA, Lake JE, et al. Antiretroviral initiation is associated with increased skeletal muscle area and fat content. AIDS 2017;31:1831–8. doi:10.1097/QAD.0000000000001558.

[76] Kalichman L, Klindukhov A, Li L, Linov L. Indices of paraspinal muscles degeneration: reliability and association with facet joint osteoarthritis: feasibility study. Clin Spine Surg 2016;29:465–70. doi:10.1097/BSD.0b013e31828be943.

[77] Sebro R, O'Brien L, Torriani M, Bredella MA. Assessment of trunk muscle density using CT and its association with degenerative disc and facet joint disease of the lumbar spine. Skeletal Radiol 2016;45:1221–6. doi:10.1007/s00256-016-2405-8.

[78] Kim MK, Kim W, Kwon H, Baek K, Kim EK, Song K. Effects of bariatric surgery on metabolic and nutritional parameters in severely obese Korean patients with type 2 diabetes: A prospective 2-year follow up. J Diabetes Investig 2014;5:221–7. doi:10.1111/jdi.12137.

[79] Ricq G, Laroche M. Acquired lumbar kyphosis caused in adults by primary paraspinal myopathy. Epidemiology, computed tomography findings, and outcomes in a cohort of 23 patients. Joint Bone Spine 2000;67:528–32.

[80] Azuma K, Sera Y, Shinjo T, Takayama M, Shiomi E, Momoshima S, et al. Maintenance of the paraspinal muscles may protect against radiographic knee osteoarthritis. Open Access Rheumatol 2017;9:151–8. doi:10.2147/OARRR.S130688.

[81] Heymsfield S, Ross R, Wang Z, Frager D. Imaging techniques of body composition: advantages of measurement and new uses. In: Carlson-Newberry S, Costello R, editors. Emerg. Technol. Nutr. Res. Potential Assess. Mil. Perform. Capab., Washington (DC): National Academies Press (US); 1997.

[82] Hopkins JJ, Sawyer MB. Interactions of lean soft-tissue and chemotherapy toxicities in patients receiving anti-cancer treatments. Cancer Chemother Pharmacol 2018;82:1–29. doi:10.1007/s00280-018-3614-8.

[83] Erlandson MC, Lorbergs AL, Mathur S, Cheung AM. Muscle analysis using pQCT, DXA and MRI. Eur J Radiol 2016;85:1505–11. doi:10.1016/j.ejrad.2016.03.001.

[84] Mota JA, Stock MS. Rectus femoris echo intensity correlates with muscle strength, but not endurance, in younger and older men. Ultrasound Med Biol 2017;43:1651–7. doi:10.1016/j.ultrasmedbio.2017.04.010.

[85] Ismail C, Zabal J, Hernandez HJ, Woletz P, Manning H, Teixeira C, et al. Diagnostic ultrasound estimates of muscle mass and muscle quality discriminate between women with and without sarcopenia. Front Physiol 2015;6:302. doi:10.3389/fphys.2015.00302.

[86] Torriani M, Hadigan C, Jensen ME, Grinspoon S. Psoas muscle attenuation measurement with computed tomography indicates intramuscular fat accumulation in patients with the HIV-lipodystrophy syndrome. J Appl Physiol 2003;95:1005–10. doi:10.1152/japplphysiol.00366.2003.

[87] Kuk JL, Church TS, Blair SN, Ross R. Associations between changes in abdominal and thigh muscle quantity and quality. Med Sci Sports Exerc 2008;40:1277–81. doi:10.1249/MSS.0b013e31816a2463.

[88] Kaibori M, Ishizaki M, Iida H, Matsui K, Sakaguchi T, Inoue K, et al. Effect of intramuscular adipose tissue content on prognosis in patients undergoing hepatocellular carcinoma resection. J Gastrointest Surg 2015;19:1315–23. doi:10.1007/s11605-015-2838-8.

[89] Yamashita M, Kamiya K, Matsunaga A, Kitamura T, Hamazaki N, Matsuzawa R, et al. Prognostic value of psoas muscle area and density in patients who undergo cardiovascular surgery. Can J Cardiol 2017;33:1652–9. doi:10.1016/j.cjca.2017.10.009.

[90] Goodpaster BH. Measuring body fat distribution and content in humans. Curr Opin Clin Nutr Metab Care 2002;5:481–7.

[91] Machann J, Bachmann OP, Brechtel K, Dahl DB, Wietek B, Klumpp B, et al. Lipid content in the musculature of the lower leg assessed by fat selective MRI: intra- and interindividual differences and correlation with anthropometric and metabolic data. J Magn Reson Imaging 2003;17:350–7. doi:10.1002/jmri.10255.

