Original Article

Long-term prognosis of patients after kidney transplantation: a comparison of those with or without diabetes mellitus

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Abstract

Background. Compared with non-diabetic subjects, patients with type 2 diabetes and end-stage renal disease (ESRD) have seldom been selected for renal transplantation. It was the aim of this study to compare the long-term prognoses of the two groups of patients after transplantation and to identify factors associated with allograft rejection.

Methods. In a retrospective analysis, we studied all 333 consecutive patients who received a kidney transplant at our centre since 1992. Mean follow-up in 302 out of 333 patients (91%) was 3.3 ± 1.5 (0.1–11.7) years. At the time of transplantation, diabetes mellitus (type 1, $n = 3$; type 2, $n = 46$) was known in 49 patients.

Results. Patients with diabetes mellitus were older [patients without diabetes ($n = 253$) *vs* patients with diabetes ($n = 49$), 52.2 ± 12.6 *vs* 58.8 ± 13.1 years, respectively; $P = 0.002$], but they had very good diabetes control [haemoglobin A1c (HbA1c) of patients with diabetes $6.3 \pm 0.9\%$ *vs* those without diabetes $5.2 \pm 1.0\%$, $P = 0.03$]. Even during their follow-up, patients with diabetes showed a tendency to further improvement (HbA1c for patients with diabetes $5.7 \pm 0.9\%$ *vs* those without diabetes $5.5 \pm 0.9\%$, $P = 0.30$). At the end of follow-up also, there were no differences between the groups with respect to blood pressure control (patients with diabetes $135.3 \pm 28.2/79.6 \pm 17.2$ mmHg *vs* patients without diabetes $130.9 \pm 28.7/78.8 \pm 17.1$ mmHg, $P = 0.33/0.78$) and renal function (creatinine, 142.9 ± 61.6 *vs* $151.8 \pm 68.2 \mu$mol/l, $P = 0.38$; glomerular filtration rate, 63.1 ± 23.3 *vs* 59.1 ± 24.0 ml/min/1.73 m^2, respectively, $P = 0.30$). In total, 26 patients had acute transplant rejections [eight patients with diabetes (prevalence 16.3%) *vs* 18 patients without diabeteses (prevalence 7.1%), $P = 0.11$]. In multivariate analysis, the most important parameter associated with the incidence of transplant rejections was the preceding fasting blood glucose ($R^2 = 0.044$, $\beta = 0.21$, $P = 0.009$). All other parameters included in the model (body mass index, time since transplantation, diabetes duration, immunosuppressive therapy, HbA1c and HLA mismatch) revealed no associations.

Conclusions. Following kidney transplantation, the prevalence of rejections in patients with diabetes mellitus is slightly but not significantly higher than in non-diabetic subjects. One of the most important risk factors seems to be fasting blood glucose. Hence, following renal transplantation, treatment strategies should focus not only on optimal immunosuppressive therapy and HLA matching, good HbA1c and blood pressure control, but also on maintaining near-normal fasting blood glucose levels.

Introduction

To date, diabetes mellitus has been an increasing and one of the most important causes, in some countries the single most important cause, of end-stage renal disease (ESRD). According to the ESRD programme in the USA, the number of existing patients with terminal renal insufficiency caused by diabetes more than tripled between 1990 and 2001. The rate per million population increased by 167%, to 491 [1]. Comparable or even higher figures were reported from European countries [2–5]. According to the data of 'QuaSi-Niere', a nationwide system to ensure quality control in patients undergoing haemodialysis (German Renal Registry-Project Quality Assurance in Renal Replacement Therapy), the prevalence of diabetes mellitus as a cause of ESRD is 22% in Germany (type 1 diabetes, 5%; type 2 diabetes, 17%). In 2002, the incidence of end-stage renal failure due to diabetic nephropathy was 36% (type 1 diabetes, 4%; type 2 diabetes, 32%) [4,5].

