# SARCOPENIA IN PATIENTS WITH DIABETES MELLITUS AND DIABETIC KIDNEY DISEASE: PATHOPHYSIOLOGICAL MECHANISMS, CLINICAL SIGNIFICANCE AND MANAGEMENT STRATEGIES

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**Abstract.** Sarcopenia is a progressive disorder characterised by reduced skeletal muscle strength, mass and physical performance. Diabetes mellitus and diabetic kidney disease (DKD) are important conditions associated with accelerated muscle loss. Hyperglycaemia, insulin resistance, chronic inflammation, oxidative stress, metabolic acidosis and uraemic toxin accumulation contribute to impaired muscle protein synthesis and increased protein degradation. Reduced physical activity, nutritional deficiencies and vitamin D deficiency further aggravate muscle dysfunction.

**Keywords**: sarcopenia, diabetes mellitus, diabetic kidney disease, chronic kidney disease, insulin resistance, muscle wasting, inflammation, renal dysfunction.

**Introduction.** Diabetes mellitus is a major metabolic disorder associated with multiple complications, including diabetic kidney disease. In addition to cardiovascular and renal damage, diabetes may negatively affect skeletal muscle metabolism, resulting in reduced muscle strength and mass. Sarcopenia is particularly important in patients with diabetes because it contributes to physical disability, falls and reduced quality of life [1,2]. Diabetic kidney disease increases the risk of muscle deterioration. Reduced kidney function is associated with

chronic inflammation, metabolic acidosis, hormonal disturbances and accumulation of uraemic toxins. These factors accelerate muscle protein breakdown and impair muscle regeneration [3,4].

**Pathophysiological mechanisms of sarcopenia in diabetes and diabetic kidney disease**

1. Insulin resistance and impaired muscle protein synthesis

Insulin plays an important role in regulating glucose uptake and protein metabolism in skeletal muscle. In patients with type 2 diabetes, insulin resistance reduces the metabolic response of muscle cells and impair anabolic signalling pathways. Reduced activation of the PI3K–Akt–mTOR pathway contributes to decreased muscle protein synthesis, activation of catabolic pathways promotes muscle protein degradation and lead to reduced muscle mass and strength [2,4].

2. Chronic inflammation and oxidative stress

Diabetes and chronic kidney disease are associated with persistent low-grade inflammation. Increased concentrations of inflammatory mediators, including TNF-α and IL-6, may activate pathways involved in muscle protein degradation. Oxidative stress additionally damages cellular structures and impairs mitochondrial function. Increased activity of the ubiquitin–proteasome system and other proteolytic pathways contributes to muscle atrophy and reduced physical performance [4,7].

3. Accumulation of uraemic toxins

As renal function deteriorates, uraemic toxins accumulate in the circulation. Indoxyl sulfate, p-cresyl sulfate and trimethylamine-N-oxide are among the metabolites associated with altered muscle metabolism. These substances may promote oxidative stress, inflammation and mitochondrial dysfunction. Experimental evidence indicates that indoxyl sulfate can negatively affect muscle

cell viability and increase muscle protein degradation. These mechanisms contribute to the development of uraemic sarcopenia [4].

**Metabolic acidosis and hormonal disturbances.** Metabolic acidosis, frequently observed in advanced chronic kidney disease, stimulates muscle protein catabolism and reduce protein synthesis. Renal dysfunction also be associated with vitamin D deficiency, secondary hyperparathyroidism and disturbances in insulin-like growth factor signalling.[3,4].

**Malnutrition and reduced physical activity.** Dietary restrictions, poor appetite, gastrointestinal symptoms and chronic illness may result in inadequate energy and protein intake. In patients with diabetes and kidney disease, nutritional management is particularly challenging because excessive protein consumption increase renal workload, whereas insufficient intake accelerate muscle wasting.

According to the revised European Working Group on Sarcopenia in Older People consensus (EWGSOP2), reduced muscle strength is the primary indicator of probable sarcopenia. Reduced muscle quantity or quality confirms the diagnosis, while impaired physical performance indicates severe sarcopenia [1].Clinical assessment should include: handgrip strength measurement using a dynamometer, chair stand test to evaluate lower-limb muscle strength.gait speed and physical performance assessment, muscle mass evaluation using bioelectrical impedance analysis (BIA) or dual-energy X-ray absorptiometry (DXA), screening questionnaires such as SARC-F. Laboratory assessment may include fasting glucose, HbA1c, Cystatin C, serum creatinine, estimated glomerular filtration rate (eGFR), urinary albumin-to-creatinine ratio (UACR), serum albumin, C-reactive protein, vitamin D and bicarbonate [7,8].

Modern approaches to prevention and management

**Glycaemic and renal protection.** Management of blood pressure and albuminuria, together with appropriate renoprotective treatment, may help slow

kidney disease progression. Sodium–glucose cotransporter-2 inhibitors (SGLT2 inhibitors) are recommended for eligible patients with type 2 diabetes and chronic kidney disease because of their kidney and cardiovascular benefits. Renin–angiotensin system inhibitors and other evidence-based therapies should be prescribed according to clinical indications and renal status [2,5].

**Individualised nutritional support.** Nutritional management should balance kidney protection and preservation of muscle mass. According to KDIGO recommendations, a protein intake of approximately 0.8 g/kg/day is suggested for adults with diabetes and CKD who are not receiving dialysis. For patients receiving dialysis, protein requirements are generally higher, approximately 1.0–1.2 g/kg/day [2].

**Physical activity and resistance training.** Regular physical activity is an important component of sarcopenia prevention. Resistance exercises help stimulate muscle protein synthesis, improve strength and maintain functional capacity. Aerobic and balance exercises may provide additional benefits.

Exercise programmes should be adapted to the patient's cardiovascular condition, renal disease stage and physical capacity. In selected patients receiving haemodialysis, supervised intradialytic exercise may also be considered [4,5].

Conclusion. Sarcopenia in patients with diabetes mellitus and diabetic kidney disease develops through several interconnected mechanisms, including insulin resistance, chronic inflammation, oxidative stress, uraemic toxin accumulation, metabolic acidosis and nutritional imbalance. A multidisciplinary approach involving endocrinologists, nephrologists, nutrition specialists and rehabilitation professionals may improve clinical outcomes and help preserve functional independence in patients with diabetes and diabetic kidney disease.

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