Review

Research progress on the effects of sedentary behavior and physical activity on diabetes mellitus

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Abstract: Diabetes mellitus (DM) has become one of the most serious and common chronic diseases around the world, leading to various complications and a reduction in life expectancy. Increased sedentary behavior (SB) and decreased physical activity (PA) are important contributors to the rising prevalence of DM. This article reviews the research progress on the pathogenesis of DM, the effects of SB and PA on the risk of DM, aiming to explore the influence of different PA intensities, amounts, frequencies, durations and types on the incidence of DM. Research has shown that blood glucose levels tend to increase with the prolongation of SB. Within a certain range, PA intensity and amount are negatively correlated with the risk of DM; Performing PA for more than 3 days per week maintains normal glucose tolerance and lower blood pressure; Engaging in 150-300 min of moderate-intensity exercise or 75-150 min of high-intensity exercise per week reduces the risk of DM; PA during leisure time reduces the risk of DM, while PA during work increases the risk of DM; Both aerobic training and resistance training reduce the risk of DM, and the combination of the two training methods produces better benefits; Various types of exercises, such as cycling, soccer, aerobics, yoga and tai chi, all reduce the risk of DM. In summary, prolonged SB increases the risk of DM, while appropriate PA reduces the risk of DM. As the intensity, amount, and frequency of PA increase, the effect of reducing DM risk becomes more significant. Different exercise methods have different effects on reducing DM risk.

Key words: sedentary behavior; physical activity; diabetes mellitus; sports rehabilitation; health promotion

久坐行为和体力活动对糖尿病的影响研究进展

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摘要:糖尿病(diabetes mellitus, DM)已成为当前最严重和最常见的慢性病之一,可引发多种并发症,缩短人们的预期寿命;而久坐行为(sedentary behavior, SB)增加和体力活动(physical activity, PA)减少是 DM 患病率上升的重要原因。本文综述了 DM 发病机制、SB和 PA对 DM 患病风险影响的研究进展,旨在探究不同 PA 强度、量、频率、时间和方式对 DM 患病率的影响。研究表明,随着 SB时间的延长,人体血糖水平呈现升高趋势;在一定范围内,PA 强度和 PA 量与 DM 患病风险呈负相关;每周进行 3 天以上的 PA 可以维持正常的葡萄糖耐量、降低血压;每周进行 150~300 min 的中等强度运动或 75~150 min 高强度运动能够降低 DM 患病风险;闲暇时的 PA 可降低 DM 患病风险,工作时的 PA 则会增加 DM 患病风险;有氧训练和抗阻训练都能对 DM 患病风险起到降低作用,且两者结合的训练方式产生的效益会更好;骑车、足球、健美操、瑜伽、太极等不同运动项目都能降低 DM 患病风险。总之,长时间 SB 会导致 DM 患病风险上升,而合适的 PA 可降低 DM 患病风险,并且随着 PA 强度、量、频率的增加,DM 患病风险降低效果愈加明显,不同的运动方式对 DM 患病风险降低作用不同。

关键词: 久坐行为; 体力活动; 糖尿病; 运动康复; 健康促进

This work was supported by Key Project of Undergraduate Teaching Reform Research of Shandong Normal University (No. 2024ZJ12), and the sixth batch of "Sports and Health" special topic of Education Research of Chinese Society of Education.

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Diabetes mellitus (DM) is a chronic metabolic disease that leads to organ dysfunction and failure, such as the eyes, kidneys, nerves, heart, and blood vessels [1,2]. The disease also causes serious infection in the legs and feet, which may lead to amputations [3]. New research published in *Lancet* estimated that the number of people with DM will increase from 529 million in 2021 to more than 1.3 billion in 2050 [4]. It has been claimed that DM will become a major disease in this century, and the health community's response to DM in the next 20 years will determine the health and life expectancy of the population in the next 80 years [5].

With the advancement of technology and the prevalence of electronic devices, sedentary behavior (SB) has become a global problem and a unique health hazard ^[6]. SB has a significant impact on people's health and may lead to an increase in risk of many diseases, including DM ^[7].

