



# Pretransplantation Oral Glucose Tolerance Test Can Prevent Posttransplant Diabetes Mellitus After Renal Transplantation: Preliminary Study

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## ABSTRACT

Posttransplant diabetes mellitus (PTDM) adversely affects renal graft and patient survival. Fasting plasma glucose (FPG) alone underestimates diagnosis of glucose metabolism disorders (GMD) detected using the oral glucose tolerance test (OGTT-75). Prediabetes including impaired fasting glucose (IFG): 100 to 125 mg/dL (5.6–6.9 mmol/L) and impaired glucose tolerance (IGT): 140 to 199 mg/dL (7.8–11 mmol/L) 2 hours post 75-g OGTT in the pretransplant period can have a connection with the occurrence of PTDM after renal transplantation (RTx).

The aim of our study was to assess the benefit of performing OGTT-75 in dialyzed chronic kidney disease (stage 5) patients on the waiting list for kidney transplantation as a useful tool to prevent PTDM.

**Materials and Methods.** Pretransplant glucose testing using OGTT-75 was performed in nondiabetic dialyzed chronic kidney disease patients on the waiting list for renal transplantation in the southwest region of Poland. GMD were diagnosed according to current criteria. Patients with recognized prediabetic stage were recommended a low carbohydrate diet, lifestyle modification, and increased physical activity. In the 12-month posttransplant period we estimated the prevalence of PTDM in the study group based on FPG >126 mg/dL (7 mmol/L) in 2 measurements or random blood glucose >200 mg/dL (11.1 mmol/L).

**Results.** A total of 80 nondiabetic dialysis patients (65 hemodialysis/15 peritoneal dialysis; 47 male/33 female) met initial entry criteria. In pretransplant glucose testing prediabetes was found in 31 out of 80 patients (39%). Among them, 5 patients (6.25%) had combined IGT/IFG, 18 patients (22.5%) had IGT, and 8 patients (10%) had IFG. One year after RTx we recognized PTDM in 14% of all analyzed patients (11/80) and noticed a significant frequency of glucose disorders status change after RTx ( $P = .002$ ).

**Conclusion.** Our findings suggest early detection of prediabetes using the OGTT-75 test in nondiabetic dialysis patients waiting for RTx to prevent occurrence of PTDM.

**G**LUCOSE METABOLISM DISORDERS (GMD), including prediabetes and posttransplant diabetes mellitus (PTDM), are common complications after kidney transplantation and are associated with adverse long-term outcomes such as premature graft failure, cardiovascular events, and mortality [1–3].

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PTDM, also called new-onset diabetes mellitus, is a serious and common complication after renal transplantation. PTDM occurs in approximately 15% to 30% of renal transplant recipients, with higher incidence in the first year after kidney transplantation. Another 30% of patients have prediabetes with impaired fasting glucose (IFG) or impaired glucose tolerance (IGT) [4–10].

The development of PTDM has serious consequences, not only for graft rejection, graft loss, and infectious complication, but also for patient survival and cardiovascular disease risk [11–13]. Early detection and management of PTDM is essential for delaying or avoiding the effects of abnormal glucose metabolism on patient and graft survival [14–16].

Diagnosis of PTDM and prediabetic stage should be performed as early as possible to allow appropriate intervention. The prediabetes stage is important for renal transplant recipients because it predicts eventual development of PTDM and increases the cardiovascular risk [17]. The published studies have shown that treatment of IGT in renal transplant recipients with lifestyle modification can reduce eventual development of PTDM [17,18].

The oral glucose tolerance test (OGTT-75) is recommended as the first-choice diagnostic test for PTDM [19]. OGTT-75 consists of fasting and postprandial glucose measurements during a 2-hour period. This diagnostic test presents the highest sensitivity for the diagnosis of PTDM and it is able to detect the majority of cases of the disease [9,20,21].

In most studies, the main attention was focused on early detection of glucose metabolism disorders and intervention in the posttransplantation period, however, no previous studies have investigated benefits of OGTT-75 in dialyzed patients with chronic kidney disease on the waiting list for kidney transplantation.

Fasting plasma glucose (FPG) alone underestimates diagnosis of GMD detected using the OGTT-75. Prediabetes including IFG: 100 to 125 mg/dL (5.6–6.9 mmol/L) and IGT: 140 to 199 mg/dL (7.8–11 mmol/L) 2 hours post 75-g OGTT in the pretransplant period can have a connection with the occurrence of PTDM after renal transplantation (RTx).

