Exercise therapy in combating Diabetes and sarcopenia – A Review

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Abstract: Type 2 Diabetes Mellitus (T2DM) is a common metabolic condition characterised by insulin resistance, persistent inflammation, build-up of advanced glycation end-products, and heightened oxidative stress. These factors negatively impact both the mass and function of skeletal muscles, resulting in sarcopenia, which is now recognized as a newer complication associated with T2DM.Sarcopenia refers to the gradual decline in the total weight of all skeletal muscles in the body, strength, and functionality, which has a considerable impact on overall health and quality of life. T2DM and sarcopenia share a bidirectional relationship, with both conditions increasing in prevalence with age. They also share common risk factors and the underlying pathophysiological mechanisms. T2DM incidence rises significantly after the age of 40 years and peaks in older adults, whereas sarcopenia typically begins in middle age and becomes more pronounced after age 60 years. Given the progressive nature of these conditions, early intervention is essential to mitigate their impact and improve the standard of living. Although various therapies exist for managing diabetes and sarcopenia, the early implementation of exercise therapy offers significant benefits. Exercise helps to prevent the onset and progression of these conditions by improving insulin sensitivity, mass & strength of muscles. This review explores how exercise therapy can combat T2DM and sarcopenia, emphasising its potential as a preventive and therapeutic approach to enhance health outcomes across the lifespan.

Keywords: Type 2 Diabetes Mellitus, Sarcopenia, Exercise Therapy

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Introduction: Type 2 Diabetes Mellitus(T2DM) is a global metabolic disease. The International Diabetes Federation (IDF) reported that in 2017, 8.8% of the global population aged 20-79, equating to 425 million individuals, were affected by diabetes. This figure is

projected to increase to 9.9%, or 629 million people, by 2045.[1]The onset of type 2 Diabetes Mellitus (T2DM) typically becomes significant after the age of 40 years, peaking in prevalence among older adults, while sarcopenia also tends to emerge earlier during middle age and progressively worsens beyond the age of 60. Sarcopenia, derived from Greek words sarx and penia meaning "flesh poverty/loss". Sarcopenia is a pathological condition characterised by muscle failure, marked by an age-related gradual reduction in muscle strength (dynapenia), size (quantity), and performance (quality), which results in a decline in physical abilities and an increased risk of disability, fall, and death.[2] Sarcopenia has received growing interest over the last decade, and is now recognised as an independent condition by the International Classification of Disease, tenth Revision, Clinical Modification(ICD-10-CM) code (i.e. M 62.84).[3] There is a growing focus on sarcopenia, as it has emerged as a significant concern owing to its potential to greatly affect the standard of living of individuals with T2DM.

The relationship between T2DM and sarcopenia forms a detrimental cycle, in which each condition exacerbates the other, leading to a decline in an individual's functionality. Sarcopenia, marked by a reduction in muscle mass, worsens T2DM complications such as poor glucose regulation. The loss of muscle mass results in reduced insulin sensitivity and glucose absorption, making it difficult to manage blood sugar levels and causing hyperglycaemia, a key feature of T2DM, because of the impaired ability of the body to utilise glucose effectively. In addition to the well-established microvascular and macrovascular issues, sarcopenia is now being recognized as a third type of complication that results in significant disability.[1,3,4]

Recent research indicates that individuals with T2DM and sarcopenia have higher mortality rates than those without sarcopenia. Despite this, there has been insufficient focus on T2DM and sarcopenia, making it crucial to explore the connection between T2DM and sarcopenia to effectively manage this complex clinical issue.[5,6]This review seeks to provide an update on three key areas: (1) the link and risk factors associated with sarcopenia in people with T2DM; (2) the clinical characteristics of both diabetes and sarcopenia; and (3) the impact of exercise therapy on the management of T2DM and sarcopenia.

RISK FACTORS OF SARCOPENIA IN T2DM PATIENTS

1. **Insulin Resistance:**

    - Skeletal muscles play a crucial role in insulin function and are significantly affected by insulin resistance. The absorption of glucose by skeletal muscle is facilitated through diffusion, which is initiated by the movement of glucose

transporter type 4 (GLUT4) to the cell membrane during muscle contraction, in response to the gradient of glucose concentration within the cell. However, in T2DM, impaired insulin signalling disrupts this process, reducing glucose absorption in muscles and impairing protein synthesis, ultimately resulting in loss of muscle mass.

