Review

Not peer-reviewed version

A Narrative Literature Review on the Role of Exercise Training in Managing Type 1 and Type 2 Diabetes Mellitus

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Posted Date: 6 September 2023

doi: 10.20944/preprints202309.0363.v1

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Review

A Narrative Literature Review on the Role of Exercise Training in Managing Type 1 and Type 2 Diabetes Mellitus

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Abstract: Diabetes mellitus (DM) is a metabolic disease characterized by chronic hyperglycemia associated with impaired carbohydrate, lipid and protein metabolism, with concomitant absence of insulin secretion or reduced sensitivity to its metabolic effects. Patients with diabetes mellitus have 30% more risk of developing heart failure and cardiovascular disease with respect to healthy people. Heart and cardiovascular problems are the first cause of death worldwide and the main complications which lead to high healthcare costs. Such complications can be delayed or avoided by taking prescribed medications in conjunction with a healthy lifestyle (i.e. diet and physical activity). The American College of Sports Medicine and the American Diabetes Association recommend that diabetic people reduce total sedentary time by incorporating physical activity in their weekly routine. This narrative literature review has the aim to summarize and present the main guidelines, pre-exercise cardiovascular screening recommendations, and considerations for patients with diabetes and comorbidities who are planning to participate in regular exercise regimens.

Keywords: resistance training; aerobic training; physical exercise; exercise guidelines; glucose; Insulin; glycemic control

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Introduction

Exercise is normally suggested in the management of type 1 (T1DM) and type 2 (T2DM) diabetes mellitus, and can improve glucose uptake by increasing insulin sensitivity, glucose transportation into the cells, and lowering body adiposity. In T2DM, the practice of physical exercise, both alone and when combined with diet and drug therapy (e.g. oral hypoglycemic agents), can result in improved glycemic control [1]. In addition, exercise can also help to prevent the onset of T2DM and has an important role in reducing the significant world-wide problem of this pathology. Recent studies have enhanced our understanding of the acute and long-term physiological benefits of physical activity, although the precise duration, intensity, and type of exercise have yet to be fully elucidated [1,2]. In T1DM, however, the expected improvements in glycemic control with exercise have not been clearly established. Instead, significant physical and psychological benefits of exercise can be achieved while careful education, screening, and planning allow the metabolic, microvascular, and macrovascular risks to be predicted and diminished [3].

The possible hypoglycemic benefits of physical activity were originally observed by Aristotle, and later re-advocated as a support of treatment by Allen and Joslin, in the 1920 [2]. Although, considered as one of the main cornerstones of diabetes management, there is relatively little guidance about the exercise protocols for diabetes. This is despite increasing evidence that many aspects of diabetes can be improved and possibly prevented by regular exercise [2,3]. At present, there are no recommendations for screening, exercise protocols, or treatment regimens, and the personal experience of people with diabetes, including elite athletes, has included frustration and a lack of support on issues of insulin dosage, nutrition, and the potential limits on performance and safety [4].

Nowadays, even though the benefits of physical activity as a therapeutic measure for diabetic patients are well known and accepted, it is difficult to put exercise recommendations into action for several reasons. Insufficient knowledge among diabetologists and exercise professionals and lack of

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dedicated facilities are indicated as important limitations [2]. Prescribing exercise is not generally undertaken, either by the general practitioner or by the diabetologist. This may be because there is insufficient awareness of the benefits of exercise or because there is a lack of specific knowledge about current recommendations. Thus, prescriptions, when suggested, are generic and more oriented towards 'physical activity' rather than 'exercise therapy', without appropriate indication about type, intensity, frequency, timing, progression and precautions [2].

This narrative literature review aims to highlight the literature available, while examining the underlying physiology of exercise in diabetes, the benefits and risks of exercise, the strategies for minimizing complications, the protocols suggested and the potential limitations.

Acute effect of exercise on sugar metabolism

Physical activity allows improving the glucose-tolerance curve by ameliorating insulin sensitivity in any subject, either with T2DM or T1DM [5]. Traditionally, exercise is promoted in T2DM where insulin action is scarce in the context of insulin resistance and/or inappropriate insulin secretion. Nevertheless, even in the dysregulation of immune system function found in T1DM, the β-cell toxicity is facilitated by a complex interaction between oxidative stress and inflammation, for which chronic exercise effect could be protective. During exercise the large changes in energy utilization require fine adjustments of glucose and fatty acid concentrations present in the blood. During the first 5–10 minutes of moderate intensity exercise, a mixture of fatty acid and glucose provide the major fuel source for skeletal muscle. As exercise duration is prolonged and maintained at the moderate intensity, the contribution of fatty acid become more significant, thanks to hormonal responses, such as increased levels of norepinephrine and glucagon that promote the release of fatty acids from adipose tissue (fat stores) into the bloodstream (lipolysis) [6]. The liberated fatty acids circulate in the blood and are available for uptake by muscle cells. There is also an upregulation of fatty acid transporters in muscle cells. This increased expression of transport proteins facilitates the uptake of fatty acids from the bloodstream into the muscle fibers, making them available for energy production. The oxidation of fatty acids produces a larger amount of ATP compared to glucose metabolism. By relying more on fatty acids for energy, the body can conserve its limited glycogen stores [7]. Preserving glycogen is crucial for sustaining exercise performance, especially during endurance activities or when exercise intensity increases. Glycogen is the primary fuel source for high-intensity exercise, and by sparing its usage, it helps delay the onset of fatigue. There is a direct relationship between exercise intensity and glucose utilization: when the exercise intensity increases, we observe an augmented glucose utilization via the glycogen deposit from muscles and liver [7]. A complex hormonal and autonomic response allows an intensification in hepatic glucose production and tissue uptake by the mobilization of non-esterified fatty acid from adipose tissue deposits [6]. This is produced both by a fall in circulating insulin concentrations and a wide variety of counterregulatory hormones (glucagon, adrenaline, cortisol and growth hormone) that counteract the hypoglycemic action of insulin [8]. Elevations in the blood concentrations of these hormones promote both increased glucose production and mobilization of non-esterified fatty acids from adipose storage sites. In addition, production of new glucose in the liver (gluconeogenesis) from substrates such as lactate is enhanced [9]. Direct sympathetic stimulation of the pancreas and liver after muscle contraction may also bypass initial hormonal control, and additional fuel supplies are provided by ketone formation and mobilization of lactate from inactive muscle glycogen. Glucose transport into muscle is again provided by the transporter protein GLUT4 which is recruited to the membrane surface in large quantities in contracting muscle, independently of insulin. All together, these changes maintain the increased fuel supply for exercising muscles and prevent hypoglycemia from excessive utilization [9].

