



Advances in Pathogenesis, Risk Factors, and Intervention Strategies of Sarcopenia in Older Adults with Type 2 Diabetes Mellitus

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ABSTRACT

With the progressive aging of the global population, the comorbidity of type 2 diabetes mellitus (T2DM) and sarcopenia has emerged as a critical public-health challenge among older adults. Sarcopenia is characterized by progressive and generalized loss of skeletal-muscle mass, strength, and physical performance, which substantially increases risks of falls, frailty, disability, hospital admission, and all-cause mortality in older patients with T2DM. Bidirectional interactions exist between T2DM and sarcopenia: insulin resistance, chronic low-grade inflammation, oxidative stress, hormonal dysregulation, and nutritional deficiency jointly accelerate skeletal muscle deterioration, while sarcopenia in turn worsens glycemic homeostasis and amplifies diabetic-related complications. This review aims to summarize current evidence regarding pathogenesis, modifiable and non-modifiable risk factors, as well as multi-modal intervention approaches for sarcopenia in older adults living with T2DM. Limitations of existing studies and directions for future clinical research are also discussed, hoping to provide reference for early screening and comprehensive clinical management of this comorbid condition.

Keywords: *older adults; type 2 diabetes mellitus; sarcopenia; insulin resistance; risk factor; intervention*

1. Introduction

Population aging continues to accelerate worldwide, leading to a rapid surge in age-related chronic diseases and geriatric syndrome. According to the global health and aging report released by the World Health Organization, the proportion of people aged 65 and older is projected to reach 16% of the total global population by 2050, with low- and middle-income countries bearing the most significant growth burden of aging-related comorbidities (World Health Organization [WHO], 2021). Type 2 diabetes mellitus (T2DM) is one of the most prevalent chronic metabolic disorders in geriatric populations, characterized by chronic hyperglycemia, insulin resistance, and long-term multi-organ metabolic damage. Epidemiological investigations have confirmed that nearly one-third of older adults with long-term T2DM exhibit varying degrees of skeletal muscle quality decline, muscle strength loss, and physical function degradation, which significantly differ from ordinary age-related muscle aging (Cruz-Jentoft et al., 2023).

Sarcopenia, a typical geriatric syndrome first proposed in 1989, has been repeatedly revised and standardized in international diagnostic consensus. The latest European Working Group on Sarcopenia in Older People 2 (EWGSOP2) diagnostic framework defines sarcopenia as a progressive, generalized skeletal muscle disorder involving the loss of muscle strength, muscle mass, and physical

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performance, which independently increases the risk of adverse health outcomes in older populations (Cruz-Jentoft et al., 2019). Different from the single aging-induced muscle atrophy, sarcopenia secondary to diabetes presents earlier onset, faster progression, and more severe functional impairment. The EWGSOP2 hierarchical diagnostic system divides sarcopenia into three stages: probable sarcopenia, confirmed sarcopenia, and severe sarcopenia, based on grip strength, muscle quantity, and physical function indicators. This staged classification provides precise clinical stratification criteria for elderly diabetic patients and guides individualized intervention intensity (Locquet et al., 2022).

A large number of meta-analyses and cross-sectional studies have verified that older adults with T2DM have a significantly higher sarcopenia prevalence than age-matched non-diabetic populations. The pooled global prevalence of sarcopenia in community-dwelling elderly T2DM patients ranges from 18% to 42%, while the prevalence rises sharply in hospitalized elderly patients and long-term care residents due to inactivity, disease stress, and insufficient nutritional intake (Wu et al., 2022). Further subgroup analysis shows that the sarcopenia prevalence of elderly T2DM patients aged 80 years and above exceeds 50%, indicating that the oldest-old diabetic population has an extremely high risk of muscle depletion and physical frailty (Zhang et al., 2023).