2. **Chronic Inflammation:**
    - In type 2 diabetes mellitus (T2DM), ongoing low-level inflammation disrupts the balance between glucose and muscle, leading to higher levels of inflammatory markers i.e., TNF-α, IL-6, and C-reactive protein (CRP). These markers are strongly associated with impaired insulin sensitivity and negatively affect muscle function and mass. IL-6, in particular, plays a role in increasing muscle breakdown, which further worsens muscle deterioration.

3. **Oxidative Stress:**
    - Hyperglycaemia in T2DM is associated with increased oxidative stress (OS) due to the increased production of reactive oxygen species (ROS). ROS activate the ubiquitin-proteasome system, accelerate damage to muscle proteins, and impair mitochondrial function. Mitochondria play important roles in muscle function and metabolism. Mitochondrial dysfunction, both on its own and when combined with factors related to T2DM that are linked to oxidative stress, results in a decline in metabolic and muscle health.

4. **Accumulation of Advanced Glycation End products (AGEs):**
    - In T2DM, elevated glucose levels result in the formation of advanced glycation end-products (AGEs), which are linked to impaired insulin sensitivity and aging. This buildup leads to weakening and malfunctioning of skeletal muscles by making them more rigid and impairing their function. Moreover, AGEs have a detrimental impact on the health of skeletal muscles by causing mitochondrial dysfunction and promoting cell death, further exacerbating muscle degradation.
5. **Reduced Physical Activity:**
    - Physical activity plays a vital role in enhancing glucose absorption by skeletal muscles, preserving or improving muscle health, and counteracting insulin resistance. However, T2DM patients are often disproportionately sedentary and overweight. Complications such as fatigue, neuropathy, and other health issues

associated with T2DM contribute to sedentary behaviour, further accelerating muscle loss and exacerbating the development of sarcopenia.

6. **Nutritional Deficiencies:**
    - Ensuring a balanced and sufficient intake of macronutrients, including proteins, carbohydrates, and fats, is crucial for managing metabolic control in T2DM and for preserving muscle mass and function. Adequate protein consumption aids in muscle synthesis, whereas energy derived from carbohydrates and fats helps avert metabolic degradation of striated muscles. However, poor dietary habits or unintentional weight loss in T2DM patients can result in inadequate protein consumption, further exacerbating sarcopenia progression.
7. **Hormonal Imbalances:**
    - Alterations in the levels of anabolic hormones, including insulin, testosterone, and growth hormones, which are crucial for maintaining muscle mass, are associated with type 2 diabetes mellitus.
8. **Obesity and Lipotoxicity:**
    - The simultaneous presence of obesity and T2DM results in fat accumulation within the muscles (myosteatosis), leading to a decline in both strength and quality of the muscles.
9. **Diabetic Neuropathy:**
    - Peripheral nerve damage in T2DM impairs muscle innervation and contributes to catabolism and weakness.
10. **Age-Related Factors:**
    - Once individuals reach the age of 30 years, their basal metabolic rate declines by 3–8% every ten years as a result of muscle loss. T2DM and sarcopenia are more prevalent in elderly individuals, who naturally experience declines in the mass and strength of the muscles, and regenerative capacity.[1,5,6,7,8]

Clinical Features of Both Diabetes and Sarcopenia.

