PUBLICATION SUMMARY

Interplay Between Sarcopenia And Type 2 Diabetes: Mechanisms, Implications, And Therapeutic Prospects

Ghosh M, Heo Y, Kushwaha GS et al. *Nutr Diabetes*. 2026 Jun 4;16(1):18.

Background:

Skeletal muscle accounts for approximately 70-80% of postprandial glucose uptake, making it a critical regulator of glucose homeostasis. Loss of muscle mass reduces glucose disposal capacity, increasing insulin resistance and T2D risk. Conversely, chronic hyperglycemia and insulin resistance promote muscle protein breakdown, accelerating sarcopenia. This creates a vicious cycle of worsening metabolic dysfunction and declining muscle health. Older adults with T2D have approximately a 1.5-fold higher risk of sarcopenia than non-diabetic individuals, and individuals with lower muscle mass demonstrate a significantly elevated risk of developing future T2D.

Key Mechanisms Linking Sarcopenia and Type 2 Diabetes:

Insulin Resistance — Insulin resistance impairs GLUT4 translocation and glucose uptake in skeletal muscle, reducing energy availability and suppressing protein synthesis through disruption of the IGF-1/PI3K/Akt/mTOR pathway. Enhanced activation of proteolytic systems promotes muscle degradation.
Chronic Inflammation — Elevated inflammatory mediators including IL-6, TNF-α, and CRP contribute to muscle catabolism via NF-κB and JAK/STAT signaling pathways, while simultaneously worsening insulin resistance.
Oxidative Stress and AGEs — Hyperglycemia increases reactive oxygen species production and AGE accumulation, which contribute to mitochondrial dysfunction, protein crosslinking, impaired muscle contractility, and muscle loss.
Myostatin Signaling — Myostatin acts as a negative regulator of muscle growth. Increased myostatin activity suppresses muscle protein synthesis, promotes proteolysis, and impairs muscle regeneration.
Ubiquitin-Proteasome System — Upregulation of muscle-specific ubiquitin ligases (MuRF1 and Atrogin-1) accelerates protein degradation and contributes significantly to muscle wasting.

Clinical Implications:

Individuals with both sarcopenia and T2D experience:

- Reduced muscle strength and physical performance
- Greater disability and loss of independence
- Increased cardiovascular risk
- Increased risk of falls and fractures
- Poorer glycemic control
- Increased mortality risk

Diagnostic Approaches:

Muscle Mass		
• DXA (appendicular lean mass)	• Bioelectrical impedance analysis (BIA)	• CT/MRI
Muscle Strength		
• Handgrip strength	• Knee extension strength	
Physical Performance		
• Gait speed	• Short Physical Performance Battery (SPPB)	• Timed Up and Go (TUG)
Biomarkers		
• Myostatin/Follistatin	• IL-6	• TNF-α
• CRP	• IGF-1	• Vitamin D

Therapeutic Strategies:

■ Foundational interventions: adequate protein intake and resistance training
■ Pharmacology and potential impact on muscle
Metformin — Improves insulin sensitivity; may support muscle metabolism
SGLT2 Inhibitors — May improve muscle function and reduce fat infiltration
SARMs — Investigational anabolic therapies
GLP-1 RA — May enhance muscle protein synthesis and improve metabolic health
Insulin — Supports muscle protein synthesis
Myostatin Inhibitors — Emerging strategy to stimulate muscle growth

Limitations:

- Narrative review rather than systematic review or meta-analysis.
- Many therapeutic approaches discussed remain investigational.
- Limited long-term clinical outcome data for several emerging treatments.
- Further studies are needed to establish optimal nutritional interventions and treatment algorithms.

Conclusion:

Sarcopenia and T2D should be viewed as interconnected conditions requiring integrated management. Early identification of muscle loss in individuals with T2D and intervention through resistance exercise, nutritional optimization, and appropriate pharmacologic therapy may improve both muscle health and metabolic outcomes. The review also highlights promising opportunities for GLP-1 receptor agonists, SGLT2 inhibitors, and myostatin-targeted therapies in future management strategies.

Journal article may be accessed at:

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