# Physical Exercise for Diabetes Mellitus: The effective programs for treatment

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**Abstract**: Evidence-based medicine (EBM) has come to be regarded as essential in all fields of medical sciences and practical medicine. Among the epidemiological studies of physical exercise, recent mega-trials such as the Diabetes Prevention Program (DPP) in the U.S. have shown that lifestyle intervention programs involving diet and/or exercise reduce the progression of impaired glucose tolerance (IGT) to type-2 diabetes. In studies examining the endocrinological and metabolic effects of exercise, it has been demonstrated that physical exercise promotes the utilization of blood glucose and free fatty acids in muscles and lowers blood glucose levels in well-controlled diabetic patients. Long-term, mild, regular jogging increases the action of insulin in both carbohydrate and lipid metabolism without influencing body mass index or maximal oxygen uptake. A significant correlation has been observed between delta MCR ($\Delta$insulin sensitivity) and the average number of steps performed in a day. Our recent data suggested that the improved effectiveness of insulin that occurs as a result of physical exercise is attributable, at least in part, to increases in GLUT4 protein, PI3 kinase, and IRS1 protein in skeletal muscle. Health insurance system in Japan recently changed so that doctors can be reimbursed for lifestyle interventions. As a prescription for exercise, aerobic exercise of mild to moderate intensity, including walking and jogging, 10–30 minutes a day, 3–5 days a week, is recommended. An active lifestyle is essential in the management of diabetes, which is one of typical lifestyle-related diseases.

**Key words**: Lifestyle-related diseases; Diabetes mellitus (type 2); Physical exercise; Insulin sensitivity

## Introduction

As the 21st century advances, evidence-based medicine (EBM) is becoming an important concept in medical sciences and practical medicine. In the area of research on the clinical

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use of physical exercise for the prevention and treatment of diabetes mellitus, an understanding of how exercise affects diabetes is being pursued through molecular biological approaches. Long-term epidemiological follow-up studies on exercise training and the prevention of diabetes have been reported. Thus, evidences demonstrating the usefulness of exercise therapy have been gradually increasing.

Related to this, the Japanese Ministry of Health and Welfare (currently the Ministry of Health, Labor and Welfare) introduced the concept of "lifestyle-related diseases" in its policies, based on the conclusion that lifestyle factors such as diet and exercise, in addition to genetic factors, are involved in the development of so-called "adult diseases," including type-2 diabetes and obesity. Health insurance system in Japan was altered to provide additional remuneration for the guidance and management of exercise for the treatment of hypertension in April 1996 and for diabetes mellitus and hyperlipidemia in April 2000. In addition, the "Healthy Japan 21" project, which is aimed at preventing the onset of diabetes mellitus and circulatory diseases and prolonging healthy longevity by modifying lifestyle habits, including physical activity and exercise, nutrition, and diet, was put into effect in April 2000.

Now that the general climate in Japan tends to favor exercise therapy, improvement in this type of therapy is desirable, particularly in the area of EBM.

## Physical Exercise and Diabetes Mellitus: Results of Epidemiological Studies

### 1. Lifestyle-related diseases and insulin resistance

In recent years, the decrease in physical exercise associated with automation and computerization has combined with western-style eating habits to lead to insufficient physical activity and overeating (high fat diet). This in turn has brought about an increase in the prevalence of the pathological conditions known as "syndrome X," "syndrome of insulin resistance," "the deadly quartet," "multiple risk factor syndrome," "visceral fat syndrome," or "metabolic syndrome" as represented by diabetes mellitus, obesity, hypertension, and hyperlipidemia.

As mentioned previously, the Ministry of Health and Welfare introduced the concept of "lifestyle-related diseases" to describe these conditions. As factors common to these diseases, the importance of insulin resistance and accompanying compensatory hyperinsulinemia have been stressed.

### 2. Prevention of type-2 diabetes mellitus and the role of physical exercise

The results of various follow-up studies have revealed that the proper diet combined with physical exercise are not only useful in preventing type-2 diabetes mellitus and improving disease status but are also effective in the prevention and treatment of all other insulin-resistance-related diseases (lifestyle-related diseases), including hypertension and hyperlipidemia, by improving *in vivo* sensitivity to insulin.

a. The incidence of diabetes mellitus decreases by 6% with every 500 kcal/week increase in energy consumption in leisure-time physical exercise (Paffenbarger Study, USA, 1994).

b. Although patients with impaired glucose tolerance (IGT) are at high risk for type-2 diabetes mellitus and death from coronary disease, the implementation of dietary counseling and physical exercise lead to the decrease in the mortality of IGT patients to the level of individuals with normal glucose tolerance (Malmö Study, Sweden, 1998).

