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REVIEW ARTICLE

A comprehensive review on the risks assessment and treatment options for Sarcopenia in people with diabetes

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Abstract

Objectives This comprehensive review aims to examine the reciprocal interplay between Type 2 diabetes mellitus (T2DM) and sarcopenia, identify prevailing research gaps, and discuss therapeutic approaches and measures to enhance healthcare practices within hospital settings.

Methods A thorough literature review was conducted to gather relevant studies and articles on the relationship between T2DM and sarcopenia. Various databases were searched, including Google Scholar, PubMed, Scopus, and Science Direct databases. The search terms included T2DM, sarcopenia, inflammation, insulin resistance, advanced glycation end products, oxidative stress, muscle dimensions, muscle strength, muscle performance, aging, nutrition, hormone levels, and physical activity. The collected articles were critically analysed to extract key findings and identify gaps in current research.

Results The prevalence and incidence of metabolic and musculoskeletal disorders, notably T2DM and sarcopenia, have surged in recent years. T2DM is marked by inflammation, insulin resistance, accumulation of advanced glycation end products, and oxidative stress, while sarcopenia involves a progressive decline in skeletal muscle mass and function. The review underscores the age-related correlation between sarcopenia and adverse outcomes like fractures, falls, and mortality. Research gaps regarding optimal nutritional interventions for individuals with T2DM and sarcopenia are identified, emphasizing the necessity for further investigation in this area.

Conclusions The reciprocal interplay between T2DM and sarcopenia holds significant importance. Further research is warranted to address knowledge gaps, particularly in utilizing precise measurement tools during clinical trials. Lifestyle modifications appear beneficial for individuals with T2DM and sarcopenia. Additionally, practical nutritional interventions require investigation to optimize healthcare practices in hospital settings.

Keywords T2DM · Obesity · Sarcopenia · Muscle · Health metabolic health

Introduction

Sarcopenia, a progressive and generalized condition characterized by rapid muscular atrophy [1], is derived from the Greek term "poor of flesh" (penia sarco) and represents the age-related inability to sustain a healthy muscular metabolism [2]. It has emerged as a prevalent health concern among the elderly population, posing a significant challenge to the public health system. The United Nations (UN) reports that 13.1% of the global population is aged 60 years or older [3]. It is widely acknowledged that advancing age leads to gradual muscle mass loss, resulting in a progressive decline in strength, mobility, and the ability to perform activities of daily living.

Despite its prominence, there is a lack of data regarding the diagnosis and incidence of sarcopenia in India. Existing research predominantly employs cutoff values based on Caucasian populations, which may not accurately reflect the characteristics of Asians. Asians exhibit lower muscle mass, and individuals in less developed nations have substantially weaker grip strength compared to those in developed nations (4–5).

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The duration of sarcopenia can serve as a classification factor, distinguishing between acute and chronic forms. Acute sarcopenia, typically resulting from illness or injury, often resolves within six months [6]. On the other hand, chronic sarcopenia persists for more than six months and is commonly associated with degenerative diseases [7]. However, due to overlapping symptoms such as cachexia and sarcopenic obesity, sarcopenia is often misdiagnosed as another disorder. Accurate clinical diagnostic criteria are crucial, as the reported prevalence of sarcopenia may vary across studies. Physical well-being during middle age has been identified as a predictor of sarcopenia, which contributes to muscle loss and weakness [8].

Sarcopenia commonly coexists with diabetes in older individuals. Recent studies have suggested a bidirectional relationship between sarcopenia and diabetes. Sarcopenia, characterized by age-related muscle loss, is associated with a higher prevalence of diabetes, and individuals with diabetes exhibit reduced bone mass index in both men and women [9–11]. The decline in muscular mass in sarcopenia contributes to diminished glucose clearance, metabolic rate, and physical activity in older individuals (Fig. 1) [12, 13]. Lifestyle modifications have been identified as potential interventions to prevent and manage both sarcopenia and diabetes. This review article explores the intricate relationship between type 2 diabetes mellitus (T2DM) and sarcopenia, sheds light on current research gaps, discusses treatment therapies, and proposes steps to improve healthcare practices in hospital settings.

Prevalence of sarcopenia

According to a 2019 report, 53% of Indian outpatients met the Asian Working Group for Sarcopenia (AWGS) 2014 criteria for sarcopenia [14]. It is important to note that most sarcopenia studies have focused on participants with secondary sarcopenia, as it is expected in the elderly population dealing with multiple chronic diseases, as reported in a 2020 meta-analysis [15]. However, recent outpatient research conducted in Thailand revealed that 10% of older individuals exhibited primary sarcopenia based on AWGS criteria [16]. Consistent with World Health Organization standards, overweight individuals were found to have a lower likelihood of experiencing sarcopenia compared to those with normal or underweight status. Similar findings have been

