

Sarcopenia – Definition, Radiological Diagnosis, Clinical Significance

Sarkopenie – Definition, radiologische Erfassung, klinische Bedeutung

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ABSTRACT

Background Sarcopenia is an age-related syndrome characterized by a loss of muscle mass and strength. As a result, the independence of the elderly is reduced and the hospitalization rate and mortality increase. The onset of sarcopenia often begins in middle age due to an unbalanced diet or malnutrition in association with a lack of physical activity. This effect is intensified by concomitant diseases such as obesity or metabolic diseases including diabetes mellitus.

Method With effective preventative diagnostic procedures and specific therapeutic treatment of sarcopenia, the negative effects on the individual can be reduced and the negative impact on health as well as socioeconomic effects can be prevented. Various diagnostic options are available for this purpose. In addition to basic clinical methods such as measuring

muscle strength, sarcopenia can also be detected using imaging techniques like dual X-ray absorptiometry (DXA), computed tomography (CT), magnetic resonance imaging (MRI), and sonography. DXA, as a simple and cost-effective method, offers a low-dose option for assessing body composition. With cross-sectional imaging techniques such as CT and MRI, further diagnostic possibilities are available, including MR spectroscopy (MRS) for noninvasive molecular analysis of muscle tissue. CT can also be used in the context of examinations performed for other indications to acquire additional parameters of the skeletal muscles (opportunistic secondary use of CT data), such as abdominal muscle mass (total abdominal muscle area – TAMA) or the psoas as well as the pectoralis muscle index. The importance of sarcopenia is already well studied for patients with various tumor entities and also infections such as SARS-COV2.

Results and Conclusion Sarcopenia will become increasingly important, not least due to demographic changes in the population. In this review, the possibilities for the diagnosis of sarcopenia, the clinical significance, and therapeutic options are described. In particular, CT examinations, which are repeatedly performed on tumor patients, can be used for diagnostics. This opportunistic use can be supported by the use of artificial intelligence.

Key Points:

- Sarcopenia is an age-related syndrome with loss of muscle mass and strength.
- Early detection and therapy can prevent negative effects of sarcopenia.
- In addition to DEXA, cross-sectional imaging techniques (CT, MRI) are available for diagnostic purposes.
- The use of artificial intelligence (AI) offers further possibilities in sarcopenia diagnostics.

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ZUSAMMENFASSUNG

Hintergrund Bei der Sarkopenie handelt es sich um ein altersabhängiges Syndrom, welches durch einen Verlust an Muskelmasse und -kraft gekennzeichnet ist. In der Folge wird die Selbständigkeit älterer Menschen eingeschränkt und die

Hospitalisierungsrate sowie die Mortalität steigen. Die Entwicklung einer Sarkopenie beginnt oftmals bereits im mittleren Lebensalter durch Fehl- und Mangelernährung bzw. in Kombination mit mangelnder körperlicher Aktivität. Verstärkt wird dieser Effekt durch Begleiterkrankungen wie Adipositas oder Stoffwechselerkrankungen wie Diabetes mellitus.

Methode Durch effektive präventiv-diagnostische Verfahren und die gezielte therapeutische Behandlung der Sarkopenie lassen sich die negativen Auswirkungen auf das Individuum reduzieren und negative gesundheitliche sowie sozioökonomische Effekte verhindern. Hierfür stehen verschiedene diagnostische Möglichkeiten zur Verfügung. Neben einfachen klinischen Methoden wie der Messung der Muskelkraft lässt sich die Sarkopenie auch mit bildgebenden Verfahren erfassen, etwa mittels der Dual-Röntgen-Absorptiometrie (DXA), der Computertomografie (CT), der Magnetresonanztomografie (MRT) oder der Sonografie. Die DXA bietet dabei als einfaches und kostengünstiges Verfahren eine dosisarme Möglichkeit der Erfassung der Körperzusammensetzung. Mit den schnittbildgebenden Verfahren der CT und MRT ergeben sich weitere diagnostische Möglichkeiten bis hin zur MR-Spektro-

skopie (MRS) zur nicht invasiven molekularen Analyse von Muskelgewebe. Durch die CT können auch bei im Rahmen anderer Fragestellungen durchgeführten Untersuchungen zusätzlich Parameter der Skelettmuskulatur erfasst werden (opportunistische sekundäre Verwendung von CT-Daten), so beispielsweise die abdominale Muskelmasse (total abdominal muscle area – TAMA) oder der Psoas- sowie der Pektoralis-Muskel-Index. Die Bedeutung der Sarkopenie ist bereits für Patienten mit verschiedenen Tumorentitäten und auch Infektionen wie SARS-COV2 gut untersucht.

Ergebnisse und Schlussfolgerung Nicht zuletzt durch den demografischen Wandel der Bevölkerung wird die Sarkopenie an Bedeutung zunehmen. In dieser Übersichtsarbeit werden die Möglichkeiten zur Diagnostik der Sarkopenie, die klinische Bedeutung und Therapiemöglichkeiten beschrieben. Dabei können insbesondere CT-Untersuchungen, die wiederholt bei Tumorpatienten durchgeführt werden, zur Diagnostik herangezogen werden. Diese opportunistische Verwendung kann dabei durch den Einsatz künstlicher Intelligenz unterstützt werden.

