

# Imaging of Sarcopenia in Type 2 Diabetes Mellitus

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**Abstract:** Sarcopenia is an age-related condition characterized by the loss of skeletal muscle mass, muscular strength, and muscle function. In older adults, type 2 diabetes mellitus (T2DM) constitutes a significant health burden. Skeletal muscle damage and deterioration have emerged as novel chronic complications in patients with diabetes, often linked to their increased longevity. Diabetic sarcopenia has been associated with increased rates of hospitalization, cardiovascular events, and mortality. Nevertheless, effectively managing metabolic disorders in patients with T2DM through appropriate therapeutic interventions could potentially mitigate the risk of sarcopenia. Utilizing imaging technologies holds substantial clinical significance in the early detection of skeletal muscle mass alterations associated with sarcopenia. Such detection is pivotal for arresting disease progression and preserving patients' quality of life. These imaging modalities offer reproducible and consistent patterns over time, as they all provide varying degrees of quantitative data. This review primarily delves into the application of dual-energy X-ray absorptiometry, computed tomography, magnetic resonance imaging, and ultrasound for both qualitative and quantitative assessments of muscle mass in patients with T2DM. It also juxtaposes the merits and limitations of these four techniques. By understanding the nuances of each method, clinicians can discern how best to apply them in diverse clinical scenarios.

**Keywords:** diagnostic imaging, older adults, sarcopenia, skeletal muscle mass, type 2 diabetes mellitus

## Introduction

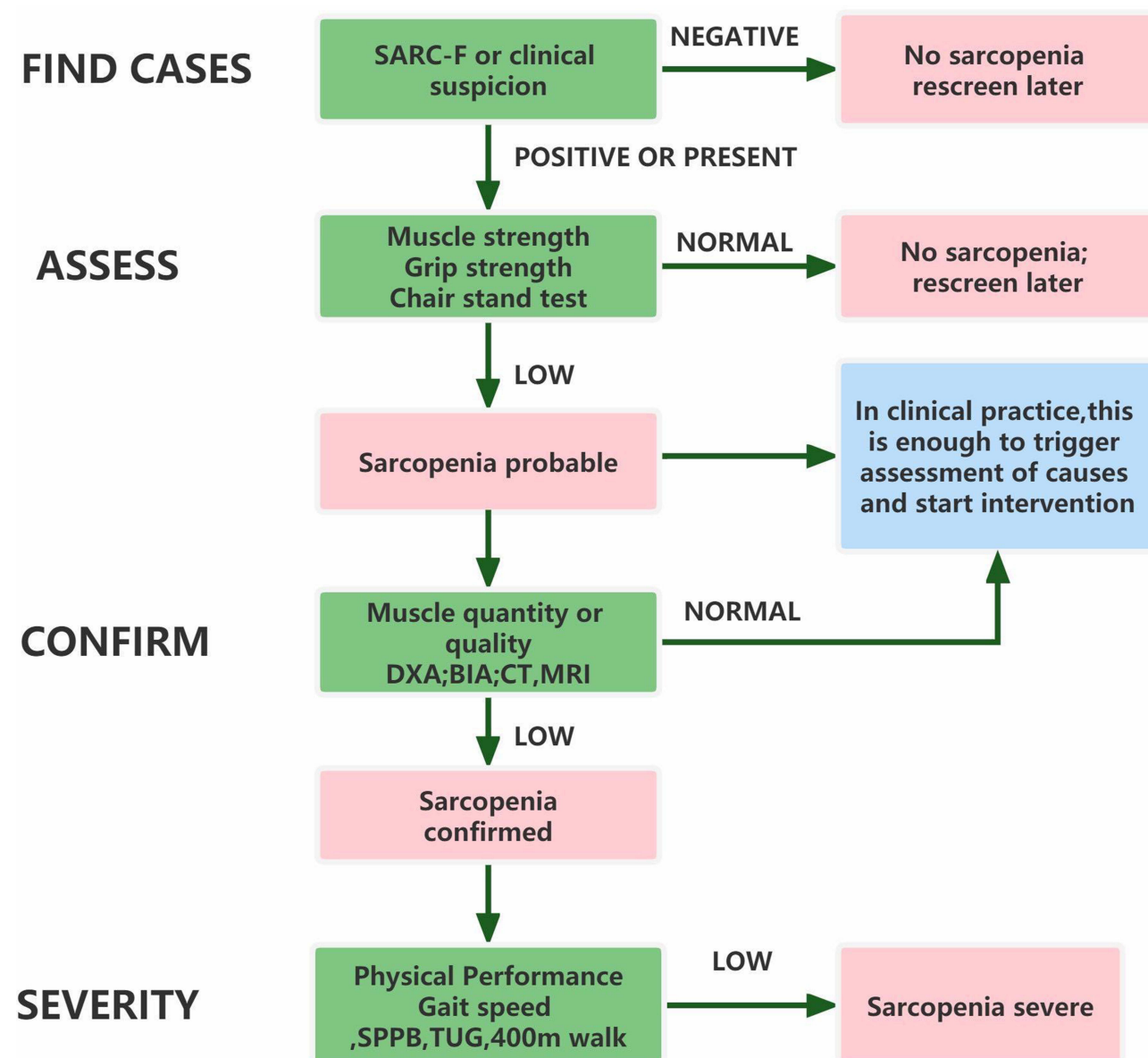
Sarcopenia, a syndrome characterized by the deterioration of muscle mass and function (including muscle strength and/or physical performance) as individuals age, has emerged as a pressing global concern. This is attributed to its association with escalated risks of mortality, frailty, and diminished mobility among the older adults.<sup>1,2</sup> Type 2 diabetes mellitus (T2DM) is one of the most prevalent metabolic disorders, affecting almost a quarter of the population aged 65 years and above. This proportion is anticipated to escalate in the forthcoming decades.<sup>3</sup> Older adults grappling with T2DM experience elevated incidences of functional disability, coexisting ailments, and various geriatric conditions, alongside microvascular and macrovascular complications.<sup>4</sup> A novel chronic complication of T2DM is the damage and degeneration of the skeletal muscle, which is attributed to the extended survival of patients with T2DM.<sup>5,6</sup> The vulnerability to sarcopenia is notably augmented in patients with T2DM. T2DM is associated with excessive loss of skeletal muscle and trunk fat mass in older adults. Older women with T2DM are at especially high risk for loss of skeletal muscle mass.<sup>7</sup> While the rate of deterioration might vary contingent on the muscle cluster, it invariably leads to compromised muscle.<sup>8</sup>