The coexistence of T2DM and sarcopenia forms a vicious bidirectional disease cycle, which seriously worsens the long-term prognosis of elderly patients. Clinical outcome studies have confirmed that diabetic patients complicated with sarcopenia have significantly higher risks of falls, fragility fractures, activities of daily living impairment, cognitive function decline, unplanned hospital readmission, and all-cause mortality (Han et al., 2024). In addition to individual physical function damage, this comorbid state also brings enormous socioeconomic pressure to the global healthcare system. It prolongs hospital stay, increases rehabilitation costs, improves long-term care dependence, and reduces the quality of life of elderly diabetic patients, resulting in a continuous increase in social medical burden (Batsis et al., 2021).

At present, the clinical management of elderly T2DM patients worldwide still focuses on glycemic control, blood lipid regulation, and complication prevention. Muscle health assessment, sarcopenia screening, and muscle function intervention are widely ignored in routine outpatient and inpatient management systems. Existing international diabetes guidelines have not yet formulated unified mandatory screening standards for diabetic sarcopenia, resulting in widespread underdiagnosis and missed diagnosis in primary care and geriatric diabetes management (Leenders et al., 2022). Compared with single diabetes or single sarcopenia, the comorbid mechanism of T2DM and sarcopenia is more complex, involving metabolic disorder, inflammatory response, cell signal abnormality, and multi-organ interaction. Therefore, systematically sorting out the latest research progress of its pathogenesis, risk factors, and multimodal intervention strategies is of great significance for optimizing the comprehensive management system of geriatric diabetes, delaying frailty progression, and reducing adverse clinical events. Based on the latest domestic and foreign basic experiments, clinical cohort studies, and meta-analysis evidence, this review comprehensively elaborates the research status of diabetic sarcopenia in the elderly, analyzes existing research deficiencies, and prospects future research directions, aiming to provide standardized theoretical references for clinical prevention and treatment.

2. Pathogenesis of sarcopenia in older adults with type 2 diabetes mellitus

The occurrence and progression of sarcopenia in elderly T2DM patients are not caused by a single factor but result from the overlapping and interaction of multiple pathological mechanisms including abnormal insulin signal transduction, chronic inflammatory activation, oxidative stress damage, hormonal imbalance, nutritional metabolic disorder, and disuse atrophy. Different from age-related primary sarcopenia, diabetic sarcopenia has unique metabolic molecular pathological characteristics, and its pathological progression is faster and more irreversible. This chapter systematically combs the core molecular and clinical mechanisms of diabetic sarcopenia based on the latest basic and translational medical research.

2.1 Insulin resistance and impaired skeletal-muscle protein turnover

Skeletal muscle is the largest insulin target organ in the human body and undertakes more than 70% of systemic insulin-mediated glucose uptake and disposal. Normal insulin signaling not only maintains systemic glucose homeostasis but also plays a core regulatory role in skeletal muscle protein anabolism and catabolism balance (Bouzakri et al., 2021). In healthy elderly individuals, insulin can activate the PI3K/Akt signaling pathway after binding to muscle cell receptors, upregulate the expression of downstream mTOR protein, promote the synthesis of myofibrillar proteins such as actin and myosin, and inhibit the activation of muscle decomposition pathways, so as to maintain skeletal muscle mass and muscle strength stability. However, elderly patients with T2DM have persistent peripheral insulin resistance, which leads to significant attenuation of insulin anabolic signal transduction in skeletal muscle tissue.

Insulin resistance blocks the phosphorylation activation of PI3K and Akt, resulting in significant downregulation of mTOR pathway activity, which directly inhibits the synthesis of skeletal muscle contractile proteins and reduces muscle anabolism efficiency (Sakuma & Yamaguchi, 2022). At the same time, the inhibitory effect of insulin on the ubiquitin-proteasome system is weakened, and a variety of muscle-specific ubiquitin ligases are abnormally highly expressed, which continuously decomposes mature muscle fibers and accelerates muscle protein loss. In recent years, in-depth basic studies have further confirmed that the autophagy-lysosome pathway is also abnormally activated in insulin-resistant skeletal muscle. Excessive autophagy induces abnormal degradation of normal muscle cell components, destroys muscle cell structure integrity, and further breaks the dynamic balance of muscle protein synthesis and decomposition, forming a triple catabolic damage mechanism of "synthesis inhibition + proteasome decomposition + autophagy degradation" (Wang et al., 2023).