The DM Prevention and Control Guidelines of World Health Organization (WHO) suggest changing unhealthy lifestyles and engaging in physical activities (PAs) to prevent and reverse DM [8]. Lack of PA has become an important factor affecting people's health [9], as shown by a large number of studies on the effects of PA on people's health. Thus, lack of PA is a major risk factor for the development of DM. A decrease in PA and an increase in SB will negatively affect people's health [10]. Therefore, increasing PA and decreasing SB are necessary to prevent DM or improve DM conditions, but the optimal PA intensity, amount, frequency, and type for preventing or improving DM, as well as the joint effects of SB and PA on DM, are not fully understood. Therefore, this article reviews the research progress on the effects of SB and PA on the risk of DM, aiming to explore the influence of different PA intensities, amounts, frequencies, durations and types on the incidence of DM, providing a theoretical reference for the development of healthy lifestyles and prevention and reversal of DM.

1 Pathogenesis and hazards of DM

DM is a metabolic disease characterized by hyperglycemia, which is caused by defective insulin secretion, the body's insensitivity to insulin, or both. Prolonged hyperglycemia leads to chronic damage and dysfunction of various organs and tissues, such as the eyes, kidneys, heart, blood vessels, and nerves [11]. DM is cat-

egorized into various types, and the most common types are type 1 DM (T1DM), type 2 DM (T2DM), and gestational DM. T2DM accounts for more than 90% of all the DM cases, and its diagnostic criteria are as follows: fasting blood glucose concentrations of ≥ 126 mg/dL (7.0 mmol/L), oral glucose tolerance test two-hour blood glucose concentrations of ≥ 200 mg/dL (11.1 mmol/L) or glycated hemoglobin (HbA1c) concentrations of $\geq 6.5\%$ (48 mmol/mol) [12, 13]. Insulin resistance is a hallmark of T2DM and detected in nearly 90% or more of patients [14, 15]. T2DM is typically accompanied by other diseases, including hypertension, high serum low density lipoprotein (LDL) cholesterol, and low serum high density lipoprotein (HDL) cholesterol, which increase cardiovascular risk as much as T2DM [16]. This constellation of metabolic disorder is known as metabolic syndrome. In addition, obesity increases the prevalence of DM, which is nearly consistently present in the majority of insulin-resistant adult and pediatric T2DM patients [17]. A new study in Molecular Cell found that DM-level glucose concentrations (> 8 mmol/L) strongly destabilized the oncogenic protein p53 within 1 h. Through a series of regulatory processes, high glucose concentrations promoted the assembly of CRL4cop1 E3 ligase and accelerated the ubiquitination degradation of p53 proteins, which promoted the uptake of glucose and glycolysis by cancer cells and ultimately, cancer cell proliferation and progression [18]. High blood glucose also promoted the degradation of tet oncogene family member 2 protein (TET2), which led to the high expression of oncogenes and promotion of cancer development [19].

A hallmark of prediabetes is impaired fasting glucose (IFG) or impaired glucose tolerance (IGT), and prediabetes and DM begin with cellular insulin resistance [20]. In most cases, individuals with early-stage T2DM exhibit insulin insensitivity, and to counteract the decline in the insulin function and maintain normal blood glucose levels, pancreatic beta cells produce more insulin, which leads to hyperinsulinemia [21]. The two main features of IFG and IGT are insulin resistance and decreased pancreatic beta-cell function [21]. Prediabetes is reversible and preventable with proper PA during this critical period [22].

2 SB increases DM risk

SB involves an energy expenditure of ≤ 1.5 metabolic

equivalent of task (MET) in a sitting or lying position while awake [23]. Studies have demonstrated that SB is positively associated with risk of developing DM [24-26], with a 1.46-fold increase in risk of developing T2DM for every additional hour of SB compared with those with normal glucose metabolism [27]. A meta-analysis of the relationship between SB and DM showed that individuals with long sedentary times have increased risk of DM by 112% compared with those with short sedentary times [28]. Another study reported that the incidence of T2DM increases by 22% for every additional hour of sedentary time [27]. In non-DM patients, SB is strongly associated with increased risk of abnormal glucose metabolism, because muscle contractions accelerate plasma glucose uptake, which slows down in SB [29]. SB leads to a significant decrease in body activity, and in order to maintain a normal metabolic state, the body needs more insulin to act on target organs to lower blood sugar levels, which leads to insulin resistance in the long term. Moreover, SB leads to abnormalities in glucose metabolism and lipid metabolism, reduced insulin sensitivity [29], elevated fasting insulin levels [30-32], IGT [33-35], etc. Furthermore, human blood glucose levels tend to rise as sedentary time increases [36]. Thus, SB has been proven to be positively associated with DM risk.

