World Journal of Biology Pharmacy and Health Sciences
eISSN: 2582-5542
Cross Ref DOI: 10.30574/wjbphs
Journal homepage: https://wjbphs.com/

(REVIEW ARTICLE)

Muscle health and type 2 diabetes mellitus: A comprehensive review of sarcopenia, inflammation, and nutritional interventions

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World Journal of Biology Pharmacy and Health Sciences, 2026, 26(03), 371-377

Publication history: Received on 17 May 2026; revised on 24 June 2026; accepted on 26 June 2026

Article DOI: https://doi.org/10.30574/wjbphs.2026.26.3.0371

Abstract

Emerging evidence suggests that skeletal muscle health plays a critical role in glucose metabolism and the development of type 2 diabetes mellitus (T2DM). While low muscle mass and low muscle strength have individually been linked to diabetes, findings regarding their independent and combined effects remain inconsistent. Recent studies have also highlighted the roles of muscle quality, sarcopenia, sarcopenic obesity, and chronic inflammation in diabetes risk. This review aims to examine the associations of muscle mass, muscle strength, muscle quality, sarcopenia, and sarcopenic obesity with diabetes and to explore inflammation as a potential biological mechanism underlying these relationships. A narrative review of published literature from 2014 to 2025 was conducted using peer-reviewed articles, systematic reviews, meta-analyses, and population-based studies examining the relationship between skeletal muscle parameters and diabetes. Evidence consistently demonstrates that low muscle mass and low muscle strength are independently associated with an increased risk of diabetes. Individuals exhibiting both conditions have a substantially greater risk compared to those with either condition alone. Reduced muscle quality is also associated with impaired glucose metabolism and elevated diabetes prevalence. Sarcopenia, characterized by concurrent declines in muscle mass and strength, shows a stronger association with diabetes than isolated muscle deficits. Furthermore, sarcopenic obesity appears to exert synergistic effects on insulin resistance and metabolic dysfunction, resulting in a significantly higher risk of diabetes. Chronic low-grade inflammation, mediated through inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and C-reactive protein (CRP), may partially explain the association between impaired muscle health and diabetes. Inflammation appears to be a key mediator linking poor muscle health and metabolic dysfunction. Future longitudinal studies are required to establish causality and evaluate interventions targeting muscle preservation and inflammatory pathways for diabetes prevention.

Keywords: Diabetes Mellitus; Muscle Mass; Muscle Strength; Muscle Quality; Sarcopenia; Sarcopenic Obesity; Inflammation; Insulin Resistance.

1. Introduction

Type 2 diabetes mellitus (T2DM) is one of the fastest-growing chronic diseases worldwide and represents a major public health challenge. According to the International Diabetes Federation, the global prevalence of diabetes continues to rise due to population aging, sedentary lifestyles, and increasing obesity rates. While obesity has long been recognized as a major risk factor for diabetes, growing evidence suggests that skeletal muscle health plays an equally important role in glucose homeostasis and metabolic regulation.

Skeletal muscle is responsible for approximately 80% of insulin-mediated glucose uptake and serves as a primary site for glucose disposal. Consequently, reductions in muscle mass, muscle strength, and muscle quality can impair glucose

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utilization and contribute to insulin resistance. In recent years, researchers have increasingly focused on sarcopenia and sarcopenic obesity as potential predictors of diabetes and metabolic disorders.

Sarcopenia is characterized by progressive loss of skeletal muscle mass and strength, whereas sarcopenic obesity refers to the coexistence of excess adiposity and reduced muscle function. Both conditions have been associated with adverse metabolic outcomes, including insulin resistance, cardiovascular disease, physical disability, and mortality.

Recent studies have also suggested that chronic low-grade inflammation may mediate the relationship between poor muscle health and diabetes. Inflammatory cytokines contribute to muscle protein degradation and interfere with insulin signaling pathways, thereby linking sarcopenia to metabolic dysfunction.