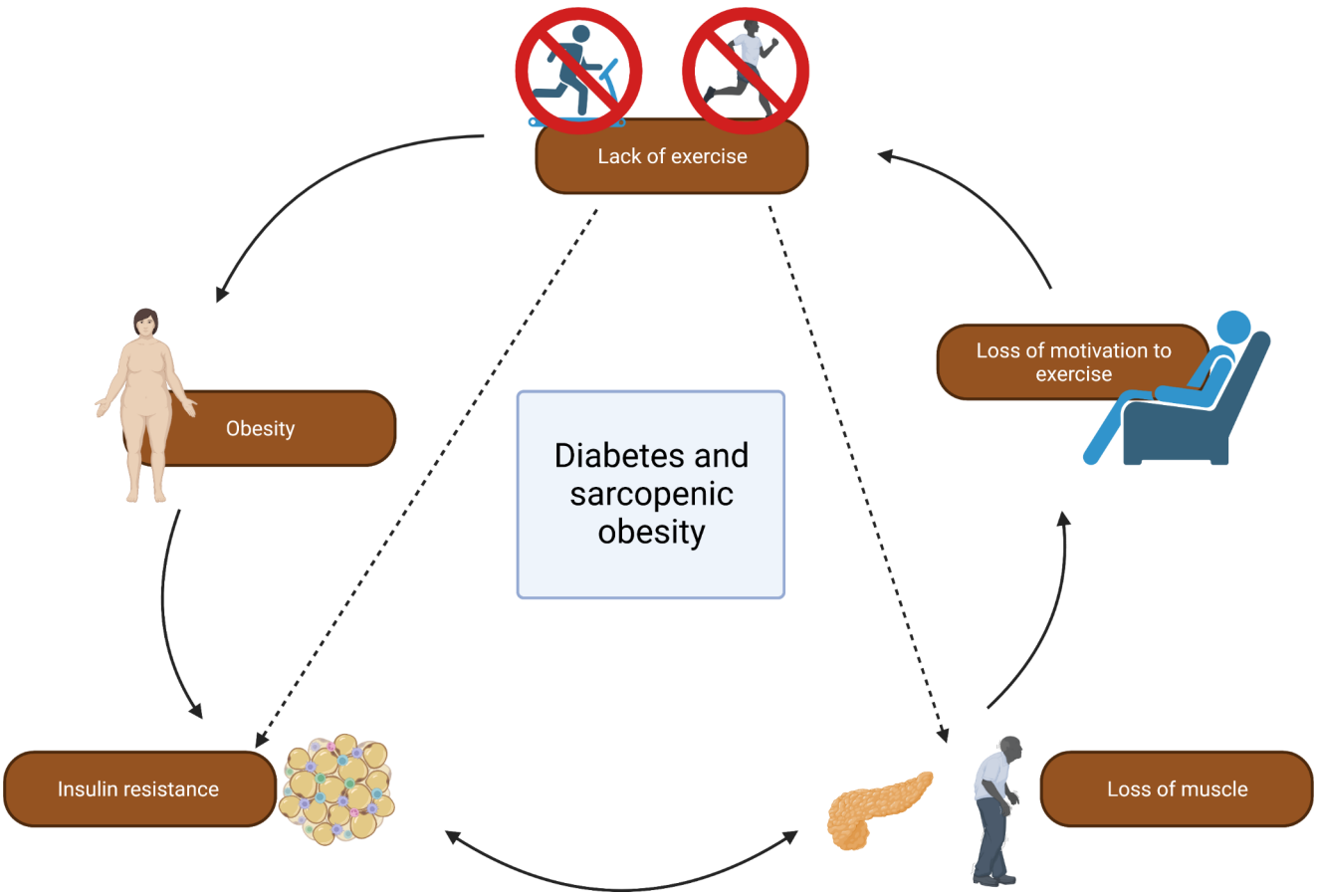

Fig. 1 Schematic representation of an unhealthy lifestyle that can lead to diabetes, sarcopenia, and other metabolic disorders

reported in recent studies involving Asian populations [17, 18].

In a study involving Asian patients aged over 60, with females constituting 53.4% of the sample, two groups were formed: 1,537 individuals with diabetes and 5,485 individuals without diabetes. Sarcopenia was diagnosed using AWGS criteria. The prevalence of sarcopenia was 15.9% among individuals with diabetes, compared to 10.8% among non-diabetic individuals, indicating a higher risk of sarcopenia in those with diabetes [19].

In some cases, a high body mass index (BMI) may indicate a healthy balance between lean skeletal mass and fat. However, in the presence of sarcopenia, a high BMI may mask the condition, emphasizing the importance of measuring adiposity to diagnose sarcopenic obesity. Cereals constitute a significant portion of the Indian diet, but their protein quality is lower compared to legumes, meat, and dairy products. Insufficient protein consumption at a young age leading to low initial muscle mass is likely a contributing factor to the increasing sarcopenia epidemic in India [20]. Figure 2 depicts the prevalence of sarcopenia in men and women according to AWGS and the Foundation for the National Institutes of Health (FNIH) criteria [21].

The impact of inflammation on muscle Mass and Strength in type 2 diabetes Mellitus

Individuals with type 2 diabetes mellitus (T2DM) commonly exhibit low-grade systemic inflammation, which disrupts glucose and muscle homeostasis [22–24]. Inflammatory markers such as IL-6, TNF-α, and C-reactive protein (CRP) are elevated in individuals with T2DM [25, 26]. Visceral adipose tissue (VAT) may contribute to inflammation in T2DM by secreting pro-inflammatory cytokines like IL-6 and TNF-α [27]. These cytokines stimulate the immune system. A recent study involving 84 overweight or obese subjects demonstrated that a larger waist circumference was associated with reduced muscle strength, quality, and performance [28] (Fig. 3).

Temporary increases in IL-6 induced by physical activity promote nutrient mobilization and muscle growth [29–31]. Furthermore, even in the absence of systemic inflammation, direct administration of IL-6 to the tibialis anterior muscle of Sprague-Dawley rats resulted in muscle atrophy [24]. In the Framingham Heart Study, IL-6 accurately predicted loss of lean mass in women but not in men over a two-year period [32]. Over a span of five years, individuals over the age of 60 with high IL-6 and CRP levels experienced five times greater muscle loss, and those with elevated IL-6 had four times higher muscle loss [33, 34]. A study conducted over three years found that older individuals with type 2 diabetes experienced greater loss of leg muscle mass and strength compared to non-diabetic controls [35].

Muscle strength is considered a fundamental aspect of sarcopenia, and inflammatory markers are believed to impact muscle mass and strength [36]. In women of both Black and Caucasian heritage, TNF-α was found to decrease grip strength, whereas this relationship was not observed in men [36]. The English Longitudinal Study of Aging reported an inverse association between C-reactive protein and handgrip strength in both women and men, as well as the time is taken to stand up from a chair [37]. T2DM-related inflammation may indeed affect muscle mass and strength.

Oxidative stress in T2DM-Associated Sarcopenia and mitochondrial dysfunction

The pathogenesis of sarcopenia is associated with age-related depletion of antioxidants [38]. T2DM induces myopathy, which is linked to increased oxidative stress [39–41].