Definition

The term “sarcopenia” is composed of the two Greek words “sarx meaning flesh” and “penia meaning loss”. Sarcopenia refers to age-related progressive and generalized loss of muscle mass and strength. The course of this primary aging process can be intensified by comorbidities and physical inactivity [1]. Sarcopenia can also be present in children and adolescents, e. g., as part of a tumor disease like hepatoblastoma, long-term steroid therapy, muscular dystrophy, or chronic liver disease [2–4]. ► **Table 1** provides a list of potential risk factors for sarcopenia. In addition to functional limitations, sarcopenia often causes an increase in trauma/falls and resulting injuries that can further limit quality of life. Approximately 20 % of 70-year-olds and about 50 % of 75-year-olds are affected by sarcopenia [5]. With respect to gender distribution, the specified or estimated prevalence is higher in men or in women depending on the definition and population [6]. There are already some studies with large case numbers addressing the prevalence, risk factors, and screening of sarcopenia [7–10]. According to the “UK Biobank” study including 168 682 participants, pre-sarcopenic men and sarcopenic women have an elevated risk of osteoporosis [10]. In their study, Soh and Won examined the relationship between sarcopenia and fall risk in older Korean adults. They used data from the “Korean Frailty and Aging Cohort Study” [11]. As a result of demographic changes in population structure, sarcopenia will play an increasing role in the future.

In addition to sarcopenia, patients often also have an elevated fat mass. So called “Sarcopenic obesity” is a special type of obesity. Muscle mass normally increases in response to an increase in weight load. This adaptive mechanism can be disrupted particularly in older people [12]. In addition, reduced energy consumption does not necessarily result in a decrease in appetite [13]. Con-

sequently, these patients have lower muscle mass and strength in relation to the increased fat mass. There is a significant prevalence of sarcopenic obesity also in children and adolescents. According to a review, the prevalence is 5.7 % to 69.7 % in girls and 7.2 % to 81.3 % in boys. A connection with cardiometabolic events, severity of non-alcoholic fatty liver disease, inflammation, and mental health has also already been described [14].

The term “cachexia” must be differentiated from sarcopenia. The diagnostic criterion for cachexia is weight loss (fat and muscle mass) of more than 5 % in the last 6 months or of more than 2 % in people who are already underweight (body mass index [BMI] < 20 kg/m²) or have sarcopenia. According to the consensus of an international group of experts, sarcopenia in tumor patients is a fundamental part of cachexia and an important element in the evaluation of tumor patients [15, 16]. The difference between cachexia and sarcopenia in tumor diseases is that sarcopenia as well as weight loss must be present in the cachexia [15].

Diagnosis

There are various screening methods to diagnose sarcopenia, which are listed, for example, by the *European Working Group on Sarcopenia in Older People (EWGSOP)* [17]. In general, these can be categorized as direct and indirect methods [18]. The indirect measurement methods include the detection of molecular and cellular changes in the skeletal muscles, e. g. based on biomarkers. The negative effects of sarcopenia can also be analyzed. This includes, for example, reduced quality of life, increased fall risk, and an increased hospitalization rate [19].

► **Table 1** Risk factors for sarcopenia and their significance.

Age	Often begins in middle age and advances with increasing age
Gender	Depending on the classification that is used, the prevalence is higher in women or men (reference Petermann-Rocha et al., Morley et al.)
Malnutrition	Especially decreased protein intake. The need for protein increases with age
Lack of physical activity	Often due to diseases like osteoarthritis/other types of degeneration or as a result of tumor diseases. This results in a vicious cycle that further aggravates muscle atrophy
Hormone deficiency	Particularly testosterone or estrogen deficiency
Inflammatory processes	Chronic inflammatory processes like in rheumatoid arthritis promote muscle atrophy
Tumor diseases	Often a consuming disease and side effects of treatment resulting in undernourishment/malnourishment Due to longer hospitalization and/or surgical interventions, there is a risk of progressive physical inactivity
Muscular dystrophy	Rare cause of progressive muscular weakness and decreased muscle mass due to genetic mutations

► **Table 2** Imaging techniques available to detect sarcopenia (modified from Mohamed Ali et al. [6]). Additional presentation of advantages and limitations. DXA: dual-energy-X-ray absorptiometry, CT: computed tomography, MRI: magnetic resonance imaging.

Imaging	Advantages	Limitations
DXA	<ul style="list-style-type: none"> ▪ Inexpensive, can be performed quickly ▪ Minimal radiation exposure 	<ul style="list-style-type: none"> ▪ Imprecise results in the case of obese patients and edema ▪ Limited comparability for examinations performed on different scanners ▪ 2D images
CT	<ul style="list-style-type: none"> ▪ Quantification of the musculature and the degree of fatty changes ▪ Can be used for the entire body or for individual muscles ▪ Evaluations can also be performed in the case of examinations for other medical questions 	<ul style="list-style-type: none"> ▪ Expensive and time-intensive ▪ Radiation exposure ▪ No cutoff values for the diagnosis of sarcopenia
MRI	<ul style="list-style-type: none"> ▪ Reliable determination of muscle quantity and quality ▪ No radiation exposure ▪ Can be used for the entire body or for individual muscles 	<ul style="list-style-type: none"> ▪ Expensive and not widely available ▪ Long examination times and technically challenging ▪ No cutoff values for the diagnosis of sarcopenia
Ultrasound	<ul style="list-style-type: none"> ▪ Simple to perform, inexpensive, safe, and noninvasive ▪ Good reproducibility 	<ul style="list-style-type: none"> ▪ No standardized measurements ▪ Unclear which anatomical regions correlate with the total muscle mass

Radiological methods

There are various radiological methods for diagnosing sarcopenia like dual X-ray absorptiometry (DXA) or cross-sectional imaging methods like computed tomography (CT) and magnetic resonance imaging (MRI). ► **Table 2** provides an overview. The most important methods are described in greater detail below.

Dual X-ray absorptiometry (DXA)

DXA is a radiodiagnostic method with comparably low radiation exposure and is the most commonly used method for analyzing body composition [20]. This measurement method is based on the different absorption rates of low and high-energy X-rays in mineralized tissue, fat, and soft tissue. [21].

