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Invited Review

Clinical Aspects of Physical Exercise for Diabetic Patients: Theory and Practice

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Abstract: In recent years, the Westernization of dietary habits and increasingly sedentary lifestyles have contributed to a marked increase in the number of patients with lifestyle-related diseases, including type 2 diabetes (T2D), worldwide. Epidemiological studies of physical exercise, such as the Diabetes Prevention Program and the Diabetes Prevention Program Outcomes Study, have shown that lifestyle intervention programs involving diet and/or exercise reduce the progression of impaired glucose tolerance to T2D. In Japan, a nationwide survey regarding exercise therapy for diabetic patients revealed that relatively few physicians provide patients with exercise guidance because of time constraints, that the physicians do not receive additional consultation fees, and there is a lack of specialized physical exercise educators. It has been demonstrated in well-controlled diabetic patients that physical exercise promotes the utilization of blood glucose and free fatty acids in the muscles and lowers blood glucose levels. Furthermore, long-term, mild, regular jogging increases the action of insulin without affecting body mass index or maximum oxygen uptake. It is suggested that people with T2D undertake at least 150 min/week of moderate-to-vigorous aerobic exercise spread out over at least 3 days/week, with no more than 2 consecutive days between bouts of aerobic activity. Mild-intensity resistance training using light dumb-bells and stretch cords is recommended for elderly individuals who have decreased muscle strength and mass (sarcopenia). An active lifestyle is essential for the management of diabetes, a typical lifestyle-related disease.

Key words: type 2 diabetes, physical exercise, insulin resistance, nationwide survey, medical support team

Introduction

In recent years, the Westernization of dietary habits (i.e. a high-protein and high-fat diet) combined with increasingly sedentary lifestyles have contributed to a marked increase in the number of patients with lifestyle-related diseases, such as type 2 diabetes (T2D) and metabolic syndrome (MetS), worldwide[1–3]. The aging population has further exacerbated

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these problems[4]. Insulin resistance is one of the characteristic features of T2D and MetS[3, 5]. Although dietary intervention in combination with physical exercise is effective for the prevention and treatment of T2D and MetS[6, 7], lifestyle improvements based on diet and exercise are difficult in practice[8].

Recently, Lee *et al*[9] reported that low cardiorespiratory fitness and obesity increase the risks of impaired fasting glucose and T2D. Furthermore, in a UK population of South Asians, Gill *et al*[10] reported a significant relationship between sitting time and 2-h glucose levels that was independent of physical activity and waist circumference. In another study, Dunstan *et al*[11] found an association between television viewing time and an increased risk of both all-cause and cardiovascular disease (CVD) mortality. It is known that breaking up periods of sitting with short bouts of light- or moderate-intensity walking lowers postprandial glucose and insulin levels in overweight and/or obese adults[10, 11]. This may improve glucose metabolism and, as such, prove to be an important public health and clinical intervention strategy for reducing cardiovascular risk[10, 11].

Overall, there is considerable evidence in the literature regarding the benefits of physical exercise for the prevention and treatment of T2D, obesity, and/or MetS[7–14].

Physical activity and T2D : results of epidemiological studies

In Japan, most diabetic patients have T2D. Decreased insulin secretion and insulin resistance play important roles in the occurrence and progression of T2D[7]. Indeed, epidemiological studies have revealed that a proper diet combined with exercise is not only useful in preventing T2D and improving disease status, but that it is also effective in preventing and treating all other insulin resistance-related diseases (lifestyle-related diseases, MetS) by improving in vivo sensitivity to insulin[7]. Furthermore, lifestyle interventions have been shown by the Diabetes Prevention Program (DPP)[8] and its Outcomes Study (DPPOS)[13] to be cost-effective[14].

The results of some of these studies are summarized below.

1. Pennsylvania University Health Study (USA ; 1991, 1994) : the findings of this study indicate that the incidence of diabetes decreases by 24% with every 2000 kcal/week increase in energy consumption during leisure-time physical exercise[15].

2. Nurses' Health Study (USA ; 1991, 1999, 2010) : prospective studies[16, 17] have provided strong evidence that increased physical activity in diabetic women is associated with substantial reductions in the risk of cardiovascular complications. Even moderate-intensity exercise, such as regular walking, is strongly associated with a lower risk of CVD in patients with diabetes[18]. In addition, van't Riet *et al*[18] reported that excess adiposity and, to a lesser extent, specific dietary habits can explain a substantial part of the association between having a family history of diabetes and the risk of T2D.