The interplay between these two factors may potentiate adverse outcomes, notably functional regression and disability.<sup>9</sup> The decline in muscle mass seems to be an inevitable part of the aging trajectory, and variations in the rate of degeneration among different populations imply that modifiable behavioral elements can influence the onset of sarcopenia.<sup>10</sup> A particularly effective strategy in thwarting sarcopenia is resistance-based training.<sup>11</sup> Moreover, alongside lifestyle modifications, due consideration must be accorded to several hypoglycemic drugs, which could yield varied effects on the underlying pathophysiological irregularities giving rise to sarcopenia. Our investigation delves into pertinent reviews on this subject, aimed at facilitating the early clinical identification of susceptibility to sarcopenia in patients with T2DM and the timely initiation of interventions to ameliorate muscle mass loss. This proactive approach seeks to minimize the incidence of falls and fractures in patients with T2DM, consequently enhancing their quality of life. Furthermore, it aids medical practitioners in selecting

appropriate imaging modalities to track alterations in the muscle structure and mass among patients with T2DM during the course of diabetes. This monitoring process is vital for evaluating the efficacy of relevant treatments.

## Definition and Diagnosis of Sarcopenia

Age-related loss of muscle mass and function is a prevalent phenomenon. Muscle strength undergoes a reduction of 20–40% during the seventh and eighth decades of life, and this decline exacerbates progressively over time.<sup>12</sup> In 1988, Irwin Rosenberg first introduced the term “sarcopenia” to delineate the age-related deterioration of skeletal muscle mass and function.<sup>13</sup> According to the European Working Group on Sarcopenia in Older People (EWGSOP), sarcopenia is currently defined as a “syndrome characterized by progressive and generalized loss of skeletal muscle mass and strength”.<sup>14</sup> This definition was revised in 2019 to describe sarcopenia as “a muscle disease originating from adverse muscle changes that accumulate over a lifetime”. EWGSOP proposes a screening and diagnostic approach for sarcopenia termed “Find-Assess-Confirm-Severity” (F-A-C-S; Figure 1).<sup>1</sup> Similarly, the Asian Sarcopenia Working Group (AWGS) adopts a comparable strategy for sarcopenia, suggesting an adjusted