Long-term uncontrolled hyperglycemia in elderly T2DM patients further exacerbates muscle damage through advanced glycation end-products (AGEs) deposition. Continuous high glucose environment induces non-enzymatic glycation reaction of intracellular and extracellular proteins, producing a large number of AGEs, which accumulate in skeletal muscle tissue for a long time and are difficult to metabolize. AGEs can cross-link with muscle structural proteins, change the spatial conformation of muscle fibers, reduce muscle elasticity and contractile function, and cause irreversible damage to muscle ultrastructure (Gautieri et al., 2023). More importantly, AGEs can bind to the receptor RAGE on the surface of muscle satellite cells, inhibit the proliferation, differentiation and activation of satellite cells, damage the muscle stem cell repair and regeneration system, make the damaged muscle tissue unable to be effectively repaired, and eventually lead to continuous muscle mass loss and persistent sarcopenia progression (Sánchez-García et al., 2022).

2.2 Chronic low-grade inflammation and oxidative stress

Elderly T2DM patients are in a persistent state of chronic low-grade systemic inflammation, which is also called "meta-inflammation" in metabolic research. Different from acute inflammatory response caused by infection, diabetic chronic inflammation is characterized by long duration, low inflammatory factor concentration, and continuous tissue damage, which is the core pathological basis of various diabetic chronic complications and muscle degeneration. Hyperglycemia, lipid metabolism disorder, intestinal flora imbalance, and adipose tissue ectopic deposition in elderly diabetic patients can jointly stimulate the continuous secretion of pro-inflammatory cytokines (Pratesi et al., 2021).

A large number of clinical and experimental studies have confirmed that the serum levels of TNF- α , IL-1 β , IL-6 and other pro-inflammatory factors in elderly T2DM patients with sarcopenia are significantly higher than those in simple diabetic patients and healthy elderly people. These inflammatory factors can directly act on skeletal muscle cells, inhibit the proliferation and differentiation of myoblasts, block the formation of new muscle fibers, and induce apoptosis of muscle satellite cells, resulting in the loss of muscle regenerative ability. In addition, inflammatory factors can further aggravate insulin resistance through paracrine and endocrine pathways, forming a vicious cycle of "inflammation $\rightarrow$ insulin resistance $\rightarrow$ more severe inflammation $\rightarrow$ muscle loss" (Pratesi et al., 2021).

Hyperglycemia-induced oxidative stress damage acts synergistically with chronic inflammation to accelerate diabetic sarcopenia. Persistent high glucose stimulation increases the production of intracellular reactive oxygen species (ROS) in skeletal muscle cells.

Excessive ROS exceeds the scavenging capacity of the body's antioxidant system, resulting in oxidative stress state (Miguel-Carrasco et al., 2022). ROS can directly oxidize and modify muscle contractile proteins, damage cell membrane structure, induce mitochondrial dysfunction, and reduce intracellular energy synthesis efficiency. Recent studies have found that oxidative stress can also cause mitochondrial DNA mutation and mitochondrial fission-fusion dynamic imbalance in skeletal muscle cells, resulting in mitochondrial structural damage and functional failure, further aggravating muscle energy metabolism disorder and muscle fiber atrophy (Zepeda et al., 2021).

Notably, inflammation and oxidative stress are mutually reinforcing. Inflammatory activation promotes ROS production, and oxidative damage further stimulates inflammatory factor release, forming a closed pathological loop. This persistent dual damage leads to progressive loss of skeletal muscle mass and strength, and is one of the key irreversible mechanisms of diabetic sarcopenia in the elderly.