The aim of our study was to assess benefits of performing the OGTT-75 before transplantation in dialysis patients as a useful tool to prevent PTDM in renal transplant recipients.

## MATERIALS AND METHODS

Pretransplant glucose testing using the OGTT-75 was performed in nondiabetic dialyzed patients on the waiting list for kidney transplantation in the southwest region of Poland. GMD were diagnosed according to current criteria. Results of the OGTT-75 were taken from qualifying documents for kidney transplantation. The patients with recognized prediabetic stage were recommended a low carbohydrate diet, lifestyle modification, and increased physical activity. Our study included 80 renal transplant recipients (47 male/33 female) treated at the Department and Outpatient Clinic of Nephrology and Transplantation Medicine, Wrocław Medical

University, Poland. All grafts were transplanted from deceased donors. Of all the study subjects 81% (n = 65) underwent hemodialysis (HD) and 19% (n = 15) underwent peritoneal dialysis (PD) before transplantation. The mean age at transplantation was 47.5 years ( $\pm 12.5$  years, median 51.0 years) and duration of dialysis treatment before kidney transplantation was 40.3 months ( $\pm 37.0$  months, median 28.5 months). Thereafter, in the 12-month post-transplant period, we estimated the prevalence of PTDM based on FPG  $> 126$  mg/dL (7 mmol/L) in 2 measurements or random blood glucose  $> 200$  mg/dL (11.1 mmol/L).

After kidney transplantation, the patients were treated with 2 main immunosuppressive protocols including 1. combination of cyclosporine A (CsA) with mycophenolate mofetil/mycophenolate sodium (MMF/MPA) and corticosteroids (CS) or, more frequently, 2. combination of tacrolimus (Tac) with MMF/MPA and CS.

In the CsA group steroid administration was as follows: perioperative intravenous (IV) bolus of methylprednisolone 500 mg followed by 250 mg IV (12 hours and 24 hours after transplantation) and 125 mg IV at day 2. From day 3 prednisone was given per os with the initial dose of prednisone 0.5 mg/kg body weight per day (but no more than 40 mg/d), and then the dose was tapered to reach 10 mg/d after 3 months and 5 mg after 6 months.

In the Tac group significantly smaller steroid doses were given: perioperative bolus of methylprednisolone 500 mg IV followed by 250 mg IV at day 1 and 125 mg IV at day 2. Since day 3, prednisone was given per os in the fixed dose of 20 mg. After reaching the stable therapeutic level of Tac, prednisone doses were gradually reduced in order to reach a daily dose of 15 mg after 4 weeks, 10 mg after 2 months, and 5 mg after 3 months.

The mean yearly cumulative prednisone dose in cyclosporine-receiving patients was about 5600 mg compared with about 3000 mg in tacrolimus-treated recipients.

In high immunological risk patients induction therapy with thymoglobulin (high risk) and anti-CD25 antibody (moderate risk) were introduced with combination of Tac, MMF/MPA, and CS. There is no withdrawal protocol for steroid after kidney transplant in our clinic.

GMD were diagnosed according to the current criteria by the World Health Organization and the American Diabetes Association.

The general principles of diagnosis of diabetes mellitus currently held by the Polish Diabetes Association do not recommend use of glycated hemoglobin (HbA1c) for the diagnosis of diabetes [22].

- Casual plasma glucose  $\geq 200$  mg/dL ( $\geq 11.1$  mmol/L) and the declaration of the typical symptoms of hyperglycemia (polyuria, polydipsia, and unexplained weight loss),
- Twice identified fasting plasma glucose  $\geq 126$  mg/dL ( $\geq 7.0$  mmol/L); fasting is defined as no caloric intake for at least 8 hours,
- Glycemia in 120 minutes of 75-g OGTT  $\geq 200$  mg/dL ( $\geq 11.1$  mmol/L) [1].

Criteria for the diagnosis of prediabetes: FPG 100 mg/dL (5.6 mmol/L) to 125 mg/dL (6.9 mmol/L) (IFG) or 2-hour PG in the 75-g OGTT 140 mg/dL (7.8 mmol/L) to 199 mg/dL (11.0 mmol/L) (IGT).

## Statistical Analysis

All variables were analyzed using Statistica 12.5 (StatSoft Inc, Palo Alto, Calif, United States). Descriptive statistical analysis was performed using numbers and frequency for categorical variables and using median, range, mean, and SD for continuous variables.

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