3 Active role of PA in DM prevention and management

PA is defined as an activity in which skeletal muscle contractions cause an increase in energy expenditure, such as PA at work, PA at home, leisure activities, and physical exercise [8]. Studies confirmed the effects of PA on the risk of DM. For example, moderate-to-highintensity PA facilitates glucose stabilization, and skeletal muscle contractions increase glucose transporter 4 (GLUT4) expression in cell membranes, increase glucose uptake, and facilitate glucose stabilization [37]. With insufficient exercise, muscles are unable to effectively convert glucose in the blood into energy, causing it to accumulate in the blood and increasing blood glucose level; In addition, no exercise for a long time will also lead to fat accumulation, further increase the burden of islet beta cells, so that the secretion of insulin is not enough to meet the needs of the body, thus inducing diabetes. PA also improves insulin sensitivity [10, 38, 39]. Lifestyle with increasing PA is more

effective than drug treatment for T2DM [40]. A prospective follow-up study found that oxidized LDL content and total antioxidant capacity determine the body's ability to resist T2DM, and moderate-intensity PA (MPA; 331-1484 MET min/week) reduces the body's level of oxidative stress and decreases 10-year incidence of T2DM by 53% [41]. PA increases glucose uptake and improves glucose homeostasis and the overall energy balance [42-44]. In addition, PA effectively controls blood glucose in T2DM patients, reduces their risk of cardiovascular diseases and weight gain, maintains their bone health, prevents metabolic diseases, and improves their quality of life [45-47]. PA affects the risk of DM, and different PA intensities, amounts, frequencies, time and types have different effects on the risk of DM. The following aims to explore the most appropriate intensity, amount, frequency, time and method of PA to reduce the risk of DM.

3.1 Under the same amount of PA, high-intensity PA has the best effect on DM risk reduction

PA is categorized into three levels based on the intensity of the exercise: low (< 3 MET), medium (3-6 MET), and high (> 6 MET). Moreover, a dose-response relationship exists between PA intensity and the risk of DM. Thus, exploring which PA intensity level will effectively reduce risk of DM is necessary.

Moderate-to-vigorous-intensity PA (MVPA) improves blood glucose levels in T2DM and prediabetes patients [47,48] and has beneficial effects on people's health. MVPA significantly increases the body's glucose uptake [49,50], and not only maintains normal lipid levels and prevents insulin resistance [51,52], but also activates the body's immune system, which has a positive impact on health. High-intensity aerobic exercise (e.g., swimming or 150 min of fast running/walking per day for a week) lowered high blood pressure, improved blood glucose and lipid profiles, and reduced risk of cardiovascular diseases in the patients with T2DM [53]. Low-intensity PA (LPA) and MPA improve the overall health status of patients with T1DM [54].

High-intensity aerobic exercise is considered to be superior to low-intensity exercise for regulating blood glucose [53]. High-intensity interval training (HIIT) is an aerobic training that involves an all-out, fast, and explosive workout in short periods to rapidly increase the heart rate and burn calories. This type of high-intensity workout increases the body's demand for oxygen, resulting in a hypoxic state that causes the body to

require high amounts of oxygen during recovery. HIIT garnered attention as a potential time-efficient modality that elicits significant physiological and metabolic adaptations, and studies demonstrated that a single session of HIIT significantly reduced postprandial hyperglycemia in adult T2DM patients [55]. HIIT also significantly improved the health of T2DM adult patients and lowered their HbA1c levels and body mass index (BMI) [56]. Furthermore, with the same energy expenditure, HIIT improves fitness and body composition compared with sustained walking and enhances insulin sensitivity and pancreatic beta-cell function [57]. However, T2DM patients who want to improve their blood glucose levels should not engage in uninterrupted HIIT for long periods and should closely monitor their response to the training, because prolonged high-intensity training has negative effects, such as transient post-exercise hyperglycemia [58]. Engagement in PA with different intensities will have different effects on T2DM risk, such as significant improvements in insulin sensitivity and fasting blood glucose in elderly men after two months of MPA [59]. People who engage in higher-intensity exercise are less likely to develop T2DM compared to those who do not exercise at all [60]. A cohort study suggested that vigorous-intensity PA (VPA) or MVPA has stronger health benefits for reducing T2DM risk than MPA [61].

