



Research protocol

A large-scale clinical study to explore the effectiveness of physiotherapy in diabetes: A research protocol

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ABSTRACT

【Background】Exercise therapy is very important for improving glycemic control in diabetes mellitus. Physical therapists should be actively involved in treating diabetes mellitus as specialists in exercise therapy; however, various issues, such as the lack of established evidence for exercise therapy, have prevented physical therapists from playing a larger role in the care of patients with diabetes mellitus. Therefore, the purpose of this study is to conduct a large-scale clinical study to obtain evidence supporting physiotherapy for diabetes mellitus.

【Methods】This is a large-scale multicenter study, which involves the participation of 200 facilities nationwide, and includes 10,000 patients with type 1 and type 2 diabetes mellitus. This exploratory study aims to evaluate the efficacy of physiotherapy and the need for the intervention of physical therapists from multiple angles over the course of 10 years.

【Discussion】As the number of Japanese diabetic patients continues to grow, so does the importance of exercise therapy as an option to treat diabetes mellitus. The knowledge and techniques of physical therapists are essential for providing optimal exercise therapy, and many healthcare professionals have high expectations regarding the role of physical therapists. Findings obtained from this study should provide evidence that increases awareness among physical therapists and encourages their participation in providing therapy for patients with diabetes.

【Trial registration】The trial registration number is UMIN-CTR (UMIN000044011).

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Introduction

Diabetes mellitus is a disease characterized by a chronic hyperglycemic state that occurs mainly due to the insufficient action of insulin, and long-term persistence of hyperglycemia can cause various complications specific to diabetes. The number of patients with type 2 diabetes mellitus (T2DM) has been increasing rapidly in Japan. In fact, it has been estimated that over 20 million patients have T2DM or impaired glucose tolerance¹⁾. Proper glycemic control is critical, and exercise is one of the major therapeutic approaches for T2DM in clinical practice. Increasing the level of physical activity/exercise is one of the main strategies for the prevention and treatment of T2DM. Although aerobic exercises, such as walking and jogging, have been recommended, there are also several reports claiming that resistance training is effective for improving T2DM²⁾.

Thus, although exercise therapy is considered an important treatment for patients with diabetes, there are very few physical therapists working with (or teaching) diabetic patients in Japan. This is because of a lack of established evidence for physiotherapy in diabetes. Although a number of studies have been reported from a single institution where individual physical therapists are affiliated, this is not sufficient for the development of solid evidence. Conducting a large-scale clinical study in collaboration with physical therapists throughout Japan to demonstrate the usefulness of

physiotherapy for diabetes treatment may provide a solution to this problem. Furthermore, these efforts may lead to future reimbursements for physical therapists for performing physiotherapy for patients with diabetes.

Therefore, this study aims to elucidate the efficacy of physical therapy in diabetes mellitus, as well as the need for guidance from a physical therapist from multiple perspectives.

Methods***Study design and subjects***

This prospective exploratory study will include Japanese patients with diabetes mellitus. The clinical study period is 10 years. Patients with type 1 and 2 diabetes mellitus between 20 and 89 years of age will be recruited from 200 facilities throughout Japan for this study. Informed consent will be obtained from all participants prior to their involvement in the study. The inclusion criteria are as follows: 1) patients whose diabetologist determines that exercise therapy is necessary; 2) inpatients and outpatients with diabetes mellitus who are able to provide written informed consent to participate in this study. Exclusion criteria are as follows: 1) diabetic patients with dementia; 2) patients with gestational diabetes; 3) patients with diabetes who have difficulty walking; 4) patients who seem inappropriate for this study based on investigations. In this study, each evaluation item will

be categorized and investigated. There will be two categories for sex (male or female), and seven categories for the age range of 20–80 years. The total number of participants will be 10,000. The research ethics committee of the Japanese Society of Physical Therapy has approved this study (approval number: ER02-003). The original study protocol has been registered in the University Hospital Medical Information Network (UMIN000044011).