**Figure 1** Screening and diagnostic approach for sarcopenia termed “Find-Assess-Confirm-Severity”. Adapted from Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T et al Sarcopenia: revised European consensus on definition and diagnosis. Age and ageing. 2019;48(1):16–31.<sup>1</sup>

cutoff value specifically suited for Asians, accounting for their anthropometric characteristics of the Asian population.<sup>15</sup> Central to the diagnosis of sarcopenia is the measurement of muscle mass. Clinical practice and research employ diverse qualitative and quantitative methodologies to ascertain muscle mass. Imaging modalities, including dual-energy X-ray absorptiometry (DXA), computed tomography (CT), magnetic resonance imaging (MRI), and ultrasound (US; Table 1), serve to evaluate muscle mass and quality, consequently facilitating sarcopenia diagnosis.

## Association Between T2DM and Sarcopenia

The skeletal muscle, which is the largest organ in the human body, also serves as a regulator of glucose homeostasis and is responsible for 80% of postprandial circulating glucose uptake.<sup>16</sup> Muscle insulin resistance, which disrupts the amount and timing of glucose uptake, is the initial metabolic defect in T2DM.<sup>17</sup> As individuals age, there is a gradual decline in mitochondrial function in human skeletal muscle along with a decrease in muscle mass, strength, and overall muscle function.<sup>18</sup> In the case of insulin resistance and T2DM, there is delayed insulin action and glucose uptake by skeletal muscle resulting in decreased overall glucose uptake.<sup>19</sup>

In addition, anomalies in lipid metabolism and obesity frequently induce insulin resistance. Altered adipose tissue growth and function lead to fluctuations in the concentrations of adipokines and cytokines, causing chronic inflammation, mitochondrial impairment, disruption of the insulin signaling pathway in the skeletal muscle, and eventual muscular atrophy. Adipose tissue secretes proinflammatory cytokines such as interleukin 6 (IL-6), interleukin 1 (IL-1), and tumor necrosis factor alpha (TNF- $\alpha$ ).<sup>20</sup> These inflammatory molecules significantly affect key nodes within the pancreatic route, consequently influencing insulin sensitivity, fostering insulin resistance, and hastening the onset of sarcopenia.

These metabolic defects overlap, and insulin resistance occurs at the junction of aging, muscle atrophy/muscle loss, and obesity, forming a toxic feedback loop where each exacerbates the other.<sup>21</sup>

## Muscle Mass and Behavioral Interaction

Although the decline in muscle mass is often considered an inevitable aspect of aging, there exists variation in the rate of muscle mass loss across different populations.<sup>10</sup> This variability suggests that certain behavioral factors might influence the onset and progression of sarcopenia. Among the strategies for preserving muscle quantity and quality, resistance exercise training is a reliable approach.<sup>1</sup> Notably, resistance-based training proves equally effective in enhancing muscle strength, size, and mass among older adults with T2DM.<sup>11</sup> Investigation into resistance training at varying intensities revealed positive outcomes in terms of muscle number, assessed through mid-thigh muscle cross-sectional area measurements.<sup>22,23</sup> However, to