Higher-intensity exercise or shorter-duration activities primarily rely on glycogen as the predominant fuel source, while lower-intensity or longer-duration exercise shifts towards a greater reliance on fatty acids for energy [7]. At the end of exercise, the body enters in a fasted state in which glycogen stores in muscle and liver are low and hepatic glucose production is accelerated. The counterregulatory hormone levels may remain elevated for some considerable time and there is a concomitant hyperglycemic and hyperinsulinaemic responses [10]. Glycogen resynthesis in the muscle occurs at first as a result of increased GLUT4 transport and insulin sensitivity. Then, when homoeostasis is reached and glycogen, glucose, and hormone levels return to normal, insulin may be

 doi:10.20944/preprints202309.0363.v1

required to produce additional glucose uptake and glycogen resynthesis in muscle and liver. In the insulin deficient or resistant state, storage of glucose may therefore be impaired within muscle due to the incomplete transport with a concomitant decrement in glycogen synthase activity [4,8].

Exercise benefits for people with diabetes

Physical activity, sports and exercise should be encouraged in people with T1DM, for the same reasons as it should be promoted in people with T2DM, or in the general population. The prescription of exercise for diabetic control should be considered for a variety of associated and independent health benefits. The full scope of these benefits can be seen in a number of reviews and include weight loss, weight loss maintenance, lipid profiles, reduction of blood pressure, good psychological profile, and the regulation of symptoms implicated in the metabolic syndrome [1,11]. It would appear that the combined effect of physical activity and diet provides the first and possibly most effective intervention in improving cardiovascular risk [12].

It has become evident that the most important effect of exercise is the improvement of blood sugar control, weight loss and weight loss maintenance. Physical activity helps in lowering blood sugar levels by increasing the uptake of glucose into muscles, even without the need for insulin. Exercise enhances insulin sensitivity, making the body more efficient at using insulin to regulate blood sugar. Regular exercise can contribute to better long-term glycemic control. Moreover, the physical exercise plays a crucial role in weight management, which is particularly important for individuals with T2DM. Regular physical activity reduces body fat, increase muscle mass, and improve overall body composition. Maintaining a healthy weight can enhance insulin sensitivity allowing a more efficient glucose utilization. This can lead to decreased insulin resistance, which is a key factor in T2DM. By improving insulin sensitivity, exercise can reduce the reliance on medication or insulin therapy in managing diabetes [4,13,14].

Exercise can also improve cardiovascular health by strengthening the heart, reducing blood pressure, lowering LDL cholesterol levels, increasing HDL cholesterol levels, and improving blood circulation, reducing significantly the risk of heart disease and stroke. Cardiovascular complications are also worsened by stress, and physical activity is an excellent stress reliever. Managing stress is important for individuals with diabetes because stress hormones can raise blood sugar levels. Exercise reduces stress levels, improve mood, and promote overall mental well-being. By improving blood sugar control, weight management, cardiovascular health, and overall well-being, regular exercise can lower the risk of diabetes-related complications such as heart disease, stroke, nerve damage, kidney disease, and eye problems [4,13,14].

Exercise and diabetes: general recommendations

All levels of physical activity, including leisure activities, recreational sports, and competitive professional performance, can be performed by people with DM who do not have complications and are in good blood glucose control. It has been largely confirmed that daily physical activity has different implication in improving people lifestyle: improve insulin sensitivity, reducing exogenous insulin injection, manage body weight and lipid profiles, boost self-confidence, improve psychological problems associated with the pathology, reduce systemic inflammation, and most importantly, enhance long-term protection against cardiovascular disease. Chronic hyperglycemia is supposed to be the mechanism by which coronary artery disease, stroke, nephropathy, retinopathy, and neuropathy, occur over decades after disease onset. Moreover, hyperglycemia is related with increased inflammation, as reflected by activation of immune cells and increased systemic concentrations of proinflammatory cytokines/chemokines [15]. This inflammatory status persists for several hours or days after hyperglycemia has been resolved [16]. Preventing hyperglycemia is the main aim of DM treatment, and may eliminate the excess inflammation caused by exercise as well. When this occurs, subject can: (i) postpone or cancel the planned exercise activity until the proinflammatory effects are reduced; (ii) perform exercise in a proinflammatory status; (iii) reduce exercise associated inflammation via medical treatment. Given that prior hyperglycemia alone (without ketosis) is not currently included in the contraindications to exercise, the second option is the good one [17]. General guidelines that may prove helpful in regulating the glycemic response to physical activity can be summarized as follows [2,18]:

Metabolic control before exercise

I. Avoid exercise if fasting glucose level is >250 mg/dl and ketosis is present, and take care if glucose level is >300 mg/dl and no ketosis is present.
II. Ingest added carbohydrate if glucose levels are <100 mg/dl.

Blood glucose monitoring before, during and after exercise

I. Identify when changes in medication (insulin/hypoglycemic agent) or food intake are necessary.
II. Learn the glycemic response to different physical activity conditions.

