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Cardiovascular Consequences of New-Onset Hyperglycemia After Kidney Transplantation

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Abstract

Background—New-onset diabetes after transplantation (NODAT) is associated with high cardiovascular (CV) risk and reduced patient survival. It is unclear whether this risk is newly acquired or represents preexisting CV disease in patients with this complication.

Methods—Included are 1146 adults, recipients of first kidney transplants from 1984 to 2008 treated with modern immunosuppressants.

Results—One year after transplantation, 29.8% of patients experienced impaired fasting glycemia and 13.4% NODAT. The risk of NODAT related to recipient variables include the following: older age, male gender, higher body mass index, higher pretransplantation glucose and triglyceride levels, and lower high-density lipoprotein level. Increasing fasting glucose levels at 1, 4, or 12 months after transplantation, independent of other factors, related to reduced patient survival (12 months hazard ratio [HR]=1.146 [1.132–1.161], $P<0.0001$ for 10mg/dL increase in glucose), and this was primarily because of an increase in CV deaths. Hyperglycemia related to all major CV events (MCVE), cardiac (HR=1.113 [1.094–1.132], $P<0.0001$), vascular (HR=1.168 [1.140–1.197], $P<0.0001$), and strokes (HR=1.156 [1.123–1.191], $P=0.003$). These relations were

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R.P.W. participated in writing the study plan, collecting most of the data (in collaboration with M.L.S.F.), writing the original version of the article, and introducing modifications as needed. F.G.C. participated by generating the hypothesis guiding the study, being the primary mentor of R.P.W. during this study, and producing the final article (together with R.P.W.). M.L.S.F. participated by collecting data and providing critical input on article production and data presentation. Y.K. and P.S. participated by providing critical input from endocrinology on this project in both the original planning of the study and selection of data to be collected and reviewing the final article. V.E.T., who was a senior advisor to R.W. during her study time, participated by assisting in the design of the study, presentation of the data, and production of the final article.

statistically independent of other risk factors. The increased risk of MCVE was noted particularly in patients without MCVE before transplantation (HR=1.145 [1.126–1.165], $P<0.0001$). Furthermore, among patients with after transplantation MCVE (n=123, 11%), hyperglycemia increases the risk of death (NODAT: HR=2.410 [1.125–5.162], $P=0.024$).

Conclusions—After transplantation hyperglycemia is a strong independent risk factor for MCVE and death, mainly from CV causes. This risk is independent of the presence of CV disease identified before transplantation.

Keywords

NODAT; Diabetes; Cardiovascular risk; Glucose

Since the early days of transplantation, it has been recognized that diabetes can develop de novo after transplantation (new-onset diabetes after transplantation [NODAT]) (1). NODAT is associated with increased cardiovascular (CV) risk and reduced patient survival (2, 3). However, the nature of this association is unclear. Possibly, this increase in CV risk reflects preexisting CV disease because NODAT develops preferentially in older recipients, in patients with high CV burden, and in those with an unfavorable CV risk profile (1–6). If that is the case, NODAT may be mainly a marker of high CV risk, and treatment of hyperglycemia may not reduce risk. Consistent with this hypothesis, CV risk and mortality increases soon after the development of NODAT, and the magnitude of the risk is similar to that observed in patients with diabetes before transplantation (2). However, it is also possible that hyperglycemia itself or the series of biochemical and physiologic anomalies associated with elevated glucose levels contribute to CV risk. This alternative or complementary hypothesis seems to be supported by the fact that all levels of fasting glucose after transplantation are associated with increased risk of CV events and mortality (2, 3). Furthermore, previous studies suggested that reversal of posttransplantation hyperglycemia may be associated with a reduction in risk (2). Finally, it should be considered that not all risk factors for NODAT relate to CV risk. For example, previous studies have shown an association between hepatitis C and NODAT (7, 8).

In this study, we analyzed a large cohort of first-time kidney transplant recipients followed up for long periods of time to examine the nature of the association between posttransplantation hyperglycemia, CV risk, and survival. We hypothesized that posttransplantation hyperglycemia is associated with increased CV risk independent of pretransplantation CV risk factors. Clarifying the variables that contribute to the increased CV risk and mortality of patients with this common complication could have significant implications for patient management after transplantation.

RESULTS

Table 1 displays the characteristics of the patient population. In this cohort, there is a predominance of recipients of the white race and of living-donor recipients, which is characteristic of our center but significantly different from other transplant centers.

