# Exercise Intervention and Implementation Key Points for Populations with Type 2 Diabetes Complications: Postprint

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## Abstract

Exercise is a cornerstone in the prevention and management of type 2 diabetes complications; however, there has been limited discussion in the academic community regarding the precautions and implementation essentials of exercise interventions for populations with type 2 diabetes complications. To address this gap, this article integrates the latest diabetes prevention and treatment guidelines, expert consensus, and corresponding research evidence to elaborate on exercise recommendations, precautions, exercise timing, and drug-exercise interactions for populations with type 2 diabetes complications, aiming to provide practical guidance and evidence-based direction for exercise therapy in this population.

## Full Text

### Key Points of Exercise Intervention and Implementation for People with Complications of Type 2 Diabetes Mellitus

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**Abstract**

Exercise remains a cornerstone in the prevention and management of diabetic complications in patients with type 2 diabetes. However, there have been few discussions about the precautions and implementation key points of exercise intervention for diabetic complications. In this study, we presented some recommendations of exercise intervention, the precautions related to exercise intervention, the selection of exercise timing, and the interactive effects between sports and medications for patients with diabetic complications, based on the latest guidelines on diabetes prevention and management, the expert consensus, and the latest research trials, aiming to provide some practical guidance and evidence-based guidelines for exercise intervention in patients with diabetic complications.

**Key words:** Diabetes mellitus, type 2; Exercise intervention; Exercise timing; Integration of sports-and-medication

## Introduction

Diabetes mellitus, particularly type 2 diabetes, has become a major chronic disease threatening human health worldwide. According to reports, in 2022, approximately 828 million adults aged 18 and older had diabetes globally, with about 148 million patients in China alone, accounting for 18% of the global adult diabetic population [1]. More critically, the prevalence of diabetic complications is alarmingly high. Studies have found that among people with diabetes, 50% may suffer from diabetic peripheral neuropathy [2], approximately 23% have diabetic retinopathy [3], and 10%-15% have diabetic kidney disease [3]. Diabetic retinopathy is the leading cause of blindness in working-age populations [4], while diabetic kidney disease represents a primary driver of excess mortality in diabetes [5]. Therefore, delaying or controlling diabetic complications is crucial for reducing the disease burden of diabetes.

Exercise represents a cornerstone in the prevention and management of type 2 diabetes and its complications. The Da Qing Study demonstrated that lifestyle interventions including exercise could reduce the cumulative incidence of diabetes by 30%-50%, decrease the risk of microvascular complications (such as retinopathy and kidney disease) by 25%-30%, and lower the risk of cardiovascular disease by 20%-25% [6]. However, to date, no clear consensus has been established regarding how or when people with diabetes, particularly those with diabetic complications, should exercise. Furthermore, individuals with diabetic complications often have comorbidities requiring multiple medications, yet how to address the synergistic effects or adverse reactions between exercise and these medications remains inadequately clarified. To address these issues, this article provides a comprehensive review based on the latest domestic and international research evidence and corresponding guidelines/expert consensus [7-10].

## 1. Exercise Recommendations for Type 2 Diabetes Patients with Complications

Current domestic and international guidelines consistently recommend that most adults with type 2 diabetes should engage in at least 150 minutes of moderate-intensity aerobic exercise per week, distributed over no fewer than three sessions [7-11]. Accordingly, individuals with diabetic complications should also adhere to these recommendations. However, since diabetic complications are often accompanied by symptoms or pathological changes in other organ systems, exercise prescription components (such as exercise precautions) should be tailored differently for various types of diabetic complications (Table 1 ).

**Table 1 Exercise Prescription Guidelines and Considerations for Type 2 Diabetes Patients with Common Complications**

**General Principles for Exercise Prescription**
Exercise Type: Both aerobic and resistance exercise are acceptable, but combined aerobic and resistance training yields superior outcomes; aerobic exercise is prioritized in clinical practice.
Exercise Intensity: Recommend starting at low intensity, with moderate intensity being optimal, gradually increasing intensity over time.
Exercise Duration: Recommend 30–45 minutes per session for aerobic exercise (no less than 10 minutes but not exceeding 60 minutes per session); recommend resistance exercise focusing on major muscle groups (suggesting 4–6 exercises, 2–4 sets each, total duration 20–60 minutes).
Exercise Frequency: Recommend 3–5 sessions per week for aerobic exercise and 2 sessions per week for resistance exercise.
Total Exercise Volume: Recommend 150 minutes of moderate-intensity aerobic exercise per week.
Exercise Progression: Suggest gradual increases in exercise intensity, duration, and volume.