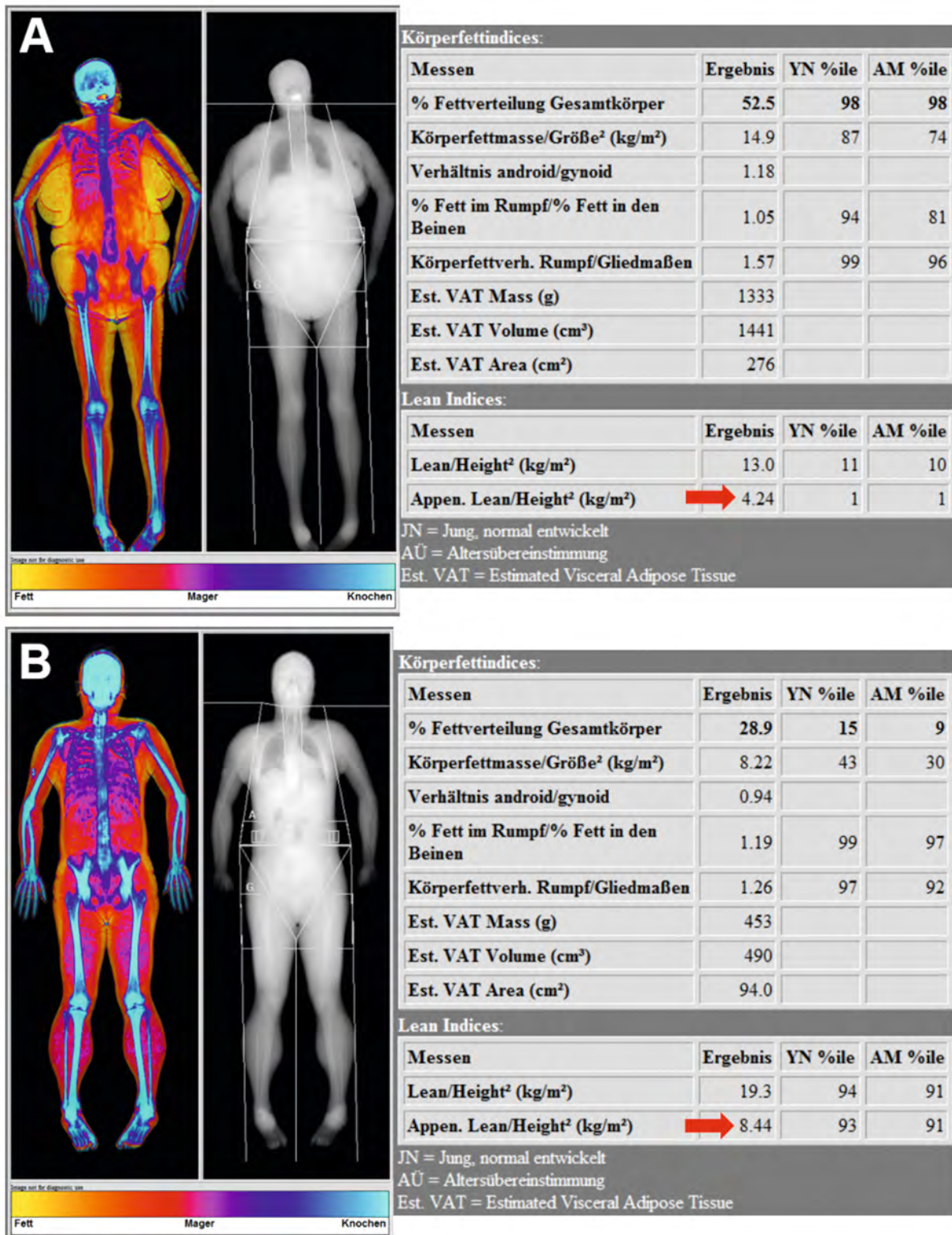
With DXA, the following values can typically be determined: lean mass (LM), fat mass (FM), bone mineral content (BMC), and areal bone mineral density (aBMD). The LM is the measurement of all types of tissue that are neither fat nor bone. The sum of the LM of the upper and lower extremities, known as the appendicular LM

(ALM), is used to determine the muscle mass. The correlation with body size is used to calculate the ALM index ($ALMI = ALM / \text{body size}^2$). The EWGSOP specifies an ALMI of $< 6 \text{ kg/m}^2$ for women and $< 7 \text{ kg/m}^2$ for men as cutoff values for reduced muscle mass [20]. ► **Fig. 1** shows examples of DXA images.

The limited comparability of the results from different manufacturers is a limitation of DXA. Compared to CT and MRI, it provides only two-dimensional images. Moreover, DXA does not allow a statement about the qualitative composition of muscle, e. g. in relation to fat deposits.

Computed tomography

Using CT as the most widely available cross-sectional imaging method, skeletal muscle in different regions of the body can be analyzed. In addition to the muscle area and volume, the density values of individual muscles or muscle groups can be determined [22]. The segmentation of the musculature and the determination of the cross-sectional area (CSA) are typically performed at



► **Fig. 1** Dual X-ray absorptiometry (DXA) of two female patients. **A** A 74-year-old obese female patient with an appendicular lean index (ALMI) of 4.24 kg/m² (red arrow). According to the European Working Group on Sarcopenia in Older People (EWGSOP), sarcopenia is, therefore, present (cut-off value for women <6 kg/m²). **B** A 40-year-old female patient without sarcopenia with an ALMI of 8.44 kg/m² (red arrow).