**Table 1** Advantages and Disadvantages of the Primary Imaging Techniques for Body Composition and Mass/Fat Assessment

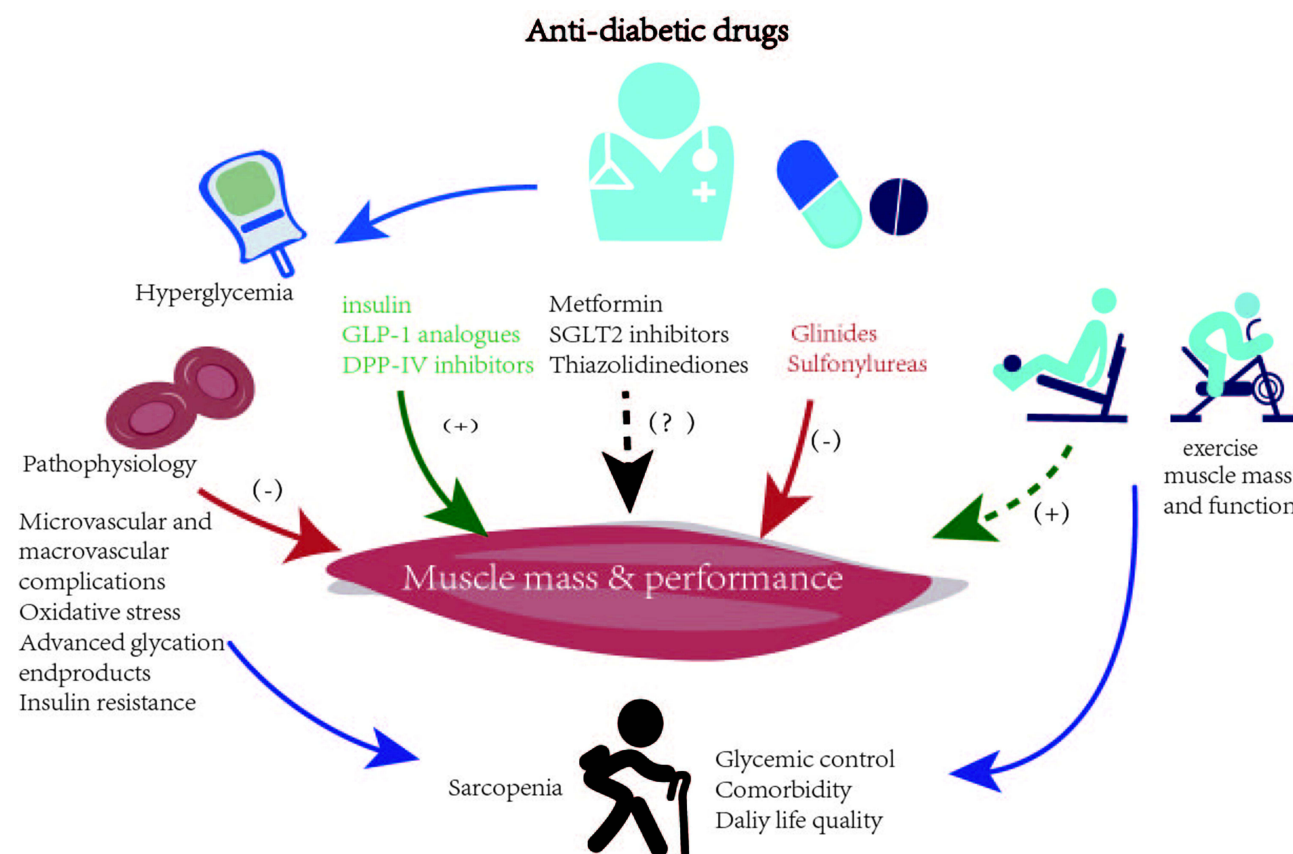
	DXA	US	CT	MRI
Measures	-Appendicular lean mass -Appendicular lean mass index	-Echo-intensity of skeletal muscle -Muscle thickness -Cross sectional area -Fascicle length -Pennation angle	-The SMA at the L3 level or height-corrected SMA (cm <sup>2</sup> /m <sup>2</sup> )	-Providing the same data on fat infiltration as CT -Muscle edema -Fiber infiltration -Fiber contraction -Elasticity
Simplicity	+	+	+	+
Cost	++	+	++\++++	++\++++
Validity	++	+\++	+++	+++
Clinical application	+	+	+	+
Research application	++\++++	+	+++	+++
New techniques	-	SWE CEUS	pQCT	IDEAL <sup>1</sup> H MRS\ <sup>31</sup> P MRS DTI BLOD

**Notes:** Use +++~+ to indicate different measurement methods in terms of simplicity, cost, validity, clinical application, and research application degree.+++; high; ++, medium; +, low.

ensure the continuous and safe engagement of older adults in training, it becomes imperative to thoroughly study and evaluate the suitable exercise intensity and duration, a task that imaging methods can facilitate.<sup>24</sup> The role of nutritional intervention in preventing and treating sarcopenia is less straightforward; nevertheless, some data suggest that adopting healthier dietary patterns, including adequate amounts of protein, vitamin D, antioxidants, and long-chain polyunsaturated fatty acids, could confer benefits.<sup>25–27</sup>