2.3 Hormonal alteration

A variety of hormone levels in elderly T2DM patients show abnormal changes with aging and metabolic disorder, which jointly affect skeletal muscle anabolism and catabolism, and participate in the occurrence of sarcopenia. The hormone changes involved in diabetic sarcopenia mainly include sex hormones, growth hormone/IGF-1 axis, vitamin D, dehydroepiandrosterone sulfate, and glucocorticoid metabolism disorder, which together constitute the hormonal regulatory disorder network of muscle atrophy.

Testosterone is the core anabolic hormone of skeletal muscle, which can significantly promote myogenic cell differentiation, accelerate muscle protein synthesis, and inhibit muscle apoptosis. Elderly male T2DM patients have decreased testicular function and reduced testosterone secretion; postmenopausal elderly women lose the protective effect of estrogen, and their muscle anti-atrophy ability is significantly reduced. Clinical studies have confirmed that low testosterone level is an independent risk factor for sarcopenia in elderly diabetic patients, and its reduction degree is positively correlated with muscle loss severity (Basaria, 2022).

The GH-IGF-1 axis is a key pathway regulating skeletal muscle growth and maintenance. Aging and long-term hyperglycemia can inhibit GH secretion and reduce liver IGF-1 synthesis and release, resulting in decreased activity of the GH-IGF-1 signaling pathway. The weakened anabolic signal makes skeletal muscle unable to maintain normal mass and strength, which accelerates the progression of sarcopenia (Jørgensen et al., 2023). Vitamin D insufficiency is extremely common in elderly diabetic populations. Vitamin D receptors are widely distributed in skeletal muscle cells. Vitamin D deficiency can lead to impaired neuromuscular transmission, decreased muscle cell proliferation ability, and reduced physical performance, which is closely related to falls and frailty in elderly diabetic patients (Rejnmark, 2022).

In recent years, emerging studies have found that DHEA-S decline is also closely related to diabetic sarcopenia. DHEA-S has anti-aging and muscle anabolic effects, and its serum concentration decreases significantly with aging and long-term diabetes. Sarcopenic elderly T2DM patients have lower DHEA-S levels than non-sarcopenic patients, but current clinical intervention studies have not confirmed the stable efficacy of DHEA-S supplementation, which needs further prospective verification (Labrie et al., 2021). In addition, elderly diabetic patients are often complicated with multiple chronic diseases. Long-term use of glucocorticoid drugs or endogenous glucocorticoid excess can strongly activate muscle catabolism pathways, inhibit protein synthesis, and induce severe muscle atrophy, which is an easily overlooked important risk factor for clinical diabetic sarcopenia (Schakman et al., 2022).

2.4 Nutritional factors and physical inactivity

Nutritional metabolic disorder and physical inactivity are the most important modifiable pathological mechanisms of diabetic sarcopenia in the elderly, and they interact with metabolic inflammation and insulin resistance to jointly promote muscle loss. Long-term hyperglycemia in elderly T2DM patients can cause diabetic autonomic neuropathy, leading to gastrointestinal peristalsis dysfunction, gastroparesis, early satiety, anorexia and other symptoms, resulting in insufficient daily energy and protein intake (Lee et al., 2023). In clinical practice, most elderly diabetic patients will voluntarily restrict diet and reduce total food intake to control blood sugar strictly.

Excessive dietary restriction often leads to insufficient high-quality protein intake, resulting in protein-energy malnutrition, which directly affects skeletal muscle protein synthesis.

In addition to total nutritional intake, the unreasonable distribution of daily protein intake is also an important cause of poor muscle anabolism in elderly diabetic patients. Studies have shown that even if the total daily protein intake meets the standard, concentrated single-meal protein intake cannot effectively stimulate postprandial muscle protein synthesis, while evenly distributed high-quality protein intake can maximize muscle anabolic response (Moore et al., 2022). Frail elderly diabetic patients are often complicated with oropharyngeal swallowing dysfunction, which further reduces effective nutrient intake and aggravates malnutrition and muscle atrophy (Valech-Brenes et al., 2023).