[92] Karampatos S, Papaioannou A, Beattie KA, Maly MR, Chan A, Adachi JD, et al. The reliability of a segmentation methodology for assessing intramuscular adipose tissue and other soft-tissue compartments of lower leg MRI images. Magma 2016;29:237–44. doi:10.1007/s10334-015-0510-7.

[93] Gomez-Perez SL, Haus JM, Sheean P, Patel B, Mar W, Chaudhry V, et al. Measuring abdominal circumference and skeletal muscle from a single cross-sectional computed tomography image: a step-by-step guide for clinicians using

national institutes of health ImageJ. J Parenter Enter Nutr 2016;40:308–18. doi:10.1177/0148607115604149.

[94] Sabel MS, Lee J, Cai S, Englesbe MJ, Holcombe S, Wang S. Sarcopenia as a prognostic factor among patients with stage III melanoma. Ann Surg Oncol 2011;18:3579–85. doi:10.1245/s10434-011-1976-9.

[95] Baracos VE. Psoas as a sentinel muscle for sarcopenia: a flawed premise. J Cachexia Sarcopenia Muscle 2017;8:527–8. doi:10.1002/jcsm.12221.

[96] Mourtzakis M, Prado CMM, Lieffers JR, Reiman T, McCargar LJ, Baracos VE. A practical and precise approach to quantification of body composition in cancer patients using computed tomography images acquired during routine care. Appl Physiol Nutr Metab 2008;33:997–1006. doi:10.1139/H08-075.

[97] Weinberg M, Shachar S, Deal A, Williams G, Nyrop K, Alston S, et al. Characterization of skeletal muscle and body mass indices in younger and older women with stage II and III breast cancer. J Am Geriatr Soc 2016;suppl:S86.

[98] Dériaz O, Dumont M, Bergeron N, Després JP, Brochu M, Prud'homme D. Skeletal muscle low attenuation area and maximal fat oxidation rate during submaximal exercise in male obese individuals. Int J Obes Relat Metab Disord 2001;25:1579–84. doi:10.1038/sj.ijo.0801809.

[99] Kelley DE, Slasky BS, Janosky J. Skeletal muscle density: effects of obesity and non-insulin-dependent diabetes mellitus. Am J Clin Nutr 1991;54:509–15. doi:10.1093/ajcn/54.3.509.

[100] Heymsfield S, Noel R, Lynn M, Kutner M. Accuracy of soft tissue density predicted by CT. J Comput Assist Tomogr 1979;3:859–60.

[101] Bulcke JA, Termote J, Palmers Y, Crolla D. Computed tomography of the human skeletal muscular system. Neuroradiology 1979;17:127–36.

[102] Baumgartner RN, Heymsfield SB, Roche AF, Bernardino M. Abdominal composition quantified by computed tomography. Am J Clin Nutr 1988;48:936–45. doi:10.1093/ajcn/48.4.936.

[103] Goodpaster BH, Thaete FL, Simoneau JA, Kelley DE. Subcutaneous abdominal fat and thigh muscle composition predict insulin sensitivity independently of visceral fat. Diabetes 1997;46:1579–85.

[104] Heymsfield S, Tighe A, Wang Z. Nutritional assessment by anthropometric and biochemical methods. In: Shils M, Olson J, Shike M, editors. Mod. Nutr. Health Dis. 8th ed., Philadelphia: Lea and Febiger; 1994.

[105] Sjöström L. A computer-tomography based multicompartment body composition technique and anthropometric predictions of lean body mass, total and subcutaneous adipose tissue. Int J Obes 1991;15 Suppl 2:19–30.

[106] Lönn L, Kvist H, Grangård U, Bengtsson B-Å, Sjöström L. CT-determined body composition changes with recombinant human growth hormone treatment to adults with growth hormone deficiency. In: Ellis KJ, Eastman JD, editors. Hum. Body Compos. Vivo Methods Models Assess., Boston (MA): Springer US; 1993, p. 229–31. doi:10.1007/978-1-4899-1268-8_53.

[107] Mitsiopoulos N, Baumgartner RN, Heymsfield SB, Lyons W, Gallagher D, Ross R. Cadaver validation of skeletal muscle measurement by magnetic resonance imaging and computerized tomography. J Appl Physiol 1998;85:115–22. doi:10.1152/jappl.1998.85.1.115.