3. DPP/DPPOS (USA ; 2002, 2009) : a randomized controlled clinical trial, the DPP demonstrated that intensive lifestyle intervention reduced the incidence of T2D by 58%

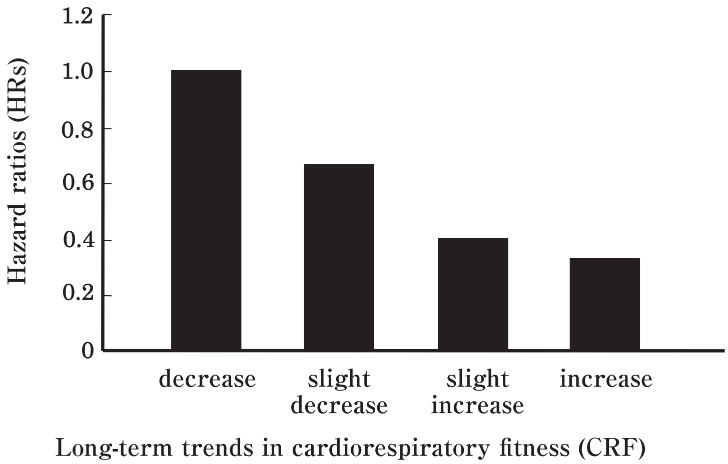
compared with placebo intervention, whereas metformin intervention reduced the incidence of T2D by 31%[8]. The DPPOS[13] is a long-term follow-up study of participants in the DPP study investigating whether the delay in the development of diabetes observed during the DPP is sustained and assessing the long-term effects of the various interventions on subjects' health. Over an average 10-year follow-up (3 years of the DPP, 7 years of the DPPOS), the incidence of diabetes after randomization was reduced by 34% and 18% in subjects initially randomized to lifestyle and metformin interventions, respectively, compared with placebo. The DPP research group concluded that the prevention or delay of diabetes using lifestyle or metformin interventions persists for at least 10 years.

4. Tokyo Gas Study (Japan, 2003, 2010): Sawada *et al*[19] investigated the relationship between long-term trends in cardiorespiratory fitness (CRF) and the incidence of T2D in a cohort of 41 787 non-diabetic Japanese men who completed annual health check-ups and fitness tests for the estimation of maximum oxygen uptake (VO_{2max}) over a period of 7 years. In that study, a strong inverse relationship was found between long-term trends in CRF and the development of T2D (Fig. 1). Sawada *et al*[19] provided evidence that low CRF due to a sedentary lifestyle is a strong predictor of the incidence of T2D in Japanese men.

Current status of exercise therapy for diabetic patients in Japan: a nationwide survey

The number of diabetic patients worldwide is increasing. In 2010, Japan was ranked as having the eighth highest number of diabetic individuals[1].

Many studies in Japan have focused on the benefits of exercise intervention in preventing



CRF: cardiorespiratory fitness
(Sawada SS et al, Diabetes Care 33(6): 1353-1357, 2010 revised)

Fig. 1. Long-term trends in CRF and the incidence of type 2 diabetes

and treating T2D[20,21]. However, these results are meaningless if effective exercise therapy is not incorporated into clinical practice by medical institutions. Thus, we undertook a nationwide survey to determine the current status of exercise therapy in Japan and to clarify the problems related to its implementation[22].

In that study, questionnaires were sent out to 1200 randomly selected diabetologists and non-specialist physicians of the Japan Medical Association[22]. Four hundred and three physicians (response rate 34%) returned completed questionnaires. The responses were then divided into two groups according to the rate of exercise guidance provided to patients at the time of their initial visit to the clinic: (i) a high rate of guidance (> 70% ; HG group ; n = 212) ; and (ii) a low rate of guidance (< 50% ; LG group ; n = 131). The results were then evaluated.

As indicated in Fig. 2a, b, the rate of exercise guidance was significantly lower ($P <$ 0.001) than that of dietary guidance. Across both groups, approximately 65% and 53% of physicians reported that a "lack of time" and the "absence of an additional consultation fee", respectively, were the main reasons why they did not provide exercise guidance to patients. A higher number of physicians in the LG compared with HG group reported that there were no specialized physical educators in their clinics ($P < 0.001$; Fig. 3). In both groups, physicians suggested that patients did not exercise primarily because they "had no time to exercise" (70%) and/or "were not eager to perform exercise" (60%)[22].

