Physical Activity/Exercise and Type 2 Diabetes

A consensus statement from the American Diabetes Association

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For decades, exercise has been considered a cornerstone of diabetes management, along with diet and medication. However, high-quality evidence on the importance of exercise and fitness in diabetes was lacking until recent years. The present document summarizes the most clinically relevant recent advances related to people with type 2 diabetes and the recommendations that follow from these. Our recently published technical review on physical activity/exercise and type 2 diabetes (1) includes greater detail on individual studies, on prevention of diabetes, and on the physiology of exercise.

The present statement focuses on type 2 diabetes. Issues primarily germane to type 1 diabetes will be covered in a subsequent technical review and ADA Statement. The levels of evidence used are defined by the ADA in ref. 2.

PHYSICAL ACTIVITY AND PREVENTION OF TYPE 2 DIABETES — Two randomized trials each found that lifestyle interventions including ~150 min/week of physical activity and diet-induced weight loss of 5–7% reduced the risk of progression from impaired glucose tolerance (IGT) to type 2 diabetes by 58% (3,4). A cluster-randomized trial found that diet alone, exercise alone, and combined diet and exercise were equally effective in reducting the progression from IGT to diabetes (5). Therefore, there is firm and consistent evidence that programs of increased physical activity and modest weight loss reduce the incidence of type 2 diabetes in individuals with IGT.

EFFECTS OF STRUCTURED EXERCISE INTERVENTIONS ON GLYCEMIC CONTROL AND BODY WEIGHT IN TYPE 2 DIABETES — Boulé et al. (6) undertook a systematic review and meta-analysis on the effects of structured exercise interventions in clinical trials of ≥8 weeks duration on HbA_{1c} (A1C) and body mass in people with type 2 diabetes. Postintervention A1C was significantly lower in exercise than control groups (7.65 vs. 8.31%, weighted mean difference −0.66%; $P < 0.001$). In contrast, postintervention body weight did not differ between the exercise and control groups. Meta-regression confirmed that the beneficial effect of exercise on A1C was independent of any effect on body weight. Therefore, structured exercise programs had a statistically and clinically significant beneficial effect on glycemic control, and this effect was not primarily mediated by weight loss. A subsequent meta-analysis by the same authors (7) showed that exercise intensity predicted postintervention weighted mean difference in A1C ($r = -0.91$, $P = 0.002$) to a larger extent than exercise volume ($r = -0.46$, $P = 0.26$). These results provide support for encouraging type 2 diabetic individuals who are already exercising at moderate intensity to consider increasing the intensity of their exercise in order to obtain additional benefits in both aerobic fitness and glycemic control.

PHYSICAL ACTIVITY, AEROBIC FITNESS, AND RISK OF CARDIOVASCULAR AND OVERALL MORTALITY — Large cohort studies have found that higher levels of habitual aerobic fitness and/or physical activity are associated with significantly lower subsequent cardiovascular and overall mortality (8–10), to a much greater extent than could be explained by glucose lowering alone. For example, Church et al. (8) found that men in the lowest, second, and third quartiles of cardiorespiratory fitness had 4.5-, 2.8-, and 1.6-fold greater risk for overall mortality than men in the highest quartile of cardiorespiratory fitness, even after adjustment for age, examination year, baseline cardiovascular disease (CVD), hypercholesterolemia, hypertriglyceridemia, BMI, hypertension, parental CVD, smoking, and baseline fasting glucose levels. Essentially all of the association between higher BMI and higher mortality was explained by confounding with cardiorespiratory fitness; there was no difference in mortality among normal-weight, overweight, and obese men after adjustment for cardiorespiratory fitness.

In the same cohort, it was shown that among moderately fit subjects (21st–60th percentile for age) whose only exercise was walking, the mean time spent per week on exercise was 130 min for men and 148 min for women (11). These times are consistent with recommendations from the U.S. Surgeon General (12) and other respected bodies (13–15) stating that 150 min/week of moderate-intensity exercise should be accumulated. Moderately fit subjects whose only exercise was jogging or running reported a mean of 90 min/week for men and 92 min/week for women. These times are consistent with

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Abbreviations: CAD, coronary artery disease; CVD, cardiovascular disease; ECG, electrocardiogram; IGT, impaired glucose tolerance.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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an alternative and equally valid recommendation for 30 min of vigorous activity three times a week.