## Muscle Mass and Hypoglycemic Medication Interaction

Given the diverse effects of hypoglycemic medications on muscle mass (Figure 2), the choice of such medications should consider not only blood glucose levels and cardiovascular conditions but also the risk of sarcopenia. When compared with patients with T2DM but without sarcopenia, those with both conditions exhibit elevated blood glucose levels and inadequate insulin production. Elevated levels of HbA1c and mean blood glucose contributed to the increased risk of sarcopenia. Metformin, the primary choice for T2DM treatment, might enhance strength and muscle growth.<sup>28</sup> However, a study<sup>29</sup> indicated that metformin might attenuate the typical increase in muscle density associated with progressive resistance exercise. Long-term effects of sodium-glucose transport protein 2 inhibitors (SGLT2i) might enhance insulin sensitivity, thereby mitigating muscle catabolism and influencing the quality and functionality of the skeletal muscle.<sup>30,31</sup> Epidemiological research indicates a link between thiazolidinediones and reduced loss of muscle mass as well as improved walking pace among patients with T2DM.<sup>28,32</sup> Nonetheless, clinical trial data remain limited and contradictory.<sup>33</sup> The notable advantage for muscle preservation seems to be the use of glucagon-like peptide-1 (GLP-1) receptor agonists<sup>34,35</sup> and dipeptidyl peptidase-4 inhibitors (DPP-4i),<sup>36–38</sup> which not only minimally affects muscle mass loss but also stimulates muscle contraction and aid in muscle recovery. A novel agent, tirzepatide, a glucose-dependent insulin polypeptide and GLP-1 receptor agonist, exhibits approximately five times higher binding affinity to the GLP-1 receptor than natural GLP-1 does,<sup>39</sup> leading to reduced blood



**Figure 2** Effects of hypoglycemic drugs and exercise on muscle mass and performance.

sugar levels in patients with T2DM, particularly those who are obese. It also results in clinically relevant weight loss and effectively improved overall body function.<sup>40</sup> Conversely, sulfonylureas and glinides appear to consistently have a negative effect on skeletal muscle.<sup>41,42</sup> While existing clinical trial and epidemiological data demonstrate a positive correlation between insulin use and measures related to sarcopenia,<sup>43–45</sup> the effect of insulin on overall body weight cannot be disregarded. In light of this, clinicians should exercise caution in prescribing these medications to diabetic patients who are susceptible to sarcopenia, shifting focus instead to monitoring changes in muscle mass. This underscores the crucial role of imaging methods in promptly and accurately assessing the muscle mass of patients.

## Imaging Techniques for Sarcopenia in Type 2 Diabetes Mellitus

### Dual-Energy X-Ray Absorptiometry

DXA can be used to assess the adipose tissue, bone mineral content, and nonbony lean tissue in the entire body or specific anatomical regions.<sup>46</sup> The appendicular lean mass (ALM) value, which represents the combined muscle mass of the upper and lower limbs as measured by DXA, is commonly utilized for assessing muscle mass. This value is then standardized to height by calculating the appendicular lean mass index ( $ALMI = ALM/height^2$ ). The recent guidelines from EWGSOP have made slight modifications to previous diagnostic cutoff values, proposing an  $ALMI < 5.5 \text{ kg/m}^2$  in women and  $ALMI < 7.0 \text{ kg/m}^2$  in men be used as criteria for defining low muscle mass (1). Additionally, the AWGS suggests an  $ALMI < 5.7 \text{ kg/m}^2$  in women and  $ALMI < 7.0 \text{ kg/m}^2$  in men, taking into account the anthropometric characteristics of the Asian population (2). Through a comparison of data across different age groups and DXA-based sarcopenia assessments, other researchers<sup>47</sup> identified significant differences in skeletal muscle mass between older and middle-aged patients with diabetes. Notably, the prevalence of sarcopenia among older adults with T2DM was markedly higher than that in their middle-aged diabetic counterparts. The link between sarcopenia and diabetes was more pronounced among individuals over the age of 75 years. Lean tissue, as determined by DXA, encompasses skin, fibrous connective tissue, body water in addition to the muscle. Consequently, estimating muscle mass solely based on lean tissue could yield inaccurate results.<sup>48</sup> Bredella et al<sup>49</sup> compared DXA with CT and observed a tendency of DXA to overestimate thigh muscle mass, especially in severely obese women, due to the influence of body thickness and level of hydration on DXA measurements, which suggests potential limitations in quantifying body composition. Obesity contributes to an increased risk of both T2DM and insulin resistance.<sup>50</sup> In cases of obese patients with sarcopenia and T2DM, DXA measurements might overstate muscle mass, potentially leading to treatment delays. Additionally, the accuracy of measurements could be compromised if a subject's body length exceeds the scanning area's dimensions or if their arm spacing exceeds the scanning area's width due to design constraints.