The results of that survey revealed that, in Japan, there is relatively little exercise guidance for patients because physicians have no time, they receive no additional consultation fees, and there is a lack of specialized physical exercise educators[22]. Although improvements in these areas may lead to higher rates of exercise guidance, we consider that the preparation of specific exercise guidelines for T2D patients is essential for the effective implementation of this therapy in clinical practice. To this end, a teaching manual based on the results of that survey, as well as current evidence, has been published[23].

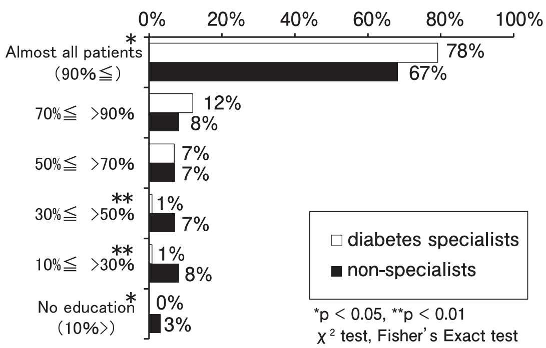


Fig. 2a. Dietary Guidance (at first visit)

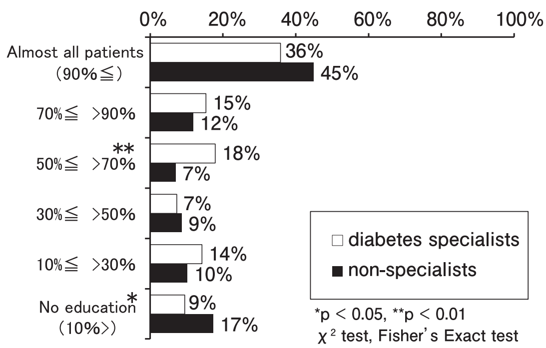


Fig. 2b. Exercise Guidance (at first visit)

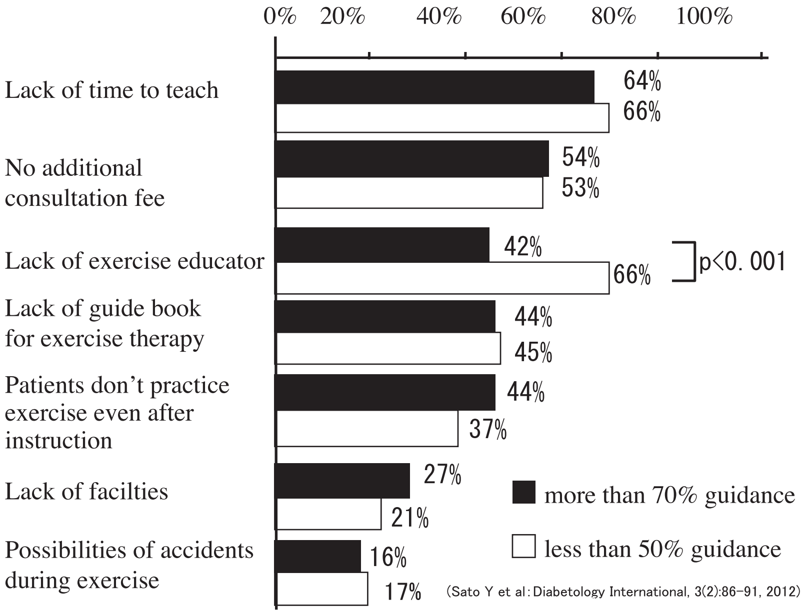


Fig. 3. Problems Related to the Practice of Exercise Therapy for Diabetic Patients (multiple answer)

Metabolic and endocrinological effects of physical exercise

Acute effects of exercise

1. Fuel metabolism during exercise: physical activity (PA) increases glucose uptake into active muscles, which is balanced by hepatic glucose production, with a greater reliance on carbohydrates to fuel muscular activity as exercise intensity increases.

2. Insulin-independent and -dependent muscle glucose uptake during exercise: insulin-stimulated blood glucose (BG) uptake (GLUT4 translocation) into skeletal muscle predominates at rest and is impaired in T2D, whereas muscular contractions stimulate BG transport via a separate additive mechanism (AMP-activated protein kinase) that is not affected by insulin resistance or T2D. Both aerobic and resistance exercise increase the abundance of GLUT4 and BG uptake, even in the presence of T2D[7,16].