There have also been reports of intervention trials (randomized controlled trials) in which a particular population is randomly allocated to a given intervention, e.g., instructions concerning diet or exercise, and the intervention group is then compared with a control group.

c. The incidence of diabetes mellitus in IGT patients decreased by 31% during a six-year

period when diet therapy alone was prescribed, by 46% when exercise therapy alone was prescribed, and by 42% when a combination of diet and exercise therapy was prescribed (DaQing Study, China, 1997).

d. Positive modification of lifestyle habits concerning diet and exercise has a greater suppressive effect on the development of diabetes mellitus than that of the oral antihyperglycemic agent metformin (58% vs. 31%) (Diabetes Prevention Program, DPP; USA, 2002).

Although the results of intervention trials have been reported from various countries, few studies of this kind have been carried out in the field of diabetes prevention in Japan. Data from the ongoing study of JDPP (Director: Dr. Kuzuya, H., National Kyoto Hospital) are awaited.

## Metabolic and Endocrinological Effects of Physical Exercise

### 1. Acute metabolic effect

The presence of insulin plays a key role in how the acute metabolic effect of exercise is manifested.

a. In patients in whom metabolic regulation is well maintained, exercise promotes the use of glucose and free fatty acids (FFA) in muscles. Therefore, exercise after meals by diabetic patients with relatively good glucose control may lead to better control of diabetes by suppressing the rapid postprandial elevation of blood glucose.

b. In patients who are in ketosis [urinary ketone (+) and fasting glucose $\geqq$ 250 mg/d*l*; and fasting glucose $\geqq$ 300 mg/d*l* in cases of urinary ketone (−)] because of severe insulin deficiency, the levels of blood glucose, FFA, and ketone bodies may increase further after exercise.

c. High-intensity exercise may aggravate abnormal carbohydrate metabolism through increased secretion of insulin-counter regulatory hormones such as glucagon and catecholamine. When diabetes mellitus is poorly controlled, secretion of these counter regulatory hormones is further increased. If diabetic control is extremely poor, physical exercise is contraindicated. Even when diabetes is favorably controlled, low-intensity exercise is recommended.

d. The implementation of moderate-intensity exercise [relative intensity up to about 50% of maximum oxygen uptake ($VO_2$max)] for several minutes causes increased utilization of carbohydrates and FFA as muscle energy sources. However, as exercise intensity increases above the lactate threshold (LT) (exercise intensity at which anaerobic metabolism begins and the blood lactate level starts to increase), the ratio of carbohydrate utilization increases, and maximal exercise (anaerobic exercise) depends on the glycolytic pathway, using only glucose, not lipids, as the source of energy.

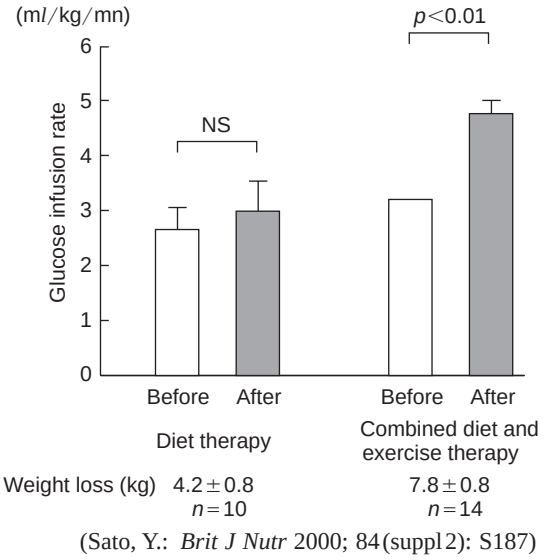
### 2. Training effect

#### (1) Physical exercise and insulin sensitivity

a. Even mild physical exercise that does not affect $VO_2$max can cause improvement in the *in vivo* insulin sensitivity if continued for a prolonged period of time. The implementation of dietary restriction and physical exercise in obese people and obese patients with type-2 diabetes will result in a selective decrease of body fat, leading to weight loss, while causing no changes in lean body mass (LBM). Thus, dietary restriction combined with physical exercise is more useful for improving insulin sensitivity than dietary restriction alone (Fig. 1). In addition, the glucose metabolic clearance rate (MCR) shows a positive correlation with the number of steps performed per day as determined by a pedometer.

b. Aerobic exercise such as jogging is more useful in improving the *in vivo* insulin sensitivity than anaerobic exercise like weightlifting. However, mild resistance exercise, if carried out in an aerobic manner, is also useful for improving insulin sensitivity in patients with type-2 diabetes and in the elderly.

c. Continued exercise training prevents




(Sato, Y.: *Brit J Nutr* 2000; 84(suppl 2): S187)

Fig. 1 Changes in insulin sensitivity (glucose infusion rate) in patients on diet therapy alone and on combined diet and exercise therapy

Even if body weight decreases in obese patients with type-2 diabetes mellitus, decreased insulin sensitivity will not improve unless physical exercise is performed.

decreased basal metabolic rate caused by implementation of dietary restriction.

d. Implementation of exercise improves physical fitness and lipid metabolism.

e. Physical exercise can improve blood glucose control in patients with type-2 diabetes, as mentioned above. However, since metabolic status can vary on a daily basis in patients with type-1 diabetes mellitus, the effect of physical exercise is not necessarily constant.