**Complication-Specific Considerations**

**Diabetic Kidney Disease**
1. For individuals with glomerular filtration rate $ $30mL \cdot min^{\{-1\}\cdot(1.73m}\{2\})\hat{}\{-1\}$ and urine microalbumin/creatinine ratio <300 mg/g, high-intensity exercise should be avoided to prevent exacerbating proteinuria, with regular monitoring of serum creatinine, urinary protein, and blood pressure.
2. For individuals with glomerular filtration rate <30 $\mathrm{mL \cdot min^{-1} \cdot (1.73\ m^2)^{-1}}$, with or without urine microalbumin/creatinine ratio $ $300 mg/g, exercise intensity should be restricted, focusing on low-to-moderate intensity daily activities.
4. Dialysis patients should maintain water-electrolyte balance during exercise and promptly correct any water or electrolyte disturbances.

**Diabetic Retinopathy**
3. Individuals with proliferative retinopathy or severe non-proliferative retinopathy are not recommended to engage in vigorous exercise.

**Diabetic Peripheral Neuropathy**
4. Select appropriate athletic shoes and socks, keep feet dry, and reduce ulcer risk from foot friction.

**Diabetic Autonomic Neuropathy**
2. Enhance blood pressure monitoring and avoid exercises involving rapid postural changes.

**Diabetic Lower Extremity Arterial Disease**
3. Exercise intensity should not exceed the threshold that induces lower extremity soreness and pain.

Diabetic kidney disease is characterized by persistent albuminuria and progressive decline in glomerular filtration rate, often accompanied by hypertension and edema. Current evidence indicates that individuals with diabetic kidney disease should engage in moderate aerobic exercise and resistance training to improve metabolic control and renal function. Specifically, those in the early-to-mid stages of diabetic kidney disease (typically defined as glomerular filtration rate $ $30mL \cdot min^{\{-1\}\cdot(1.73m}\{2\})\^{}\{-1\}$ and urine microalbumin/creatinine ratio <300 mg/g) should perform at least 150 minutes per week of moderate-intensity aerobic exercise (such as brisk walking or cycling) along with 2–3 sessions per week of resistance training (using dumbbells or resistance bands) to enhance muscular strength and cardiovascular health [12-13]. Exercise intensity should be maintained at 50%–70% of maximum heart rate, avoiding excessive vigorous exercise to prevent triggering or worsening proteinuria [14]. For advanced-stage diabetic kidney disease patients (typically glomerular filtration rate <30 $\mathrm{mL \cdot min^{-1} \cdot (1.73\ m^2)^{-1}}$, with or without urine microalbumin/creatinine ratio $ $300 mg/g), exercise intensity must be limited, focusing on low-to-moderate intensity daily activities. Those undergoing dialysis may engage in low-intensity exercise (such as bedside cycling or resistance bands) 1–2 hours after dialysis completion [15]. Due to fluid loss associated with exercise, dialysis patients should also maintain water-electrolyte and acid-base balance [11]. Diabetic kidney disease patients frequently develop sarcopenia, with studies reporting prevalence rates of 32.7%–73.5% in hemodialysis patients and 25.6%–44% in peritoneal dialysis patients [15]. Therefore, resistance exercise in diabetic kidney disease patients can help reduce or delay the risk of sarcopenia development and progression. However, given the significantly increased cardiovascular disease risk and common malnutrition issues in these patients, exercise intensity should be initiated at low levels. Vital signs must be closely monitored during exercise intervention, and exercise should be immediately discontinued if symptoms such as dizziness, chest pain, or dyspnea occur, with the exercise regimen adjusted under medical supervision [13].

Diabetic retinopathy can cause visual disturbances such as floaters, visual dis-

tortion, and blurred vision, with severe cases leading to retinal detachment and complete or partial vision loss [16]. Existing research has confirmed that exercise can improve retinal microvascular blood supply and oxygen delivery, thereby helping maintain retinal cell health and function [17]. However, studies on exercise in diabetic retinopathy populations remain relatively limited. Some research indicates that moderate-intensity aerobic exercise and physical activity offer greater benefits for diabetic retinopathy patients compared to low- or high-intensity exercise, primarily by helping prevent or delay retinopathy progression [18]. Notably, BROWNING et al. [19] found that diabetic retinopathy patients with concurrent macular edema should avoid short-term high-intensity exercise (such as handstands or vigorous head movements) to prevent increased intraocular pressure that could heighten the risk of vitreous hemorrhage or retinal detachment.