3. Mild-intensity exercise, such as tai chi and yoga, improves BG management[16].

4. Intense PA: plasma catecholamine levels rise markedly during intense PA, which may result in transient hyperglycemia.

Chronic effects of exercise training

1. Metabolic control (BG levels and insulin resistance): intramyocellular lipids and intrahepatic lipids are associated with a reduction in insulin action in both obese and non-obese individuals. Both aerobic and resistance training improve insulin action, BG control,

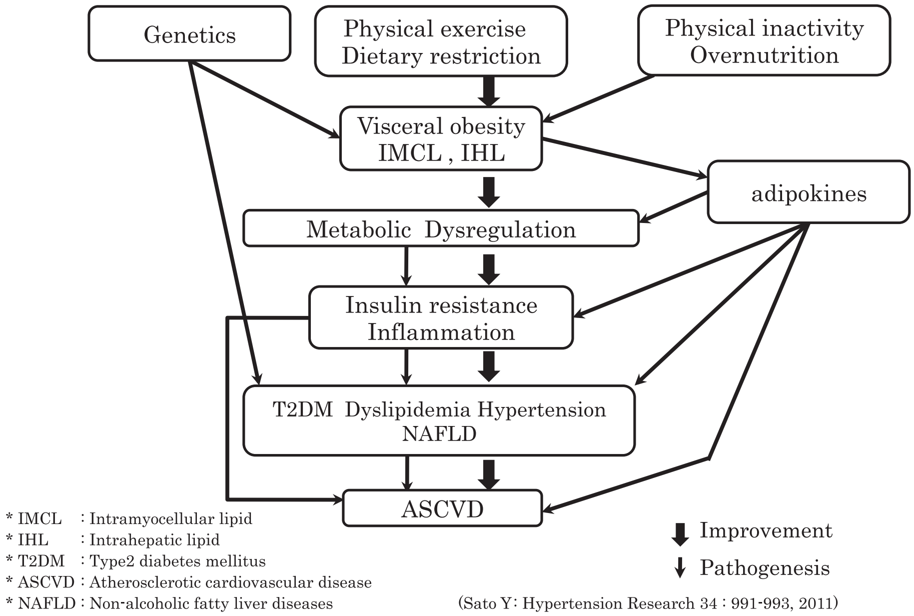


Fig. 4. Physical exercise improves or prevents metabolic syndrome-associated disorders.

and fat oxidation and storage in the muscles and liver (Fig. 4)[3, 5, 24, 25].

2. Muscle mass : in older people, diabetes is associated with reductions in muscle strength and muscle quality. These impairments are significant contributors to walking limitations related to diabetes[26]. Resistance exercise enhances skeletal muscle mass, and the increased muscle mass resulting from resistance training may contribute to BG uptake (i.e. mass effect). Heavy weight training in particular may reverse or prevent the further loss of skeletal muscle as a result of disuse and aging.

3. Lipids and lipoproteins : mixed results have been reported for blood lipid responses to training, but exercise training may result in a small reduction in low-density lipoprotein-cholesterol and no change in high-density lipoprotein-cholesterol or triglyceride levels. Combined weight loss and PA may be more effective in improving lipids than aerobic exercise training alone[16].

4. Hypertension : aerobic training may reduce systolic blood pressure (BP) slightly, but reductions in diastolic BP are less common in individuals with T2D[7, 16].

5. Mortality and cardiovascular risk : greater PA and fitness are associated with a lower risk of all-cause and cardiovascular mortality. Furthermore, PA- and/or exercise-induced increases in fitness, particularly muscular, predict improvements in cardiovascular risk factors in subjects with T2D independent of weight loss, thus indicating a need for targeted fitness programs in these individuals, particularly those who struggle to lose weight[27]. Williams *et al*[28] reported that the combination of diabetes plus impaired health-related functioning (HRF) is associated with substantially higher CVD mortality. This suggests that for

individuals with diabetes, impaired HRF is likely to be important for the identification of those at increased risk of CVD mortality.

6. Body weight maintenance and loss: the most successful programs for long-term weight control use combinations of diet, exercise, and behavior modification[7,16]. Recommended levels of PA may help to induce weight loss; however, up to 60 min/day may be required when relying on exercise alone for weight loss[16].

Matsushita *et al*[29] reported that changes in body weight are not accurate surrogate markers of changes in visceral fat area (VFA) and that repeated VFA measurements over time are useful. Adopting a lifestyle that does not increase VFA is important for the prevention of MetS.