To our knowledge, no meta-analysis of the effects of exercise training on lipids or blood pressure in people with diabetes has been published. In the general, predominantly nondiabetic population, the effects of exercise training on blood pressure (16) and lipids (17) are relatively modest. Greater increases in HDL cholesterol and decreases in plasma triglycerides have been seen with exercise programs that are more rigorous in terms of both volume and intensity than those that have been evaluated in diabetic subjects (18). Potential mechanisms through which exercise could improve cardiovascular health were reviewed by Stewart (19). These include decreased systemic inflammation, improved early diastolic filling (reduced diastolic dysfunction), improved endothelial vasodilator function, and decreased abdominal visceral fat accumulation.

FREQUENCY OF EXERCISE

The U.S. Surgeon General's report (12) recommended that most people accumulate ≥30 min of moderate-intensity activity on most, ideally all, days of the week. However, most clinical trials evaluating exercise interventions in people with type 2 diabetes have used a three-times-per-week frequency (6), and many people find it easier to schedule fewer longer sessions rather than five or more weekly shorter sessions. The effect of a single bout of aerobic exercise on insulin sensitivity lasts 24–72 h depending on the duration and intensity of the activity (20). Because the duration of increased insulin sensitivity is generally not >72 h, we recommend that there should not be more than 2 consecutive days without aerobic physical activity. The effect of resistance exercise training on insulin sensitivity may last somewhat longer (21), perhaps because some of its effects are mediated by increases in muscle mass.

EXERCISE FOR WEIGHT LOSS AND WEIGHT MAINTENANCE

The most successful programs for long-term weight control have involved combinations of diet, exercise, and behavior modification (22). Exercise alone, without concomitant dietary caloric restriction and behavior modification, tends to produce only modest weight loss of ~2 kg. Weight loss is typically this small primarily because obese people often have difficulty performing sufficient exercise to create a large energy deficit, and it is relatively easy to counterbalance increased energy expenditure through exercise by eating more or becoming less active outside of exercise sessions (22). However, in a randomized trial, high-volume aerobic exercise (700 kcal/day, ~1 h/day of moderate-intensity aerobic exercise) produced at least as much fat loss as the equivalent degree of caloric restriction and with greater resulting improvements in insulin sensitivity (23).

The optimal volume of exercise to achieve sustained major weight loss is probably much larger than needed to achieve improved glycemic control and cardiovascular health. In observational studies (24–27), individuals who successfully maintain large weight loss over at least a year have typically performed ~7 h/week of moderate- to vigorous-intensity exercise. Two randomized trials found that higher exercise volumes (2,000 and 2,500 kcal/week) produced greater and more sustained weight loss than lower exercise volumes (1,000 kcal/week) (28,29).

Because of the increased evidence for health benefits from resistance training during the past 10–15 years, the American College of Sports Medicine (ACSM) now recommends that resistance training be included in fitness programs for healthy young and middle-aged adults (13), older adults (30), and adults with type 2 diabetes (15). With increased age, there is a tendency for progressive declines in muscle mass, leading to "sarcopenia," decreased functional capacity, decreased resting metabolic rate, increased adiposity, and increased insulin resistance, and resistance training can have a major positive impact on each of these (30). Resistance exercise improves insulin sensitivity to about the same extent as aerobic exercise (31).

RESISTANCE TRAINING

Studies of resistance training in type 2 diabetes

Two clinical trials provided the strongest evidence for the value of resistance training in type 2 diabetes (32,33). In both studies, the average age of participants was 66 years, and the resistance-training regimen involved multiple exercises at high intensity (three sets, three times per week), and absolute A1C declined 1.1–1.2% in resistance-training subjects versus no significant change in control subjects. One of these trials had a second phase (months 7–12), where training was home based rather than facility based (34). Body composition changes were maintained, but exercise intensity and adherence were lower than in the first 6 months and the A1C difference between groups became statistically nonsignificant. Other published studies of resistance exercise in type 2 diabetic participants have used less intense exercise regimens (35–40). All showed beneficial effects of the resistance exercise program but to a lesser extent than the Dunstan et al. (32) and Castaneda et al. (33) trials.