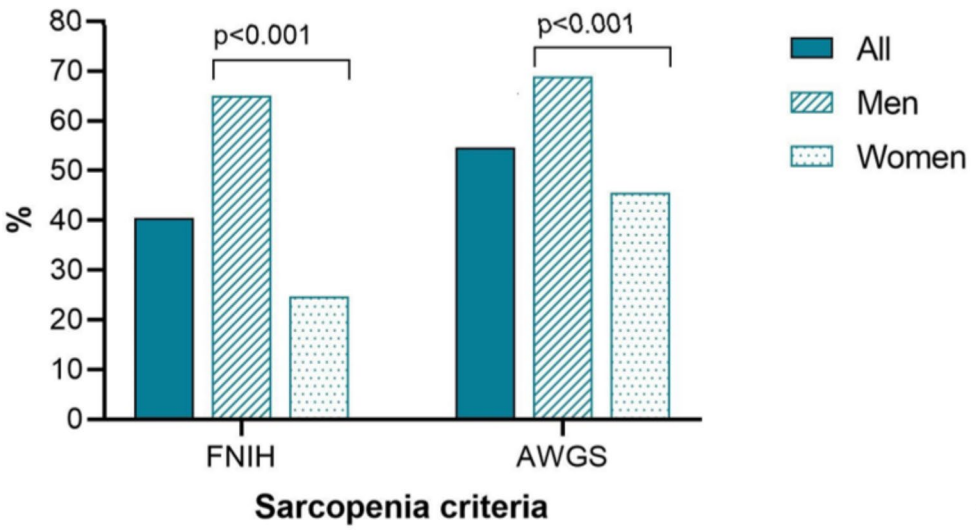

Fig. 2 The prevalence of sarcopenia in men and women
FNIH, Foundation for the National Institutes of Health, AWGS, Asian Working Group for Sarcopenia

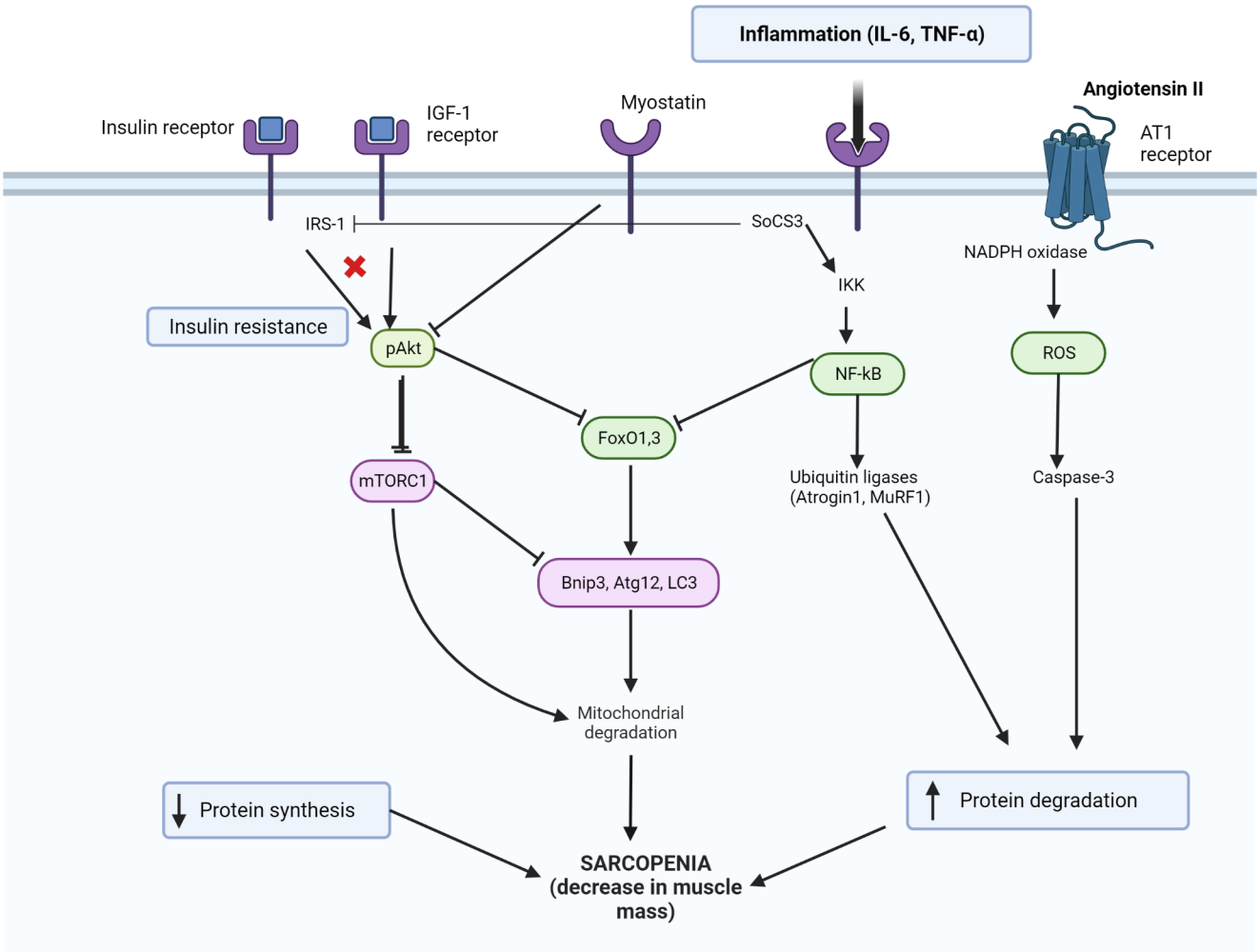

Fig. 3 Molecular mechanism of sarcopenia in diabetes

Studies conducted on premenopausal and postmenopausal women have revealed an inverse relationship between oxidative stress and skeletal muscle mass [42]. The detrimental effects of oxidative stress on cell growth and DNA synthesis [43] contribute to the disruption of various cellular mechanisms in type 2 diabetic myopathy. Further investigation is required to elucidate the underlying pathways and potential intervention targets.

Mitochondrial dysfunction is intricately connected to aging, T2DM, and the metabolic and muscular deterioration induced by oxidative stress. Aged individuals may experience a 50% reduction in oxidative capacity compared to younger individuals due to increased mitochondrial DNA mutations (44–45). Impaired oxidative capacity leads to slowed macronutrient metabolism and reduced physical performance. In offspring of individuals with diabetes, T2DM reduces mitochondrial density in insulin-sensitive individuals by 38% compared to non-diabetic offspring, even in those without diabetes in their lineage [46]. Given the critical role of mitochondria in skeletal muscle function and metabolism, further research is warranted to explore the relationship between T2DM, sarcopenia, and mitochondrial dysfunction in humans.

Role of advanced glycation end-products in muscular health

Advanced glycation end-products (AGEs) are formed through non-enzymatic interactions between glucose and amino groups in lipids, proteins, and nucleic acids. There is a strong association between insulin resistance, obesity, and age-related oxidative damage [47–49]. Although the

precise mechanism by which AGEs contribute to poor muscle health is not fully understood, increased protein cross-linking within the muscle is implicated. These cross-linking hampers muscular contraction, promotes inflammation, and induces oxidative stress. Moreover, AGE levels in skeletal muscle tend to elevate with age. Measurement of autofluorescence serves as a surrogate marker for AGEs and provides insights into long-term glycaemic control [50].