Therefore, this review examines the current evidence regarding the associations between muscle mass, muscle strength, muscle quality, sarcopenia, sarcopenic obesity, and diabetes, with particular emphasis on the potential mediating role of inflammation.

2. Low Muscle Mass and Diabetes

Skeletal muscle mass is an important determinant of metabolic health because it regulates insulin sensitivity and glucose disposal. Reduced muscle mass decreases the body's capacity to utilize glucose efficiently, contributing to insulin resistance and hyperglycemia.

Kalyani et al. (2014) reported that age-related and disease-related muscle loss contributes significantly to metabolic dysfunction and diabetes development. The authors proposed a bidirectional relationship in which diabetes accelerates muscle degradation while muscle loss further worsens glucose metabolism.More recently, Zhang et al. (2024) analyzed data from large national cohorts in China and the United States and found that low muscle mass was independently associated with diabetes after adjusting for demographic and lifestyle factors. Individuals with reduced muscle mass exhibited significantly higher odds of diabetes compared to those with normal muscle mass.

These findings suggest that preserving skeletal muscle mass may be an important strategy for reducing diabetes risk and improving metabolic health.

3. Low Muscle Strength and Diabetes

Muscle strength reflects functional muscle capacity and has emerged as a stronger predictor of metabolic health than muscle mass alone. Reduced muscle strength may indicate neuromuscular dysfunction, impaired muscle quality, and decreased physical performance.

Several studies have demonstrated that lower handgrip strength and reduced lower-limb strength are independently associated with diabetes prevalence and incidence. Zhang et al. (2024) reported that low muscle strength remained significantly associated with diabetes even after controlling for muscle mass and obesity, indicating an independent effect. The growing importance of muscle strength is reflected in contemporary sarcopenia definitions proposed by the European Working Group on Sarcopenia in Older People (EWGSOP2), which prioritize low muscle strength as the primary criterion for sarcopenia diagnosis.(Cruz-Jentoft et al., 2019).

These findings indicate that assessments of muscle strength may provide valuable information for identifying individuals at increased risk of diabetes.

4. Muscle Quality and Diabetes

Muscle quality refers to muscle performance relative to muscle mass and encompasses factors such as intramuscular fat infiltration, fibrosis, mitochondrial function, and neuromuscular efficiency.

Emerging evidence suggests that poor muscle quality may be more strongly associated with metabolic dysfunction than muscle quantity alone. Obesity and diabetes promote ectopic fat accumulation within skeletal muscle, resulting in reduced muscle function and impaired insulin sensitivity.

Recent studies have demonstrated that lower muscle quality is associated with elevated diabetes risk, even among individuals with normal muscle mass. These findings support the notion that functional characteristics of muscle are critical determinants of metabolic health.

5. Sarcopenia and Diabetes

Sarcopenia combines reductions in both muscle mass and muscle strength and is increasingly recognized as a metabolic disorder.

A meta-analysis conducted by Veronese et al. reported that individuals with sarcopenia have significantly greater odds of developing diabetes compared with non-sarcopenic individuals. Similarly, diabetes patients demonstrate a higher prevalence of sarcopenia than healthy populations.

In 2025, the European Society for Clinical Nutrition and Metabolism described "sarcopenic diabetes" as an under-recognized clinical condition requiring greater attention in diabetes management. Shared mechanisms include insulin resistance, mitochondrial dysfunction, oxidative stress, hormonal changes, and chronic inflammation.

Evidence suggests that the combination of low muscle mass and low muscle strength exerts a greater metabolic burden than either factor alone, explaining the stronger association observed between sarcopenia and diabetes.(Mesinovic et al., 2019)."

6. Sarcopenic Obesity and Diabetes

Sarcopenic obesity represents a particularly harmful phenotype because it combines two major metabolic risk factors: excess adiposity and reduced muscle function.