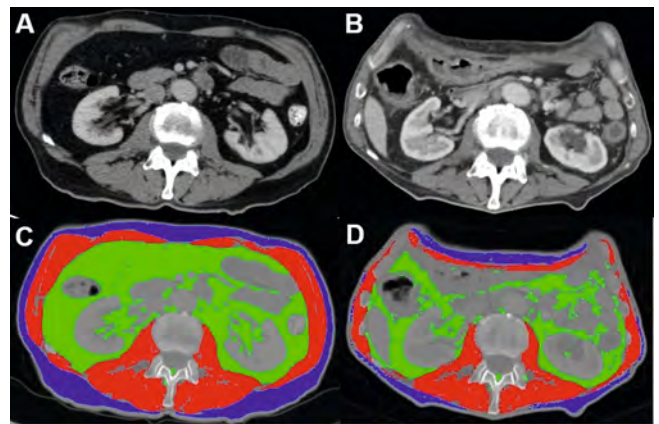
the level of L3 or L4. The psoas muscle alone is analyzed at this level or the entire muscle area is analyzed at the corresponding level [23]. The abdominal wall musculature, the psoas muscle, the autochthonous back muscles, and the quadratus lumborum muscle are segmented for this purpose. In addition, the subcutaneous and visceral fat tissue can also be quantified. In principle, muscle segmentation is performed manually. Alternatively, masks with predefined Hounsfield units (HU) can also be used. Goodpaster et al. defined a range between 0 and 100 HU for the musculature, while Mitsiopoulos et al. used a density range of -29 to 150 HU [24, 25]. A direct comparison of the two HU ranges showed significant differences in the calculated muscle areas [26]. Due to the larger HU range, interstitial adipose tissue in the muscle tissue is also taken into consideration. In contrast, when using the lower HU range, only the adipose tissue-free muscle (ATFSM) is taken into consideration. In healthy young adults, anatomical skeletal muscle is only slightly greater than the ATFSM. However, the IAT increases with age, in the case of obesity, and also in the case of certain diseases, e. g. muscular dystrophy [25]. For this reason, the range of -29 to 150 HU has become established.

Moreover, the direct comparison of the skeletal muscle areas calculated from non-contrast and contrast-enhanced CT examinations resulted in some significant differences depending on the HU range being used [26]. The range between -29 and 150 HU yielded the most reliable results also in this study. Therefore, the HU range must be taken into consideration in the evaluation, interpretation, and comparison of results.

The muscle areas calculated based on a CT scan correlate very well with the total body muscle mass [27, 28]. The ratio of muscle area to body size determines the skeletal muscle index (SMI) ($SMI = CSA/body\ size^2$). For the diagnosis of sarcopenia, the EWG-SOP currently only defines cutoff values for DXA and the bioelectric impedance analysis (BIA) [17]. Some studies also specify corresponding cutoff values for the SMI [23, 29, 30]. In tumor patients, the CT data of Prado et al. and Martin et al. were used most frequently as a reference. The data of Prado et al. was based on the analysis of a total of 2115 patients with solid tumors of the gastrointestinal tract or the respiratory system [29]. In the study by Martin et al., the skeletal muscle index (SMI) of 1473 patients with a malignancy of the lung or the gastrointestinal tract was determined [30]. There are already age- and gender-specific percentile curves for the total psoas muscle area (tPMA) for children [31].

An advantage of these indices is that the muscle mass can be determined in all CT examinations of the trunk in addition to the primary clinical question and the corresponding calculations can be performed (secondary use of CT data). CT is suitable particularly in tumor patients for diagnosing sarcopenia since it is often performed already during diagnosis and subsequently in defined intervals for evaluating treatment response.

The muscles can only be analyzed at the indicated level (L3 and L4) in abdominal examinations. For this reason, Derstine et al. evaluated examination of skeletal muscle from Th10 to L5 [32]. As a result, sarcopenia diagnosis can also be performed during chest CT. An additional advantage of abdominal CT is that skeletal muscle as well as the abdominal fat distribution are determined (subcutaneous and intra-abdominal fat tissue). These supplement-



► **Fig. 2** Body composition analysis at L3 level of a 67-year-old patient with an AEG tumor before **A, C** and after **B, D** neoadjuvant chemotherapy with a marked reduction of skeletal muscle area and subcutaneous and visceral adipose tissue. Skeletal muscle area decreased from 123.40 cm² to 65.06 cm². Skeletal muscle index decreased from 36.85 cm²/m² to 19.43 cm²/m². Skeletal muscle area is red, subcutaneous adipose tissue is blue, and visceral adipose tissue is green. Segmentation was performed semiautomatically with an own Python application based on SimpleITK. For skeletal muscle, Hounsfield unit (HU) mask was between -5 and 135 HU and for adipose tissue between -190 and -30 HU.

tary measurements thus allow a body composition analysis based on DXA [33].

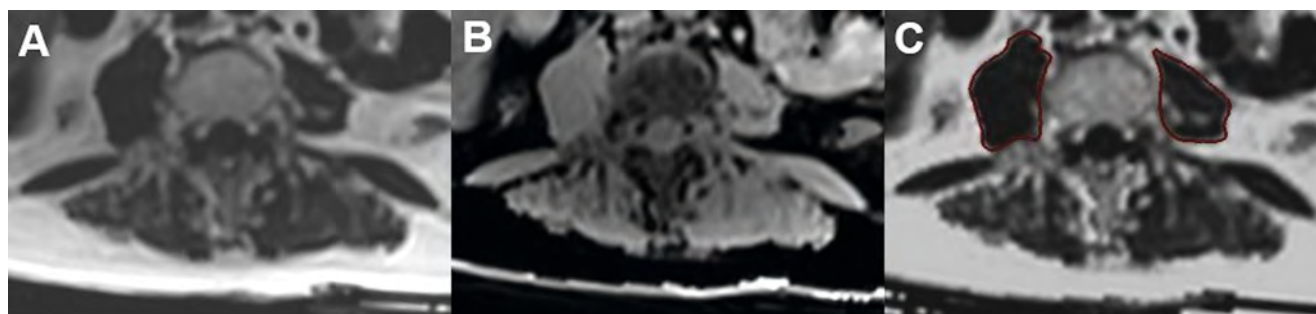
An example of an analysis of body composition based on routine CT is shown in ► **Fig. 2**.