[108] Sjöström L, Alpsten M, Andersson B, Bengtsson B-Å, Bengtsson C, Björntorp P, et al. Hormones, body composition and cardiovascular risk. In: Ellis KJ, Eastman JD, editors. Hum. Body Compos. Vivo Methods Models Assess., Boston (MA): Springer US; 1993, p. 233–43. doi:10.1007/978-1-4899-1268-8_54.

[109] Chowdhury B, Sjöström L, Alpsten M, Kostanty J, Kvist H, Löfgren R. A multicompartment body composition technique based on computerized tomography. Int J Obes Relat Metab Disord 1994;18:219–34.

[110] Chowdhury B, Lantz H, Sjostrom L. Computed tomography-determined body composition in relation to cardiovascular risk factors in Indian and matched Swedish males. Metabolism 1996;45:634–44.

[111] Heymsfield SB, Wang Z, Baumgartner RN, Ross R. Human body composition: advances in models and methods. Annu Rev Nutr 1997;17:527–58. doi:10.1146/annurev.nutr.17.1.527.

[112] Goodpaster BH, Thaete FL, Kelley DE. Composition of skeletal muscle evaluated with computed tomography. Ann N Y Acad Sci 2000;904:18–24.

[113] Chabowski A, Zendzian-Piotrowska M, Nawrocki A, Górski J. Not only accumulation, but also saturation status of intramuscular lipids is significantly affected by PPARγ activation. Acta Physiol 2012;205:145–58. doi:10.1111/j.1748-1716.2011.02380.x.

[114] Doyle SL, Bennett AM, Donohoe CL, Mongan AM, Howard JM, Lithander FE, et al. Establishing computed tomography-defined visceral fat area thresholds for use in obesity-related cancer research. Nutr Res 2013;33:171–9. doi:10.1016/j.nutres.2012.12.007.

[115] Prado CMM, Lieffers JR, McCargar LJ, Reiman T, Sawyer MB, Martin L, 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;9:629–35. doi:10.1016/S1470-2045(08)70153-0.

[116] Oxford Dictionaries: English Dictionary, Thesaurus, & grammar help n.d. https://en.oxforddictionaries.com/ (accessed January 11, 2019).

[117] Dicionário Cambridge: Significados, Definições e Traduções n.d. https://dictionary.cambridge.org/pt/ (accessed January 11, 2019).

[118] Rivas DA, McDonald DJ, Rice NP, Haran PH, Dolnikowski GG, Fielding RA. Diminished anabolic signaling response to insulin induced by intramuscular lipid accumulation is associated with inflammation in aging but not obesity. Am J Physiol Regul Integr Comp Physiol 2016;310:R561-569. doi:10.1152/ajpregu.00198.2015.

[119] Dong Y, Silva KAS, Dong Y, Zhang L. Glucocorticoids increase adipocytes in muscle by affecting IL-4 regulated FAP activity. FASEB J 2014;28:4123–32. doi:10.1096/fj.14-254011.

[120] Farup J, Madaro L, Puri PL, Mikkelsen UR. Interactions between muscle stem cells, mesenchymal-derived cells and immune cells in muscle homeostasis, regeneration and disease. Cell Death Dis 2015;6:e1830. doi:10.1038/cddis.2015.198.

[121] Hamrick MW, McGee-Lawrence ME, Frechette DM. Fatty infiltration of skeletal muscle: mechanisms and comparisons with bone marrow adiposity. Front Endocrinol 2016;7:69. doi:10.3389/fendo.2016.00069.

[122] Agley CC, Rowlerson AM, Velloso CP, Lazarus NR, Harridge SDR. Human skeletal muscle fibroblasts, but not myogenic cells, readily undergo adipogenic differentiation. J Cell Sci 2013;126:5610–25. doi:10.1242/jcs.132563.

[123] Arsenault BJ, Beaumont EP, Després J-P, Larose E. Mapping body fat distribution: a key step towards the identification of the vulnerable patient? Ann Med 2012;44:758–72. doi:10.3109/07853890.2011.605387.

[124] Almasud AA, Giles KH, Miklavcic JJ, Martins KJB, Baracos VE, Putman CT, et al. Fish oil mitigates myosteatosis and improves chemotherapy efficacy in a

preclinical model of colon cancer. PloS One 2017;12:e0183576. doi:10.1371/journal.pone.0183576.

[125] Penton CM, Thomas-Ahner JM, Johnson EK, McAllister C, Montanaro F. Muscle side population cells from dystrophic or injured muscle adopt a fibro-adipogenic fate. PloS One 2013;8:e54553. doi:10.1371/journal.pone.0054553.