Safety of resistance training

Some medical practitioners have concerns about the safety of higher-intensity resistance exercise in middle-aged and older people who are at risk of CVD. Often, the main concern is that the acute rises in blood pressure associated with higher-intensity resistance exercise might be harmful, possibly provoking stroke, myocardial ischemia, or retinal hemorrhage. We have found no evidence that resistance training actually increases these risks. No serious adverse events have been reported in any research study of resistance training in patients with type 2 diabetes, although the total number of subjects enrolled in these studies was small (32,33,35–37,40). A review of 12 resistance exercise studies in a total of 246 male cardiac rehabilitation patients found no angina, ST depression, abnormal hemodynamics, ventricular dysrhythmias, or other cardiovascular complications (41). A study of 12 men with known coronary ischemia and electrocardiogram (ECG) changes inducible by moderate aerobic exercise found that even maximal-intensity resistance exercise did not induce ECG changes (42). Therefore, moderate- to high-intensity resistance training was found to be safe even in men at significant risk of cardiac events.

While it is well known that blood pressure rises while lifting a heavy weight, it is often not appreciated that blood pressure can also rise considerably in healthy older people performing aerobic exercise. Benn et al. (43) demonstrated that in healthy older men, the myocardial demands of high-intensity resistance exercise were comparable to those occasionally needed for activities of daily living, such as climbing stairs, walking up a hill, or carrying 20–30 lb of groceries.

FLEXIBILITY EXERCISE — Flexibility exercise (stretching) has frequently been recommended as a means of increasing range of motion and hopefully reducing risk of injury. However, two systematic reviews found that flexibility exercise did not reduce risk of exercise-induced injury (44,45). Most studies included in these systematic reviews evaluated younger subjects undertaking very vigorous activity programs, such as those in military basic training; these results may not be generalizable to older subjects. Flexibility exercise has been successfully used in clinical trials as a "placebo" exercise (32,46), since there is no evidence that flexibility exercise affects metabolic control or quality of life. One small randomized trial ($n = 19$) found that range-of-motion exercises modestly decreased peak plantar pressures (47). We found no studies that directly evaluated whether flexibility training reduced the risk of ulceration or injury in people with diabetes. Therefore, we feel that there is insufficient evidence to recommend for or against flexibility exercise as a routine part of the exercise prescription.

EVALUATION OF THE DIABETIC PATIENT BEFORE RECOMMENDING AN EXERCISE PROGRAM — For a more detailed review on this subject, see ref. 48. Before beginning a program of physical activity more vigorous than brisk walking, people with diabetes should be assessed for conditions that might be associated with increased likelihood of CVD or that might contraindicate certain types of exercise or predispose to injury, such as severe autonomic neuropathy, severe peripheral neuropathy, and preproliferative or proliferative retinopathy. The patient's age and previous physical activity level should be considered.

The role of stress testing before beginning an exercise program is controversial. There is no evidence that such testing is routinely necessary for those planning moderate-intensity activity such as walking, but it should be considered for previously sedentary individuals at moderate to high risk of CVD who want to undertake vigorous aerobic exercise exceeding the demands of everyday living (49). The prevalence of both symptomatic and asymptomatic coronary artery disease (CAD) is greater in diabetic individuals compared with nondiabetic individuals of the same age-group. However, many younger diabetic patients have relatively low absolute risk for a coronary event. Ten-year CVD risk can be estimated using the UKPDS (U.K. Prosepctive Diabetes Study) Risk Engine (50) (http://www.dtu.ox.ac.uk/index.html?maindoc%20=%20/riskengine/), while 30-year risk of a wide variety of outcomes, including CVD, can be estimated using the American Diabetes Association's Diabetes PHD (Personal Health Decisions) (51) (http://diabetes.org/diabetesPHD). The lower the absolute CAD risk, the higher the likelihood of a false-positive test. A recent systematic review for the U.S. Preventive Services Task Force came to the conclusion that stress tests should usually not be recommended to detect ischemia in asymptomatic individuals at low CAD risk (<10% risk of a cardiac event over 10 years) because the risks of subsequent invasive testing triggered by false-positive tests outweighed the expected benefits from detection of previously unsuspected ischemia (52,53).

There is little or no evidence to guide practitioners in terms of whether stress testing before undertaking resistance training is necessary. One might ask whether such testing should use resistance exercise rather than the usual aerobic exercise during a stress test in such circumstances. Very few test centers would currently be equipped for such testing, and such tests have not been standardized. In contrast, aerobic exercise stress testing is widely available, standardized, and of proven prognostic value.