Research has established a correlation between sarcopenia and higher levels of skin autofluorescence, accompanied by reduced muscle strength and lean body mass. A Japanese study involving 232 adult males found that increased skin autofluorescence was associated with lower hand grip and leg extension strength [51, 52]. Additionally, in a cohort of 9,203 Japanese men and women (mean age 58 years), skin autofluorescence showed a negative correlation with BMI [53]. Another study on 1,934 older individuals revealed an adverse association between skin autofluorescence and grip strength, hip strength, and overall muscular strength [53]. However, the use of skin autofluorescence as a proxy for AGE concentrations has been questioned due to factors such as skin pigmentation, application of body lotions, and variations in blood flow [54, 55].

While skin autofluorescence offers a convenient and non-invasive assessment of AGE accumulation, further investigations employing more rigorous measurements of AGE concentrations, such as tissue biopsies and analysis of serum or urinary samples, are necessary to thoroughly examine the impact of AGEs on sarcopenia. Such long-term studies will provide a comprehensive understanding of the influence of AGEs on metabolic and muscular health.

Vascular complications in type 2 diabetes Mellitus: microvascular and macrovascular impact

Long-term hyperglycemia, along with the accumulation of advanced glycation end-products (AGEs), oxidative stress, and inflammation, exerts detrimental effects on skeletal muscle [56, 57]. Like other tissues, skeletal muscles rely on an intact circulatory system to receive oxygen, nutrients, and efficient waste removal. The loss of muscle mass and strength is strongly associated with decreased mobility, an elevated risk of falls and fractures, impaired physical function, and an increased dependency on assistance. In individuals with type 2 diabetes mellitus (T2DM), both microvascular and macrovascular complications further contribute to these issues.

Microvascular complications

Type 2 diabetes mellitus (T2DM) is known to give rise to microvascular complications, including retinopathy, neuropathy, and nephropathy. The destruction of muscle nerve cells leads to a decrease in contractility and muscle strength. Notably, a study has demonstrated that individuals with type 2 diabetes and neuropathy, aged over 50, exhibit lower knee extension strength [58]. Furthermore, nerve damage contributes to muscle atrophy [59], ultimately resulting in impaired muscle function and restricted movement. In a cross-sectional study involving 2,364 older individuals (aged 73–82 years), a negative correlation was observed between gait, standing balance ratio, and peripheral nerve function [60]. Remarkably, T2DM patients exhibited poorer physical performance compared to controls, even after controlling for peripheral nerve function [60].

While diabetic retinopathy may not have an immediate impact on muscle function, it can affect eyesight, which is crucial for maintaining balance during movement and other physical activities [61]. Researchers have found that individuals with T2DM and diabetic retinopathy have an increased likelihood of experiencing falls compared to those without diabetes [61]. Furthermore, individuals with mild or severe non-proliferative diabetic retinopathy are more prone to falls [61]. Falls are responsible for 75% of injury-related deaths worldwide [62] and result in substantial healthcare expenditures [63].

Recent investigations have also highlighted the relationship between diabetic retinopathy, sarcopenia, and quality of life, taking into consideration the body mass index (BMI) [61]. Chronic kidney disease (CKD) associated with diabetes exacerbates muscular atrophy [64]. Notably, the Asian Working Group for Sarcopenia (AWGS) reported that 387 older Asians with T2DM and diabetic nephropathy have a 2.5 times higher prevalence of sarcopenia [65]. Sarcopenia has been linked to more severe CKD and can serve as a predictor of mortality in CKD patients [66, 67]. CKD can induce sarcopenia through various mechanisms, such as mitochondrial dysfunction, inflammation, protein loss, and impaired vitamin D production. The glomerular filtration rate (GFR) has been found to correlate with lean body mass [68]. Moreover, CKD leads to a reduction in muscular and respiratory capacity, potentially contributing to the development of sarcopenia. In muscle samples from individuals with stage 5 CKD, a decrease in mitochondrial volume density has been observed [69]. Enhancing muscle mass and promoting mitochondrial synthesis may help reduce mortality rates in this population.

Macrovascular complications

The development of atherosclerosis is a significant macrovascular complication associated with T2DM, and individuals with T2DM appear to experience a more rapid progression of this condition. Metabolic dysfunction contributes to the worsening of atherosclerosis. In a study involving hypertensive Turkish adults over 18 years without T2DM, researchers discovered an inverse relationship between a lower percentage of body fat and a higher percentage of skeletal muscle with hypertension and retinopathy [70]. While high blood pressure has been linked to organ damage in previous studies, this particular study did not find a correlation between serious mental illness (SMI) and high blood pressure. Nevertheless, there is evidence suggesting that muscle mass can influence blood pressure, and it is possible that myocytes are susceptible to damage in the presence of hypertension. The deletion of myostatin, a protein that inhibits muscle growth, leads to increased muscle mass and reduced blood pressure. However, it is challenging to determine whether an increase in muscle mass would produce similar vascular benefits in humans, as exercise is currently the primary method for enhancing muscle mass. Therefore, there is an ongoing debate about whether the positive effects of exercise on vascular health are primarily attributed to gains in muscle mass or if other favourable effects of exercise play a crucial role, considering that gains in muscle mass are an incidental outcome of the exercise. Macrovascular complications affect approximately one-quarter of individuals with diabetes, further emphasizing the health risks faced by this population.

In individuals aged 60 and older, strength in lower hip extension, knee flexion, and hip flexion has been associated with the ankle-brachial index, an indirect and non-invasive indicator of peripheral arterial disease (PAD) [57]. Moreover, it has been observed that individuals affected by PAD exhibit slower walking speeds in their later years compared to their peers without PAD at the same age [71]. Ischemia resulting from reduced blood flow, a characteristic feature of PAD, can lead to decreased muscle strength and compromised performance [72]. Additionally, the discomfort associated with PAD may discourage individuals from engaging in regular exercise, which can have adverse effects on muscle health. Consequently, individuals with T2DM are exposed to a significant health risk due to the consequences of sarcopenia, which encompass alterations in muscle composition and function.