6. TABLES

Table 1. Characteristics of the populations addressed by the studies.

Characteristics	% (n)	References
Cancer patients	61,2% (n=41)	[3,11,16–23,28,33–62]
Healthy individuals	14,9% (n=10)	[5,12,13,68–74]
Orthopedic and neuromuscular diseases patients	8,9% (n=6)	[8,63,76,77,79,80]
CNCD patients (overweight, obesity, diabetes mellitus, hepatic steatosis, cirrhosis) – excluding cancer	7,5% (n=5)	[9,14,64,65,78]
Other patients (critical, in renal transplant, pancreatitis, apnea and seropositive)	7,5% (n=5)	[15,24,66,67,75]

CNCD - Chronic non-communicable diseases

Table 2. Summarization of the methodologies used to evaluate the abdominal region and muscle groups by computed tomography.

	Evaluated points	% (n)	References
Abdominal region	L3	70,1% (n=47)	[3,8,11,12,15–23,28,33–39,41–53,55–67]
	L4 and L5	8,9% (n=6)	[5,13,68,71,75,76]
	L3, L4 and L5	7,5% (n=5)	[14,69,73,74,77]
	Mid abdominal level	4,5% (n=3)	[70,72,78]
	L3 and L4	3% (n=2)	[24,40]
	Umbilical level	3% (n=2)	[9,80]
	L3 and L5	1,5% (n=1)	[79]
	L4	1,5% (n=1)	[54]
Muscle groups	Paraspinal, psoas, transversus abdominus, internal and external obliques and rectus abdominus muscles or all abdominal region muscles (when the study did not inform which were the evaluated muscles)	76,1% (n=51)	[3,11,15–23,28,33–53,55–62,64–67,71,73–75,77,80]
	Paraspinal muscles	11,9% (n=8)	[9,63,69,70,72,76,78,79]
	Paraspinal and psoas muscles	4,5% (n=3)	[5,24,54]
	Paraspinal and abdominal (rectus and lateral) muscles	3% (n=2)	[13,68]
	Paraspinal, psoas, internal and external obliques and rectus abdominus muscles	1,5% (n=1)	[8]
	Paraspinal, psoas, internal and external obliques, rectus abdominus, transversus spinae and latissimus dorsi muscles	1,5% (n=1)	[12]
	Paraspinal, psoas, transversus abdominus, internal and external obliques, rectus abdominus and gluteus maximus muscles	1,5% (n=1)	[14]

L3 – third lumbar vertebrae; L4 –fourth lumbar vertebrae; L5 – fifth lumbar vertebrae;

Table 3 – Summarization of the methodologies used for skeletal muscle quality classification by computed tomography.

	Evaluated points	% (n)	References
SM areas selection	Mean attenuation of the total abdominal muscles area	74,6% (n=50)	[5,8,9,11–13,15–24,33–48,50–53,55,57–60,64–68,71,73,75,79]
	Regions of interest	13,4% (n=9)	[14,54,69,70,72,76–78,80]
	Mean attenuation of the total abdominal muscles area and skeletal muscle gauge	6% (n=4)	[49,56,61,62]
	High or low radiodensity SM indexes area	3% (n=2)	[3,28]
	High or low density SM area	1,5% (n=1)	[74]
	Did not inform the methodology used for this topic	1,5% (n=1)	[63]
Radiodensity ranges	SM: -29HU to +150HU	37,3% (n=25)	[15–18,22,23,34–37,39,40,42,46,47,49,51,52,56,58,60–62,64,67]
	Did not inform the methodology used for this topic	20,9% (n=14)	[8,9,11,13,14,33,42,50,63,68,69,76,77,79]
	SM: -29HU to +150HU; Intramuscular fat: -190HU to -30HU	10,4% (n=7)	[20,21,38,43,45,55,59]
	SM: -29HU to +150HU; Intermuscular fat: -190HU to -30HU	7,5% (n=5)	[44,48,57,65,66]
	Fat range (general)	4,5% (n=3)	[70,72,78]
	SM: 0HU to +100HU	3% (n=2)	[5,80]
	SM: −50HU to +150HU	3% (n=2)	[12,73]
	Low radiodensity SM: –29HU to +29HU; High radiodensity SM: +30HU to +150HU; Intramuscular fat: -190HU to -30HU	1,5% (n=1)	[28]
	Low radiodensity SM: –29HU to +29HU; High radiodensity SM: +30HU to +150HU	1,5% (n=1)	[3]
	SM: 0HU to +100HU; Intermuscular fat: -190HU to -30HU	1,5% (n=1)	[71]

Table 3 (continuation) – Summarization of the methodologies used for skeletal muscle quality classification by computed tomography.