Food intake the exercise day

I. Consume added carbohydrate as needed to avoid hypoglycemia.
II. Carbohydrate-based foods should be readily available during and after physical activity.

Food intake the rest day

I. Reduce carbohydrate intake (< 50 grams/day).
II. A low carbohydrate diet has been shown to be effective for weight loss due to its effect on decreasing appetite and calorie intake.
III. Lowering dietary carbohydrate intake demonstrated benefits on insulin resistance, the underlying cause of T2DM, by independently promoting both weight loss and a reduction in insulin levels.

Exercise in managing T1DM

The ability to adjust the therapeutic regimen (insulin administration; timing, type and quantity of food ingestion before and after exercise) that allows safe participation and high performance has recently been recognized as an important management strategy in individuals with T1DM. In particular, the important role played by the patient in collecting self-monitored blood glucose data related to exercise responses to improve performance and enhance safety is now fully accepted [1,2,19].

During a prolonged exercise made below the anaerobic threshold, which occurs in amateurs at 50%-60% of VO2max, the availability of glucose can rise due to the increased uptake of skeletal muscle. Glycemic level normally drops by a few mg/dL from 30 to 45 min after exercise, and it is kept within the physiological range by two process: a rapid increase in endogenous glucose production, and due to the reduction in systemic insulin values [17]. Subjects should decrease, or may completely suspend, their insulin infusion during exercise. This is because the excess of insulin in the body have the dual effect of increasing glucose uptake in the skeletal muscle, and to suppress endogenous glucose production, leading to the hypoglycemic effect.

Different is the situation in which subject is involved in exercise above the anaerobic threshold and close to the VO2max. In this condition, the body produces a higher adrenergic activation, that made, beyond cardiovascular response, an endogenous increase in glucose level, exceeding the metabolic need at peripheral level. This makes a state of moderate, transient hyperglycemia that not exceed 140 mg/dL in healthy people. In T1DM, given that insulin cannot be secreted in response to this hyperglycemic response, the hyperglycemia value often continues to increase after exercise, sometimes becoming dangerous (>400 mg/dL) [17].

Hypoglycemia, which can occur during, immediately after, or many hours after physical activity, can be avoided. Indeed, during physical exercise the body requires about 30%-50% less insulin than in resting conditions to transport glucose across the cell membrane of myocytes. This is due to a considerable fraction of exercise-stimulated transmembrane glucose transport that occurs via noninsulin-dependent mechanisms [20]. In this case it is important that the patient has both an adequate knowledge of the metabolic and hormonal responses to physical activity and well-tuned self-management skills. The increasing use of intensive insulin therapy has provided patients with the flexibility to make appropriate insulin dose adjustments for various activities. Moreover, in T1DM, after 2-4 years disease onset, the ability to increase glucagon secretion (the main counterregulatory hormone) in response to hypoglycemia is permanently and completely abolished.

However, in T1DM hypoglycemia is caused by excessive exogenous insulin injection, involving low glycemia and high insulinemia that blocks glucagon release [17].

Aerobic performance is reduced in T1DM because of cardiovascular, muscular, and metabolic impairments. When compared to their nondiabetic counterparts, young patients with T1DM showed a reduction in VO2max despite insulin therapy [21], difference exacerbated in adults with neuropathic complications or sedentary lifestyles [22]. Different is the situation in which athletes with T1DM is compared to nondiabetic counterparts, where VO2 peak was found similar [23]. Moreover, in T1DM, various cardiovascular parameters, such as end-diastolic volume and left ventricular ejection fraction, do not show a normal increment due to exercise, meaning that exercise can lead them to normal aerobic and cardiovascular parameters [17].

In general, the principles recommended for dealing with physical activity in adults with T1DM, free of complications, apply to children, with the caveat that children may be prone to greater variability in blood glucose levels. In children, particular attention needs to be paid to balancing glycemic control with exercise, and for this the assistance of parents, teachers, and athletic coaches may be necessary. In the case of adolescents, hormonal changes can contribute to the difficulty in controlling blood glucose levels. Despite these added problems, it is clear that with careful instructions in self-management and the treatment of hypoglycemia, physical activity can be a safe and rewarding experience for the great majority of children and adolescents with T1DM [18].

Exercise in managing T2DM

A standard recommendation for diabetic patients, as for nondiabetic individuals, is that physical activity includes a proper warm-up and cool-down period. A warm-up should consist of 5–10 min of aerobic activity (walking, cycling, etc.) at a low intensity level. The warm-up session is to prepare the skeletal muscles, heart, and lungs for a progressive increase in exercise intensity. After a short warm-up, muscles should be gently stretched for another 5–10 min, to maintain a range of motion in the joints. Without it, the muscles shorten and become tight. The active warm-up can either take place before or after stretching [24]. After the activity session, a cool-down should be structured similarly to the warmup. The cool-down should last about 5–10 min and gradually bring the heart rate down to its pre-exercise level. There are several considerations that are particularly important and specific for the individual with T2DM. Moderate weight training programs that utilize light weights and high repetitions can be used for maintaining or enhancing upper body strength in nearly all patients with diabetes. Several long-term studies have demonstrated a consistent beneficial effect of regular physical activity training on carbohydrate metabolism and insulin sensitivity, which can be maintained for at least 5 years. These studies used physical activity regimens at an intensity of 50–80% VO2max three to four times a week for 30–60 min a session. Aerobic physical activity should be recommended, but taking precautionary measures for physical activity involving the feet is essential for many patients with diabetes [1,2,24–27]. High resistance exercise using weights may be acceptable for young individuals with diabetes, but not for older individuals or those with long-standing diabetes.

Proper hydration is also essential, as dehydration can affect blood glucose levels and heart function adversely. During physical activity, fluid should be frequently taken in an amount sufficient to compensate for losses in sweat reflected in body weight loss, or the maximal amount of fluid tolerated (e.g., 0.5 L of fluid consumed 2 h before physical activity). Precautions should be taken when exercising in extremely hot or cold environments.