Impact of intermuscular adipose tissue (IMAT) on type 2 diabetes Mellitus (T2DM) and Sarcopenia

Sarcopenia, a condition often overlooked, encompasses various aspects affecting muscle quality. Advanced age is associated with several neuromuscular changes that contribute significantly to reduced force production [73]. These changes include the accumulation of adipose tissue within and between muscles, as well as normal muscle atrophy. Intermuscular adipose tissue (IMAT), also known as ectopic fat deposition, has been implicated in metabolic and muscle health impairments [74–76]. Elevated levels of IMAT have been observed in the thighs of individuals with obesity and type 2 diabetes compared to healthy individuals without these conditions [77].

Research has demonstrated a negative correlation between calf IMAT and insulin sensitivity in overweight or obese individuals without diabetes, utilizing gold-standard techniques such as magnetic resonance imaging (MRI) and glucose clamp [78, 79]. The authors of the study suggested that IMAT may exacerbate insulin resistance and related conditions [80]. The presence of non-contractile IMAT within the skeletal muscle can lead to alterations in the elastic properties of the muscle [81]. Undoubtedly, IMAT plays a significant role in the intricate relationship between sarcopenia and T2DM in the elderly population. Therefore, IMAT should be considered a primary outcome measure in future interventional studies investigating this subject. Furthermore, the deficits in muscular function experienced by patients with type 2 diabetes mellitus may contribute to prolonged periods of inactivity, compounding the impact of the disease.

Management and prevention strategies for type 2 diabetes mellitus (T2DM) and Sarcopenia

Glucose-lowering medications are commonly employed in the treatment of T2DM. While the impact of most of these medications on the various aspects of sarcopenia remains uncertain, some evidence suggests potential effects on muscle mass. Metformin, a commonly used medication, has been shown to inhibit muscle growth by targeting the molecular target of rapamycin and increasing AMP-activated protein kinase activity [82, 83].

In a subset of users, sulfonylureas have been associated with muscular atrophy, although this association has not been investigated through randomized clinical trials [84]. Table 1 provides an overview of the potential effects of glucose-lowering medications on body weight and muscle

Table 1 Treatments for people with sarcopenia in diabetes mellitus

Study	Design	Duration	Exercise intervention	Sarcopenic marker	T2DM marker
Mitranun et al., 2014 (90)	A randomized controlled experiment with two groups Patients with diabetes (50–70 years) 16 males and 29 females total Breaking Continual AT Down Into Intermittent AT	12 weeks	3 sessions/week AT: 30–40 min walking	Strength in the thighs and calves has improved dramatically for both The upper-body power has not changed noticeably.	Reductions in fasting glucose concentration and insulin resistance were statistically significant across both workout groups. HbA1c drops substantially during the interval AT.
Tan et al., 2015 (91)	Trial with Randomized Subjects people above the age of 60 with diabetes 13 males and 12 females total There are 2 categories: CT and CON.	6-month	Three times a week CT: 30 min of moderate AT, followed by 10 min of RT	Leg muscle strength significantly increased in the CT group.	For the CT group, there was a notable rise in 6-MWD.
Egger et al., 2013 (92)	A controlled experiment with parallel groups Patients with diabetes (median age 64.8, standard deviation 7.8 years; n = 13 males and 19 women) Consisting of two groups (CON and Hypertrophy CT/Endurance CT)	8 weeks	7 meetings a week Exercise for muscle growth: 10–12 reps at 70% of one's one-repetition maximum (RM); aerobic training for one hour every day To improve your endurance, you should perform the following CT protocol: RT: 25–30 repetitions, 40% 1-RM; AT: 1 h daily.	Both groups showed a notable rise in muscle strength and mass.	The level of HbA1c did not significantly shift. Rapid decreases in both fasting glucose and fructosamine
Chen et al., 2017 (93)	Trial with Randomized Subjects Sarcopenia patients who were overweight (aged 65+) = 60 Classes: AT, RT, CT, and CON	12 weeks	RT: 60–70% Overhead, one repetition maximum, three sets 8–10 sets, twice weekly Time Commitment: 1 h, Twice Weekly Physical Therapy: Once Weekly CT Sessions AT, once weekly RT	AT, RT and CT beat CON in muscle mass and strength improvements.	RT outperformed AT, CT, and CON in grip strength at weeks 8 and 12. At week 8, RT and CT had higher IGF-1 concentrations than AT and CON. In Week 12, the four groups were similar.
Lustosa et al. 2011 (94)	A controlled, randomized, crossover trial Women over 65 living in the community at risk for developing frailty were split into two groups (RT and CON), totaling 322.	10 weeks	Three times a week for one repeat at 75% of one's maximum effort, eight times.	The TUG, the 10-minute walk, and the muscle strength of the knee extensors all saw significant increases.	Not measured
Latham et al., 2013 (95)	Frail patients (> 65) were randomly assigned to RT, CON, Vitamin D, and placebo groups.	10 weeks	RT 60–80% 1-RM	Both the TUG and MWD tests yielded insignificant results. Musculoskeletal injuries were somewhat more likely to occur after exercise.	Not measured
Terada et al., 2013 (96)	Diabetic individuals were randomly assigned to two parallel groups (55–75 years) Eight men and seven women make up the total population of 15. Two classes: continuous and intermittent AT	12 weeks	Five times a week, for a total of 20 h AT high-intensity interval exercise	Not measured	The first measurements showed no significant change in HbA1c or fasting blood glucose levels.

mass in T2DM; however, studies exploring the interplay between these variables and their impact on human health are lacking.

Effective management and prevention strategies for T2DM and sarcopenia require further research to elucidate the optimal treatment approaches and their impact on muscle-related parameters. Future studies should focus on

understanding the complex interactions between glucose-lowering medications, muscle mass, and the multifaceted aspects of sarcopenia to guide evidence-based interventions in clinical practice.

Testosterone supplementation

Testosterone supplementation has been investigated as a potential intervention to address the muscle loss associated with sarcopenia. Transdermal testosterone gels have demonstrated the ability to increase serum androgen concentrations, thereby exerting anabolic effects on skeletal muscle [85]. Clinical trials focusing on Selective Androgen Receptor Modulators (SARMs) have also reported positive outcomes in terms of body composition and functional capacity [86, 87]. Furthermore, the inhibition of myostatin, a negative regulator of muscle growth, through myostatin blockades has shown promise in animal models, leading to significant increases in skeletal muscle hypertrophy [88, 89]. However, further research is necessary to establish the safety and efficacy of these interventions before their widespread use in humans.