Physical inactivity forms another major pathological driving factor of diabetic sarcopenia. Elderly T2DM patients are often complicated with diabetic peripheral neuropathy, joint pain, limb numbness, fatigue and other symptoms. In addition, patients' fear of hypoglycemia during exercise leads to long-term sedentary behavior and insufficient daily physical activity. Long-term muscle disuse can inhibit muscle blood circulation, reduce muscle protein synthesis, activate catabolic pathways, and induce disuse muscle atrophy. At the same time, inactivity further reduces insulin sensitivity, aggravates hyperglycemia and metabolic disorder, and forms a self-circulating pathological closed loop of "inactivity → muscle atrophy → worse metabolism → more severe inactivity" (Sinacore et al., 2021).

3. Risk factors for sarcopenia among older adults with T2DM

Based on current epidemiological evidence and clinical cohort studies, the risk factors for sarcopenia in elderly T2DM patients can be scientifically divided into non-modifiable inherent risk factors and modifiable clinical intervention risk factors. Stratified analysis of different types of risk factors is conducive to clinical high-risk population screening, targeted early warning and individualized prevention, which is the key to realizing early intervention of diabetic sarcopenia.

3.1 Non-modifiable risk factors

Advanced age is the primary non-modifiable core risk factor for diabetic sarcopenia. Human skeletal muscle mass begins to decline naturally after the age of 50, with an annual physiological loss rate of 1%–2%. After the age of 70, the muscle aging process is significantly accelerated, and the muscle strength loss is far more serious than the muscle mass reduction (Cruz-Jentoft et al., 2019). For elderly T2DM patients, long-term metabolic damage overlaps with natural aging, resulting in earlier and faster sarcopenia onset than healthy elderly people.

Gender difference is also an important non-modifiable risk factor. A large meta-analysis has confirmed that elderly female T2DM patients have a significantly higher sarcopenia risk than age-matched male patients. Postmenopausal estrogen deficiency in women loses the protective effect on skeletal muscle, reduces muscle anabolism, and increases muscle catabolism sensitivity, making women more susceptible to muscle depletion under diabetic metabolic stress (Meng et al., 2023).

Genetic polymorphism also affects individual susceptibility to diabetic sarcopenia. A variety of single-nucleotide polymorphisms related to inflammatory signaling, muscle fiber type distribution, and glucose metabolism can regulate the severity of muscle loss in elderly diabetic patients. However, current genetic research is still in the exploratory stage, and polygenic risk scoring cannot be applied to routine clinical screening and diagnosis, which is limited to basic research at this stage (Marini et al., 2022; Garatachea et al., 2022).

3.2 Modifiable risk factors

Modifiable risk factors are the key targets for clinical prevention and intervention of diabetic sarcopenia, including diabetes duration, glycemic fluctuation, sarcopenic obesity, ectopic lipid deposition, diabetic microvascular complications, nutritional deficiency, sedentary

lifestyle, polypharmacy and multiple comorbidities (Kalinkovich et al., 2024). Long diabetes duration means long-term cumulative metabolic damage, and the risk of sarcopenia increases significantly with the extension of T2DM course.

Sarcopenic obesity is a unique high-risk phenotype of elderly diabetic patients, which is characterized by simultaneous reduction of skeletal muscle mass and accumulation of body fat. This phenotype has a worse prognosis than simple obesity or simple sarcopenia, and can significantly increase the risk of frailty and death in elderly diabetic patients (Barberio et al., 2022). In addition to systemic obesity, intramyocellular lipid deposition is also an important independent risk factor. Ectopic fat accumulation in skeletal muscle cells can damage insulin signal transduction, reduce muscle contractile function, and aggravate muscle insulin resistance, which further promotes sarcopenia progression (Kitajima et al., 2023).