EXERCISE IN THE PRESENCE OF NONOPTIMAL GLYCEMIC CONTROL

Hyperglycemia

When people with type 1 diabetes are deprived of insulin for 12–48 h and ketotic, exercise can worsen the hyperglycemia and ketosis (54). Previous ADA exercise position statements suggested that physical activity be avoided if fasting glucose levels are >13.9 mmol/l (>250 mg/dl) and ketosis is present and that it be performed with caution if glucose levels are >16.7 mmol/l (300 mg/dl), even if no ketosis is present (55). We agree that vigorous activity should probably be avoided in the presence of ketosis. However, the recommendation to avoid physical activity if plasma glucose is >300 mg/dl, even in the absence of ketosis, is probably more cautious than necessary for a person with type 2 diabetes, especially in a postprandial state. In the absence of very severe insulin deficiency, light- or moderate-intensity exercise would tend to decrease plasma glucose. Therefore, provided the patient feels well, the patient is adequately hydrated, and urine and/or blood ketones are negative, it is not necessary to postpone exercise based solely on hyperglycemia.

Hypoglycemia

In individuals taking insulin and/or insulin secretagogues, physical activity can cause hypoglycemia if medication dose or carbohydrate consumption is not altered. This is particularly so at times when exogenous insulin levels are at their peaks and if physical activity is prolonged. Hypoglycemia would be rare in diabetic individuals who are not treated with insulin or insulin secretagogues. Previous ADA guidelines suggested that added carbohydrate should be ingested if preexercise glucose levels are <5.6 mmol/l (100 mg/dl) (55). We agree with this recommendation for individuals on insulin and/or an insulin secretagogue. However, the revised guidelines clarify that supplementary carbohydrate is generally not necessary for individuals treated only with diet, metformin, α-glucosidase inhibitors, and/or thiazolidinediones without insulin or a secretagogue. We found no published studies examining responses to exercise in subjects taking pramlintide (synthetic amylin analog) or exenatide (incretin analog). Neither is likely to cause hypoglycemia when used as monotherapy or combined with only metformin or a thiazolidinedione. However, patients taking either of these drugs in combination with insulin or a secretagogue may need to take additional carbohydrate before physical activity and/or reduce doses of insulin or secretagogue to avoid hypoglycemia. For a detailed discussion of medication adjustments to reduce risk of hypoglycemia, see ref. 56.

Concomitant medications other than hypoglycemic agents. Diabetic patients frequently take diuretics, β-blockers, ACE inhibitors, aspirin, and lipid-lowering agents. In most type 2 diabetic individuals, medications will not interfere with the physical activities they choose to perform, but patients and health care providers should be aware of potential problems to minimize their impact. Diuretics, especially in higher doses, can interfere with fluid and electrolyte balance. β-Blockers can blunt the adrenergic symptoms of hypoglycemia, possibly increasing risk of hypoglycemia unawareness. They can reduce maximal exercise capacity to ~87% of what it would be without β blockade (57) through their negative inotropic and chronotropic effects. However, most people with type 2 diabetes do not choose to exercise at very high intensity, so this reduction of maximum capacity is generally not problematic. In people with CAD, β blockade actually increases exercise capacity by reducing coronary ischemia (58). For additional discussion on the impact of concomitant medications on physical activity, see ref. 48.

EXERCISE IN THE PRESENCE OF SPECIFIC LONG-TERM COMPLICATIONS OF DIABETES

— There is a paucity of research on the risks and benefits of exercise in the presence of diabetes complications. Therefore, recommendations in this section are based largely on "expert opinion."

Retinopathy

Exercise and physical activity are not known to have any adverse effects on vision or the progression of nonproliferative diabetic retinopathy or macular edema (59). This applies to both resistance and aerobic training. However, in the presence of proliferative or severe nonproliferative diabetic retinopathy, vigorous aerobic or resistance exercise may be contraindicated because of the potential risk of triggering vitreous hemorrhage or retinal detachment (59). We found no research studies providing guidance as to an appropriate time interval between successful laser photocoagulation and initiation or resumption of resistance exercise. Ophthalmologists, with whom one of us (C.C.-S.) consulted, suggested waiting 3–6 months after laser photocoagulation before initiating or resuming this type of exercise.