It is important to note that interventions aimed at improving muscle mass, quality, and function may indirectly enhance metabolic health. However, the precise impact of these interventions on overall health outcomes requires additional investigation. While lifestyle changes, such as exercise, will likely remain the cornerstone of therapy for managing both T2DM and sarcopenia, anti-diabetic medications and other lifestyle factors can also modify the risk of developing sarcopenia in individuals with diabetes. Figure 4 illustrates the use of anti-diabetic medications in the context of sarcopenia among individuals with diabetes.

Physical activity and exercise

Physical activity plays a crucial role in the prevention and management of both T2DM and sarcopenia. Adopting a more physically active lifestyle can not only delay the onset of T2DM but also potentially lead to complete remission of the condition [97, 98]. Studies comparing lifestyle interventions with standard diabetes support and education have demonstrated that approximately 12% of individuals who engaged in lifestyle interventions experienced partial or

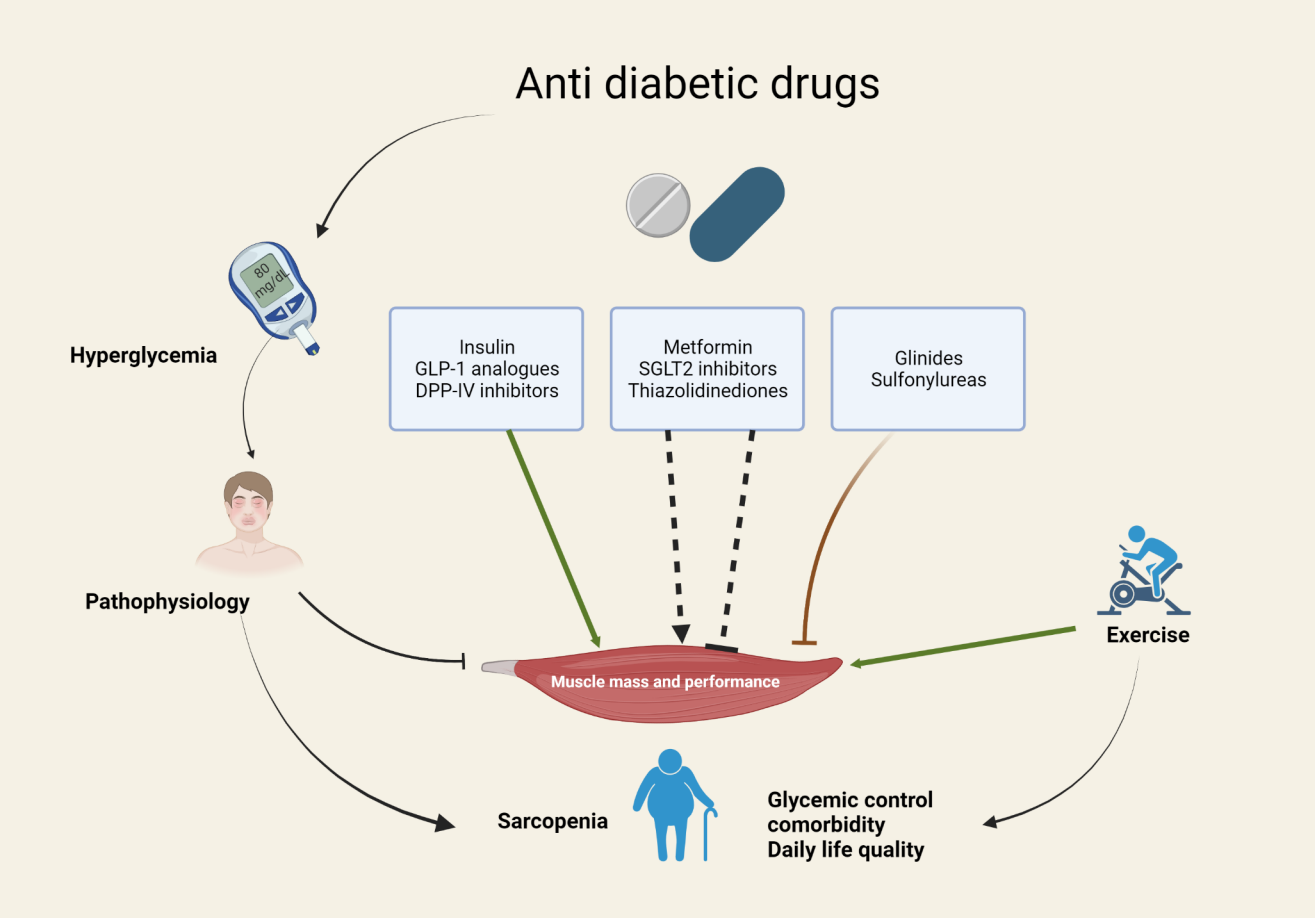

Fig. 4 Anti-diabetic medications play a role in controlling muscle size and function in people with diabetes
DPP-IV, glucagon-like peptide-1 (GLP-1), and sodium-glucose cotransporter 2 (SGLT-2)

complete remission of T2DM [98]. Furthermore, engaging in regular physical activity has been shown to reduce the incidence of sarcopenia in individuals aged 40 and above, as indicated by a meta-analysis [99].

Long-term follow-up studies have revealed additional benefits of lifestyle interventions in individuals with T2DM. Participants who engaged in a lifestyle intervention demonstrated improved lower-limb function and a reduced risk of impaired gait speed after 11 years [100]. In a study involving 2,208 adults with T2DM, supervised aerobic and strength training proved to be more effective than no exercise in reducing HbA1c levels. Moreover, overweight older individuals who combined resistance and aerobic training experienced a 21% increase in physical performance compared to those who performed either type of exercise alone. This enhancement can be attributed to the preservation of muscle mass and strength achieved through combined training [100].

Furthermore, for overweight or obese individuals intentionally seeking weight loss over an 18-month period, a combination of resistance training and calorie restriction led to less loss of lean mass compared to other interventions [100]. Therefore, physical activity and exercise interventions hold significant potential for managing T2DM and mitigating the impact of sarcopenia. These interventions should be tailored to individual needs and preferences to maximize their effectiveness in improving metabolic health and preserving muscle mass and function.

Nutritional and dietary strategies

Proper dietary strategies play a crucial role in the management of T2DM and sarcopenia. While weight loss is beneficial for T2DM, it can promote muscle atrophy [101]. Therefore, it is important to consider the impact of dietary restrictions on muscle health. During calorie restriction, low protein intake and inadequate loading may contribute to muscle loss. Protein is vital for muscle building and maintenance, and the recommended dietary intake (RDI) of protein for older adults in many countries is 0.8 g/kg/day [102–104].