Posttransplant Hyperglycemia, Risk Factors

At 1, 4, and 12 months after transplantation, impaired fasting glycemia (IFG) was observed in 27%, 34.3%, and 29.8% of recipients, respectively, and NODAT was diagnosed in 14.1%, 11.1%, and 13.4% of recipients, respectively. Compared with patients who received transplantations before 1998 (n=248), the incidence of IFG and NODAT increased since 1998 (n=898): 16.1% versus 33.6% for IFG and 6.5% versus 15.3% for NODAT ($P<0.0001$). Among patients with NODAT at 1 year, 51.5% were not receiving pharmacologic therapy for their diabetes, 18.8% were receiving oral hypoglycemic agents, and 37.0% were receiving insulin.

The following pretransplantation variables related to risk of NODAT at 1 year: increasing recipient age (presented as odds ratio [OR]=1.06 [95% confidence interval {CI}, 1.05–1.08], $P<0.0001$ per year of age), increasing body mass index (BMI) (1.13 [1.10–1.17], $P<0.0001$), male gender (0.438 [0.30–0.65], $P<0.0001$), and history of major CV events (MCVE) before transplantation (2.10 [1.35–3.28], $P=0.001$). The incidence of NODAT also related to higher fasting plasma glucose (FPG) levels before transplantation (1.10 [1.07–1.120], $P<0.0001$), higher triglycerides (TG; 1.003 [1.001–1.004], $P<0.0001$), or lower high-density lipoprotein (HDL) cholesterol (0.95 [0.94–0.97], $P<0.0001$). By multivariate analysis, the risk of NODAT was independently associated with all of these pretransplantation variables with the exception of TG and pretransplantation MCVE. The risk factors for posttransplantation IFG were similar to those for NODAT, although high TG and/or low HDL levels did not relate to IFG.

NODAT was more common in patients with the renal diagnosis of atherosclerotic kidney disease (HTN/AKD; 24.4%) than in patients with glomerulonephritis (GN; 11.0%), autosomal dominant polycystic kidney disease (13.9%), other diagnoses (12.4%), or unknown diagnosis (10.7%) ($P<0.0001$, chi-square test). Compared to patients with GN, the risk of NODAT at 1 year was increased in patients with HTN/AKD (OR=3.170 [95% CI, 1.89–5.31], $P<0.0001$) but not in patients with other diagnoses. Patients with HTN/AKD were significantly older than those with GN, and after correcting for recipient age, the incidence of NODAT was not significantly different between these two groups (data not shown).

Regarding posttransplantation variables, NODAT developed in 14.9% of patients on tacrolimus (n=762), in 14.1% of patients on sirolimus (n=63), in 37.5% of patients on combination of tacrolimus and sirolimus (n=16), and in 8.5% of patients on cyclosporine ($P<0.0001$, chi-square test). The incidence of NODAT was not statistically different in patients taking tacrolimus and steroids (15.8%) and in those taking tacrolimus but no steroids (n=49, 10.2%, $P=0.382$). The following variables were not associated with the risk of NODAT: pretransplantation dialysis, months on dialysis, total cholesterol, low-density lipoprotein, uric acid, the use of angiotensin-converting enzyme inhibitors or statins, donor characteristics, induction immunosuppression, change in BMI during the first year, graft function, acute rejection, and number of human leukocyte antigen mismatches.

Posttransplantation Hyperglycemia and Patient Survival

For a follow-up period of 90.4+52.6 months (range, 12.2–300 months), 137 patients died (12%), and 150 (13.1%) lost their allograft not because of patient death. Death-censored graft survival did not relate significantly with FPG levels measured at any time point after transplantation (data not shown). However, patient survival censored at graft failure was significantly reduced in patients with hyperglycemia at 1 month (hazard ratio [HR]=1.026 [1.022–1.022], $P<0.0001$ for every 10 mg/dL increment in FPG), 4 months (HR=1.044 [1.037–1.051], $P<0.0001$), or 1 year after transplantation (HR=1.146 [1.132–1.161], $P<0.0001$). Figure 1A displays the association between FPG at 1 year and patient survival. Compared to normal FPG, patients with IFG showed significantly reduced survival (HR=1.714 [1.147–2.561], $P=0.009$), and survival was reduced further in patients with NODAT (HR=3.477 [2.249–5.377], $P<0.0001$). Among patients with NODAT at 1 year, there were no survival differences among those not receiving pharmacologic therapy, those on oral hypoglycemic agents, and those receiving insulin ($P=0.173$, log-rank test). In patients who received transplantations since 1998, the associations between patient survival and glycemia at 4 and 12 months were similar to those shown previously (data not shown).