Diabetic peripheral neuropathy represents another microvascular complication following diabetic kidney disease and diabetic retinopathy. It commonly manifests as bilateral symmetric numbness, tingling, and pain, predominantly affecting the feet [20]. Studies on diabetic peripheral neuropathy populations have found that exercise, particularly endurance training, can significantly improve peripheral nerve conduction velocity, likely by modulating metabolic factors such as lowering blood glucose and improving circulation, thereby benefiting patients with diabetic peripheral neuropathy [21]. However, exercise intensity should be selected based on individual disease characteristics. Due to abnormal or diminished foot sensation and impaired balance, patients with diabetic peripheral neuropathy face significantly increased risks of falls and fractures [22]. Therefore, this population, especially those with a history of diabetic foot ulcers, should carefully inspect feet for redness, swelling, or lesions before and after exercise, avoid barefoot exercise during activity, and prevent friction or thermal injuries (such as in hot yoga). Notably, research by MATOS et al. [23] indicates that weight-bearing exercise does not necessarily increase diabetic foot ulcer risk; rather, appropriate weight-bearing exercise can enhance muscle strength and improve nerve function, potentially reducing the risk of diabetic foot ulcer development.

Unlike patients with diabetic microvascular complications, those with diabetic macrovascular disease face significantly increased risk of cardiovascular events or recurrence. Therefore, exercise intervention in diabetic macrovascular disease patients requires extra attention to cardiovascular safety and should be conducted under professional medical supervision. During exercise, patients with diabetic macrovascular disease should closely monitor heart rate and watch for symptoms such as chest tightness, chest pain, or dyspnea. Exercise intensity should start at low levels and gradually progress to a tolerable intensity (for example, in patients with coronary heart disease, exercise heart rate should be 10 beats/min lower than the heart rate at which angina symptoms or ST-segment depression occur) [10]. When performing resistance exercise, attention should be paid to breathing coordination, avoiding breath-holding maneuvers (such as the Valsalva maneuver) to prevent sudden blood pressure elevation.

However, regardless of whether patients have diabetic microvascular or macrovascular complications, blood glucose should be monitored before exercise to reduce exercise-related hypoglycemia risk. If pre-exercise blood glucose is <5.6 mmol/L, appropriate carbohydrate supplementation is recommended; if pre-exercise blood glucose is >13.9 mmol/L with positive urinary ketones, exercise should be suspended.

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## 2. Timing of Exercise Intervention in Type 2 Diabetes Complications

Existing guidelines and consensus statements on exercise intervention for type 2 diabetes primarily address basic principles from a health promotion perspective, yet offer no explicit recommendations regarding exercise timing (such as whether to exercise pre- or post-meal, or in the morning versus evening). Although current guidelines do not specify optimal exercise timing for particular complication populations, their recommendations for exercise timing in general type 2 diabetes patients [7-10] can nonetheless help guide exercise implementation for most individuals with diabetic complications.

Regarding the clinical question of whether pre- or post-meal exercise better facilitates glycemic control, multiple studies suggest that postprandial exercise may be more beneficial, particularly when performing prolonged (45 minutes) moderate-intensity aerobic exercise after meals [24]. COLBERG et al. [25] found that post-dinner walking was more effective than pre-dinner walking in reducing the glycemic impact of dinner and minimizing glucose fluctuations. Additional research indicates that initiating exercise 30 minutes to 1 hour after meals can effectively reduce postprandial glucose, with postprandial exercise being more effective than pre-meal exercise. Regarding exercise duration, studies suggest that exercise lasting more than 30 minutes may provide greater glycemic control benefits, while shorter durations are less effective [26].

Whether morning or evening exercise is more beneficial represents another clinical consideration. Research has shown that among individuals with type 2 diabetes and obesity, engaging in moderate-to-vigorous physical activity in the evening is associated with the lowest risks of all-cause mortality, cardiovascular disease, and microvascular disease compared to morning or afternoon activity [27]. Additionally, while morning exercise may help improve insulin resistance, its effects are relatively modest; evening exercise demonstrates superior benefits, with moderate-to-vigorous evening physical activity reducing insulin resistance by 25% in adults [28]. Furthermore, in overweight/obese men, although both morning and evening exercise improve cardiorespiratory fitness, only evening exercise improves postprandial glycemic control or partially reverses metabolic profile changes induced by high-fat diets [29].

However, it is noteworthy that individuals with type 2 diabetes should avoid vigorous exercise within 1 hour before bedtime, as intense activity may disrupt sleep latency, reduce deep sleep (slow-wave sleep) duration, or affect overall sleep

architecture, thereby compromising sleep quality [23]. On the other hand, since diabetes itself and diabetic retinopathy may cause vision decline, individuals with visual impairment, particularly those with concurrent retinopathy, should enhance safety precautions during evening exercise to prevent exercise-related accidents.