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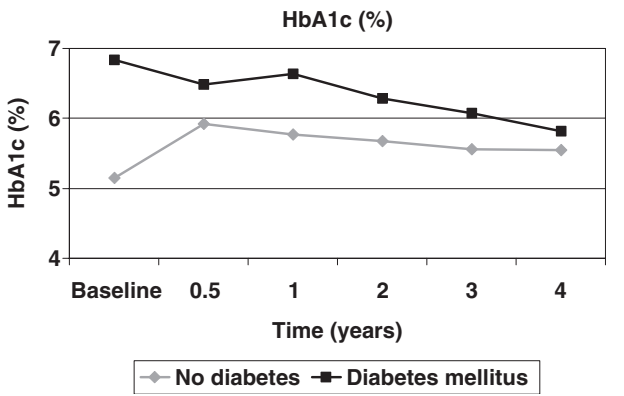
HbA1c (%)

n	Baseline	0.5 years	1 year	2 years	3 years	4 years
No diabetes	253	252	246	214	192	155
Diabetes mellitus	49	48	46	42	35	29

Fig. 1. HbA1c values in patients with or without diabetes mellitus during a follow-up of 4 years after renal transplantation

Fasting blood glucose (mmol/l)
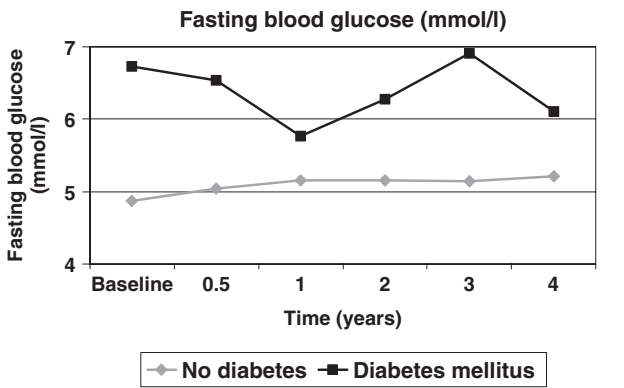
n	Baseline	0.5 years	1 year	2 years	3 years	4 years
No diabetes	253	252	246	214	192	155
Diabetes mellitus	49	48	46	42	35	29

Fig. 2. Fasting blood glucose values in patients with or without diabetes mellitus during a follow-up of 4 years after renal transplantation

However, although kidney transplantation has been established as probably the best modality of renal replacement therapy in patients with type 1 diabetes mellitus and ESRD (a procedure currently often being simultaneously performed with pancreas transplantation), information concerning the results of kidney transplantation in patients with type 2 diabetes mellitus is scarce. To date, there is controversy about the frequency of scheduling diabetic patients for kidney transplantation: according to data from the ESRD programme in the USA, only patients with a body mass index (BMI) <21.3 kg/m² had lower rates of being placed on transplantation lists than subjects with

diabetes [1]. In other reports [4,6], in comparison with non-diabetic subjects, patients with type 2 diabetes mellitus and ESRD were less frequently selected for renal transplantation than non-diabetic patients. Moreover, compared with non-diabetic subjects, patients with type 2 diabetes are mostly older and often have diabetes-related long-term complications and a wide range of co-morbidities [6]. For example, studying a random sample of 4025 patients entering renal replacement programmes in the USA, Stack and Bloembergen found a prevalence of coronary heart disease of 38%. It was significantly ($P < 0.05$) more common in patients with diabetes mellitus (46.4%) than in non-diabetic patients (32.2%) [7]. Similar results were found in a cohort of 433 Canadian patients [8]. Apart from cardiac complications, the diabetic patients are also more subject to a wide range of other vascular complications (peripheral vascular disease ~7%, stroke ~1%) [9] and infections [10]. All these co-factors, which make renal transplantation in patients with type 2 diabetes mellitus much more complicated than in non-diabetic patients, result in patients with type 2 diabetes rarely being selected for renal transplantation [11,12]. Moreover, transplantation outcomes in patients with type 2 diabetes mellitus have been worse than in other patient groups [12]. One reason for the poor outcomes may be elevated blood glucose levels, with their resultant glucotoxic effects, and underlying inflammation or specific immune defects. On the other hand, the higher risk of diabetes for patients makes several other variables important for an analysis of graft and patient outcomes—factors such as immunological status, immunosuppressive regimen, quality of diabetes control and strategy of diabetes treatment, which have often been insufficiently controlled for. Therefore, the current trial was undertaken to evaluate the results of kidney transplantation and to identify factors associated with allograft rejection and long-term prognosis in a non-selected cohort of patients with type 2 diabetes mellitus, who were compared with non-diabetic patients who received a renal transplantation during the same period.