By multivariate analysis, the following variables related to reduced patient survival (Table 2): increasing recipient age, lower graft function at 1 year, and higher FPG at 4 months or at 1 year. Additional variables included in this model were not statistically significant, although these variables were associated with patient survival by univariate analysis (Table 2). In this multivariate model, the association between MCVE before or after transplantation and mortality became statistically not significant when recipient age was added to the model. These variables were not statistically related to patient survival: donor age, sex and race, recipient race and BMI, history of smoking, acute rejection, and type of induction or maintenance immunosuppression. The use of statins at 1 year after transplantation was not related to patient survival. However, during the study period, statins were used in our program selectively in patients with high CV risk. Table 3 displays causes of death in patients classified according to FPG levels at 1 year. NODAT was associated with increased risk of death due to CV causes.

Posttransplantation Hyperglycemia and Posttransplantation MCVE

Increasing FPG levels at 1 year related to more risk of posttransplantation MCVE (Fig. 1B) whether FPG levels were measured at 1 month (HR=1.019 [1.014–1.025], $P=0.023$), 4 months (HR=1.031 [1.022–1.040], $P=0.043$), or 1 year (HR=1.113 [1.097–1.130], $P<0.0001$). Hyperglycemia at 1 year was associated with more risk of fatal or nonfatal cardiac events (n=94 events) (HR=1.113 [1.094–1.132], $P<0.0001$ for every 10mg/dL increase in FPG level), vascular events (n=27) (HR=1.168 [1.140–1.197], $P<0.0001$), and central nervous system (CNS) events (n=25) (HR=1.156 [1.123–1.191], $P=0.003$). All of these associations were also noted in patients who received transplantations since 1998: cardiac events (HR=1.160, $P<0.0001$), vascular (HR=1.171, $P=0.007$), and CNS (HR=1.178, $P=0.037$).

Among patients without MCVE pretransplantation (n=922) development of posttransplantation hyperglycemia was associated with more risk of posttransplantation

MCVE (74 events; HR=1.145 [1.126–1.165], $P<0.0001$). In contrast, among patients with MCVE before transplantation ($n=193$), posttransplantation hyperglycemia was not associated with more risk of posttransplantation MCVE (45 events; HR=0.994[0.962–1.028], $P=0.916$). Compared with a reference group of patients with neither pretransplantation MCVE nor posttransplantation hyperglycemia (Fig. 2A), the risk of posttransplantation MCVE was increased significantly in patients without pretransplantation MCVE but with posttransplantation hyperglycemia (HR=1.991 [1.215–3.264], $P=0.006$), and the risk was much higher in patients with pretransplantation MCVE (HR=4.990 [3.046–8.175], $P<0.0001$) whether or not they developed posttransplantation hyperglycemia (all of the patients with pretransplantation MCVE are shown as a single line in Figure 2A to simplify the figure). Analysis of patient survival in these three groups of individuals (Fig. 2B) showed somewhat different results. Thus, compared to the reference group of patients, mortality was similarly increased in patients without pretransplantation MCVE and posttransplantation hyperglycemia (HR=2.387 [1.585–3.595], $P<0.0001$) and in patients with pretransplantation MCVE (HR=2.507 [1.488–4.224], $P=0.001$) whether or not they developed hyperglycemia. This is somewhat surprising because patients with pretransplantation MCVE showed significantly more MCVE after transplantation (see Figure 2A). One hypothesis that may explain these findings is that hyperglycemia increases mortality in patients with MCVE. In fact, among patients with posttransplantation MCVE, compared to patients with normoglycemia, patient survival was significantly reduced in patients with IFG (HR=2.186 [1.123–4.256], $P=0.021$) and in patients with NODAT (HR=2.410 [1.125–5.162], $P=0.024$).