MVPA during leisure time reduces T2DM risk by 63%-65%, according to a randomized controlled trial in Finland [62]. A UK cohort study of self-reported daily PA (regular walking and cycling, recreational activities, and exercise) found that MPA significantly reduces T2DM risk [63]. In addition, in a prospective cohort study of a Chinese population with IFG, risk of T2DM was reduced by 12%, 20%, and 25% for the individuals who engaged in LPA, MPA, and VPA, respectively, during their leisure time compared with those who did not exercise [64]. Chinese scholars used an isochronous substitution model to explore the replacement of sedentary time with LPA, MPA, and VPA and the theoretical effects of the replacement of SB with PA of different intensities on risk of 45 common noncommunicable diseases. Specifically, the replacement of 1 h/d of sedentary time with an equivalent amount of LPA is associated with a 2%-5% reduction in DM risk. In addition, the replacement of 1 h/d of sedentary time with an equivalent amount of MPA is associated with a 2%-12% reduction in DM risk. By contrast, the

replacement of 1 h/d of sedentary time with an equivalent amount of VPA results in a 7%-19% reduction in DM risk. The experiments demonstrated that replacing 1 h of sedentary time with VPA led to the greatest reduction in diabetes risk ^[65].

Different PA intensities have different effects on DM risk, and within a certain range, the higher the PA intensity, the more effective the PA in reducing DM risk and improving physical conditions. Given an equal amount of PA, different intensity levels will have different reducing effects on DM risk, with the DM risk reducing effect diminishing from VPA to MPA, and then to LPA.

3.2 Activity with the amount recommended by WHO Physical Activity Guidelines effectively reduces the risk of DM

PA enhances glycemic control and improves insulin resistance, thus reducing the risk of T2DM and facilitates the maintenance of overall health conditions [66]. Different amounts of PA are associated with different DM risk reductions, and the WHO 2020 Guidelines for PA and SB recommend children and adolescents (5-17 years old) to engage in moderate-to-vigorous-intensity aerobic exercise, as well as muscle- and bone-strengthening exercises, for at least 60 min a day, 3 days a week, on average. Meanwhile, the Guidelines recommend adults (18-64 years old) to engage in at least 150-300 min of moderate-intensity aerobic exercise or at least 75-150 min of vigorous-intensity aerobic exercise or a combination of moderate- and vigorous-intensity exercise a week to gain substantial health benefits. In addition, adults should engage in moderate- or vigorousintensity muscle-strengthening exercises, which involve using the body's major muscle groups, two or more days a week. For elderly adults (≥ 65 years old), the Guidelines recommend a variety of MPA or higher 3 or more days a week to enhance their functional capacity and prevent falls [67].

A meta-analysis investigated the ideal amount of exercise for reducing DM risk and reported a 26% reduction in DM risk from no exercise to 11.25 MET/h per week. In the study, MVPA of over 37.5 MET/h per week (equivalent to 300 min of VPA) was found to have a similar reduction effect on T2DM risk [68]. High-intensity PA (33.3-120.0 MET/h per week), such as weightlifting, excavation, or construction work, minimized DM risk compared with inactivity [60], and 150-300 min of MPA a week was beneficial for reducing and negatively associated with T2DM risk [10]. How-

ever, the effects were not particularly pronounced. A study based on NHANES data from 2011 to 2016 found that people who engaged in adequate levels of PA and occupational, recreational, and transportation PA had a 22%, 16%, 18%, and 22% lower risk of T2DM, respectively, than those who do not meet the recommendations of the 2018 Physical Activity Guidelines for Americans [69].

The amount of PA recommended by the WHO is the amount that is effective in reducing the risk of DM, and 150-300 min of MPA a week has considerable health benefits. As the amount of PA increases, the risk of DM decreases significantly; thus, the amount of PA is negatively correlated with the risk of DM.