It has been shown that improvements in glycated hemoglobin (HbA1c) are generally 10–20% of baseline and are most marked in patients with mild T2DM and in those who are likely to show insulin resistance [28]. It remains true, unfortunately, that most of these studies suffer from inadequate randomization and controls, and are confounded by associated lifestyle changes. The general agreement is that regular exercise should not be expected to dramatically affect HbA1c values, other variables such as increased food intake or reduced insulin dosages compensate for any increases in glucose disposal. Nonetheless, epidemiological evidence confirmed that being physically active, rather than sedentary, can lower mortality and morbidity for any given level of HbA1c [29].

It now appears that long-term programs of regular physical activity are indeed feasible for patients with impaired glucose tolerance or uncomplicated T2DM with acceptable adherence rates. Those studies with the best adherence have used an initial period of supervision, followed by relatively informal home physical activity programs with regular, frequent follow-up assessments [3]. A number of such programs have demonstrated sustained relative improvements in VO2max over many years with little in the way of significant complications [30].

Psychological profile, muscular and cardiovascular evaluations

Other important aspects to keep into account when prescribing an exercise program are the evaluation of motor responses and the consideration of the psychological profile. Evaluations represent a fundamental moment for understanding the real capabilities of an individual, setting up the protocols and assessing the results over time. People with diabetes show both impaired exercise tolerance and an excessive risk of developing heart failure, which are not entirely explained by known cardiovascular risk factors or coronary artery disease [31]. The risk for cardiovascular disease and other diabetes related complications including neuropathy, retinopathy, and nephropathy in persons with long-standing disease is high and care should be taken to properly screen individuals before recommending a new exercise program. Caution is warranted for those with advanced disease complications and medical screening; before initiating any new vigorous exercise program, a graded exercise stress test with ECG and blood pressure monitoring should be performed. The main assessments that should be made, before carrying out any type of physical exercise, are in order: i) Health Assessment Questionnaire; ii) Assessment of balance level and risk of falls; iii) Cardiopulmonary exercise testing; iv) The assessment of muscle strength.

Health assessment questionnaires [32]. While several tools are available to measure health-related quality of life (HRQoL) for patients with diabetes, the design and therefore duration of these measurements may limit their feasibility in the daily routine of a sports facility. Furthermore, these measures do not distinguish items for diabetes-specific quality of life. Thus, a specific questionnaire on the diabetics' quality of life (DMQoL) was developed with only 10 questions, sensitive to the change related to the progression of diabetes compared to the initial stages (e.g. glycemic changes). The combination of the DMQoL and the WHOQOL-BREF (the shortened version of the quality of life questionnaire designed by WHO) provides a comprehensive picture of overall health-related quality of life in patients with diabetes, and improves the ability to detect changes clinically significant in the pathology.

Tests the level of balance and the risk of falls. Patients with T2DM, particularly those ≥65 years old, exhibit an increased rate of falls. It is therefore important to assess the risk of falling before the prescription of an exercise intervention. The most used tests are the Timed Up & Go Test – TUG, the Functional Reach Test – FRT, the Berg Balance Scale – BBS, and the Dynamic Gait Index – DGI. Among those tests, the TUG showed the greatest sensitivity (90%) and specificity (88%) to the phenomenon [33]. In this assessment the patient gets up from a chair, walks 3 m, turns around, returns to the chair and sits down again. This task must be completed within 10.6 seconds. Times between 11 and 20 seconds are within the normal range for frail elderly and disabled patients; times ≥ 20 seconds indicate that the person needs external assistance. A score ≥ 30 seconds predicts a higher risk of falling.

Cardiopulmonary exercise testing (CPET). Measurements of ventilation, gas exchange, and electrocardiography during an incremental exercise test, is a noninvasive protocol that provides assessment of pulmonary, cardiovascular, and muscle function during exercise (see Table 1). The addition of echocardiographic monitoring ("imaging-CPET") may provide further insight into different aspects of cardiac function during exercise and their impact on exercise intolerance, mainly used in patients with heart failure [34].

Table 1. Physiological variables measured during CPET.

Physiological mechanism	Direct measurement	Indirect measurement
General	VO_2; peak power	VO_2 %
Cardiovascular system	HR; blood pressure	VO_2/HR
Cardiac electrical system	ECG	Chronotropic insufficiency; change in heart rate of recovery
Ventilation	Ventilation; Tidal volume	VE/VO_2; VE/VCO_2

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Gases exchange	SpO_2; $PETO_2$; $PETCO_2$	Anaerobic threshold
Skeletal muscles	Scala di Borg	$\Delta(a\text{-}v)O_2$; Anaerobic threshold
Metabolism	RER	Anaerobic threshold
Systolic function	LVEF; TAPSE	Systolic reserve
Diastolic function	E/A; DT	Systolic reserve

Legend: VO_2%, percentage of peak oxygen uptake; HR, heart rate; BP, blood pressure; ECG, electrocardiography; VE/VO_2; VE/VCO_2, ventilator equivalents of oxygen and carbon dioxide; SpO_2, arterial oxygen saturation; $PETO_2$ and $PETCO_2$, end-expiratory pressure of oxygen and carbon dioxide; $\Delta(a\text{-}v)O_2$, arteriovenous difference in oxygen; RER, respiratory exchange ratio; LVEF, left ventricular ejection fraction; TAPSE, tricuspid annular plane systolic excursion; E/A, transmittal flow velocity; DT, deceleration time.