By multivariate analysis, the risk of posttransplantation MCVE related to the following variables: increasing recipient age (HR=1.063 [1.038–1.089], $P<0.0001$ per year), history of MCVE before transplantation (HR=2.608 [1.554–4.378], $P<0.0001$), higher creatinine levels 1 year before transplantation (HR=2.155 [1.422–3.266], $P<0.0001$), and increasing FPG at 1 year (HR=1.083 [1.058–1.110], $P=0.018$). Similar models using 1- or 4-months FPG confirmed the independent association between MCVE and FPG levels at all time points (not shown). Variables not statistically related to posttransplantation MCVE included the following: donor variables (age, sex, and race), recipient variables (BMI, sex, and race), immunosuppression, preemptive transplantation, delayed graft function, history of smoking, acute rejection, or the use of statins at 1 year after transplantation.

DISCUSSION

Between 41% and 45% of patients have hyperglycemia after receiving their first kidney transplant, and this complication is associated with increased CV risk and reduced survival (2, 9). As shown here and previously, the incidence of posttransplantation hyperglycemia has increased in more recent years (5), but the CV and survival implications of this complication have not changed significantly with the use of more modern immunosuppression. Posttransplantation hyperglycemia develops preferentially but not exclusively in patients with a high CV risk profile including older recipients with higher BMI or with biochemical indicators suggestive of insulin resistance (1–6). These analyses also showed a higher risk of hyperglycemia in patients with atherosclerotic kidney disease, although this association was explained, statistically, by the fact that these patients were

older. We did not find a significant increased risk of hyperglycemia in patients with autosomal dominant polycystic kidney disease, which is consistent with some studies (6, 10) but inconsistent with others (11, 12).

These analyses suggest that the increased CV risk and reduced survival of patients with posttransplantation hyperglycemia can be attributed to at least three factors: (1) an unfavorable CV risk profile before transplantation; (2) additional factors independent of pretransplantation variables; and (3) reduced survival in patients with MCVE after transplantation if they also have hyperglycemia.

Patients with history of MCVE before transplantation have a marked increased risk of additional MCVE after transplantation. In these patients, posttransplantation hyperglycemia did not increase the risk of additional MCVE. This finding may not indicate a lack of effect of hyperglycemia but may reflect a relatively low number of patients in this subgroup (n=193) and a very high risk of additional MCVE in these patients (see Fig. 2A) even in the absence of hyperglycemia. It may also be that, in these patients, hyperglycemia is solely a marker of an unfavorable CV risk profile and that interventions directed to either prevent or treat hyperglycemia may be futile. Disputing this interpretation, these analyses showed that the mortality associated with a posttransplantation MCVE is significantly increased in patients with hyperglycemia. Recent studies showed that tight control of glucose levels reduces the number of CV events in nontransplant patients with type 2 diabetes (13). However, those same studies showed no differences in survival, perhaps reflecting the fact that the increased mortality of patients with type 2 diabetes is because of multiple causes, not only CV (14). Consistently, in transplant patients, NODAT is associated preferentially with an increase in CV deaths. However, it should be noted that the increase mortality of transplant patients with hyperglycemia greatly exceeds the number of patients with MCVE after transplantation (see Fig. 1), suggesting that other causes of death are also likely increased in these patients.

Consistent with observations made in the general population (15, 16), these results showed that increasing FPG levels relate to increasing CV risk. We showed that this risk is particularly prominent in patients with no history of MCVE before transplantation. Thus, quantitatively in these patients, posttransplantation hyperglycemia doubles the risk of posttransplantation MCVE. It could be argued that patients with posttransplantation hyperglycemia may have showed subclinical CV disease because we defined MCVE clinically. However, the relationship between hyperglycemia and MCVE is independent of other variables that also increase CV risk particularly, time on dialysis (17) and age. The cause for the increased CV risk associated with hyperglycemia is unknown. However, in previous studies, we showed that hyperglycemia is associated with significant anomalies in other CV risk factors including hypertension, lower HDL cholesterol, and higher TG (2, 18).

It is likely that this study underestimated that true incidence of posttransplantation hyperglycemia. Thus, only FPG was considered, and previous studies showed that postprandial hyperglycemia is common after transplantation even in patients with normal FPG (19). Perhaps, glycated hemoglobin may be a better marker of CV risk than FPG levels in transplant patients (20, 21), but unfortunately, this parameter was not available for

analysis. Furthermore, this study included a low percent of African Americans and patients with hepatitis C, patient groups with high incidence of NODAT (3, 7, 8). Thus, in other populations with a higher representation of these patient groups, the incidence of hyperglycemia is expected to be higher than described here.