3.3 Different exercise frequencies have different effects on DM risk reduction, and high-frequency PA has the best effect

PA frequency also affects DM risk, and different exercise frequencies have different effects on DM risk. Studies reported that people who run ≥ 3 times a week during their leisure time had a reduced risk of T2DM by 28% [70]. In addition, 3-7 d a week of PA for the elderly increased their muscle strength, enhanced their cardiorespiratory fitness, lowered their blood pressure, maintained their normal glucose tolerance, and so on [71]. Another study noted that participating in VPA at least once a week reduced the risk of T2DM, and engaging in at least 120 min of VPA, 240 min of MPA, or 240 min of LPA a day resulted in a significant reduction in T2DM risk [10].

3.4 Long-term LPA effectively improves blood glucose control, and the longer the PA, the lower the risk of DM

A randomized controlled trial showed that LPA for at least 3 h a day improved glycemic control in elderly adults ^[72]. Another randomized controlled trial showed an average decrease in HbA1c levels of approximately 1% in DM patients when they engaged in LPA for > 55.2 min/day or MVPA for > 7.33 min/day. These findings demonstrated that the longer the PA, the lower the risk of T2DM ^[73]. The WHO recommends adults to engage in at least 150-300 min of moderate-intensity aerobic exercise or at least 75-150 min of vigorous-intensity aerobic exercise a week ^[8].

3.5 Different types of PA have different effects on DM risk

The following section discusses DM in terms of work and leisure PA, aerobic and resistance exercises, and other types of exercises.

3.5.1 Domestic and work-related PA (DWPA) increases the risk of DM, while leisure-time PA (LTPA) reduces DM risk

PA plays a preventive and ameliorative role in DM, but a clear and detailed description of the relationship between different types of PAs and risk of DM has yet to be provided. PA is categorized as DWPA and LTPA. DWPA includes occupational, academic, and voluntary activities, such as going up and down stairs to carry objects, cleaning, doing housework, and so on. Meanwhile, LTPA includes sports, exercise, and recreational activities, such as hiking, jumping rope, running, playing golf, and bowling. A Korean study showed that the risk of IFG and T2DM was higher in the individuals who engaged in moderate-intensity DWPA compared with those who engaged in low-intensity DWPA. However, the risk of IFG and T2DM was lower in the individuals who engaged in medium-to-high-intensity LTPA compared with those who engaged in lowintensity LTPA. In a comparison between DWPA and LTPA, it was found that medium-to-high-intensity LTPA reduced the risk of T2DM, whereas medium-tohigh-intensity DWPA increased the risk of T2DM, and the higher the intensity, the higher the risk of T2DM. Therefore, this study concluded that, regardless of the intensity, DWPA had a negative effect, and LTPA had a positive effect [74]. A study on the effects of LTPA and DWPA on the cardiovascular system in healthy workers found that DWPA was detrimental to the cardiovascular system, whereas LTPA had beneficial effects on the cardiovascular system [75]. However, there were few studies on the effect of LTPA and DWPA of the same amount or intensity on DM, and future studies may be limited to grouping the effects of LTPA and DWPA of the same amount or intensity on DM.

3.5.2 Regular exercise significantly improves the metabolism of DM patients, and the combination of aerobic and resistance exercises demonstrates the best effect Regular exercise has favorable effects on the metabolism of DM patients. Aerobic and resistance exercises gradually improved insulin activity, which was beneficial for glycemic control, and promoted fat oxidation and storage in muscles for 24-72 h [76]. Aerobic exercise increased insulin sensitivity and thus improved blood glucose uptake, and long-term regular aerobic exercise significantly reduced T2DM risk. During an

aerobic exercise, the body's oxygen uptake and oxygen demand were roughly equal owing to the low-intensity, long-duration, and rhythmic nature, safety, and other characteristics of the exercise [77]. Meanwhile, resistance exercise increased blood glucose uptake by increasing muscle mass [78]. The hypoglycemic effects of increased aerobic capacity and muscle mass were independent of each other, and the combination of aerobic and resistance exercises was more effective in improving glycemic control than either form of exercise alone [79]. Low-intensity exercise, such as tai chi and yoga, improved glycemic control, and stretching decreased blood glucose levels. Regular exercise decreased systolic blood pressure and had a slight effect on diastolic blood pressure in patients with T2DM, relieved depressive symptoms in patients with T2DM, and reduced maternal blood glucose levels in gestational DM and the risk of gestational DM [80].