Assessment of muscle strength. A significant percentage of T2DM patients (prevalence 16%, mean age 58 years old) are sarcopenic compared to age-matched healthy individuals [35]. Furthermore, muscle strength is reduced by 30% to 50% in T2DM patients compared to their healthy counterparts. Dynamometry is considered the gold standard for examining muscle strength. However, considering the cost of this device and the technical skills required, this test is not feasible for those working in private and home care settings. There are different types of tests, such as handgrip strength and sit-to-stand tests (Figures 1 and 2). Handgrip strength shows moderate to high correlations with extremity muscle strength. The patient sits in a chair with the elbow flexed to 90 degrees and with a force device in one hand. Subsequently, the patient grips the device as tightly as possible for 3 seconds. This test is performed 3 times, alternating hands. Another strength test that could be considered to assess muscle strength in T2DM patients is the sit-to-stand test, although the validity of this test is currently under an intense debate. Briefly, in this test the person, without the help of the hands and arms, but with only the work of the legs, must perform, in 1 minute as many reps as possible and sit with legs bent at 90 degrees (Figure 2). Another version foresees 30 seconds - 30s-STS [36], another one 5 reps as quickly as possible – FTSST [37].

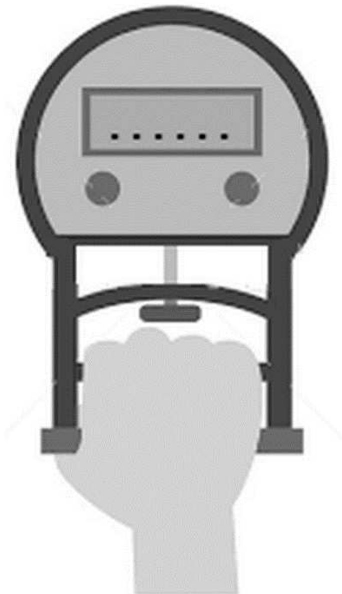

Figure 1. Image represents a hand that grip a dynamometer to measure the maximum isometric strength of the body.

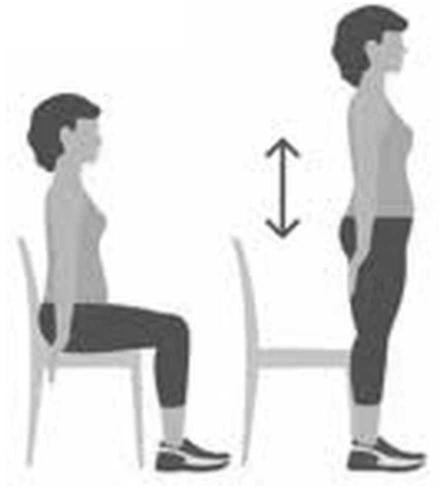

Figure 2. Image represent a participant that seat on a chair and stand up from that using only leg muscles doing as many reps as possible in a precise time.

Exercise prescription

Regular exercise enhances overall fitness, strength, and endurance. It boosts energy levels and can alleviate symptoms of fatigue commonly experienced by individuals with diabetes. It's important for individuals with diabetes to consult with their healthcare team before starting an exercise program. They can provide guidance on the type, intensity, duration, and frequency of exercise that suits individual needs and medical conditions. Additionally, monitoring blood sugar levels before, during, and after exercise is crucial to prevent hypoglycemia or hyperglycemia episodes.

Once a patient has been screened and the risk factors and exercise capacity determined, regular exercise may then be considered. The typical patient with T2DM is sedentary, overweight, and middle aged or older. In this group of patients, exercise may well be beneficial but needs to be carefully implemented. Guidelines issued jointly by the American Diabetes Association (ADA) and the American College of Sports Medicine (ACSM) suggest a gentle warm up period of 5–10 minutes, a period of stretching before the activity session, and then an active cool down period of 5–10 minutes to allow gradual adjustment of heart rate and blood pressure [25]. The intensity, duration, and frequency of exercise necessary for good health has been adjusted from the 60–80% of maximal oxygen consumption (VO2max) outlined in the ACSM guidelines in 1976 [14]. The target of an adult should be to achieve 30 minutes of continuous moderate activity, equivalent to brisk walking, on five or six days a week, with the flexibility of shorter bouts of more intense activity. Vigorous activity is widely implicated in health benefits and can be safely undertaken in diabetics if cardiovascular and hypertensive problems are taken into consideration [4,14]. Until now, to our knowledge, no studies have accurately defined the most suitable exercise programs for diabetics, it is inappropriate to be too prescriptive and instead we should concentrate on adherence and compliance. When ACSM guidelines are used, there is a dropout rate of 40–70% after 12–18 months despite an active intervention program [24]. However, the recent guidelines have gained wider acceptance and much greater success has been reported in the Malmo intervention studies with mixed high and low intensity exercises, although exercise below 30% of VO2max may have smaller benefit [38].

Physical activity guidelines for patients with DM are the same as for healthy people, unless co-occurring health conditions or advanced age affect their physical ability. In particular, interventions that combine aerobic and resistance training appear to show greater efficacy than the two training modalities taken individually [39]. Combined exercise 3 times/week may be of greater benefit for glycemic control than aerobic or resistance exercise alone. Additionally, total exercise duration and calorie expenditure were greater with the combo workout than with the individual workouts [39]. Several types of exercise protocols enhance health and glycemic management in individuals with DM, although structured exercise training has been studied most frequently, with benefits resulted from enhanced insulin sensitivity, reduced postprandial hyperglycemia, and reduced cardiovascular risk.

High intensity interval training (HIIT)

There has been a growing interest in high intensity interval training (HIIT) over the past 20 years. HIIT involves alternating short sets of high-intensity exercise, typically achieving values ≥85% peak heart rate (HRmax), with passive recovery periods or light exercise typically performed at ≤70% HRmax. HIIT has been proposed as a time-efficient form of exercise. A typical HIIT session can be up to 3 time shorter than that of traditional moderate-intensity continuous training (MICT) and can lead to both cardiovascular and metabolic improvements in less time than MICT. Several authors have studied the potential benefits of HIIT for multiple aspects, including cardiorespiratory fitness, anthropometric variables, mental health, cardiovascular and cardiometabolic diseases in different populations, both healthy and with pathologies. In individuals with T2DM and without complications, training adaptations induced by HIIT and MICT are equally capable of rapidly attenuating some local limiting factors governing the initially impaired VO2 kinetics response during submaximal exercise [40]. For this reason, HIIT at low-volume should also be considered a suitable and effective exercise modality to enhance oxidative metabolism in individuals living with T2DM.