### Computed Tomography

Although Steven Heymsfield utilized CT for analyzing body composition in the 1980s,<sup>51</sup> Shen et al<sup>52</sup> did not present a method for calculating whole-body skeletal muscle and adipose tissue from a single abdomen CT cross-sectional scan until 2004. A commonly used approach for evaluating sarcopenia involves quantifying the skeletal muscle area (SMA) at the lumbar 3 (L3) level by delineating regions of interest (ROIs) and applying standardized thresholds ( $-29 \text{ Hounsfield units (HU)}/+150 \text{ HU}$ ) to identify the muscle tissue, thereby obtaining the cross-sectional area (CSA) of the muscle.<sup>53,54</sup> The skeletal muscle index (SMI) is typically calculated by dividing the cross-sectional area (CSA) by height squared ( $CSA/height^2$ ). According to a recent meta-analysis, the commonly used SMI cutoff values for assessing muscle mass on CT scans range from  $39 \text{ to } 41 \text{ cm}^2/\text{m}^2$  for females and from  $52 \text{ to } 55 \text{ cm}^2/\text{m}^2$  for males.<sup>55</sup> A study<sup>56</sup> utilized CT to analyze the body composition of 1787 healthy individuals across four northern Chinese cities and established diagnostic thresholds for skeletal muscle mass loss based on 700 younger healthy adults. In a prospective study of Japanese Americans, Han et al<sup>57</sup> used CT to investigate the relationship between cumulative changes in visceral fat, thigh muscle cross-sectional area, and the occurrence of T2DM over 5 years. Their findings indicated that simultaneous changes in visceral fat and thigh muscle area were associated with an increased risk of T2DM. These reference values and research outcomes could aid doctors in predicting outcomes, enhancing nutritional therapy, and diagnosing malnutrition, though further research is necessary to determine the predictive effect of these reference values across various disease groups. However, because of variations in population characteristics and criteria, there is no



universally recognized standard for CT-based sarcopenia diagnosis.<sup>58</sup> Moreover, the high radiation dose, cost, and operational complexity of CT for assessing skeletal muscle quality limit its practical applicability.

The exploration of the link between sarcopenia, osteoporosis, and diabetes is facilitated by quantitative CT (QCT), which mitigates the impact of unstable CT results on measurements and quantifies true volumetric bone mineral density. Peripheral QCT (pQCT), based on peripheral body layer imaging, is a compact scanning device that gauges muscle area, muscle density, and intra-muscular fat content in limb cross sections. Researchers<sup>59</sup> investigated longitudinal changes in pQCT-measured calf myosteatosis and skeletal muscle density. Intermuscular adipose tissue (IMAT) has been associated with alterations in lipid and glucose metabolism, emerging as a noteworthy concern. Studies suggest that increased intermuscular fat with aging correlates with the onset of T2DM, raising the possibility that intermuscular fat could serve as an independent predictor of T2DM in males of African descent.<sup>60</sup> pQCT offers advantages over standard CT, including reduced radiation exposure, shorter scan times, and lower costs.<sup>60</sup> The main drawbacks of pQCT include the lack of image acquisition and processing protocol homogeneity and limitations in scanning range, potentially leading to measurement errors.<sup>61</sup>

## Magnetic Resonance Imaging

Through the manipulation of radiofrequency pulse sequences, MRI technology can evaluate the adipose tissue and fat-free tissue by assessing the absorption and release of radiofrequency energy from hydrogen nuclei under the influence of an external magnetic field.<sup>62</sup> MRI can diagnose sarcopenia and is considered the gold standard for determining body composition, similar to CT. It not only provides data on fat infiltration akin to CT but also offers additional insights into muscle quality by detailing muscle edema, fiber infiltration, fiber contraction, and elasticity. These aberrant changes can lead to reduced muscle mass and strength, both crucial components of sarcopenia.<sup>63–65</sup> However, studies on MR have been conducted on various muscular regions without standardized imaging protocols and biomarkers.<sup>66</sup> Studies have correlated skeletal muscle fat infiltration with insulin resistance, diabetes, and sarcopenia.<sup>67</sup> In a study,<sup>68</sup> whole-body MRI quantified intermuscular adipose tissue (IMAT), visceral adipose tissue (VAT), subcutaneous adipose tissue, and total adipose tissue to determine changes in body composition associated with aging. The results revealed a decline in skeletal muscle mass coupled with an increase in VAT and IMAT. Animal studies have shown<sup>69</sup> that diabetes mellitus leads to reduced skeletal muscle weight, strength, and cross-sectional area of muscle fibers, while intramyocellular (IMCL) lipid content increases. The rise in IMCL correlates with the loss of skeletal muscle mass.<sup>68</sup> Researchers<sup>70</sup> suggest that specific patterns of fat infiltration, rather than overall fat content, might serve as more significant risk factors for T2DM and metabolic syndrome. Consequently, changes in skeletal muscle fat content and infiltration represent a pivotal focus in sarcopenia and T2DM research.