Blood glucose levels drop fastest during lowintensity aerobic or endurance exercises. These activities, performed for extended periods, increase glucose uptake by muscles and lower blood sugar levels, while also boosting energy expenditure and promoting weight loss [77]. Recently, resistance exercise training was recognized as an effective class of exercises that had a positive impact on patients with T2DM, such as controlling their blood glucose, improving their insulin sensitivity, and reducing the risk of DM [81]. Moreover, resistance exercise training was found to improve strength, bone density, lean mass, blood pressure, and blood lipids by 10%-15% among elderly T2DM patients [47, 82] and reduced HbA1c levels in elderly T2DM patients [83]. Aerobic and resistance training reduced T2DM risk, and interventions that combined aerobic and resistance training were superior to those that used either types of exercise alone [84-86].

3.5.3 A variety of daily exercises, such as cycling and football, significantly reduce the risk of DM

Cycling to and from work increases daily PA and is a healthy lifestyle practice ^[87]. A Japanese study showed that cycling to work was associated with a significant reduction in T2DM risk, that is, the cycling commuting time was negatively associated with the risk of DM ^[88,89]. This finding is consistent with the findings of a study on working women in China ^[90]. A study based on NHANES data from 2007 to 2018 found that exercise, such as walking, did not have a substantial effect on

DM prevention, but brisk walking or cycling reduced T2DM risk by 24% [60].

Epidemiological studies demonstrated that playing soccer reduces risk of insulin resistance and oxidative stress, increased the levels of proteins associated with mitochondrial biogenesis, and improved the antioxidant capacity of active individuals with glucose intake, thereby leading to reduced T2DM risk [91]. Another study investigated the prevalence of prediabetes and T2DM among soccer players by interviewing 378 male soccer players (who played soccer an average of 3 days a week, 2 h a day) and 378 male control subjects who did not participate in regular sports, such as soccer, running, or swimming. The results showed that in the soccer players, the prevalence of prediabetes was 7.93%, and the prevalence of T2DM was 1.59%, whereas in the control group, the prevalence of prediabetes was 18.78%, and the prevalence of T2DM was 23.54%. The prevalence of T2DM in the control group was seven times higher than that of football players [92], which demonstrated that playing soccer significantly reduced the prevalence of prediabetes and T2DM.

Aerobics has considerable benefits for strengthening the body, improving mental outlook, and enhancing body flexibility and is proven to play a significant role in lowering blood glucose in patients with DM. A study showed that 6 months of aerobic exercise training in 60 adults with T2DM resulted in significant improvements compared to the control group. Participants experienced reductions in HbA1c, fasting plasma glucose, insulin resistance, fasting insulin, and systolic blood pressure [93]. Thus, aerobics is effective in reducing hyperglycemia in patients with T2DM.

Other leisure-time exercises affect DM risk to varying degrees. Yoga, tai chi, and other types of PAs had beneficial effects on blood glucose, and yoga improved the overall blood glucose and lipid levels and body composition of people with T2DM [94-97]. Tai chi training, which combined a variety of balance, stretching, and resistance exercises, improved blood glucose levels and reduced BMI and neuropathy symptoms, thus enhancing the quality of life for patients with T2DM and neuropathy [98,99]. Qigong reduced HbA1c levels and helped patients achieve improvements in other health parameters, such as blood pressure, cholesterol levels, body weight, blood glucose variability, and

mental health ^[98, 100, 101], and Pilates improved glycemic management and glycemic function in middle-aged and elderly T2DM patients ^[102]. In sum, many different exercises in daily life, such as cycling, soccer, aerobics, yoga, tai chi, qigong, and Pilates, reduce the risk of T2DM.