One of the limitations of CT is the higher dose in comparison to DXA. According to the German Commission on Radiological Protection, the applied effective dose of whole-body DXA is 1–10 µSv [34]. The typical effective dose for CT of the abdomen and pelvis is approximately 11 mSv [35]. However, this can vary based on individual factors, such as sex, age, and constitution. This disadvantage is balanced out when acquisition is performed as part of examinations regarding other medical questions, e. g. in routine staging examinations for tumor patients as mentioned above.

Magnetic resonance imaging (MRI)

In addition to the advantage of excellent soft-tissue contrast, MRI can be used as a radiation-free alternative. In addition to the targeted imaging of individual muscles or muscle groups, whole-body examinations are also possible. Moreover, MRI allows not only qualitative visualization, e. g. fatty infiltration or fibrosis, but also quantitative determination of muscle mass and fat mass [36]. According to Pons et al., using MRI to determine the volumetry of muscles has proven to be a valid and reliable method. In addition to manual segmentation, (semi-) automated segmentation of certain muscles is also possible [37].

In addition to muscle segmentation, the Dixon method and MR spectroscopy (MRS) are special techniques for the diagnosis of sarcopenia. Fatty infiltration of skeletal muscle is an important factor in the limited mobility of patients with sarcopenia [38–40]. The DIXON method can be used to determine fatty infiltration of skeletal muscle. The various resonance frequencies of wa-



► **Fig. 3** Magnetic resonance imaging (MRI) with multi-echo (ME) Dixon technique. Calculated water-only image **A**, fat-only image **B**, and results from the Dixon dataset to define fat fraction **C** with segmentation of the psoas muscle. Area of the right psoas muscle is 12.0 cm² and 8.40 cm² on the left side. Fat fraction is 7.5 % on the right side and 16.3 % on the left side.

ter and fat are used to analyze the percentages of fat and water based on all proton signals. With the original DIXON sequence, two echoes are acquired, one with water and fat in-phase (IP) and one with water and fat opposed-phase (OP) [41]. The fat and water images can be generated by adding and subtracting the OP and IP. Qualitative fat detection can be performed with the original DIXON method based on the acquired images. In the clinical routine, this method is used, for example, for the differentiation of adrenal tumors. The further development of the DIXON method uses echoes at multiple time points and is referred to as the multi-echo (ME) method. This approach allows direct water and fat quantification based on the calculation of parametric maps. In clinical studies, the ME technique has already been used for the quantification of liver fat [42, 43]. In addition it allows analysis of fat distribution in the musculature via mapping [44, 45]. ► **Fig. 3** shows an example of fat quantification using the ME-Dixon method.

MRS is a further option for investigating sarcopenia [21]. In contrast to MR imaging, the result of spectroscopy measurement is not a cross-sectional image but an intensity spectrum of frequency signals [46]. These volume-selective measurements make it possible to examine metabolic processes in the human body, e. g., in skeletal muscles. Particularly with ³¹P-spectroscopy, the spectrum of phosphor metabolites and the changes in the concentrations of these metabolites during muscular work can be analyzed [47], for example in patients with type II diabetes or peripheral arterial disease [48–50]. A relationship between changes in skeletal muscle metabolism and decreasing muscle mass or changes in muscle function on MRS has also been described in connection with sarcopenia. Additional studies are needed to confirm and further investigate these results.

Reproducibility and intermodal concordance between MRI and CT in abdominal muscle segmentation has already been shown in patients with renal cell carcinoma [51]. Examples of qualitative muscle changes are shown in ► **Fig. 4, 5**.

In addition to cost and the sometimes limited availability, the long examination times compared to other methods are limitations of MRI. Moreover, there are no absolute cutoff values for the definition of sarcopenia. The method is normally used within the framework of research at specialized centers.

Ultrasound

As an inexpensive, widely available, and radiation-free method, ultrasound represents an alternative with good reproducibility [52]. Ticinesi et al. were able to determine the volume of the entire quadriceps muscle by determining the cross-section of the rectus femoris muscle. In addition, there was very good correlation with MRI measurement [53]. The lack of standardization of ultrasound examination and the partly examiner-dependent quality of implementation are limitations of the method. Moreover, if too much pressure is applied to the ultrasound transducer, the muscle compartments can be overly compressed, resulting in incorrectly small muscle volumes.

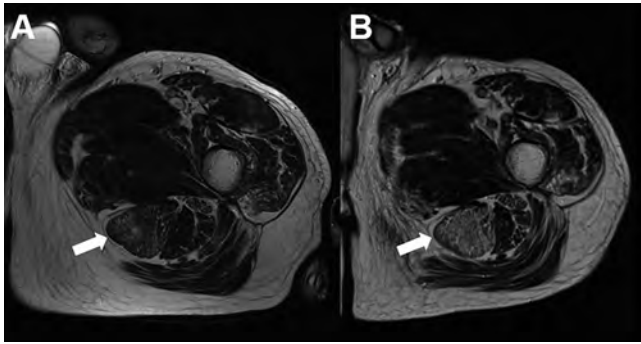
Non-radiological diagnostic methods

Further non-radiological diagnostic methods include bioelectric impedance analysis (BIA), electromyography (EMG), determination of potassium level, and anthropometric measurements, e. g., the circumference of the upper arm.

Artificial intelligence in sarcopenia diagnosis

In some studies, muscle and fat tissue in CT and MRI datasets has already been analyzed using artificial intelligence (AI) [9, 54–57]. In their study including 1143 CT datasets, Nowak et al. used two neuronal networks [57]. The CT scan to be analyzed at the level of L3 / L4 was selected with the first neuronal network and the skeletal muscle and fat tissue were segmented with the second. There was significant agreement between manual analysis and automatic analysis using the two neuronal networks. Pickhardt et al. used an automated deep-learning approach to analyze skeletal muscle at the level of the first and third lumbar vertebral body from 9223 CT datasets [9]. The acquired data on sarcopenia and particularly on fatty infiltration of muscle was comparable to clinical risk scores in the prediction of hip fractures and mortality. As a result of an AI-based evaluation, the time expenditure for segmentation can be reduced and the additionally acquired data can be included in the radiology report.