Studies have demonstrated the significance of protein intake in relation to muscle mass preservation and the risk of T2DM. Older individuals in the highest protein consumption quintile (1.20 g/kg/day) experienced approximately 40% less loss of appendicular lean mass (ALM) and total lean mass (TLM) over a three-year period [105]. Furthermore, the quality of protein consumed can affect the risk of T2DM. The Melbourne Collaborative Cohort Study (MCCS) and a meta-analysis have indicated increased risk ratios for incident T2DM in the highest categories of animal and total protein intake. Conversely, high consumption of protein were associated with a decreased risk of T2DM [106]. The MCCS cohort study specifically found a decreased risk of T2DM in women (n = 21,523). For individuals at risk of T2DM over the age of 50, incorporating plant-based protein sources into their diet may be beneficial. Although plant proteins have lower anabolic properties compared to animal proteins, strategies such as improving amino acid profiles and combining different plant-based protein sources can enhance their effectiveness [107].

In older individuals, protein supplementation combined with resistance training has shown promising results in terms of muscle outcomes, although the effects may vary. A study by Morton et al. demonstrated that protein supplementation improved lean mass in resistance-trained individuals but had limited impact on older persons [108]. Another meta-analysis indicated that protein intakes exceeding 1.6 g/kg/day did not significantly enhance lean body mass. Moreover, only 3 out of 12 randomized controlled trials showed that protein supplementation combined with exercise increased muscle growth and strength in sarcopenic older adults [109]. Nevertheless, adequate protein intake is important for muscle maintenance, growth, and metabolism.

Role of vitamin D and Omega-3 in metabolic and muscular health

Vitamin D, an important hormone, plays a significant role in muscle and metabolism. Insufficient levels of vitamin D have been linked to impaired metabolism [110–111]. The presence of vitamin D receptors in skeletal muscle and the pancreas suggests that this hormone regulates glucose and muscle function. However, a randomized controlled trial involving aged individuals administering 800 IU/day of vitamin D showed no significant effect on lower-extremity power, strength, or lean mass when vitamin D levels were 8 and 20 ng/mL [112].

Meta-analyses have indicated that vitamin D supplementation can enhance muscle strength, but this effect seems to be limited to individuals with adequate 25(OH) D levels. Combining vitamin D supplementation with exercise has demonstrated small improvements in lower limb muscle strength, as shown in a meta-analysis by Antoniak and Greig [113]. Nevertheless, due to the limited number of studies included in the meta-analysis, further research is needed to better understand the potential benefits of vitamin D supplementation in conjunction with exercise. Additionally, clinical studies are warranted to investigate the impact of vitamin D on muscle health in individuals with T2DM and sarcopenia who have vitamin D deficiency.

Although vitamin D supplementation does not appear to increase insulin sensitivity in individuals with type 2 diabetes and vitamin D deficiency (25(OH)D < 50 nmol/L), it

does affect glucose management in patients with prediabetes and diabetes but not in individuals without these conditions [114–118]. The effects of vitamin D supplementation on glucose metabolism, particularly in larger populations with T2DM and non-T2DM individuals who have moderate to severe vitamin D insufficiency (25(OH)D), require further exploration, including whether these effects are specific to individuals with poorer metabolic health.

Omega-3 supplements, either alone or in combination with exercise, have shown potential in improving metabolic and muscular health. These supplements have been found to enhance muscle protein synthesis and reduce systemic inflammation. In a study involving postmenopausal women, omega-3-rich fish oil supplementation for 6 months improved gait speed [119]. Another study demonstrated that omega-3 fatty acid treatment increased thigh muscle volume, handgrip strength, and composite 1 repetition maximum muscular strength over a 6-month period [120]. While omega-3 supplements alone may not significantly improve muscle health in older individuals [121], combining them with exercise has shown promising effects. In a 12-week resistance training study with older men, alpha-linolenic acid (ALA) supplementation increased knee flexor muscle thickness and reduced IL-6 levels (mean age 64 years) [122]. However, further investigation is needed to determine the most effective omega-3 supplement and dosage for treating sarcopenia and slowing the aging process.

Regarding metabolic health, the benefits of omega-3 supplements appear to be modest, if any. Limited evidence suggests minimal or negligible effects on fasting glucose, insulin resistance, and T2DM. Further studies focusing on well-defined populations, particularly those with dietary deficits, are necessary to elucidate the impact of nutritional interventions on both metabolic and muscular health.

Challenges and strategies in sarcopenia diagnostics and therapies implementation in healthcare institutions

Healthcare institutions vary considerably in their inclination and capacity to embrace innovative practices and procedures [123]. Overcoming these change barriers and effectively implementing diagnostics and therapies for sarcopenia requires addressing three primary components. The transformation process involves three stages: (i) initial success, (ii) change maintenance, and (iii) dissemination. Achieving successful practice alteration necessitates obtaining buy-in from all relevant stakeholders and comprehending the obstacles specific to the organizational setting.

Addressing Change Barriers: To overcome the challenges associated with introducing new procedures, active involvement and education of stakeholders, including the multidisciplinary team, operational personnel, logistics staff, and patients, are crucial for supporting the justification for change [124]. Adequate time should be allocated for planning and piloting the new procedure with key individuals before its implementation.

Educating and Raising Awareness: Healthcare providers and patients/caregivers require education, training, and awareness campaigns to elevate the importance of sarcopenia and weakness as critical aspects of acute treatment. Screening and identifying sarcopenia and weakness in patients, followed by appropriate instructions on managing these conditions, are imperative [125]. The selection of sarcopenia screening and diagnosis technologies should consider their validity, reliability, and practicality.

Sustaining Change for Long-term Success: The long-term enhancement of patient care depends on the ability to maintain newly implemented practices. As more healthcare organizations adopt environmentally friendly procedures, a positive transformation in company culture can be observed [126–127]. Canada's research on the sustain and spread approach has demonstrated its utility in promoting a shift in attitudes toward nutrition treatment and its beneficial effects on patients. This framework holds the potential for disseminating knowledge on sarcopenia. Sustaining these changes and disseminating knowledge through appropriate frameworks can further enhance the adoption of innovative practices in healthcare settings.