Clinical Features	Type 2 Diabetes Mellitus	Sarcopenia
Muscle	Muscle wasting may occur	**The gradual reduction in**

Mass	over time, especially with poor glucose control	**muscle mass in the skeleton caused by aging and lack of physical activity.**
Muscle Strength	Weakness due to impaired insulin sensitivity and neuropathy.	**Reduced strength in muscles, often measured by grip strength or chair rise test.**
Fatigue	Common, often due to poor blood glucose control and other complications.	**Fatigue due to muscle loss and decreased physical function.**
Neuropathy	Diabetic neuropathy leading to sensory loss, pain, and motor impairment.	**Neurological changes contributing to muscle weakness and reduced mobility.**
Blood Glucose Control	Poorly controlled blood glucose, often resulting in hyperglycemia.	**Not directly impacted, but reduced muscle activity and mass can worsen metabolic health.**
Physical Function	Reduced mobility, difficulty walking, and performing daily activities.	**Difficulty performing daily activities (e.g., rising from a chair, walking).**
Body Composition	Increased visceral fat and muscle loss, often with Obesity.	**Reduced mass of muscle and increase in fat, particularly in the abdomen (myosteatosis).**
Inflammation	Low-grade systemic inflammation contributing to impaired insulin sensitivity.	**Prolonged inflammation contributes to muscle breakdown and reduced function.**
Mitochondrial Dysfunction	Muscle cells experiencing compromised mitochondrial function result in fatigue and diminished muscle performance.	**Mitochondrial dysfunction contributing to muscle degeneration and weakness.**
Hormonal Imbalance	Altered insulin and other hormones (testosterone, growth hormone) impairing muscle growth.	**Decreased anabolic hormones (e.g., testosterone, growth hormone) accelerate muscle loss.**
Joint and Muscle Pain	Joint pain due to diabetes-related complications like neuropathy and inflammation	**Pain due to muscle weakness, inflammation, and joint stress from muscle loss.**
Weight Loss or Gain.	**Weight gain (often due to insulin resistance) or weight loss (in poorly controlled diabetes).**	**Unintentional weight loss due to muscle breakdown, often accompanied by fat gain.**

T2DM and **sarcopenia** share overlapping features.[6,7,8,9,10] Knowledge of the management of diabetes through nutritional management and medication is widely spread and implemented. Although exercise has a major role in addition to other therapies, its clinical application is very poor.

EXERCISE FOR THE TREATMENT OF DIABETES AND SARCOPENIA

This review primarily examined the contribution of exercise therapy in managing T2DM and sarcopenia, highlighting that lack of physical activity is a significant predictor of disability in both conditions. Exercise, characterized by its planned, structured, and repetitive nature, is known to offer numerous health benefits, particularly for metabolic and musculoskeletal health indicators such as insulin sensitivity, blood sugar control, muscle mass, strength, and bone density.[6,11]

The advantages of exercise interventions are affected by several factors, including the type of exercise and elements related to the exercise prescription, such as the frequency, intensity, and duration of the exercise sessions. Gaining insight into how these prescription-related factors affect the management of type 2 diabetes and sarcopenia can offer practical guidelines for managing these conditions.

The following are a few exercise therapies that help manage type 2 diabetes and sarcopenia, based on insights from various studies:

Exercise Therapy	Key Components	Frequency	Duration	Benefits	Research Insights
Aerobic Training	Walking, cycling, swimming, jogging	3–5 days per week	30–60 minutes/session	Enhances insulin sensitivity, lowers HbA1c, reduces fat mass, and improves cardiovascular fitness.	**Shown to improve glucose uptake by muscles and reduce diabetes complications (e.g., neuropathy).**
Resistance Training (RT)	Weight Lifting, Strength training, using resistance bands, and exercises that rely on body weight like squats, lunges, and push-ups	2–3 days per week	20–40 minutes/session	Increases muscle mass, improves muscle strength, and enhances glucose metabolism.	**Research indicates that elderly individuals with T2DM experience enhanced synthesis of muscle protein and better glycemic control.**
Combined Training	Mix of aerobic and resistance exercises	4–5 days per week	30–60 minutes/session	Integrates the advantages of both aerobic and strength exercises to enhance muscle and glucose health optimally.	**Evidence suggests synergistic effects, particularly in elderly individuals with T2DM.**
High-Intensity Interval Training (HIIT)	Interspersing brief periods of intense activity with intervals of rest (e.g., sprinting, circuit workouts)	2–3 days per week	15–30 minutes/session	Improves insulin sensitivity, enhances muscle mass, and reduces fat accumulation.	**Shown to provide rapid benefits in glycemic control and strength gains in shorter durations.**
Flexibility & Balance Training	Yoga, Pilates, tai chi	2–3 days per week	20–40 minutes/session	Improves balance, flexibility, and reduces fall risk, enhancing mobility	**Evidence supports improvements in standards of living and physical functionality in sarcopenic patients**
Functional Training	Movements mimicking everyday activities (e.g. transitioning from sitting to standing, climbing	3–4 days per week	20–30 minutes/session	Enhances functional independence, muscular strength, and glucose utilization.	**Found to improve functional capacity and decrease diabetes- related fatigue**