	Evaluated points	% (n)	References
Radiodensity ranges	SM: -29HU to +150HU; Low MA: -29HU to +29 HU	1,5% (n=1)	[19]
	SM: -29HU to +160HU	1,5% (n=1)	[24]
	Intermuscular fat: ≤30HU	1,5% (n=1)	[75]
	SM: -29HU to +150HU; Intramuscular fat: -190HU to -90HU	1,5% (n=1)	[53]
	SM: -30HU to +150HU	1,5% (n=1)	[54]
	SM: 0HU to +100 HU, considering low density SM: 0HU to +29HU and high density SM: +30HU to +100HU	1,5% (n=1)	[74]
Cut-off points	Cut-off points did not established, findings continuously analyzed and, mean and median values of the entire abdominal region were compared among groups	37,3% (n=25)	[5,8,9,11–13,15,24,33,40,45,47,49,53,55,56,61,62,66,68,69,75,78–80]
	Cut-off points established for the evaluated population, through statistical analyzes, tercile and quartile	29,8% (n=20)	[3,17,19,21,22,28,34,36,38,43,52,54,58,59,67,70–72,74,77]
	Cut-off points pre-established by Martin et al. (2013)[19]	22,4% (n=15)	[16,18,20,23,35,37,39,41,44,46,50,51,57,64,65]
	Cut-off points pre-established for visceral, subcutaneous and total fat [114] and sarcopenia (the study showed only the mean MA for its population) [115]	1,5% (n=1)	[42]
	Cut-off point <30HU [4,5]	1,5% (n=1)	[60]
	Mean of the entire abdominal region continuously, correlation tests and linear regression	1,5% (n=1)	[73]
	Values of each muscle group alone as continuous variables.	1,5% (n=1)	[14]
	Mean of the continuous variable of all groups and terciles, did not stratified by sex.	1,5% (n=1)	[48]
	Mean of the continuous variable of all groups and cut-off points created for a MQ Index: Radiographic Density Ratio = Radiographic Muscle Density/Standard Deviation of Density.	1,5% (n=1)	[76]
	Did not inform the methodology used for this topic.	1,5% (n=1)	[63]

HU – Hounsfield Units; MA – muscle attenuation; MQ – muscle quality; SM – skeletal muscle;

Table 4. Summarization of the terms used to evaluate and refer to skeletal muscle quality by computed tomography.

Used terms	% (n)	References
SM attenuation/MA	62,7% (n=42)	[5,9,12,13,17–19,21–24,28,34,35,37,38,41,42,45–49,51,53–58,62,64–68,70,72–74,78,80]
SM density/Muscle density	35,8% (n=24)	[8,11,14–16,33,39,45,49,50,52,53,56,60–62,66,67,69,74–77,79]
SM radiodensity/Muscle radiodensity/Radiological SM attenuation	25,4% (n=17)	[3,11,16,20,28,33,36,43,44,46,48,50,52,57,59,60,66]
Intramuscular AT/Intramuscular fat	23,9% (n=16)	[9,17,20,21,28,34,38,43,45,50,53,55,67,70,72,78]
SM quality/MQ	19,4% (n=13)	[3,17,34,40,47,56,58,64,66,67,74,76,80]
Myosteatosis	17,9% (n=12)	[20,28,35,40–42,53,64,65,68,74,76]
Muscle fat infiltration	14,9% (n=10)	[13,15,46,48,53,64,65,68,74,76]
Muscle fat content/Muscle lipid content/Lipid in muscle/Triglyceride muscle content	14,9% (n=10)	[33,39,47,49,55,56,62,70,72,80]
Intermuscular AT	10,4% (n=7)	[5,13,48,57,65,66,71]
Fatty muscle infiltration	8,9% (n=6)	[11,33,36,40,63,75]
Intermuscular fat	4,5% (n=3)	[45,50,75]
Muscle composition	3% (n=2)	[13,68]
Intramyocellular triglycerides	3% (n=2)	[3,28]
Fat deposits	1,5% (n=1)	[69]
Muscle lipid infiltration	1,5% (n=1)	[66]
Sarcopenia (considering area and MA)	1,5% (n=1)	[56]

AT – adipose tissue; MA – muscle attenuation; MQ – muscle quality; SM – skeletal muscle;