Radiomics analysis of skeletal muscle represents another approach to sarcopenia diagnosis [58]. In one study radiomics was



► **Fig. 4** Magnetic resonance imaging (MRI) of a 45-year-old patient diagnosed with malignant peripheral nerve sheath tumor (MPNST). Transverse T2 turbo spin echo (TSE) sequence of the left femur 1 year after **A** and 6 years after **B** distal femoral amputation. There is a progressive reduction in the volume of the thigh muscles and fat deposits, which is most pronounced in the semitendinosus muscle (arrows).

used to detect sarcopenia from the CT datasets of 247 patients with small-cell bronchial carcinoma. A machine learning model was used for the analysis. However, additional studies are needed to further examine this promising approach.

Clinical significance

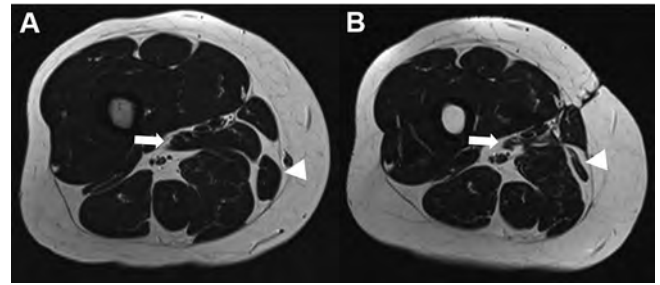
As the world population ages, the frequency of sarcopenia will increase significantly, with additional negative consequences. However, age-independent severe diseases like malignancies, COPD, chronic heart or kidney diseases can cause a secondary loss of muscle mass and strength. Early screening and intervention can significantly lower costs for the public health care system.

Diverse clinical applications result from the described modality-based methods for diagnosing sarcopenia. Some examples involving tumors and inflammatory/infectious diseases are discussed in the following.

Tumor

Sarcopenia diagnosis is mainly used in tumorous diseases. Particularly patients with malignancies often suffer from pronounced weight loss and the resulting consequences due to the disease itself or treatment-associated side effects. In addition, major surgeries and long hospital stays pose a risk in this patient population in particular.

In a group of patients with malignancies of the upper gastrointestinal tract, a prevalence of sarcopenia of 11.5% was seen with DXA based on the cutoff values according to Suetta in a Danish reference collective [59] or 19.1% compared to an Australian reference collective [60]. However, there was a significant discrepancy with respect to the cutoff values for sarcopenia diagnosis based on CT in the same collective [61]. In detail, there was an average difference in the quantification of lean tissue of 1.4 kg [61]. In particular, CT imaging is often used in this connection to determine body composition since staging and follow-up examinations in patients with tumors are performed repeatedly over



► **Fig. 5** Magnetic resonance imaging (MRI) of a 36-year-old female patient diagnosed with Ewing's sarcoma. Transverse T2 turbo spin echo (TSE) sequence of the right thigh before **A** and 3 years after **B** resection. There is a reduction in the volume of the thigh muscles over time most markedly of the adductor magnus muscle (arrows) and the gracilis muscle (arrowhead). The musculature shows increasing streaky fat deposits.

the course of the disease so that the focus is on the secondary use of CT data.

In relation to the CT-based SMI for diagnosing sarcopenia, it was shown that particularly the cutoff values of Martin et al. [30] and Prado et al. [29] were used in the available studies in oncology patients with a percentage of approx. 30% and 45%, respectively [62]. Patients with colorectal cancer were examined most frequently in the studies to date, with a prevalence of low SMI values being seen in 46.0% of cases (median percentage of patients with a low SMI: 41.1% in the curative cohort, 49.1% in the cohort without a curative approach) [62]. However, the highest prevalence of a low CT-based SMI was seen in patients with esophageal and pulmonary cancer (49.8% and 49.5%, respectively), with the cohorts with non-curative cancer being characterized by a higher prevalence comparable to colorectal cancer [62]. For the individual tumor entities, there was a prevalence of low SMI values between 35% and 50%, which was approximately comparable among the individual tumor types, cutoff values, and disease stages, so that reduced muscle mass or muscle quality based on CT-based SMI values seems endemic among oncology patients [62]. It should be mentioned here that a reduced SMI – together with the slightly more rarely used skeletal muscle density (SMD) – seems to have a negative effect on the survival of oncology patients and thus has direct clinical relevance [63–65]. 38 studies with a total of 7843 patients with a diagnosis of a solid tumor were included in a meta-analysis by Shachar et al. [63]. The tumor diseases most commonly examined in the studies were hepatocellular carcinoma (n = 11), pancreaticobiliary tumors (n = 6), gastroesophageal tumors (n = 4), urothelial carcinomas, renal cell carcinomas, and colorectal cancers (n = 3 in each case). In all included studies, the SMI determined during diagnosis was a negative predictive factor for survival. This was true for patients with and without metastases. In a retrospective analysis in patients with pancreatic cancer undergoing first-line chemotherapy, Kim et al. determined the SMI, SMD, and presence of sarcopenia [65]. A low SMI or SMD was a negative prognostic factor for survival. This effect was even greater if both the SMI and SMD were low. Side effects of chemotherapy were also observed more frequently in patients with a low SMI. In contrast, the broader use of MRI-based methods

for diagnosis or follow-up imaging of sarcopenia is still largely absent. In a study including patients with various primary oncological diseases, there was a strong positive intermodal correlation between the CSA and the paraspinous muscular fatty infiltration according to CT and MRI [55]. Particularly the good correlation between the CS-MRI-based quantification of muscle fat content and density values from CT imaging seems promising for being able to opportunistically acquire comparatively valid markers from CT imaging that are not inferior to MRI [55]. DTI or MRS could allow further characterization of compartments affected by sarcopenia, but these are not yet used on a representative basis particularly in patients with tumor diseases.