(2) **Mechanisms of training effects**

a. Improved insulin sensitivity is the major beneficial effect of exercise. Muscular factors including postreceptor steps, such as muscle weight gain, glycolytic pathway in muscle, increase in enzyme activity in the tricarboxylic acid (TCA) cycle, and glucose transporter (GLUT4), play a role in its manifestation.

b. Adipose tissue factors such as decreases in body fat and the size of fat cells cannot be disregarded. As the amount of fat tissue decreases, plasma TNF-$\alpha$ levels secreted from adipose tissue may decrease, resulting in improved *in vivo* insulin sensitivity.

## Practical Aspects of Prescribed Exercise

### 1. Indications of physical exercise and medical check-up

Before patients undertake programs of physical exercise, various medical examinations are needed to determine that they have good diabetic control and are without progressive complications.

### 2. Type and intensity of exercise

The effect of exercise that manifests in improved insulin sensitivity decreases within 3 days after exercise, and is no longer apparent after 1 week. As noted previously, moderate or lower intensity exercise is preferable.

Specifically, moderate-intensity exercise that results in $VO_2$max of about 50% (pulse rate of about 120/min for those in their 50s or younger and about 100/min for those in their 60s and 70s) should be performed for 10–30 min at a time (2–3 times a day, preferably after meals), at least 3–5 days a week. Recommended types of exercise are aerobic exercises that use muscles throughout the body, such as walking, jogging, radio gymnastic exercises, stationary bicycle exercise, and swimming. If resistance exercise is adopted, the level of the load should be low.

Diabetes mellitus is a typical lifestyle-related disease. It is necessary to instruct patients to incorporate some exercise into their daily life, e.g., getting off the bus at a stop before the destination and walking the rest of the way (Table 1). The use of a pedometer and Lifecorder® are useful for motivating patients and for determining how much exercise has been performed. The recorded figures should be checked during regular inpatient rounds or in the outpatient clinic, with the goal set at 10,000 steps (or at least 7,500 steps) per day.

### 3. Precautions in implementing physical exercise

a. If diet therapy is not followed, good

Table 1 Yardsticks of Energy Consumption during Exercise

| Intensity of exercise | Time 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: 70 m/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.