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## 3. Medication Use Considerations in Exercise Intervention for Type 2 Diabetes Complications

Compared to individuals with uncomplicated type 2 diabetes, those with diabetic complications often have more complex medication regimens, as they may require not only glucose-lowering agents but also antihypertensive, lipid-lowering, and antiplatelet medications. However, interactions between exercise and medications can further complicate exercise intervention. Therefore, from an "integration of sports and medicine" perspective, attention to exercise-drug interactions is crucial for implementing safe and effective exercise interventions in diabetic complication populations.

Exercise-drug interactions can be considered from several perspectives: (1) whether drug efficacy synergizes with exercise, such as exercise-induced glucose lowering through increased energy expenditure potentially superimposed on the glucose-lowering effects of sulfonylureas, producing enhanced hypoglycemic effects; (2) whether drug-related adverse effects are amplified by exercise, such as the increased risk of hypoglycemia from sulfonylureas potentially being further elevated by the synergistic glucose-lowering effects of exercise; and (3) whether exercise alters drug pharmacokinetics, such as increased sweating during exercise potentially accelerating drug excretion, modifying pharmacokinetic profiles, and consequently affecting blood drug concentrations and efficacy.

Although current guidelines detail medication precautions during exercise intervention for type 2 diabetes patients (including those with complications) (Table 2 ), it should be noted that literature on exercise-drug interactions remains relatively scarce.

Metformin is a first-line medication for type 2 diabetes treatment. Some studies have found that metformin may affect the efficacy of aerobic exercise in improving cardiovascular health and insulin sensitivity, potentially attenuating the improvement in maximal oxygen uptake ($VO_2$max) from aerobic training [30-31]. However, other research indicates that metformin use does not significantly impact $VO_2$max or the fat-burning effects of exercise [32].

Beyond metformin, studies have examined the impact of sodium-glucose co-transporter 2 (SGLT2) inhibitors on exercise capacity. Research shows that empagliflozin use in type 2 diabetes patients can improve cardiorespiratory health indicators, such as increasing peak oxygen uptake and reducing the ventilatory equivalent for carbon dioxide [33]. However, in clinical practice, considering

that exercise may increase the risk of hyperketonemia associated with SGLT2 inhibitors, it is recommended to discontinue SGLT2 inhibitors at least 24 hours before engaging in substantial physical activity [10].

For individuals on insulin therapy (particularly those with long disease duration and poor pancreatic function), exercise can improve insulin sensitivity and enhance insulin action [34], significantly increasing hypoglycemia risk [35]. Therefore, this population should intensify blood glucose monitoring before exercise and supplement with appropriate carbohydrates when necessary.

**Table 2 Medication Use Considerations During Exercise Intervention for Type 2 Diabetes Patients with Complications**

| Drug Category | Adverse Reactions | Precautions with Exercise |
|---|---|---|
| **Metformin** | Gastrointestinal discomfort, hypoglycemia, lactic acidosis | May reduce cardiovascular benefits and glycemic improvements from aerobic exercise |
| **Insulin Secretagogues** | Hypoglycemia, gastrointestinal discomfort, weight gain | Be vigilant about synergistic hypoglycemia risk with exercise; caution about fall risk to avoid fractures |
| **Insulin Sensitizers** | Weight gain, edema, increased fracture risk | – |
| **Alpha-glucosidase Inhibitors** | GI symptoms (bloating, abdominal pain) | Exercise 30 min after taking medication; treat hypoglycemia with simple sugars |
| **SGLT2 Inhibitors** | Ketoacidosis, weight loss (muscle mass) | Ensure adequate hydration; adjust medication based on exercise intensity/duration; add resistance exercise |
| **Incretin-based Drugs** | Nausea, vomiting, diarrhea, bloating | – |
| **Statins** | Rhabdomyolysis | Start with low-intensity, short-duration exercise; monitor for rhabdomyolysis |
| **Antiplatelet/Anticoagulant** | Bleeding risk | Avoid high-impact exercise; assess fall risk; stop exercise and seek care if hematuria or bruising occurs |

## 4. Summary and Outlook

The emergence of type 2 diabetes complications significantly increases disease burden and affects quality of life in this population. Although active exercise engagement can delay complication progression and reduce mortality risk, individuals with type 2 diabetes complications must pay extra attention to exercise safety and consider the interactions and influences between exercise and medications. On the other hand, as primary healthcare institutions serve as the main frontline for chronic disease prevention and treatment of type 2 diabetes in China, how to strengthen their capacity for screening diabetic complications and enhance healthcare professionals' knowledge application abilities in integrating sports with medicine or health [36], thereby developing more scientific, effective, and reasonable personalized exercise prescriptions for different diabetic complication populations, remains to be further explored and implemented.

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*Note: Figure translations are in progress. See original paper for figures.*