Inflammation/infection

Another large patient group of interest for sarcopenia diagnosis includes inflammatory and infectious diseases. These also promote catabolic metabolic reactions and result in a decrease in muscle mass that is also intensified by long periods of inpatient or outpatient bed rest [66, 67].

Particularly in chronic inflammatory diseases like rheumatic diseases or in chronic inflammatory bowel diseases, the correlation with sarcopenia has been shown usually by DXA measurements in multiple studies like the systematic analysis by An et al. [68].

With respect to inflammatory changes, Modesto et al. examined a healthy control group and three patient groups with various stages of pancreatitis [69]. An initial episode of acute pancreatitis was differentiated from a recurrent acute form of chronic pancreatitis. A modified psoas index was used in the analysis. The group was able to show that the muscle volume of the psoas musculature is a suitable biomarker to allow timely identification of the transition from recurrent acute to chronic pancreatitis so that corresponding therapeutic measures can be initiated early. However, there was a lack of a cutoff value for the absolute muscle volume so that only comparative analyses between the patient groups were possible. In a further study, a relationship between the loss of muscle mass and mortality with a month of hospitalization was able to be shown in patients with necrotizing pancreatitis [70]. ▶ **Fig. 6** shows an example of a decrease in skeletal muscle in a patient with necrotizing pancreatitis.

Multiple studies on sarcopenia have also recently been published with regard to the novel disease COVID-19. Gualtieri et al. were able to use CT to document a decrease in muscle mass during a stay in the ICU [71]. A prediction about the duration of hospital stay, intubation, and mortality in COVID-19 patients can be made based on the pectoralis muscle area [72]. ▶ **Fig. 7, 8** show a decrease in skeletal muscle as a result of a severe COVID-19 infection.

Complications, length of hospitalization, morbidity

Another interesting option for sarcopenia diagnosis is the possibility to better estimate the risk of postoperative complications based on the perioperative determination of muscle mass. This information can lead to better personalization of the indication for surgery with more comprehensive physiotherapeutic preparation and workup if needed. Jang et al. examined 284 patients prior to

planned pancreatic surgery [73]. Preoperative determination of the muscle area standardized to body weight on abdominal CT was able to show that highly significant and often feared postoperative pancreatic fistulas requiring correspondingly long inpatient treatment and resulting in immobilization are seen in sarcopenia patients. In contrast, other examined parameters such as the preoperative diameter of the main pancreatic duct as is typically used for risk assessment did not have any effect on the postoperative formation of fistulas. Moreover, a correlation between the psoas index in older patients and in trauma patients and morbidity, duration of hospitalization, and complication rate during inpatient care was able to be shown [74, 75].

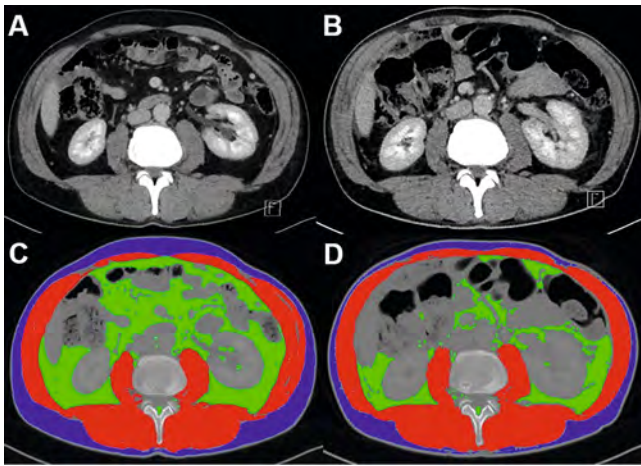
Prophylaxis and treatment

Physical activity is the most important intervention in connection with prophylaxis and the treatment of sarcopenia. Physical activity has a positive effect on muscle mass, muscle strength, and physical function by mitigating age-related loss [76, 77].

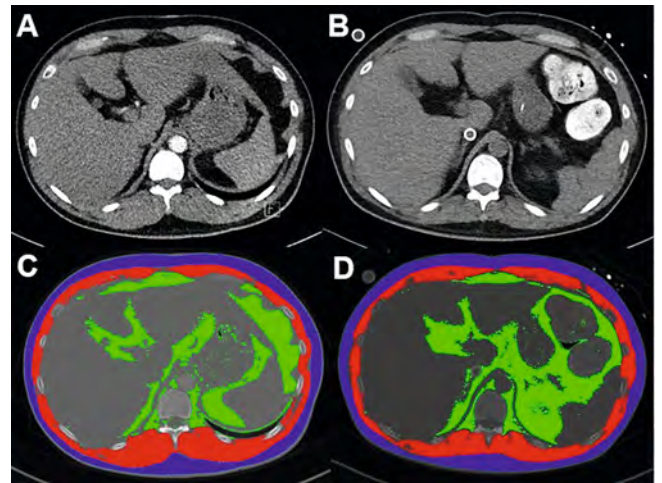
Although there is currently no specific treatment for sarcopenia, it is usually reversible. The goal is to improve muscle mass, strength, and performance. Particularly in the case of early intervention, the atrophy processes can be actively counteracted by individualized physical training and proper diet [7, 78]. Due to the targeted use of the muscles, age-appropriate and individualized progressive strength and resistance training is particularly suitable for prevention and treatment [79, 80]. In addition to muscle strength, stamina can also be improved. Intensive daily activities (e. g. housework and yard work) also help to optimize the musculature and quality of life. To minimize the fall risk, training should also include balance training [81]. To improve muscle protein synthesis, a personalized protein regimen with a sufficiently high leucine percentage (e. g. present in whey protein) is recommended [82, 83].