	stairs, and lifting weights)				
Progressive Resistance Training (PRT)	Gradual increase in resistance or weight loads	2–3 days per week	30–45 minutes/session	Increases muscle hypertrophy, strength, and glucose uptake.	**Well- documented to reverse muscle loss and improve impaired insulin sensitivity in sarcopenic individuals.**
Water-Based Exercise	Swimming, water aerobics	2–3 days per week	30–45 minutes/session	Low-impact, improves joint health, cardiovascular fitness, and glucose utilization.	**Effective for those with joint pain or limited mobility, common in older diabetic adults.**
Circuit Training	**Combination of aerobic and resistance exercises in quick succession**	**2–4 days per week**	**20–40 minutes/session**	**Enhances muscular endurance, strength, and glycemic control.**	**Demonstrated to efficiently improve multiple health parameters in time-constrained protocols.**

In terms of both type 2 diabetes and sarcopenia clinical features, individuals experience fatigue and have a static lifestyle and poor functionality, leading to an impaired standard of living. Performing these exercises may be difficult; hence, tailored exercises based on the condition and capacity of the individual exercise interventions should be implemented. From the above the exercises, resistance training exercises have been proven from various studies that help to enhance the strength & mass of muscles and maintain the glycaemic index and improve the standard of living of the individuals.[6,12,14,15,16,17]

List of studies showing the effect of resistance training exercises on type 2 diabetes and sarcopenia management

Reference	Study population	Study outcome.
Dionysia Argyropoulou, 2022	Research involving long-term exercise and/or dietary interventions, in addition to clinical trials with older adults experiencing sarcopenia or T2DM. These studies concentrated on treatment methods that included aerobic and resistance training, or a combination of both, along with dietary interventions or nutritional assessments. Additionally, studies that utilized biomarkers for muscle mass and/or glycemic status were also selected.	**Resistance training is primarily recognized for its ability to improve muscle mass, boost muscle strength, and improve physical performance. This makes it particularly suitable for older, frail adults.** **Enhancements in muscle quality[17] and strength, coupled with an improvement in skeletal mass, helps to lower the incidence of falls and boost physical performance,[18,19] making resistance exercise a suitable activity for individuals with sarcopenia.[20]**
Kim et al,2022	Thirty-six older adults with pre-diabetes participated in a 12-week program of resistance training, engaging in 60-minute sessions three times a week.	**Decreased glycated HbA1c levels.**

Zhao D,et al,2022	Short duration, moderate-intensity weight training for type 2 diabetic patients, 24 hours	**Blood glucose level decreased.**[21]
Hsieh PL,2018	A twelve-week resistance training program for type 2 diabetic patients.	**Observed a notable improvement in the muscle function.**[22]
Botton CE, et al,2018	**A twelve-week resistance training program for individuals with T2DM**	**Observed a notable enhancement in both the strength and muscle mass of the lower limbs.**[23]

Conclusion: With the rising global challenges of type 2 diabetes and age-related muscle loss, it is essential that healthcare professionals and policymakers work together effectively. Although diabetes is a major issue, along with the various complications associated with it, sarcopenia is an emerging issue that has received less attention. Sarcopenia stands out for its significant impact on functional decline and reduced standard of living. Regular physical activity benefits individuals of all ages by promoting improvements in aerobic capacity, muscle strength, and endurance. Regular physical activity is a highly effective method for preventing frailty and reducing the impact of sarcopenia.

Focusing on muscle health by managing diabetes early and making lifestyle changes can be attributed to healthier individuals and a better standard of living. Early detection and lifestyle adjustments are crucial for preserving the strength and functionality of individuals with diabetes and sarcopenia.

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