Peripheral heart action training

A particular form of HIIT is PHA (Peripheral Heart Action) training [41]. The PHA is a circuit training that involves several stations that involve different muscles or muscle groups, following a well-defined pattern: the alternation between the exercises that involve the muscles located "above and below" the heart, in such a way as to avoid passive breaks between stations. The HIIT session is repeated 5 times in the first 2 days of training and gradually increased in subsequent sessions according to the subject's heart rate, which is monitored with the heart rate monitor. In the PHA session the subjects perform 15 repetitions on each piece of equipment and then move on to the next station with active breaks until the completion of the circuit of training. Active breaks implies that the subjects trains the lower limbs as soon as they finish the upper limbs and vice versa. This circuit training is performed 4 times, separated by 1 minute of rest, resistance is increased for the next exercise session if the subject is able to perform 15 full repetitions during the final set for each exercise. Subjects wear a heart rate monitor and maintain intensity at 55-60% of 1RM, which corresponded to approximately 60-80% of HRmax.

Water exercise

Compared to land-based exercise, aquatic exercise displays different advantages, including its effects on cardiovascular regulation because the blood flow to the lower limbs decreases due to the existence of hydrostatic pressure. This increase the redistribution of blood flow and the cardiac preload, thus increasing the stroke volume. Moreover, due to the height of the water, the pressure on the systemic circulation increases further affecting respiratory effort. These changes are helpful in increasing the elasticity and strength of the respiratory muscles, improving the oxygen uptake [42]. The resistance and heat dissipation effects of water are conducive to energy expenditure and improve the effects of exercise [42]. Therefore, exercise in the water could be considered as an alternative protocol to land-based exercise. Such protocol could be started with a 5 min warm-up consisting of articular mobilization, followed by 30 minutes of easy swimming (alternating the various swimming styles – front crawl, breaststroke, backstroke and butterfly), 5 min of leg-only swimming and 5 min of arm-only swimming, 5 min of aquatic skills, and 5 minutes of cool-down. An alternative protocol, with head-out water immersion may be used successfully and induce positive metabolic adaptations in patients with diabetes [43].

Exercise prescription must also consider patients' readiness to exercise, attitudes, and belief systems, while positively encouraging decisions to exercise. Support can be provided through a team of doctors, nurses, physiotherapists, lifestyle counsellors, and exercise consultants and even through health policy decision-making at government and local level. Moreover, exercise should be prescribed based on the type of diabetes, distinguishing between type 1 and type 2.

Conclusions and future recommendations

The major challenge is to persuade diabetic people to practice physical activity and to follow dietary recommendations. Sedentary and in particular persons with disabilities are very resistant to change their lifestyle, and in particular, adult diabetic people are resistant to change their habits, maybe because this pathology, except for those who have complications, it is not so much disabling.

 doi:10.20944/preprints202309.0363.v1

Successful interventions to promote long-term changes have used specific strategies to promote sustainable effects of interventions [44]. Considering that drug-resistant diseases could become leading cause of death by 2050, an intervention aiming at sustainable lifestyle change must therefore include components that facilitate maintenance of physical activity levels and dietary changes over time.

It is well known that men and women of all ages and abilities can improve their quality of life through regular physical activity associated to a well-designed dietary recommendations and nutrition therapy. Being physically active is one of the most important action that people of all ages can take to improve their health. The regular practice of physical exercise fosters normal growth and development, make people feel better, function better, sleep better, and reduce the risk of a large number of chronic diseases. Health benefits start immediately after exercising, and even short episodes of physical activity are beneficial. The evidence about the health benefits of regular physical activity is well established, and research continues to provide insight into what works to get people moving, both at the individual and community level. Achieving the benefits of physical activity depends on our personal efforts to increase activity in ourselves, family, friends, patients, and colleagues. Action is also required at the school, workplace, and community levels. Future recommendations for elderly interventions should emphasize the importance of naturalistic or personally meaningful environments and designs that should be inducing a mismatch of supply and demand, with high task variability, fulfilling basic individual senior needs, but be engaging, so as to maximize long-term adherence to physical exercise and active lifestyle.

Author Contributions: All authors contributed to the conception of the article. The corresponding author drafted the article and performed the literature search and analysis. All authors contributed to interpretation of the results and critically revised the work. All authors read and approved the final manuscript.

Funding: The authors declare that no funds, grants, or other support were received during the preparation of this manuscript.

Conflicts of Interest: The authors have no relevant financial or non-financial interests to disclose.

Appendix A

The appendix is an optional section that can contain details and data supplemental to the main text—for example, explanations of experimental details that would disrupt the flow of the main text but nonetheless remain crucial to understanding and reproducing the research shown; figures of replicates for experiments of which representative data is shown in the main text can be added here if brief, or as Supplementary data. Mathematical proofs of results not central to the paper can be added as an appendix.

Appendix B

All appendix sections must be cited in the main text. In the appendices, Figures, Tables, etc. should be labeled starting with "A"—e.g., Figure A1, Figure A2, etc.