Conclusion/outlook

Due to changing demographics, sarcopenia as a chronic disease will become increasingly important. Sarcopenia is associated with a negative effect on the course of diverse diseases frequently in combination with an increased hospitalization rate and morbidity not only in older patients. For numerous tumor diseases, sarcopenia was able to be identified as a negative prognostic factor. Detection and follow-up can be performed with various radiological methods. CT plays an important role since it is often performed in the framework of other medical questions, e. g., in the routine staging of tumor patients. Data and information regarding sarcopenia can be acquired at the same time. The increasing use of AI-based segmentation of the skeletal muscles can additionally reduce the time expenditure. The results can be included in the radiology report on a supplementary basis. The planning of individualized treatment and follow-up can help to improve the course of the disease. The analysis of radiomics data regarding the skeletal muscles in sarcopenia diagnosis was already examined in patients with non-small-cell bronchial carcinoma [58, 84]. Dual-



► **Fig. 6** Computed tomography (CT) of a 68-year-old patient with necrotizing pancreatitis at the time of diagnosis **A, C** and four weeks later under therapy **B, D**. A significant reduction in subcutaneous (blue) and visceral (green) adipose tissue can be seen. Skeletal muscle area (red) decreased from 179.32 cm² to 162.69 cm². Skeletal muscle index showed a moderate decrease from 53.24 cm²/m² to 47.44 cm²/m². Segmentation was performed semiautomatically with an own Python application based on SimpleITK. For skeletal muscle, the Hounsfield unit (HU) mask was between -5 and 135 HU and for adipose tissue between -190 and -30 HU.



► **Fig. 7** Computed tomography (CT) of a 44-year-old patient with COVID-19 pneumonia and severe acute respiratory distress syndrome (ARDS) at baseline **A, C** and five weeks later **B, D**. The patient received intensive care treatment including invasive ventilation and a veno-venous extracorporeal membrane oxygenation (ECMO). There is a decrease in skeletal muscle area at the level of T12 from 99.38 cm² to 87.13 cm². Segmentation was performed semiautomatically with an own Python application based on SimpleITK. For skeletal muscle, the Hounsfield unit (HU) mask was between -5 and 135 HU and for adipose tissue between -190 and -30 HU.

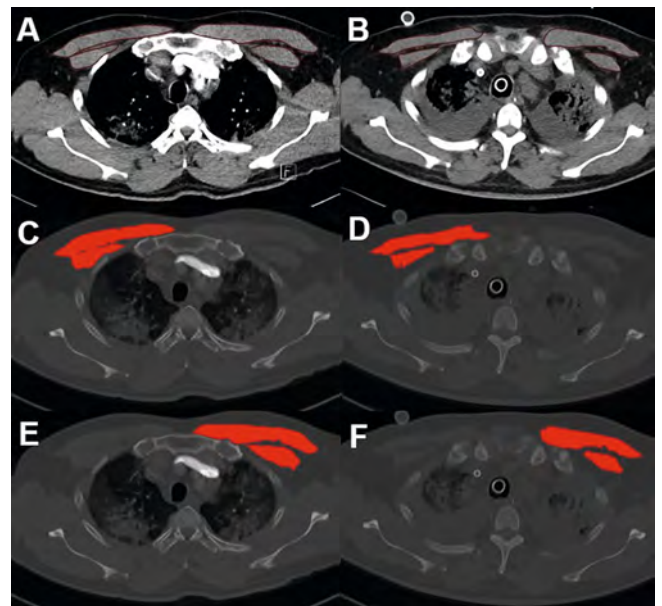
energy CT techniques and photon-counting CT are additional possibilities for sarcopenia diagnosis.

Established absolute reference values are a major requirement to be able to make generally valid statements regarding sarcopenia diagnosis in the clinical routine. Some study results on this topic are already available [23, 29–31]. Large population studies, e. g. the UK Biobank study and the NAKO study [85, 86], can provide information in this regard. Whole-body MRI examinations of approximately 30 000 participants were acquired in the NAKO study and can be used to establish reference values or to analyze MR radiomics.

It will certainly not take much longer for sarcopenia diagnosis to become established as a fixed variable in the therapeutic decision tree, at least in tumor patients. In the future not only sarcopenia screening but also the early detection of risk factors may become more important. For example, certain radiomics analyses could act as potential biomarkers, particularly in tumor patients.

KEY POINTS

- Sarcopenia is a primarily age-dependent syndrome that can manifest to a greater degree in patients with malignant tumor diseases.
- Negative effects on the course of the disease in tumor patients can be prevented by early detection and individualized treatment.



► **Fig. 8** Comparison of the area of the pectoralis major et minor muscle measured directly above the aortic arch at baseline **A** and five weeks later **B**. The measured area of the pectoralis major et minor muscle showed a decrease from 20.14 cm² to 14.95 cm² on the right **C, D** and from 26.23 cm² to 16.81 cm² on the left **E, F**. Segmentation was performed semiautomatically with an own Python application based on SimpleITK. For skeletal muscle, the Hounsfield unit (HU) mask was between -5 and 135 HU.

- In radiological diagnosis, computed tomography (CT) has the advantage of being able to be used to acquire additional parameters regarding sarcopenia (opportunistic use).
- Comprehensive use requires generally accepted and established reference values.
- Data can be quickly evaluated and implemented in the radiology report with artificial intelligence (AI).
- Radiomics analysis, dual-energy CT, and photon-counting CT are further options for sarcopenia diagnosis.

Conflict of Interest

The authors declare that they have no conflict of interest.

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