Individuals with sarcopenic obesity experience greater insulin resistance, systemic inflammation, and metabolic impairment than those with obesity or sarcopenia alone. Excess adipose tissue releases inflammatory cytokines that accelerate muscle degradation while simultaneously worsening glucose metabolism.

Recent reviews published in 2025 concluded that sarcopenic obesity significantly increases the risk of type 2 diabetes, cardiovascular disease, frailty, and mortality. The synergistic interaction between obesity and sarcopenia appears to amplify metabolic dysfunction beyond the effects of either condition independently.

These findings underscore the importance of evaluating both body composition and muscle function in diabetes risk assessment.

7. Inflammation as a Mediating Mechanism

Inflammation has emerged as a central biological mechanism linking poor muscle health and diabetes.

Chronic low-grade inflammation is characterized by elevated circulating levels of inflammatory markers, including tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and C-reactive protein (CRP). These cytokines contribute to muscle catabolism, mitochondrial dysfunction, and impaired insulin signaling.

Zhang et al. (2024) provided evidence that inflammation partially mediates the relationship between muscle deficits and diabetes. Individuals with low muscle mass and strength exhibited higher inflammatory marker levels, which in turn were associated with increased diabetes prevalence.

A systematic review by Feng et al. (2025) further confirmed that inflammatory biomarkers are consistently associated with sarcopenia, sarcopenic obesity, and insulin resistance. These findings suggest that chronic inflammation may represent a key pathway through which impaired muscle health contributes to diabetes development.

7.1. Clinical Implications

The evidence reviewed highlights the importance of incorporating muscle health assessment into diabetes prevention and management strategies. Routine evaluation of skeletal muscle mass, handgrip strength, physical performance, muscle quality, and body composition may help identify individuals at elevated risk of diabetes. Routine assessment of

muscle mass, muscle strength, and physical performance has been recommended in international clinical practice guidelines for sarcopenia management (Dent et al., 2019).

Lifestyle interventions involving resistance exercise, adequate protein intake, and weight management have demonstrated beneficial effects on muscle mass, muscle strength, inflammatory status, and glycemic control. Such interventions may be particularly effective in individuals with sarcopenia or sarcopenic obesity.

8. Nutritional Interventions for Preventing Low Muscle Mass and Diabetes

Nutrition plays a central role in maintaining skeletal muscle mass, preserving muscle function, and preventing the development of type 2 diabetes mellitus (T2DM). Skeletal muscle is a highly metabolically active tissue that serves as the primary site for insulin-mediated glucose disposal. Consequently, inadequate dietary intake, poor protein quality, micronutrient deficiencies, and chronic energy imbalance can accelerate muscle loss and impair glucose metabolism (Kalyani et al., 2014; Masih, 2023, Morley, 2024).

Recent evidence suggests that nutritional interventions targeting muscle preservation may reduce the risk of sarcopenia, sarcopenic obesity, insulin resistance, and diabetes (Cruz-Jentoft et al., 2023; Barazzoni et al., 2025). Nutritional strategies primarily focus on optimizing protein intake, improving dietary quality, reducing chronic inflammation, and enhancing anabolic signaling pathways responsible for muscle protein synthesis.

8.1. Dietary Protein and Muscle Protein Synthesis

Protein intake is the most important nutritional factor influencing skeletal muscle maintenance. Dietary amino acids, particularly leucine, stimulate muscle protein synthesis through activation of the mechanistic target of rapamycin complex 1 (mTORC1) pathway (Deutz et al., 2024).

Following protein ingestion, leucine activates mTORC1 signaling, resulting in increased translation initiation and muscle protein synthesis. This process promotes muscle hypertrophy, preserves muscle strength, and improves insulin sensitivity (Morley, 2024).

In older adults, anabolic resistance reduces the muscle's responsiveness to dietary protein. Therefore, higher protein intakes (1.0–1.5 g/kg/day) are often recommended to maintain muscle mass and function (Cruz-Jentoft et al., 2023, Masih, 2026).