References

1. Sigal RJ, Kenny GP, Wasserman DH, Castaneda-Sceppa C. Physical activity/exercise and type 2 diabetes: a consensus statement from the American Diabetes Association. Diabetes Care 2004;29:1433–8.
2. Peirce NS. Diabetes and exercise. Br J Sports Med 1999;33:161–72. https://doi.org/10.1136/bjsm.33.3.161.
3. Zinman B, Ruderman N, Campaigne BN, Devlin JT, Schneider SH. Diabetes mellitus and exercise. Diabetes Care 2002;25:S64–S64. https://doi.org/10.2337/diacare.25.2007.S64.
4. Wasserman DH, Abuad NN. Physiological Bases for the Treatment of the Physically Active Individual with Diabetes. Sport Med 1989;7:376–92. https://doi.org/10.2165/00007256-198907060-00003.
5. Kahn SE, Prigeon RL, McCulloch DK, Boyko EJ, Bergman RN, Schwartz MW, et al. Quantification of the relationship between insulin sensitivity and β- cell function in human subjects: Evidence for a hyperbolic function. Diabetes 1993;42:1663–72. https://doi.org/10.2337/diabetes.42.11.1663.
6. Stokie JR, Abbott G, Howlett KF, Hamilton DL, Shaw CS. Intramuscular lipid utilization during exercise: a systematic review, meta-analysis, and meta-regression. J Appl Physiol 2023;134:581–92. https://doi.org/10.1152/japplphysiol.00637.2021.
7. Coyle EF. Substrate utilization during exercise in active people. Am. J. Clin. Nutr., vol. 61, Oxford Academic; 1995, p. 968S-979S. https://doi.org/10.1093/ajcn/61.4.968S.

8. Frid A, Ostman J, Linde B. Hypoglycemia risk during exercise after intramuscular injection of insulin in thigh in IDDM. Diabetes Care 1990;13:473–7. https://doi.org/10.2337/diacare.13.5.473.
9. Berger M, Assal JP, Jorgens V. Physical exercise in the diabetic. The importance of understanding endocrine and metabolic responses. Diabete Metab 1980;6:59–69.
10. Wasserman DH, Vranic M. Interaction between insulin and counterregulatory hormones in control of substrate utilization in health and diabetes during exercise. Diabetes Metab Rev 1986;1:359–84. https://doi.org/10.1002/dmr.5610010403.
11. Sato Y. Overview of Exercise Prescription for Diabetes Patients and Its Application in Japan. J Sci Sport Exerc 2020;2:226–35. https://doi.org/10.1007/s42978-020-00061-6.
12. Anderssen S, Holme I, Urdal P, Hjermann I. Diet and exercise intervention have favourable effects on blood pressure in mild hypertensives: The Oslo diet and exercise study (ODES). Blood Press 1995;4:343–9. https://doi.org/10.3109/08037059509077619.
13. Roglic G. WHO Global report on diabetes: A summary. Int J Noncommunicable Dis 2016;1:3. https://doi.org/10.4103/2468-8827.184853.
14. Wasserman DH, Zinman B. Exercise in individuals with IDDM. Diabetes Care 1994;17:924–37. https://doi.org/10.2337/diacare.17.8.924.
15. Gordin D, Forsblom C, Rönnback M, Parkkonen M, Wadén J, Hietala K, et al. Acute hyperglycaemia induces an inflammatory response in young patients with type 1 diabetes. Ann Med 2008;40:627–33. https://doi.org/10.1080/07853890802126547.
16. El-Osta A, Brasacchio D, Yao D, Pocai A, Jones PL, Roeder RG, et al. Transient high glucose causes persistent epigenetic changes and altered gene expression during subsequent normoglycemia. J Exp Med 2008;205:2409–17. https://doi.org/10.1084/jem.20081188.
17. Galassetti P, Riddell MC. Exercise and type 1 diabetes (T1DM). Compr Physiol 2013;3:1309–36. https://doi.org/10.1002/cphy.c110040.
18. Sonnenberg GE, Kemmer FW, Berger M. Exercise in Type 1 (insulin-dependent) diabetic patients treated with continuous subcutaneous insulin infusion - Prevention of exercise induced hypoglycaemia. Diabetologia 1990;33:696–703. https://doi.org/10.1007/BF00400572.
19. AlShorman O, AlShorman B, Alkahtani F. A review of wearable sensors based monitoring with daily physical activity to manage type 2 diabetes. Int J Electr Comput Eng 2021;11:646–53. https://doi.org/10.11591/ijece.v11i1.pp646-653.
20. Hayashi T, Wojtaszewski JFP, Goodyear LJ. Exercise regulation of glucose transport in skeletal muscle. Am J Physiol - Endocrinol Metab 1997;273. https://doi.org/10.1152/ajpendo.1997.273.6.e1039.
21. Komatsu WR, Lima Gabbay MA, Castro ML, Saraiva GL, Chacra AR, Leite de Barros Neto T, et al. Aerobic exercise capacity in normal adolescents and those with type 1 diabetes mellitus. Pediatr Diabetes 2005;6:145–9. https://doi.org/10.1111/j.1399-543X.2005.00120.x.
22. Veves A, Saouaf R, Donaghue VM, Mullooly CA, Kistler JA, Giurini JM, et al. Aerobic exercise capacity remains normal despite impaired endothelial function in the micro- and macrocirculation of physically active IDDM patients. Diabetes 1997;46:1846–52. https://doi.org/10.2337/diab.46.11.1846.
23. Komatsu WR, Neto TLB, Chacra AR, Dib SA. Aerobic exercise capacity and pulmonary function in athletes with and without type 1 diabetes. Diabetes Care 2010;33:2555–7. https://doi.org/10.2337/dc10-0769.
24. Colberg SR, Sigal RJ, Fernhall B, Regensteiner JG, Blissmer BJ, Rubin RR, et al. Exercise and type 2 diabetes: The American College of Sports Medicine and the American Diabetes Association: Joint position statement. Diabetes Care 2010;33:e147–67. https://doi.org/10.2337/dc10-9990.
25. Warburton DER, Katzmarzyk PT, Rhodes RE, Shephard RJ. Evidence-informed physical activity guidelines for Canadian adults. Appl Physiol Nutr Metab 2007;32. https://doi.org/10.1139/H07-123.
26. Tuomilehto J, Lindström J, Eriksson JG, Valle TT, Hämäläinen H, Ilanne-Parikka P, et al. Prevention of Type 2 Diabetes Mellitus by Changes in Lifestyle among Subjects with Impaired Glucose Tolerance. N Engl J Med 2001;344:1343–50. https://doi.org/10.1056/nejm200105033441801.
27. Samuelson G. Global strategy on diet, physical activity and health. Scand J Nutr 2004;48:57. https://doi.org/10.1080/11026480410034349.
28. Sherwani SI, Khan HA, Ekhzaimy A, Masood A, Sakharkar MK. Significance of HbA1c test in diagnosis and prognosis of diabetic patients. Biomark Insights 2016;11:95–104. https://doi.org/10.4137/Bmi.s38440.
29. Jansson AK, Chan LX, Lubans DR, Duncan MJ, Plotnikoff RC. Effect of resistance training on HbA1c in adults with type 2 diabetes mellitus and the moderating effect of changes in muscular strength: A systematic review and meta-analysis. BMJ Open Diabetes Res Care 2022;10. https://doi.org/10.1136/bmjdrc-2021-002595.
30. Najafipour F, Mobasseri M, Yavari A, Nadrian H, Aliasgarzadeh A, Abbasi NM, et al. Effect of regular exercise training on changes in HbA1c, BMI and VO 2 max among patients with type 2 diabetes mellitus: An 8-year trial. BMJ Open Diabetes Res Care 2017;5. https://doi.org/10.1136/bmjdrc-2017-000414.
31. Johnston CA, Moreno JP, Foreyt JP. Cardiovascular Effects of Intensive Lifestyle Intervention in Type 2 Diabetes. Curr Atheroscler Rep 2014;16:1–8. https://doi.org/10.1007/S11883-014-0457-6.