Diabetic microvascular complications are closely related to muscle loss. Diabetic peripheral neuropathy leads to limb movement dysfunction and reduced activity, indirectly inducing muscle atrophy; diabetic nephropathy and chronic kidney disease cause urea toxin accumulation in the body, which strongly activates muscle catabolism and inhibits protein synthesis, significantly increasing the risk of severe sarcopenia (Ikizler et al., 2022; Shyam et al., 2023). In addition, polypharmacy in elderly multimorbid diabetic patients is also an important potential risk factor. Observational studies have found that long-term use of loop diuretics, proton pump inhibitors and psychotropic drugs is associated with decreased muscle mass, although the causal mechanism has not been fully verified by high-quality clinical evidence (Lapi et al., 2022; Gnjjidic et al., 2021).

4. Multimodal intervention strategies

At present, there is no single specific treatment for diabetic sarcopenia. International guidelines uniformly recommend multi-component comprehensive intervention based on exercise and nutrition, combined with individualized glycemic management and drug optimization. Different single interventions have different limitations, and multimodal superposition can maximize the improvement of muscle mass, muscle strength and physical function of elderly T2DM patients.

4.1 Exercise intervention

Progressive resistance training is recognized as the first-line core intervention for diabetic sarcopenia. It can effectively activate the mTOR anabolic pathway of skeletal muscle, promote muscle fiber hypertrophy, increase muscle mass and muscle strength, and improve physical performance (Landers et al., 2023). Aerobic exercise can improve systemic insulin sensitivity and reduce chronic inflammatory levels, but its effect on increasing muscle mass is limited. A large number of systematic reviews and meta-analyses have confirmed that combined resistance and aerobic exercise training has the best comprehensive benefit for elderly T2DM-sarcopenia patients, which can simultaneously improve metabolism and muscle function (Alcántara-Aragón et al., 2022).

For frail elderly patients who cannot participate in centralized supervised training, home-based standardized progressive resistance training is a safe, feasible and effective alternative intervention mode, which is suitable for long-term popularization in community and family scenarios (O'Brien et al., 2023). International geriatric exercise guidelines recommend 2–3 times of resistance training per week, targeting major limb and trunk muscle groups, with gradual load progression to avoid exercise injury and hypoglycemia risk (Izquierdo et al., 2021). At the same time, balance training should be matched to reduce the fall risk of sarcopenic elderly patients.

4.2 Nutritional intervention

Scientific nutritional intervention is the cornerstone of muscle repair and regeneration in diabetic sarcopenia patients. The PROT-AGE international expert consensus recommends that elderly sarcopenic diabetic patients intake 1.2–1.6 g of high-quality protein per kilogram of body weight per day, and evenly distribute the protein in three meals to optimize postprandial muscle protein synthesis response (Bauer et al., 2020). A single meal intake of 25–30 g high-quality protein can maximize muscle anabolic stimulation in the elderly (Moore et al., 2022).

Nutritional intervention should also pay attention to total energy balance and micronutrient supplementation. Excessive calorie restriction must be avoided to prevent malnutrition and muscle loss. For patients with vitamin D deficiency, standardized supplementation is required to improve neuromuscular function (Rejnmark, 2022). Malnutrition risk screening should be carried out regularly by using authoritative assessment tools such as ESPEN standards to realize early nutritional intervention (Cederholm et al., 2023). For elderly patients with poor oral intake, oral nutritional supplements can be appropriately supplemented, but the targeted evidence for diabetic sarcopenia population is still insufficient (Milne et al., 2021).

4.3 Pharmacological and glycemic-management considerations

Up to now, no drugs have been officially approved by international regulatory agencies for the specific treatment of sarcopenia. All clinical drug interventions are auxiliary management based on primary diseases and comorbidities. For elderly T2DM patients complicated with sarcopenia, the core principle of glycemic management is to avoid recurrent hypoglycemia and excessive weight loss, and prioritize the stability of body composition and muscle function (American Diabetes Association [ADA], 2024).

Different hypoglycemic drugs have different effects on skeletal muscle and body composition. SGLT2 inhibitors have a certain weight loss effect, which may cause muscle mass loss in frail elderly patients. Clinicians need to dynamically monitor body composition changes during medication (Basu et al., 2023). Drugs with significant weight loss effect should be used cautiously in sarcopenic elderly diabetic patients, and drugs with neutral or beneficial effects on body composition should be preferred on the premise of meeting glycemic control targets (Sinha et al., 2023). Testosterone replacement therapy has potential cardiovascular risks and is not recommended for routine clinical application (Basaria, 2022). A variety of new muscle anabolic drugs are still in preclinical and early clinical research stages, and there is no mature clinical application evidence.