Iterative Decomposition of Water and Fat with Echo Asymmetry and Least-Squares Estimation (IDEAL) is one of the most advanced hydro-lipid imaging methods available.<sup>71</sup> In light of clinical study stability criteria, imaging techniques advocate employing the three-point Dixon approach for quantifying muscle fat content. Precise measurement of muscle<sup>72</sup> cell lipid content can be achieved through <sup>1</sup>H magnetic resonance spectroscopy (<sup>1</sup>H MRS).<sup>73</sup> This technique quantifies IMCL and extracellular (EMCL) lipids, minimizing potential errors related to manual EMCL adipose tissue removal.<sup>74</sup> The model provides a non-invasive assessment method and can also indicate muscle lipid metabolism during exercise.<sup>75</sup> Magnetization transfer <sup>31</sup>P magnetic resonance spectroscopy (<sup>31</sup>P MRS) can measure ATP synthase rates and forward creatine kinase activity in humans and animals. ATP levels and other phosphorus metabolites are linked to metabolic changes in insulin-resistant T2DM.<sup>76</sup> Using saturation transfer <sup>31</sup>P MRS, ATP production rates were found to be reduced in muscles of the older adults and offspring of patients with T2DM.<sup>77,78</sup> Thus, <sup>31</sup>P MRS assessment of enzyme activity and mitochondrial function plays a crucial role in studying metabolic shifts, aging, and diseases.

The MRI technique called diffusion tensor imaging (DTI) has shown sensitivity to muscle microstructure alterations.<sup>79,80</sup> In skeletal muscles, fiber size significantly influences  $\lambda_2$ ,  $\lambda_3$ , mean diffusion, and fractional anisotropy (FA). DTI serves as a sensitive tool for tracking muscle atrophy, although its applicability in measuring muscles with larger fibers may be limited.<sup>81</sup> Blood oxygen level-dependent imaging (BOLD) can assess skeletal muscle oxygenation and microcirculation. In a study by Liu et al,<sup>82</sup> adult nonobese T2DM rats exhibited lower BOLD signal intensity in the gastrocnemius muscle during the ischemia-reperfusion period compared to the control group.

MRI stands as the most modern and dependable method for studying body composition. However, challenges such as high costs, complexity, and limited availability restrict its clinical usage, making it primarily applicable in research settings.

## Ultrasound

US of the musculoskeletal system offers advantages of high resolution, noninvasiveness, portability, and safety. It can be employed for both static and dynamic assessments, making it a reliable tool for evaluating muscle quality. Key metrics used by US to assess muscle mass include skeletal muscle thickness, cross-sectional area, fascicle length, and pennation angle.<sup>83</sup> Additionally, new parameters have been introduced, such as muscle volume, stiffness, contraction potential, and microcirculation.

Significant reduction in total muscle mass occurs relatively late in the natural progression of sarcopenia, even after the loss of physical capabilities. Muscle mass loss varies across different body areas as we age. Sarcopenia predominantly affects lower limb muscles rather than upper limb muscles.<sup>84</sup> Studies have indicated that rapidly contracting type II muscle fibers are more affected in patients with sarcopenia compared with type I fibers.<sup>85</sup> Utilizing high-frequency musculoskeletal ultrasonography to assess the thickness of plantar tissue and intrinsic foot muscles under the metatarsals, patients with T2DM exhibited notably thinner plantar tissue and intrinsic foot muscles compared with people without diabetes.<sup>86</sup> Although IMAT accounts for only 5% of total thigh fat, research has linked it to insulin resistance.<sup>87</sup> IMAT appears hyperechoic (white) on US, while skeletal muscle appears hypoechoic (black).<sup>88</sup> Standardizing ultrasonic measurement techniques may assist in identifying causal links or predicting disease changes. Nevertheless, relying solely on US for measuring IMAT lacks accuracy, and consistency in the results is compromised because of scanner subjectivity, probe angle, pressure, and other factors. US-guided skeletal muscle biopsy can enhance IMAT extraction from the body and serve as an effective imaging method for monitoring precise IMAT metabolic activity.<sup>89</sup>

From a technical standpoint, image acquisition is quick, straightforward, and does not demand advanced operator expertise. The integration of portable US with smartphones makes this technology suitable for predicting sarcopenia in community and inpatient settings. Studies with limited sample sizes have demonstrated a strong correlation between DXA,<sup>90</sup> MRI<sup>91</sup> measurements, and US-based muscle mass measurements.

