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Original Research

Impact of Resistance Training on Factors Involved in the Development of New-Onset Diabetes After Transplantation in Renal Transplant Recipients: An Open Randomized Pilot Study

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ABSTRACT

Objectives: New-onsetdiabetes after transplant (NODAT) is a major contributor to cardiovascular disease after transplantation. Kidney transplantation (KT) recipients have low levels of exercise capacity. Resistance training (RT) might be of special benefit in this population because underlying disease and immunosuppressive drugs favour muscle loss and insulin resistance. The aim of this study was to assess the feasibility of implementing an RT program within a population of KT recipients and its impact on the incidence of NODAT and cardiometabolic risk factors.
Methods: This pilot study was an open-randomized study. We randomized 24 patients with a 1:1 allocation to 2 parallel groups, the exercise group (E) or the control group (C). The E group was submitted to RT 3 times a week for 16 weeks. Anthropometric, body composition, cardiometabolic risk factors, muscle strength, cardiorespiratory fitness and well-being were measured before and after 16 weeks.
Results: Of the 24 recruited participants, 20 completed the study (10 in the E group and 10 in the C group). No injuries were reported. The intervention was associated with a significant increase in muscle strength ($p=0.003$). A significant group effect, in favour of the E group, was detected for the well-being score ($p=0.03$). However, no changes in body composition, cardiometabolic risk factors or cardiorespiratory fitness were noted for either group after the intervention.
Conclusions: This pilot study suggests that RT appears to be secure and feasible and improves strength and well-being in patients after KT. However, it does not improve cardiometabolic risk factors.

Mots clés :
risque cardiométabolique
sensibilité à l'insuline
transplantation rénale
diabète de novo après transplantation
entraînement musculaire

RÉSUMÉ

Objectifs : Le diabète de novo après transplantation (NODAT) contribue grandement aux maladies cardiovasculaires après la transplantation. Les receveurs de transplantation rénale (TR) ont une faible capacité à l'effort. L'entraînement musculaire (EM) serait particulièrement bénéfique dans cette population en raison de maladies sous-jacentes. De plus, les médicaments immunosuppresseurs favorisent la fonte musculaire et l'insulinorésistance. L'objectif de la présente étude était d'évaluer la faisabilité de la mise en œuvre d'un programme d'EM au sein d'une population de receveurs de TR et ses répercussions sur l'incidence du NODAT et les facteurs de risque cardiométabolique.
Méthodes : Cette étude pilote était une étude à répartition aléatoire, ouverte. Nous avons réparti de manière aléatoire 24 patients selon un ratio 1:1 en 2 groupes parallèles le groupe entraîné (E) ou le groupe témoin (T). Le groupe E était soumis à l'EM 3 fois par semaine durant 16 semaines. L'anthropométrie, la composition corporelle, les facteurs de risque cardiométabolique, la force musculaire, la capacité cardiorespiratoire et le bien-être ont été mesurés avant et après 16 semaines.

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Résultats : Parmi les 24 participants recrutés, 20 ont réalisé l'étude (10 du groupe E et 10 du groupe T). Aucune blessure n'a été rapportée. L'intervention a été associée à une augmentation significative de la force musculaire (p=0,003). Un effet de groupe significatif qui favorisait le groupe E a été détecté par le score de bien-être (p=0,03). Cependant, aucun changement dans la composition corporelle, les facteurs de risque métabolique ou la capacité cardiorespiratoire n'a été noté pour l'un ou l'autre groupe après l'intervention. *Conclusions :* Cette étude pilote suggère que l'EM semble être sûr et réalisable, et qu'il améliore la force et le bien-être des patients après la TR. Cependant, il n'améliore pas les facteurs de risque cardiométabolique.

Introduction

Kidney transplantation (KT) is a lifesaving intervention for people with end stage kidney disease. Short-term survival lengths have greatly improved and cardiovascular disease (CVD) has become the main cause of death (1,2). New-onset diabetes after transplant (NODAT) is a common complication of KT and contributes to the development of CVD complications. About 15% to 30% of patients develop NODAT during the first year (3-5). Risk factors for NODAT include modifiable risk factors (obesity, corticosteroids, calcineurin inhibitors, hepatitis C, inflammation) and nonmodifiable risk factors (genetic factors, older age and African American, Hispanic or Native American ethnic backgrounds) (6). In addition, as observed in type 2 diabetes, insulin resistance and decreased insulin secretion favour the development of NODAT (7).