Clearly, the question that needs to be answered is whether or not prevention and treatment of posttransplantation hyperglycemia reduces CV risk and improves survival. We showed here that whether the patient received pharmacologic treatment of NODAT or not did not relate to CV risk or survival. It would be premature to conclude that treatment of hyperglycemia is ineffective because treatment of NODAT in our program was not protocolized, and it is likely that patients receiving pharmacologic treatment showed more severe hyperglycemia. Still, it is sobering to consider that, in nontransplant patients with type 2 diabetes mellitus, tight control of glucose levels does not reduce mortality (13). These results suggest that glycemia control would be beneficial and that CV preventive measures should be intensified in patients with any degree of posttransplantation hyperglycemia. However, the effectiveness of glucose control after transplantation can only be answered in long-term prospective studies.

MATERIALS AND METHODS

Patient Population

The study includes 1146 adults, recipients of their first kidney transplant at the Mayo Clinic Rochester between 1984 and 2008. All patients were on calcineurin inhibitors or sirolimus as maintenance immunosuppressive therapy after transplantation. Patients were required to have a minimal patient follow-up of 12 months and a minimum of two determinations of FPG 12 months after transplantation. Recipients of bone marrow transplant or other solid organs before or at the time of transplantation were excluded. Patients with diabetes mellitus before the transplant (FPG ≥ 126 mg/dL or treatment with glucose-lowering medications) were also excluded. Clinical information was retrieved from electronic databases. The extraction and reporting of these data were approved by the institutional review board.

Definitions/Criteria

Fasting laboratory tests, including glucose levels (FPG), were measured at least weekly during the first 2 months after transplantation, twice monthly until month 4, and monthly until month 12 and every 3 months thereafter. The average of all FPG levels obtained at different periods of time was calculated, including the following: 2 to 4 weeks (designated as one month), months 2 to 5 (designated as 4 months), and months 11 to 13 (designated as 12 months). IFG was defined as a FPG between 101 and 125 mg/dL (5.6–6.9 mM); and diabetes (NODAT), as the presence of FPG ≥ 126 mg/dL (7.0 mM) or more (20, 22). Patients with FPG ≥ 126 mg/dL or less but are using insulin or oral glucose-lowering agents were also considered to have NODAT. Glycated hemoglobin and postprandial glucose levels were not routinely obtained in these patients.

Pretransplantation and posttransplantation MCVE were defined as follows: Cardiac events included acute myocardial infarction and coronary revascularization either surgical or

percutaneous (angioplasty or stents); vascular events included amputations, revascularization for peripheral vascular disease either surgical or percutaneous, and also central vascular events such as abdominal aortic aneurysm and carotid artery or renal artery stenosis requiring intervention; CNS events included all cerebrovascular accidents.

Immunosuppression

Immunosuppression consisted of induction with antithymocyte globulin in 731 patients (74.6%), anti-CD25 antibodies in 97 (9.9%), alemtuzumab in 49 (5.0%), and OKT3 in 4 (0.4%). Ninety seven patients (9.9%) did not receive induction immunosuppression, and in 166 patients (14.4%), this information was not available. At 1 year after transplantation, 762 patients (66.5%) were receiving tacrolimus, mycophenolate mofetil, and corticosteroids. Cyclosporine was used instead of tacrolimus in 305 patients (26.6%); sirolimus, instead of a calcineurin inhibitor in 63 (5.5%). Sixteen patients (1.4%) received combinations of tacrolimus and sirolimus. Forty-nine patients (5.0%) received steroid-free maintenance immunosuppression.

Data Analyses

Proportions were compared by chi-square test. Two groups of data were compared by Student *t* test or by nonparametric tests if the data were not normally distributed. Comparison among more than two groups of data were performed using analysis of variance or Kruskal-Wallis test. Relationship between different levels of FPG and other variables were assessed by logistic regression. Survival analyses were performed using Kaplan-Meier plots and Cox regression. In some analyses, we considered separately those patients who received transplantations since 1998 to assess whether the use of modern immunosuppressive agents changed the associations noted here.

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FIGURE 1.

Kaplan-Meier plots showing cumulative mortality (A) and cumulative incidence of posttransplantation major cardiovascular events (B) in patients classified according to fasting plasma glucose (FPG) levels 1 year after transplantation: Normal FPG (—), impaired fasting glycemia (IFG) (---), and new-onset diabetes after transplantation (NODAT) (+--+). Log-rank test: (A) $P=0.0001$, (B) $P<0.0001$. A, shows the numbers of patients in each group at different time points. These numbers apply to both (A) and (B).