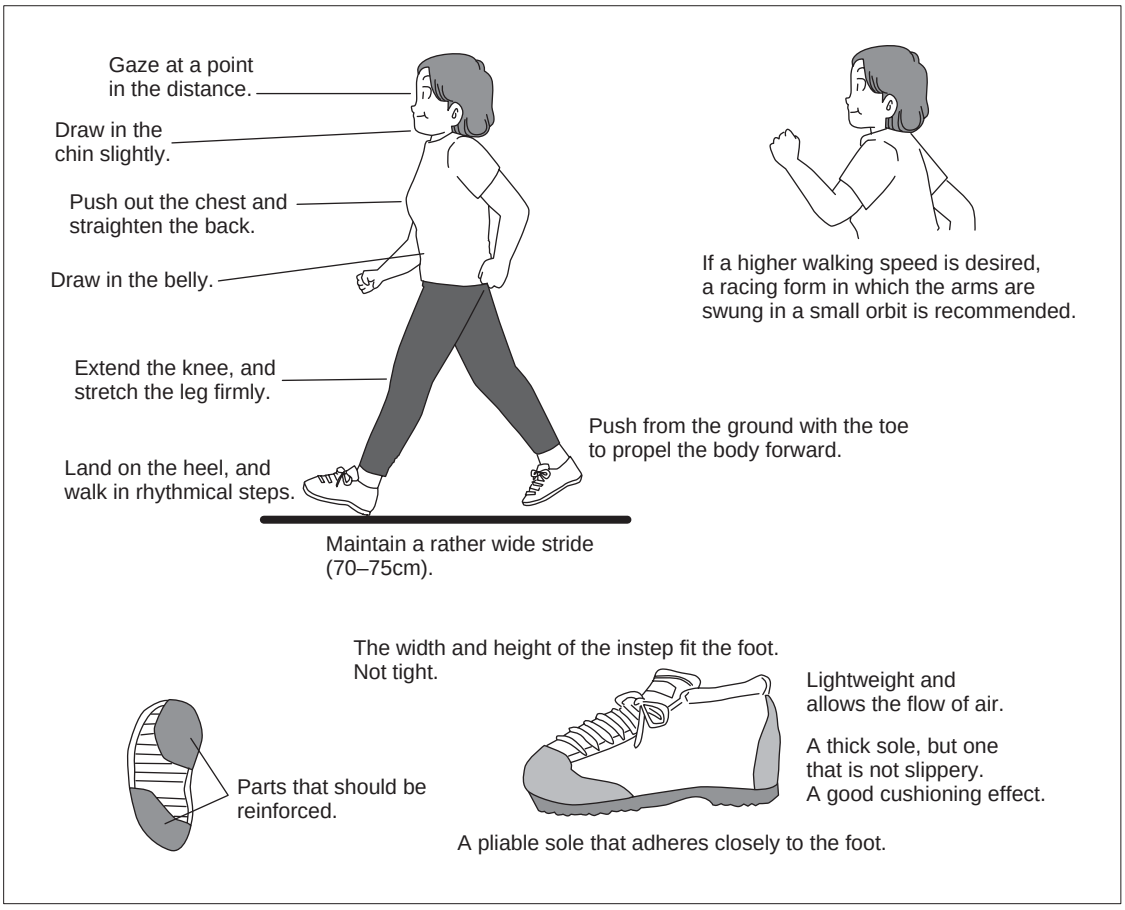



Fig. 2 Recommended posture while walking and choice of walking shoes
(Ed. Japan Medical Association: Exercise therapy prescription manual. Japan Medical Association, Tokyo, 1996; 9)

Patients name Mr・Ms

Date:

| | |
|---|---|
| Name of disease | Principal disease:<br>Others: |
| Signs and symptoms | |
| Instructions for medication | |
| Instructions for physical exercise, rest and diet | |
| Instructions for smoking and alcohol | |
| Other instructions | |

Comments: Above items are suggestions based present medical conditions, but might be variable because of changes in conditions of diseases soon.

Name of patient:

Chief physician:

Fig. 3 Care plan for the life-style related diseases

control of blood glucose will not be achieved. Dietary restriction should be instructed.

b. Usually, exercise should be performed after meals.

c. In patients on insulin therapy, the insulin dose should be reduced prior to exercise. If exercise extends over a prolonged period of time, dietary supplementation is necessary before, during, and after exercise. If hypoglycemia occurs during exercise, a cola drink or glucose (pet sugar) dissolved in lukewarm water should be taken. Cookies, cheese, and milk are suitable before and after exercise to prevent hypoglycemia. Table 1 provides a guide to food intake.

d. General precautions including the use of sports shoes and incorporation of warm-up and cool-down exercises should be given (Fig. 2).

**4. Preparing prescriptions for exercise**

As mentioned previously, Japan's national health insurance system, recognizing that comprehensive guidance and management are important in the treatment of lifestyle-related diseases, initiated a new system of reimbursement for the guidance and management of physical exercise (charges for the guidance and management of lifestyle-related diseases) in April 2002.

(1) **Point calculations for reimbursement**

a. When hyperlipidemia is the main disease
   Out-of-hospital prescription: 1,050 points
   In-hospital prescription: 1,550 points
b. When hypertension is the main disease
   Out-of-hospital prescription: 1,100 points
   In-hospital prescription: 1,400 points
c. When diabetes mellitus is the main disease
   Out-of-hospital prescription: 1,200 points
   In-hospital prescription: 1,650 points

(2) **Frequency of reimbursement**

Exercise prescriptions are counted for reimbursement no more than once per month when a treatment plan is made for an outpatient with the above diseases and when comprehensive guidance in lifestyle habits and therapeutic management are performed according to the treatment plan. In addition, a care plan (Fig. 3) is issued to the patient at a frequency of at least once every 3 months, and a duplicate is appended to the medical record.

(3) **Items included**

Charges for guidance and management and expenses for tests, medications, and injections.

(4) **Others**

An exercise prescription issued in the same month as the patient's first visit cannot be included. Patients who are and are not included may coexist in the same medical institution. The same patient may be counted one month and not another. The patient is exempted from drug cost sharing, and a certain indication of exemption should be indicated in the prescription.

Reimbursement for the guidance and management of lifestyle-related diseases can be claimed by medical clinics and hospitals with fewer than 200 beds.

## Conclusion

The effective programs of exercise therapy for diabetes mellitus have been outlined with descriptions of its rationale.

Now that exercise therapy for diabetes mellitus is acknowledged in Japan's national health insurance system, higher quality guidance in exercise can be expected, particularly in terms of EBM, i.e., based on the rationale derived from recent experimental and clinical studies.

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