Subjects and methods

In this cohort study with a retrospective design, we studied all 333 consecutive patients with ESRD who received first kidney transplants from non-related cadaveric donors at the University of Jena Medical School between 1992 and 2003. In 302 out of 333 patients (91%), mean follow-up was 3.29 ± 1.54 (0.04–11.66) years. Of the 31 patients lost to follow-up, three patients died (one male, age 68 years, 1.2 years after transplantation from myocardial infarction; one male, age 64 years, of carcinoma 3.1 years after transplantation; and one female, age 58 years, from unknown causes 3.2 years after transplantation). Information about the missing 28 patients life and kidney function-status could be obtained from general practitioners but, because the patients were not treated at our centre, no additional valid information was available.

Prior to the transplantation surgeries, the presence and the type of diabetes mellitus were established using World Health Organization (WHO) criteria published in 1999 [13]. According to these criteria, 49 patients were diagnosed as having diabetes mellitus (type 1, $n = 3$; type 2, $n = 46$) at the time of transplantation.

Data assessment

The following data were assessed in each patient: age, sex, renal disease leading to the end-stage renal failure (histological diagnosis), year of transplantation, number of donor human leukocyte antigen (HLA) A, B and DR antigen mismatches (± 2 maximum), time of the initiation and the type of dialysis treatment, history of myocardial infarction, results of extensive cardiovascular examinations (thallium scintigraphy or coronary angiography), stroke, amputation, smoking status and the use of anti-hypertensive or anti-lipidaemic treatments. Post-transplant information was obtained from standard transplantation follow-up protocols and from all post-transplant hospitalization records. This information included: use of anti-T-cell induction therapy, the type and dosage of immunosuppressive regimen, serum creatinine, proteinuria, blood pressure, lipid status and the occurrence of complications requiring hospitalization. Clinically, allograft rejection occurred with episodes of renal dysfunction after transplantation. A renal biopsy was performed in each patient with a clinically diagnosed allograft rejection with episodes of renal dysfunction after transplantation. Allograft rejection was diagnosed according to the Banff schema, i.e. acute rejection is recognized by the presence of tubulitis and intimal arteritis. Tubulitis is defined as the infiltration of the tubular epithelium by leukocytes, usually lymphocytes. Infiltration of the arterial intima is referred to as intimal arteritis. The intensity of the infiltrate and the severity of tubulitis and intimal arteritis are used to classify acute rejection into mild, moderate and severe categories. The grading system is used to indicate how urgently and intensively a particular episode of rejection needs to be treated. Biopsies with histopathological alterations insufficient for a firm diagnosis of rejection are said to show borderline changes.

The measurements of haemoglobin A1c (HbA1c; HPLC, Tosho®) were standardized according to the Diabetes Control and Complications Trial (DCCT) [14] (with an estimated reliability coefficient of 99% and a mean normal of 5.05%) and measurements of fasting blood glucose were made 6–8 weeks after transplantation and at the beginning of each trimester, during the time patients were free of rejection episodes. Urine albumin concentration was measured using nephelometry (normal range <20 mg/l). Serum creatinine was measured using the Jaffé reaction. Creatinine clearance was estimated using the Cockroft–Gault formula, as follows: $1.23 \times ([140 - \text{age}]/\text{serum creatinine [µmol]}) \times \text{weight (kg)}$. Height and body weight were assessed with patients wearing light clothing and without shoes. Blood pressure in the sitting position was measured with a standard sphygmomanometer after the patient had rested for 10 min, according to the WHO recommendations [15].