FIGURE 2.

A, Cumulative incidence of posttransplantation major cardiovascular events (MCVE) in patients with no MCVE before transplantation (Tx) and no post-Tx hyperglycemia (—), patients with no MCVE before Tx but with post-Tx hyperglycemia (---), and patients with pre-Tx MCVE whether or not they showed post-Tx hyperglycemia (· · ·) (Log-rank test: $P < 0.0001$). B, Cumulative mortality in the same three groups of patients (Log-rank test: $P < 0.0001$). B, indicates the numbers of patients in each group at different time points. These numbers apply to both (A) and (B). FPG, fasting plasma glucose.

TABLE 1

Patient characteristics (N=1146)

Parameter	n ^a	Value (%)
Recipient age, yr	1146	49.5 ± 14.4
Recipient sex (males), n (%)	1146	666 (58.1)
Recipient race (white), n (%)	1028	950 (92.4)
Recipient BMI before transplant	1102	27.3 ± 5.7
Recipient obesity (BMI>30), n (%)	1102	275 (25.0)
Dialysis before transplants (no), n (%)	971	513 (52.8)
Smoking, n (%)	959	98 (10.2)
Hepatitis C (positive), n (%)	1114	8 (0.7)
Primary renal disease, n (%)	1146	
Glomerular disease		511 (44.6)
Polycystic kidney disease		230 (20.1)
Hypertension/Atherosclerotic ^b		135 (11.8)
Other		186 (16.2)
Unknown		84 (7.3)
Donor age, yr	1058	42.2 ± 12.9
Donor sex (male), n (%)	1050	504 (48.0)
Donor type (living), n (%)	1146	852 (74.3)
Follow-up time, median, mo	1146	90.4 ± 52.7 (78.5)

^aNumber of observations.^bThe diagnosis of hypertensive/atherosclerotic (HTN/AKD) includes patients with the clinical diagnosis of hypertensive nephrosclerosis and those with renal failure secondary to renal artery stenosis.

BMI, body mass index.

TABLE 2

Factors related to patient survival censored at graft loss

Variable	Univariate Analysis		Multivariate Analysis	
	HR (CI)	P	HR (CI)	P
Recipient age	1.078 (1.062–1.094)	<0.0001	1.085 (1.064–1.107)	<0.0001
Recipient sex	0.645 (0.450–0.924)	0.017		0.402
Preemptive Tx	1.794 (1.180–2.727)	0.006		0.208
Pre-Tx MCVE	1.837 (1.175–2.872)	0.008		0.363 ^a
Post-Tx MCVE	1.939 (1.288–2.918)	0.002		0.961 ^a
Creatinine level 1 yr	1.408 (1.073–1.847)	0.014	2.050 (1.454–2.890)	<0.0001
FPG 1 mo ^b	1.020 (1.014–1.026)	0.001		0.081 ^c
FPG 4 mo ^b	1.041 (1.035–1.047)	<0.0001	1.051 (1.039–1.064)	0.001 ^c
FPG 12 mo ^b	1.139 (1.125–1.153)	<0.0001	1.094 (1.075–1.114)	0.001 ^c

^aPre-Tx and post-Tx MCVE were incorporated into two separate models including the other variables listed.

^bHazard ratio calculated for each 10 mg/dL increment in FPG.

^cThree different multivariate models were constructed incorporating 1-month, 4-months, or 12-months FPG.

CI, confidence index; HR, hazard ratio; FPG, fasting plasma glucose; MCVE, major cardiovascular events; Tx, transplantation.

TABLE 3

Causes of death post-transplant in patients classified according their level of glucose levels at one year post-transplant

Cause of Death	Glycemia 1 Yr After Transplantation			<i>P</i>
	Normal	IFG	NODAT	
No. patients	651	342	153	
Cardiovascular	14 (21.1%)	7 (17.9%)	10 (31.3%)	0.004
Infections	4 (6.1%)	2 (5.1%)	3 (9.4%)	NS
Malignancy	11 (16.7%)	7 (17.9%)	3 (9.4%)	NS
Other	12 (18.2%)	9 (23.1%)	4 (12.5%)	NS
Unknown	25 (37.9%)	14 (35.9%)	12 (37.5%)	NS
Total	66 (10.1%)	39 (11.4%)	32 (20.9%)	0.001

IFG, impaired fasting glycemia; NODAT, new-onset diabetes after transplantation.