Shear-wave elastography (SWE) is a fully quantitative technique for determining the absolute elasticity of soft tissues.<sup>92</sup> Changes in muscle hardness can be influenced by age-related alterations in muscle structure and organization, including muscle fat infiltration, muscle fiber tissue growth, collagen tissue loss, increased collagen fiber, and enhanced muscle glycosylation.<sup>93,94</sup> Thus, elastic ultrasonography can identify early sarcopenia-related changes in muscle function. A study evaluated the effects of aging on skeletal muscle stiffness in relaxed and contracted status using SWE. The average stiffness values of the medial head of the gastrocnemius muscle were  $12.51 \pm 2.56$  kPa and  $81.74 \pm 15.77$  kPa in the relaxed and contracted states,<sup>95</sup> respectively. Chen et al<sup>96</sup> developed a diagnostic model with excellent performance for identifying T2DM individuals with sarcopenia. The skeletal muscle microcirculation, the body's largest and most crucial capillary system, facilitates nutrient, oxygen, and hormone exchange, especially during physical activity. Although individual circulatory capacity decreases with age, physical activity can enhance microcirculation.<sup>97</sup> Contrast-enhanced ultrasonography (CEUS) can reveal muscle microcirculation changes. T2DM affects both macro- and microvessels, yet comprehensive CEUS studies on T2DM with sarcopenia remain lacking. Analyzing microcirculation under CEUS during different sarcopenia phases under appropriate CEUS conditions holds diagnostic potential that can be fully utilized.

Additionally, bioelectrical impedance analysis (BIA) has been recognized as a tool for assessing skeletal muscle mass (quantity).<sup>98</sup> As US, BIA is non-invasive, simple and less expensive than other techniques. However, it is important to note that BIA does not directly measure muscle mass. BIA relies on the correlation between total body water and electrical body impedance. Nevertheless, it is widely acknowledged that numerous physiological factors (such as gender, race, age, pregnancy, hormonal cycles, and exercise) as well as pathological conditions (including obesity, medications, and various diseases) can influence hydration status.<sup>99,100</sup> Given the potential for significant alterations in body fluids among older adults with T2DM due to diabetes-related complications and treatments,<sup>101,102</sup> the accuracy of BIA in assessing body composition could be substantially impacted.

## Future Perspectives and Conclusions

Prediabetes is believed to be reversible.<sup>103</sup> The combination of exercise and medication can prevent the progression from prediabetes to T2DM by enhancing muscle blood flow, regulating muscle insulin sensitivity, and reducing chronic low-

grade inflammation in order to optimize muscle mass. These hypotheses should be tested in both animal models and human subjects using imaging techniques to monitor the impact of a comprehensive intervention approach encompassing physical activity, dietary control, nutritional supplementation, and medication on preserving muscle mass and strength while safeguarding against age-related muscle loss.

The realm of imaging-based diagnostic methods for sarcopenia presents variations in terms of diagnosis techniques, standards, and clinical applications. Addressing these discrepancies necessitates further investigation. Artificial intelligence holds promise as a valuable tool in sarcopenia detection. Similar to commercial systems employing AI algorithms for automated osteoporosis detection on CT<sup>59</sup> scans, AI could prove beneficial in detecting sarcopenia. Another emerging avenue of exploration is radiomics, a field utilizing high-throughput methodologies to extract and analyze intricate quantitative imaging features from medical images like DXA, CT, and MRI. The integration of supplementary imaging omics focused on sarcopenia has the potential to refine existing diagnostic criteria, improve predictions of clinical outcomes, and deepen our understanding of the impact of sarcopenia. Before imaging techniques can be effectively employed in clinical settings, it is imperative to establish reference values for various stages of diabetes and for healthy blood glucose levels. Moreover, there should be a heightened focus on comprehending how fluctuations in blood sugar and other pertinent factors influence muscle size and function. The early identification of predilections toward sarcopenia in patients with T2DM and tailored exercise and treatment regimens to mitigate, halt, or reverse the loss of muscle mass, strength, or quality can greatly enhance the well-being of patients in their later years.

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## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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