Visceral, rather than subcutaneous, fat promotes the formation of insulin resistance-related atherosclerosis. Physical exercise combined with dietary restriction decreases visceral fat[7]. Conversely, liposuction from abdominal subcutaneous adipose tissue has been reported to have no effect on either insulin action or the risk factors for coronary heart disease[30]. In their study, Klein *et al*[30] reported that the decreases in adipose tissue mass seen following abdominal liposuction will not result in the metabolic benefits seen following weight loss.

7. Supervision of training: in the national survey into exercise guidance[22], we found that the proportion of exercise guidance is low because there is a lack of specialized physical exercise educators. Exercise intervention studies demonstrating the greatest effect on BG control have all involved the supervision of exercise sessions by qualified exercise trainers[16]. Recently Balducci *et al*[31] showed that supervised exercise is safe and effective in improving glycemic control and markers of adiposity and inflammation in insulin-treated individuals with T2D, thus counterbalancing the adverse effects of insulin on these parameters.

8. Psychological effects: increased PA and physical fitness can reduce symptoms of depression and improve health-related quality of life in individuals with T2D[16].

9. Basal metabolic rate and dietary-induced thermogenesis: continued physical exercise has been reported to increase the basal metabolic rate (which tends to decrease with dietary restriction) and dietary-induced thermogenesis in obese individuals[7].

Phisical activity and the prevention of T2D

Regular PA improves BG control and can prevent or delay the onset of T2D[16]. According to the Strong Heart Family Study[32], modest levels of PA are associated with a lower risk of incident diabetes compared with lower levels of activity (i.e.$<$3500 steps/day). Prospective cohort and cross-sectional observational studies reveal that at least 2.5 h/week of moderate to vigorous PA should be performed as a part of lifestyle changes to prevent the onset of T2D in high-risk adults[16].

Practical aspects of prescribed exercise

Pre-exercise evaluation

Before undertaking any exercise greater than brisk walking, sedentary people with T2D will likely benefit from an evaluation by a physician. Electrocardiogram exercise testing for asymptomatic individuals at low risk of coronary artery disease is not routinely recommended, but may be indicated for individuals at higher risk[16]. Various medical examinations are needed to confirm that the diabetes is well controlled and that diabetic patients do not have progressive severe complications[7].

Recommended PA for people with T2D

For most people with T2D, exercise is recommended for the management of diabetes and can be undertaken safely and effectively.

1. Aerobic exercise training

Frequency: aerobic exercise should be performed at least 3–5 days/week with no more than 2 consecutive days between bouts of activity because of the transient nature of exercise-induced improvements in insulin action[16].

Intensity: aerobic exercise should be of a moderate intensity, corresponding to approximately 40%–60% VO_{2max}. For most people with T2D, brisk walking is a moderate-intensity exercise[16].

Duration: the American Diabetes Association (ADA) states that patients with T2D should engage in a minimum of 150 min/week exercise undertaken at moderate intensity[16]. At this level, moderate-intensity exercise has been associated with reduced morbidity and mortality in observational studies in all populations[16].

2. Resistance exercise training

Frequency: in addition to regular aerobic activity, resistance exercise should be undertaken at least twice weekly on non-consecutive days, ideally 3 times/week, as a part of a PA program for patients with T2D[16].

Intensity: for optimal gains in strength and insulin action, training should be moderate (50% of 1-repetition maximum [1-RM]) or vigorous (75%–80% of 1-RM)[16].

Duration: each training session should, at a minimum, include five to 10 exercises involving the major muscle groups (in the upper body, lower body, and core), as well as the completion of 10–15 repetitions to near fatigue per set early in training[16].

Mode: resistance machines and free weights (e.g. dumb-bells, stretch cords) can result in fairly equivalent gains in the strength and mass of target muscles[16].

Aged diabetic patients: for elderly diabetic patients in whom there is a tendency for muscle atrophy (sarcopenia), mild-intensity resistance training, such as the use of dumb-bells and half squats, should be performed in addition to aerobic exercise[33]. In addition, horseback riding equipment (Joba®; Panasonic) is useful for older patients and patients with knee or foot problems[34, 35].

3. Supervised training: initial instruction and periodic supervision by qualified health fitness programmers and instructors is recommended for most patients with T2D, particularly if they undertake resistance exercise training, to ensure optimal benefits in terms of BG control, BP, lipids, and cardiovascular risk, as well as to minimize the risk of injury[16].