Patients with chronic kidney failure demonstrate limitations in exercise capacity secondary to muscle weakness (8–12). There is also impairment in cardiorespiratory fitness levels related to peripheral muscle dysfunction (13,14). Furthermore, the addition of corticosteroids administered to these patients after transplantation contributes to muscle weakness, and calcineurin inhibitors have also been shown to affect muscle function (15). Therefore, resistance training (RT) might be of special benefit in this population. Accordingly, numerous guidelines recommend the use of progressive RT as part of an exercise program for individuals with type 2 diabetes (16-18). Furthermore, several studies have shown that RT improves the metabolic profile, insulin sensitivity and glycemic control of patients with type 2 diabetes (19-26). To our knowledge, only 3 randomized studies have been published concerning exercise training in KT (27-29), and only 1 has studied RT (27). This study by Juskowa et al (27) included 69 renal transplant recipients recruited within 2 or 3 days after renal transplantation and randomized to a physical-exercise intervention group for 4 or 5 weeks along with the standard care controls. The patients in the exercise group performed whole-body strength training exercises every other day for 30-minute sessions, assisted by a physiotherapist, and they repeated the program on alternate days on their own. Results showed a positive correlation between muscle strength and improved graft function in the exercise group vs. the control group. However, therapeutic exercise after kidney transplantation produced no significant effects on the markers of atherosclerosis.

No study has investigated the efficacy of any type of exercise training in the prevention of NODAT development. Therefore, the purpose of this study was to evaluate the feasibility of implementing an RT program after kidney transplantation and to examine the impact of RT on cardiometabolic risk factors (insulin resistance and body composition) involved in the occurrence of NODAT in patients after KT. We hypothesized that an RT program would be feasible, improve cardiometabolic risk factors and decrease the incidence of NODAT.

Methods

Design

This was an open, parallel group pilot study with 1:1 randomization. For allocation of the participants, a concealed computer-generated randomization list was created by an independent person before the inclusion of the first patient. Patients were randomized to the exercise group or the control group. The primary objective was to assess the feasibility of introducing a resistance training program in patients after KT. The secondary objectives were to assess the effects of a resistance training program on incidence of NODAT, insulin sensitivity, body composition, muscle strength and health-related quality of life to facilitate the determination of sample-size calculations in future trials.

Subjects

We recruited a total of 24 patients during the follow-up appointments at the transplant clinic of Notre-Dame's hospital in Montreal (Figure 1). Patients were included in the study if they met the following criteria: ambulatory outpatients; women and men of at least 18 years of age (no upper age limit); cadaveric, living related or living unrelated donor KT 6 to 8 weeks before the inclusion in the study; nonsmokers, low to moderate alcohol consumers (<2 drinks per day) and sedentary (<2 hours of structured exercise per week). Exclusion criteria were pretransplant diabetes, posttransplant long-acting insulin-treated diabetes, patients with multiorgan transplants at the time of transplant, hypoxemia in room air (PaO_2 less than 80 mm Hg), allergies to nickel or latex, histories of acute rejection, mental or physical conditions preventing the patients from exercising, uncontrolled hypertension (systolic blood pressure 160/diastolic blood pressure 100 mm Hg), cardiac arrhythmias or any absolute contraindications to exercise testing established by the American Heart Association (30). The Centre Hospitalier de l'Université de Montréal and the Institut de Recherches Cliniques de Montréal ethic and scientific committee approved the study, and a written informed consent was obtained from all subjects.

Procedures

After inclusion, patients were invited to the Institut de Recherches Cliniques de Montréal in the fasting state in the morning for a series of tests. Upon their arrival, fasting blood glucose, glycated hemoglobin (A1C), lipid profile, anthropometric measurements, body composition and blood pressure were measured. A 75 gram oral glucose tolerance test was administered, and glucose and insulin were measured at 0, 30, 60, 90 and 120 minutes. Afterwards, a light breakfast was served. Thereafter, a cardiorespiratory fitness test was performed. Following their morning assessment, participants were invited to answer a small well-being questionnaire. After 16 weeks, the same testing was performed a second time for all patients. For the subjects randomized to the exercise group, testing was performed 48 hours after the last training session.

Measurements

Feasibility

In this pilot study, we evaluated the number of eligible patients in our centre, the injuries or adverse events as well as the adherence and dropout rates of the exercise intervention.