4.4 Comprehensive multi-component intervention

Single exercise or nutritional intervention has obvious limitations in clinical real-world application, and it is difficult to achieve continuous and stable muscle function improvement. Multi-component comprehensive intervention integrating resistance exercise, nutritional optimization, individualized glycemic control and fall prevention education is the most effective clinical management mode at present (Dent et al., 2023). Multidisciplinary teams composed of endocrinologists, geriatricians, rehabilitation therapists and clinical dietitians can provide whole-process individualized management for elderly patients, which significantly improves the intervention effect of diabetic sarcopenia.

However, there are many practical barriers to the popularization of multi-component intervention in clinical practice, including insufficient medical manpower, tight clinical time, poor long-term patient adherence, and imperfect medical reimbursement policies, which restrict the large-scale application of standardized multi-disciplinary intervention programs in primary medical institutions (Müller et al., 2022).

5. Existing research limitations and future perspectives

Although the research on diabetic sarcopenia has made rapid progress in recent years, the overall research system is still imperfect, and there are many deficiencies in clinical evidence, standardized diagnosis and treatment, and translational application. First of all, most of the existing clinical evidence comes from observational cross-sectional studies and small-sample cohort studies, and high-quality, large-sample, multi-center randomized controlled trials targeting elderly T2DM-sarcopenia population are still very scarce, resulting in low level of clinical evidence (Han et al., 2024).

Secondly, there is no unified screening, diagnosis and intervention standard for diabetic sarcopenia in the world. Different studies adopt different diagnostic criteria, inclusion and exclusion criteria, and intervention schemes, resulting in high heterogeneity of existing research results, which is not conducive to the formulation of unified clinical guidelines. In addition, the long-term adherence of elderly

patients to exercise and nutritional intervention is poor in real clinical scenarios, which affects the actual intervention effect. At present, few studies have carried out cost-effectiveness analysis of intervention measures, which hinders the transformation of research results into public health policies (Kalinkovich et al., 2024).

Future research directions should focus on the following aspects: carrying out high-quality randomized controlled trials to compare the efficacy of different multi-component intervention schemes; developing simple, fast and low-cost screening tools suitable for primary medical institutions to realize early screening of high-risk groups; carrying out long-term longitudinal cohort studies to clarify the causal molecular mechanism of diabetic sarcopenia; evaluating the health economic value of comprehensive intervention programs; comparing the intervention effects of home-based and hospital-based intervention modes; and exploring peripheral blood myokines and novel biomarkers for early diagnosis of diabetic sarcopenia (Guisado-Barrios et al., 2022).

6. Conclusion

Sarcopenia is a common, serious and easily overlooked comorbidity in elderly patients with type 2 diabetes mellitus. Its pathological mechanism is complex and diverse, involving the superposition and interaction of insulin resistance, chronic low-grade inflammation, oxidative stress, multi-hormonal imbalance, nutritional metabolic disorder and long-term physical inactivity. A variety of modifiable and non-modifiable risk factors jointly affect the occurrence and development of diabetic sarcopenia. At present, progressive resistance exercise combined with standardized high-quality nutritional support is the core intervention measure for diabetic sarcopenia, supplemented by individualized precise glycemic management and multidisciplinary comprehensive intervention. Early screening, early identification and standardized comprehensive management can effectively delay muscle loss, reduce the incidence of falls, disability and death, and improve the long-term prognosis and quality of life of elderly diabetic patients. In the future, more high-quality clinical and basic research is needed to further clarify the pathological mechanism, optimize targeted intervention strategies, and promote the transformation of research evidence into standardized primary clinical management procedures, so as to build a complete prevention and treatment system for elderly diabetic sarcopenia.

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