4. Daily movement (unstructured activity): T2D is a typical lifestyle-related disease. Patients should be instructed to incorporate some type of exercise into their daily lives (e.g. getting off the bus one stop earlier than their destination and walking the rest of the way)[7]. Non-exercise activity thermogenesis (energy expending for activities of daily living) can create a considerable daily calorie deficit to prevent excessive weight gain[36].

Using a pedometer and/or the Lifecorder® (Suzuken-Kenz) may be useful for motivating patients and determining how much exercise they have performed[7]. A meta-analysis of 26 studies with a total of 2767 (primarily non-diabetic) participants (eight randomized controlled trials, 18 observational studies) found that individuals who used pedometers increased their PA by 26.8% over baseline, resulting in a 0.38 kg/m^2 decrease in body mass index and a 3.8 mmHg decrease in systolic BP over an average intervention period of 18 weeks[37].

If using a pedometer or some other instrument to record activity, the data should be checked during regular inpatient rounds or in the outpatient clinic, with a goal of 10000 (or at least 7500) steps/day[7].

5. Flexibility training: older adults are advised to perform exercises that maintain or improve their balance, including flexibility exercise (stretching). Many older people, particularly those with T2D, are at a higher risk of falling.

Precautions when implementing physical exercise

Diet: if dietary changes are not implemented, it is unlikely that good BG control will be achieved. Patients should also be instructed regarding dietary restrictions.

Generally, exercise should be performed after meals.

The insulin dose should be reduced prior to undertaking physical exercise. If exercise extends over a prolonged period of time, dietary supplementation is necessary before, during, and after exercise.

If hypoglycemia occurs during exercise, patients should be advised to have a cola drink or glucose dissolved in lukewarm water. Cookies and/or rice balls are suitable before and after exercise to prevent hypoglycemia. Patients should undertake self-monitoring of BG before, during, and after exercise. Table 1 provides a guide to food intake before, during, and after exercise[7].

According to large-scale trials, such as the DPP[8], successful lifestyle interventions, including incorporation of goal setting, self-monitoring of training effects, frequent contact by teaching staff, and stepped-care protocols, promote PA[16].

Table 1. Mesurements of Energy Consumption during Exercise

Intensity of exercise	Times required per unit exercise	Type of exercise (energy consumption, kcal / kg / min)
Very low	Exercise continued for about 30 min to achieve 1 unit.	A stroll (0.0464), on a vehicle : standing in a train or bus (0.0375), cooking (0.0481), housework : laundry, cleaning (0.0471–0.0499), general clerical work (0.0304), shopping (0.0481), gymnastic exercise : low intensity (0.0552)
Low	Exercise continued for about 20 min to achieve 1 unit.	Walking : 70m/min (0.0623), bathing (0.0606), stairs : descending (0.0658), radio gymnastic exercise (0.0552–0.1083), bicycle : level ground (0.0658), and golf [males (0.0640), females (0.0500)]
Moderate	Exercise continued for about 10 min to achieve 1 unit.	Jogging : mild (0.1384), stairs : ascending (0.1349), bicycle : slope (0.1472), cross-country skiing (0.0782–0.1348), skating (0.1437), volleyball (0.1437), mountain climbing (0.1048–0.1508), tennis : practice (0.1437)
High	Exercise continued for about 5 min to achieve 1 unit.	Marathon running (0.2959), rope skipping (0.2667), basketball (0.2588), rugby : forward (0.2234), swimming : breaststroke (0.1968), kendo (0.2125)

Note : A single unit corresponds to about 80 kcal. It should be used as a yardstick for supplementary feeding in patients on insulin therapy.

(Sato Y et al : Diabetes Res. Clin. Pract. 75 : 135–140, 2007)

Patients should be instructed to wear appropriate sports shoes and should be provided with appropriate warm-up and cool-down exercises.

These exercise interventions should be provided by a medical support team consisting of physicians, physiotherapists, health fitness programmers and instructors, registered dieticians, pharmacists, and nurses[4, 7].

In conclusion, physical exercise plays a major role in the prevention and control of insulin resistance and T2D. Most people with T2D can perform exercises safely as long as certain precautions are taken. However, lifestyle improvements based on diet and exercise are difficult in practice and adherence to lifestyle interventions is lower than for medications (metformin). Therefore, efforts to promote PA should focus on developing self-efficacy and fostering social support from a medical support team.

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Disclosure statement

The author declares no conflict of interest.

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