Recent studies have shown that diets rich in high-quality proteins such as dairy products, eggs, fish, lean meat, soy products, and whey protein improve muscle mass and glycemic control in individuals at risk of diabetes ((Landi et al., 2018; Barazzoni et al., 2025).

8.2. Essential Amino Acids and Leucine

Among the essential amino acids, leucine is considered the most potent stimulator of muscle protein synthesis. Leucine activates the phosphatidylinositol 3-kinase (PI3K)/Akt/mTOR pathway, which enhances muscle growth and inhibits proteolysis.

Leucine supplementation has been associated with increased muscle protein synthesis, improved muscle strength, enhanced glucose uptake, improved insulin sensitivity, and reduced sarcopenia progression (Morley, 2024; Cruz-Jentoft et al., 2023).

Branched-chain amino acids (BCAAs), particularly leucine, isoleucine, and valine, may support skeletal muscle preservation when combined with resistance exercise and adequate caloric intake (Deutz et al., 2024).

8.3. Vitamin D and Skeletal Muscle Function

Vitamin D deficiency is common among older adults and individuals with diabetes. Vitamin D receptors are expressed in skeletal muscle tissue and influence muscle cell differentiation, protein synthesis, and mitochondrial function (Cruz-Jentoft et al., 2023).

Several studies have demonstrated that adequate vitamin D status is associated with greater muscle strength, improved physical performance, reduced risk of falls, and better insulin sensitivity (Morley, 2024; Barazzoni et al., 2025).

Vitamin D may also suppress inflammatory cytokines and improve pancreatic β-cell function, thereby contributing to diabetes prevention (Feng et al., 2025).

8.4. Omega-3 Fatty Acids and Inflammation

Omega-3 polyunsaturated fatty acids (PUFAs), particularly eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), possess anti-inflammatory properties that may protect against muscle loss and metabolic dysfunction.

Omega-3 fatty acids contribute to reduced TNF-α production, lower IL-6 concentrations, improved muscle protein synthesis, enhanced mitochondrial function, and improved insulin signaling (Hong & Choi, 2020; Feng et al., 2025).

Clinical trials suggest that omega-3 supplementation may improve muscle quality and reduce chronic inflammation in older adults with sarcopenia and obesity (Borba & Costa, 2025).

8.5. Mediterranean and Anti-inflammatory Dietary Patterns

The Mediterranean diet has received considerable attention for its protective effects against both sarcopenia and diabetes. This dietary pattern is characterized by high consumption of fruits and vegetables, whole grains, legumes, nuts, olive oil, and fish, together with limited intake of processed foods and refined sugars (Morley, 2024,).

The Mediterranean diet provides antioxidants, polyphenols, fiber, and healthy fats that reduce oxidative stress and inflammation while supporting muscle function (Hong & Choi, 2020).

Longitudinal studies have shown that adherence to Mediterranean dietary patterns is associated with higher muscle mass, better muscle strength, lower insulin resistance, and reduced diabetes incidence (Barazzoni et al., 2025; Morley, 2024).

8.6. Nutritional Strategies for Sarcopenic Obesity

Individuals with sarcopenic obesity require interventions that simultaneously reduce adiposity and preserve muscle mass. Current recommendations include moderate caloric restriction, high-protein diets, resistance exercise, adequate vitamin D intake, and omega-3 supplementation (Batsis & Villareal, 2018; Borba & Costa, 2025).

These combined approaches help maintain lean tissue while promoting fat loss and improving metabolic health, thereby reducing the risk of diabetes and functional decline (Barazzoni et al., 2025).

9. Metabolic Biochemistry Linking Nutrition, Muscle Health, and Diabetes

The relationship between nutrition, muscle preservation, and diabetes is mediated through several interconnected biochemical pathways.