32. Lin CY, Lee TY, Sun ZJ, Yang YC, Wu JS, Ou HT. Development of diabetes-specific quality of life module to be in conjunction with the World Health Organization quality of life scale brief version (WHOQOL-BREF). Health Qual Life Outcomes 2017;15. https://doi.org/10.1186/s12955-017-0744-3.
33. Dominguez-Muñoz FJ, Hernández-Mocholi MA, Manso LJ, Collado-Mateo D, Villafaina S, Adsuar JC, et al. Test-retest reliability of kinematic parameters of timed up and go in people with type 2 diabetes. Appl Sci 2019;9. https://doi.org/10.3390/app9214709.
34. Guazzi M, Bandera F, Ozemek C, Systrom D, Arena R. Cardiopulmonary Exercise Testing: What Is its Value? J Am Coll Cardiol 2017;70:1618–36. https://doi.org/10.1016/J.JACC.2017.08.012.
35. Purnamasari D, Tetrasiwi EN, Kartiko GJ, Astrella C, Husam K, Laksmi PW. Sarcopenia and Chronic Complications of Type 2 Diabetes Mellitus. Rev Diabet Stud 2022;18:157–65. https://doi.org/10.1900/RDS.2022.18.157.
36. Alfonso-Rosa RM, Del Pozo-Cruz B, Del Pozo-Cruz J, Sañudo B, Rogers ME. Test-retest reliability and minimal detectable change scores for fitness assessment in older adults with type 2 diabetes. Rehabil Nurs 2014;39:260–8. https://doi.org/10.1002/rnj.111.
37. Vaz MM, Costa GC, Reis JG, Junior WM, De Paula FJA, Abreu DC. Postural control and functional strength in patients with type 2 diabetes mellitus with and without peripheral neuropathy. Arch Phys Med Rehabil 2013;94:2465–70. https://doi.org/10.1016/j.apmr.2013.06.007.
38. Eriksson KF, Lindgärde F. Prevention of Type 2 (non-insulin-dependent) diabetes mellitus by diet and physical exercise The 6-year Malmö feasibility study. Diabetologia 1991;34:891–8. https://doi.org/10.1007/BF00400196.
39. Ghodrat L, Razeghian Jahromi I, Koushkie Jahromi M, Nemati J. Effect of performing high-intensity interval training and resistance training on the same day vs. different days in women with type 2 diabetes. Eur J Appl Physiol 2022;122:2037–47. https://doi.org/10.1007/S00421-022-04980-W.
40. Gildea N, McDermott A, Rocha J, O'Shea D, Green S, Egaña M. Time-course of V-O2 kinetics responses during moderate-intensity exercise subsequent to HIIT versus moderate-intensity continuous training in type 2 diabetes. J Appl Physiol 2021;130:1646–59. https://doi.org/10.1152/japplphysiol.00952.2020.
41. Piras A, Persiani M, Damiani N, Perazzolo M, Raffi M. Peripheral heart action (PHA) training as a valid substitute to high intensity interval training to improve resting cardiovascular changes and autonomic adaptation. Eur J Appl Physiol 2015;115:763–73. https://doi.org/10.1007/s00421-014-3057-9.
42. Pendergast DR, Moon RE, Krasney JJ, Held HE, Zamparo P. Human physiology in an aquatic environment. Compr Physiol 2015;5:1705–50. https://doi.org/10.1002/cphy.c140018.
43. Barbosa TM, Marinho DA, Reis VM, Silva AJ, Bragada JA. Physiological assessment of head-out aquatic exercises in healthy subjects: A qualitative review. J Sport Sci Med 2009;8:179–89.
44. Evangelista LS, Hamilton MA, Fonarow GC, Dracup K. Is exercise adherence associated with clinical outcomes in patients with advanced heart failure? Phys Sportsmed 2010;38:28–36. https://doi.org/10.3810/psm.2010.04.1759.