Peripheral neuropathy

We are unaware of research studies assessing the risk of exercise-induced injury in people with peripheral sensory neuropathy. Common sense, however, would indicate that decreased pain sensation in the extremities would result in increased risk of skin breakdown and infection and of Charcot joint destruction. Therefore, in the presence of severe peripheral neuropathy, it may be best to encourage non–weight-bearing activities such as swimming, bicycling, or arm exercises (60,61).

Autonomic neuropathy

Autonomic neuropathy can increase the risk of exercise-induced injury by decreasing cardiac responsiveness to exercise, postural hypotension, impaired thermoregulation due to impaired skin blood flow and sweating, impaired night vision due to impaired papillary reaction, and impaired thirst, which increases the risk of dehydration and gastroparesis with unpredictable food delivery (60). Autonomic neuropathy is also strongly associated with CVD in people with diabetes (62,63). Individuals with diabetic autonomic neuropathy should undergo cardiac investigation before beginning physical activity more intense than that to which they are accustomed. Some experts advocate thallium scintigraphy as the preferred screening technique for CVD in this high-risk population (60).

Microalbuminuria and nephropathy

Physical activity can acutely increase urinary protein excretion. The magnitude of this increase is in proportion to the acute increase in blood pressure. This finding has led some experts to recommend that people with diabetic kidney disease perform only light or moderate exercise, such that blood pressure during exercise would not rise to more than 200 mmHg (64). However, there is no evidence from clinical trials or cohort studies demonstrating that vigorous exercise increases the rate of progression of diabetic kidney disease. Several randomized trials in animals with diabetes and proteinuria showed that aerobic exercise training decreased urine protein excretion (65,66), possibly in part due to improved glycemic control, blood pressure, and insulin sensitivity. Resistance training also may be of benefit in terms of muscle mass, nutritional status, functional capacity, and glomerular filtration rate (67). Because of these encouraging findings, we believe there may be no need for any specific exercise restrictions for people with diabetic kidney disease. However, because microalbuminuria and proteinuria are associated with increased risk for CVD, it is important to perform an exercise ECG stress test in previously sedentary individuals with these conditions before beginning exercise significantly more intense than the demands of everyday living.

RECOMMENDATIONS

— Levels of evidence used are those defined by the ADA in ref. 2.

Lifestyle measures for prevention of type 2 diabetes

In people with IGT, a program of weight control is recommended, including at least 150 min/week of moderate to vigorous physical activity and a healthful diet with modest energy restriction. *Level of evidence*: A (3,4,68,69).

Aerobic exercise

The amount and intensity recommended for aerobic exercise vary according to goals.

- To improve glycemic control (6,7), assist with weight maintenance, and reduce risk of CVD (9,10), we recommend at least 150 min/week of moderate-intensity aerobic physical activity (40–60% of $\dot{V}O_{2max}$ or 50–70% of maximum heart rate) and/or at least 90 min/week of vigorous aerobic exercise (>60% of $\dot{V}O_{2max}$ or >70% of maximum heart rate). The physical activity should be distributed over at least 3 days/week and with no more than 2 consecutive days without physical activity. *Level of evidence*: A (6,7).
- Performing ≥4 h/week of moderate to vigorous aerobic and/or resistance exercise physical activity is associated with greater CVD risk reduction compared with lower volumes of activity (10). *Level of evidence*: B (9,10).
- For long-term maintenance of major weight loss (≥13.6 kg/30 lb), larger volumes of exercise (7 h/week of moderate or vigorous aerobic physical activity) may be helpful (24–27,70). *Level of evidence*: B (24–27,70).

Resistance exercise

In the absence of contraindications, people with type 2 diabetes should be encouraged to perform resistance exercise three times a week, targeting all major muscle groups, progressing to three sets of 8–10 repetitions at a weight that cannot be lifted more than 8–10 times (8–10 RM). *Level of evidence*: A (32,33). To ensure resistance exercises are performed correctly, maximize health benefits, and minimize the risk of injury, we recommend initial supervision and periodic reassessments by a qualified exercise specialist, as was done in the clinical trials (32,33).

Prevention of hypoglycemia

Those who take insulin or secretagogues should check capillary blood glucose before, after, and several hours after completing a session of physical activity, at least until they know their usual glycemic responses to such activity. For those who show a tendency to hypoglycemia during or after exercise, several strategies can be used. Doses of insulin or secretagogues can be reduced before sessions of physical activity, extra carbohydrate can be consumed before or during physical activity, or both strategies can be implemented. *Level of evidence*: E (consensus, clinical experience).

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