9.1. Insulin Signaling Pathway

Under normal physiological conditions, insulin binds to insulin receptors on skeletal muscle cells, activating insulin receptor substrate (IRS) proteins and the PI3K/Akt signaling cascade. This signaling pathway promotes GLUT4 translocation to the cell membrane, increased glucose uptake, glycogen synthesis, and suppression of muscle protein breakdown (Kalyani et al., 2014).

When muscle mass declines, the body's capacity for glucose disposal decreases, resulting in elevated blood glucose concentrations and insulin resistance (Zhang et al., 2024).

9.2. mTOR Signaling and Muscle Protein Synthesis

The mechanistic target of rapamycin (mTOR) pathway serves as the central regulator of muscle growth. Protein intake, especially leucine-rich protein, stimulates mTOR activation, leading to increased protein synthesis, muscle fiber growth, improved muscle quality, and enhanced insulin sensitivity (Deutz et al., 2024).

Conversely, inadequate protein intake suppresses mTOR signaling and promotes muscle atrophy, increasing susceptibility to sarcopenia and diabetes (Cruz-Jentoft et al., 2023).

9.3. Inflammation-Induced Muscle Catabolism

Chronic low-grade inflammation activates catabolic pathways involving nuclear factor-kappa B (NF-κB), the ubiquitin–proteasome system, and autophagy-related proteins (Feng et al., 2025).

Elevated inflammatory cytokines increase muscle protein degradation while impairing insulin signaling. Consequently, inflammation promotes muscle loss, reduces glucose uptake, and accelerates the development of insulin resistance and diabetes (Hong & Choi, 2020; Zhang et al., 2024).

9.4. Mitochondrial Dysfunction

Mitochondria regulate energy production and glucose oxidation within skeletal muscle. Aging, obesity, and chronic inflammation contribute to reduced mitochondrial biogenesis, increased reactive oxygen species (ROS) production, decreased ATP synthesis, and impaired fatty acid oxidation (Feng et al., 2025).

These alterations reduce muscle quality and increase insulin resistance, contributing to the progression of diabetes (Hong & Choi, 2020).

9.5. Adipose-Muscle Crosstalk in Sarcopenic Obesity

In sarcopenic obesity, excess adipose tissue secretes adipokines such as TNF-α, IL-6, and resistin. These inflammatory mediators accelerate muscle degradation and impair insulin signaling (Batsis & Villareal, 2018).

Simultaneously, reduced muscle mass decreases glucose disposal capacity, creating a vicious cycle whereby obesity promotes inflammation, inflammation accelerates muscle loss, and muscle loss worsens insulin resistance and diabetes (Borba & Costa, 2025; Zhang et al., 2024).

The synergistic interaction between adiposity and sarcopenia explains the substantially higher diabetes risk observed in individuals with sarcopenic obesity (Barazzoni et al., 2025; Borba & Costa, 2025).

Recent international guidelines emphasize that the prevention and management of sarcopenia should incorporate regular screening of muscle strength, muscle mass, and physical performance, particularly among individuals with obesity, metabolic syndrome, and type 2 diabetes mellitus (Dent et al., 2019; Cruz-Jentoft et al., 2019). Early identification of muscle deterioration may facilitate timely nutritional and lifestyle interventions, thereby reducing future metabolic complications.

10. Conclusion

Current evidence indicates that low muscle mass and low muscle strength are independently associated with diabetes and that their combined presence substantially increases diabetes risk. Reduced muscle quality further contributes to metabolic dysfunction. Sarcopenia exhibits a stronger association with diabetes than isolated deficits in muscle mass or strength, while sarcopenic obesity appears to have synergistic effects that markedly increase metabolic risk.

Inflammation represents a plausible biological mechanism linking impaired muscle health with diabetes through its effects on insulin resistance and muscle degradation. Future prospective studies are needed to clarify causal relationships and identify effective interventions aimed at preserving muscle health and reducing diabetes burden.

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