4 PA significantly reduces the risk of DM in middle-aged and elderly people

DM is prevalent among non-white, male, middle-aged, and elderly adults (≥ 45 years old) [103], which may be related to their lifestyle (e.g., SB, smoking, and so on). The prevalence of DM was low in individuals who regularly engaged in PA, and the prevalence of T2DM decreased significantly as PA intensity increased [104]. Young people (20-44 years old) had lower risk of diseases such as hypertension and hyperlipidemia and participate in MVPA in their daily lives, compared with middle-aged and elderly adults; moreover, the prevalence of T2DM was significantly lower in the former group than in the latter [60]. PA reduced the risk of DM in people of all ages, but its protective effect was strong and highly pronounced in elderly adults. A National Health and Nutrition Examination Survey on the effects of LTPA on prediabetes showed that MVPA was significantly protective against prediabetes in middleaged and elderly adults between the ages of 45 and 65 years [105]. A study on PA and DM risk in middle-aged and elderly Chinese populations noted that in terms of duration and amount, VPA/MPA was strongly negatively associated with DM risk in the middle-aged population, and MPA/LPA was significantly negatively associated with T2DM risk in the elderly population [10]. The finding suggested that PA played a positive role in reducing risk of T2DM in middle-aged versus elderly adults, but PA reduced the risk of DM significantly more in elderly adults [106, 107]. In sum, DM is prevalent among non-white individuals, and elderly adults are more likely to develop T2DM than young adults, and LPA, MPA, and VPA contribute to reducing T2DM risk in elderly adults, with VPA or MPA being strongly negatively correlated with the risk of T2DM in middleaged and elderly adults.

5 SB increases DM risk, and PA (non-DWPA) reduces DM risk

Studies found that the longer the SB time, the higher the blood glucose level, and the longer the LPA time, and the lower the blood glucose level [36]. It indicates that sitting for longer periods raises blood sugar levels, while spending more time on light physical activity lowers blood sugar levels, as shown above, and a positive correlation existed between SB and DM prevalence in inactive individuals [108-110]. According to a recent study by Chinese scholars, the replacement of 1 h/ day of VPA with the same amount of sedentary time increased DM risk by 17% [65]. Meanwhile, a three-year study in Italy showed that a 3.3 MET/h per week increase in MVPA resulted in a 0.85% decrease in HbA1c concentrations [111], because PA increased the total energy expenditure and thus counteracted the adverse effects of SB and improved the body's uptake and use of plasma glucose (Fig. 1).

In sum, prolonged SB leads to a substantially high risk of DM, but PA (non-DWPA) counteracts the negative effects of SB. In addition, people should recognize inactivity as a health hazard and reduce their SB by getting up and moving around for 5 min every 30 or 40 min [112].

6 Conclusion

DM is a chronic metabolic disease caused by various factors, such as insulin resistance, abnormal glucoselipid metabolism, and obesity, which causes different degrees of chronic damage to various organs and tissues. SB increases the prevalence of DM by elevating fasting insulin levels and IGT. Meanwhile, PA reduces risk of DM and is an effective way to reverse prediabetes and DM. Long-term SB will lead to increased risk of DM, whereas PA reduces the risk of DM. DM risk reduction increases as PA intensity, amount, frequency, and duration increase, and different exercise modalities have different effects on DM risk reduction. PA plays an important role in improving and reversing DM through exercise, but some questions remain unanswered. For instance, (1) what is the relationship between DM risk and exercise when it is performed at different time of the day? How is exercise associated

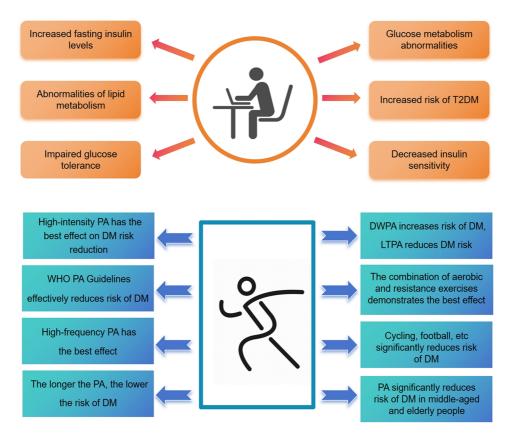


Fig. 1. Sedentary behavior (SB) increases diabetes mellitus (DM) risk, whereas physical activity (PA) (non-DWPA) has the opposite effect. Prolonged sitting increases type 2 DM (T2DM) risk, while regular high-intensity or combined exercise, like cycling or football, lowers it, especially in older adults. DWPA, domestic and work-related PA; LTPA, leisure-time PA.

with DM risk, what is its intervention effect, and what time is best for exercise? (2) What is the effect of the same level of PA on the risk of DM in different age groups, and in what age group is the protection effect highly pronounced? (3) What is the cross-over effect of PA and SB on DM? For example, can sedentary populations reduce their risk of DM by increasing their PA, and can non-sedentary populations forgo PA? The questions should be examined and explored further to clearly understand the effects of PA and SB on DM risk and develop effective interventions.

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