Measurements of clinical and laboratory parameters

We plan to collect data on the disease type, sex, age, height, body weight, body mass index (BMI), waist circumference, body composition, duration of diabetes, comorbidities (e.g., musculoskeletal and cerebrovascular diseases), systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), cognitive function, duration of exercise therapy, exercise tolerance, diet, medications, and laboratory test results. The levels of fasting plasma glucose (FBG), hemoglobin A1c (HbA1c), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides (TG), γ -glutamyl transpeptidase (γ -GPT), aspartate aminotransferase (AST), alanine aminotransferase (ALT), AST/ALT ratio, C-peptide (CPR), blood insulin, serum creatinine, microalbuminuria, and estimated glomerular filtration rate (eGFR) will be measured using standard laboratory methods. A well-trained physical therapist will interview each patient to evaluate the level of physical activity, health-related quality of life (HRQOL), drinking, smoking, and exercise habits. Physical activity and HRQOL will be evaluated using the International Physical Activity Questionnaire (IPAQ) short version³⁾ and EuroQol 5-dimensional (EQ-5D) questionnaire⁴⁾. The diagnosis of

T2DM will be based on the levels of FBG and HbA1c, and performed according to the guidelines of the Japan Diabetes Society (JDS)⁵⁾. The definitions of diabetic retinopathy, nephropathy, neuropathy, and diabetic foot are also based on the diagnostic guidelines of the JDS⁵⁾. As parameters of motor function, we will evaluate the lower extremity strength (30 s chair-stand test: CS-30)⁶⁾, lower extremity range of motion test, one-leg standing test⁷⁾, functional reach test⁸⁾, and 10 m walking speed test⁹⁾, as previously described.

Survey contents

This study will investigate changes in the clinical indicators and motor function over time during the 10-year study period. A few examples of what the study entails are as follows: (1) the relationship between blood glucose control and physical activity; (2) relationship between exercise function and chronic complications; (3) changes in the HRQOL over time; (4) comparison of exercise habits and incidence of chronic complications; and (5) exercise function in different stages of diabetic nephropathy. These survey contents may be subject to additions and changes. The timings of the assessments for clinical indicators and motor function have been set as follows: (1) for inpatients, on admission, at discharge, and subsequently every 3 months (or every 6 months) from the time of discharge until the end of the study; (2) outpatients will be assessed for the first time, and then every 3 months (or every 6 months) from the initial assessment until the end of the study.

Statistical analysis

Data will be expressed as means \pm standard deviation. Statistical analyses include univariate analysis, multivariate analysis, and trend tests. For these

analyses, $p < 0.05$ is considered statistically significant. All statistical analyses will be conducted using the JMP 12.2.0 software (SAS Institute, Cary, NC, USA) and SPSS Statistics 28 software (SPSS Inc., Chicago, USA).

Discussion

Therapy for diabetes mellitus aims to prevent the onset or progression of diabetic complications, maintain the quality of life (QOL), and ensure a life expectancy that is comparable to that of healthy individuals. Maintaining good blood glucose control throughout the lifetime is essential for this, and active interventions by physical therapists can help in treating abnormal sugar metabolism¹⁰. Furthermore, hyperglycemia and diabetic neuropathy are the main causes of various motor function impairments, such as muscle weakness^{11,12}, amyotrophy¹³, limited range of motion of joints¹⁴, decline in the balance ability¹⁵, and decline in the walking ability¹⁶ in patients with diabetes. In addition, frailty and sarcopenia in diabetic patients have become serious problems. These are precisely the areas that can benefit from the specialized knowledge of physical therapists; thus, it is clear that physical therapists need to actively participate in the treatment of patients with diabetes. However, in Japan, there are very few physical therapists involved in the therapy of patients with diabetes. Furthermore, many diseases that are treated by physical therapists in routine clinical care, such as cerebrovascular diseases, musculoskeletal disease, and cardiovascular diseases, are highly likely to be complications of diabetes mellitus. Consequently, it is important that physiotherapy for these diseases be provided with adequate knowledge of the pathology and risk management, although many physical therapists are not always aware of this.

Therefore, this study aims to elucidate the efficacy

of physical therapy in diabetes mellitus, as well as the need for guidance from a physical therapist from multiple perspectives in a large-scale clinical study with the participation of physical therapists nationwide. Currently, it is very common for exercise therapy for patients with diabetes to be provided by other medical professionals, such as nurses and nutritionists in healthcare settings. It is our hope that the findings obtained from this study will provide evidence that physical therapists should provide exercise therapy guidance. This should also help physical therapists in earning payments for medical services and contributing to the eventual expansion of job categories for physical therapists.

Conflict of interest

The authors declare that they have no competing interests.

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