Diagnostic techniques, and assessment strategies for sarcopenia in the hospital setting

The assessment and diagnosis of sarcopenia in the hospital setting pose significant challenges due to a myriad of factors involving the hospital infrastructure, healthcare providers, patients, and caregivers [128]. These challenges include a lack of qualified personnel, inadequate allocation of resources, and deficiencies in communication, all of which can impede the accurate diagnosis and treatment of sarcopenia [129]. Furthermore, patients and caregivers often have limited awareness and understanding of sarcopenia, its management, and their role in care planning, leading to suboptimal adherence to evidence-based therapies [130].

Recognizing the inherent complexities of care coordination and provision is paramount to ensuring the effective management of sarcopenia. A collaborative approach involving the interdisciplinary clinical team, management personnel, logistical staff, and service delivery personnel within the hospital is essential to provide optimal care for patients with sarcopenia. It is imperative to foster effective communication and coordination among these stakeholders to overcome the challenges associated with sarcopenia assessment and diagnosis.

Furthermore, current evidence provides limited support for the notion that outsourcing public services to private companies, such as privatizing hospital operations, leads to improved patient outcomes in the context of sarcopenia [131]. Additionally, anxiety may be experienced by both management and clinical staff, which can be either generalized or situation-specific, depending on the urgency of care needs. The lack of a sense of urgency, combined with a dearth of clinical expertise or clear guidelines, can contribute to heightened levels of anxiety among healthcare professionals [132].

Given the dynamic nature of the field and the ongoing debates surrounding the definition, diagnosis, and treatment of sarcopenia, it is understandable that uncertainties persist. It is crucial for healthcare professionals involved in sarcopenia care to stay abreast of the latest literature and research advancements to enhance their knowledge and address these uncertainties effectively. By promoting interdisciplinary collaboration, improving resources and communication, and ensuring a comprehensive understanding of sarcopenia among patients and caregivers, hospitals can strive towards providing optimal care for individuals affected by sarcopenia in the hospital setting.

Techniques for assessing lean body Mass (LBM)

Imaging techniques

In the hospital setting, the assessment of lean body mass (LBM) for sarcopenia requires the utilization of various diagnostic techniques. Imaging techniques such as magnetic resonance imaging (MRI), computed tomography (CT), bioimpedance analysis (BIA), and dual-energy X-ray absorptiometry (DXA) are commonly employed methods. MRI and CT scans are convenient and offer reduced variability related to volume status, making them frequently used for evaluating skeletal muscle mass in cirrhotic patients [133]. However, BIA, which considers total body water, may underestimate muscle mass in individuals with cirrhosis and volume overload.

Anthropometric measurement techniques

Anthropometric measurement techniques also play a role in assessing LBM in sarcopenia. Measurements such as mid-upper arm circumference (MUAC), skinfold thickness, and calf circumference [134] can be utilized to estimate muscle mass. MUAC shows a strong correlation with total protein stores in the body, while skinfold thickness measurement provides an approximate estimation of body fat. Calf circumference, which is considered the most accurate anthropometric measurement, has demonstrated its predictive value for physical performance and survival. However, anthropometry has limitations due to potential human error, changes in skin elasticity, age-related body mass alterations, and variations in user skills, making it less precise compared to other methods.

Muscle Strength Measurement

Assessing muscle strength is another crucial aspect of diagnosing sarcopenia. Reliable methods for measuring muscle strength include handgrip strength and the chair stand test. Handgrip strength, evaluated using a dynamometer, serves as an indicator of lower extremity strength (135–136). The chair stand test measures the time required for a patient to perform five chair stands and serves as a surrogate for quadriceps strength. Additionally, the number of chair stands a patient can complete in 30 s is recorded as a timed test. These measurements provide valuable insights into muscle strength and overall functional capacity.

Physical Performance Measurements

Assessing physical performance is crucial in the evaluation of sarcopenia. Reliable methods such as the Short Physical Performance Battery (SPPB) and the Stair Climb Power Test (SCPT) are commonly used. The SCPT is a simple method that evaluates leg strength by having the patient ascend a set of stairs. While stairs are readily available and cost-effective in most healthcare settings, they may pose challenges for weak and deconditioned patients. The Timed "Get Up and Go" test (TGUG) assesses muscular speed, and the SPPB evaluates a patient's leg function through various measures.

Blood-based biomarkers

Blood-based biomarkers have garnered significant attention in the field of sarcopenia identification and prognostication, with potential candidates including insulin-like growth factor-1 (IGF-1), myostatin, and inflammatory markers such as C-reactive protein (CRP). These biomarkers hold promise in facilitating the detection of sarcopenia and predicting adverse outcomes in affected individuals. Circulating levels of IGF-1, a powerful regulator of muscle growth and maintenance, have been linked to the pathophysiology of sarcopenia and may be useful in evaluating muscle mass and function [137]. Similarly, myostatin, a negative regulator of muscle growth, has demonstrated associations with muscle wasting and loss of strength, making it a potential biomarker for sarcopenia assessment [138]. Furthermore, inflammatory markers like CRP, reflecting systemic inflammation, have been linked to muscle wasting and impaired muscle function in various clinical contexts. While these

blood-based biomarkers show promise, further comprehensive research is necessary to determine their precise clinical utility in routine hospital settings, thus paving the way for the development of targeted interventions and personalized management strategies for sarcopenia patients.

Conclusion

The coexistence of type 2 diabetes mellitus (T2DM) and sarcopenia mutually influences their development, with T2DM exhibiting characteristics such as inflammation, insulin resistance, heightened oxidative stress, accumulation of advanced glycation end-products (AGEs), and vascular dysfunction, all of which can significantly impact muscle health. While several lifestyle interventions have shown improvements in functional and metabolic health for individuals with T2DM and sarcopenia, evidence for the most effective and feasible therapy remains limited. Sarcopenia, a gradual decline in muscle mass and function associated with aging, can be partially prevented and treated through healthy lifestyle choices encompassing diet, exercise, and other factors. Hence, it is crucial to identify the underlying pathogenic factors and clinical characteristics that influence treatment options, aiming for effective management. The focus of future research should revolve around defining therapeutic approaches and developing effective therapies for sarcopenia in the context of chronic illnesses, with emphasis on diagnosis, evaluation, and treatment of neuromuscular, musculoskeletal, and functional impairments, ultimately restoring and sustaining patients' previous levels of functioning and quality of life.

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Declarations

This paper is devoid of any conflict of interest.

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