Statistical analysis

Statistical analysis was performed using SPSS® (Statistical Package for Social Science). All data are presented as
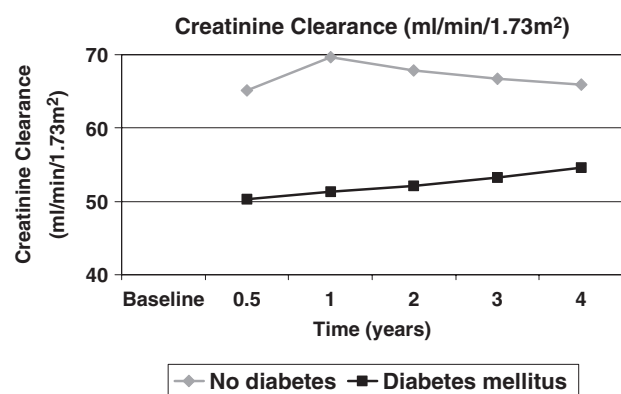
Fig. 3. Creatinine clearance values in patients with or without diabetes mellitus during a follow-up of 4 years after renal transplantation

n	Baseline	0.5 years	1 year	2 years	3 years	4 years
No diabetes	253	252	246	214	192	155
Diabetes mellitus	49	48	46	42	35	29

mean $\pm$ SD or, for data without normal distribution, as median and range. Group differences in discrete variables were compared using the χ^2 test, or Fisher's exact test for frequencies ≤ 5. For continuous variables, the Student t-test or the Mann–Whitney U-test were used as appropriate. We used analysis of variance (ANOVA) to analyse changes in continuous variables (i.e. fasting blood glucose, HbA1c, creatinine and creatinine clearance) from baseline values, by the groups of patients (with and without diabetes mellitus) and adjusted for the baseline value. Statistical tests, for interaction were done with Cox's regression. Significance was defined at the 0.05 level.

Results

Baseline examination

Comparing patients with and without diabetes mellitus at baseline, it was found that patients with diabetes were significantly older and had higher fasting blood glucose values and HbA1c levels. Additional characteristics of the cohort are shown in Table 1.

Diabetes control

At the time of transplantation, the treatment of diabetes mellitus consisted of insulin in five out of 49 patients (10%), oral anti-diabetic drugs (a combination of sulfonylurea and acarbose) in one of 49 patients (2%) and diet alone in 43 out of 49 patients (88%). During the follow-up, diabetes treatment changed in six patients (in all of them insulin was started within 1–3 weeks). During the same period, HbA1c showed a tendency to improve further ($5.67 \pm 0.93\%$). In contrast, in patients without diabetes mellitus before renal transplantation, there was a slight, but significant,

Table 1. Pre-transplant clinical and laboratory data of kidney transplant recipients with or without diabetes mellitus

	With diabetes mellitus	Without diabetes mellitus	*P*-value
n	49	253	–
Females [*n* (%)]	18 (37%)	98 (39%)	0.917
Age (years)	52.2 ± 12.6	58.8 ± 13.1	0.002
Duration of dialysis (months)	16.2 ± 4.4	16.4 ± 5.0	0.742
Insulin therapy [*n* (%)]	5 (10%)	–	–
Duration of insulin therapy (years)	7.79 ± 9.01	–	–
Insulin dosage (IU/kg body weight)	0.39 ± 0.15	–	–
BMI (kg/m^2)	25.2 ± 3.6	24.4 ± 3.6	0.151
Systolic blood pressure (mmHg)	131.1 ± 12.7	132.7 ± 15.2	0.506
Diastolic blood pressure (mmHg)	78.1 ± 7.5	80.3 ± 9.4	0.150
HbA1c (%)	6.33 ± 0.93	5.15 ± 0.98	0.031
Fasting blood glucose (mmol/l)	6.9 ± 2.3	4.9 ± 0.9	<0.001
Creatinine (µmol/l)	855.1 ± 238.1	862.3 ± 241.6	0.188
Albumin (g/l)	44.4 ± 8.3	42.4 ± 6.3	0.147
No. of HLA mismatches (*n*)	2.0 ± 1.0	2.1 ± 1.7	0.870
Induction anti-T-cell therapy [*n* (%)]	11 (22%)	53 (21%)	
Renal disease			
Glomerulonephritis [*n* (%)]	17 (34%)	133 (53%)	0.032
Diabetic nephropathy [*n* (%)]	8 (16%)	0	<0.001
Vascular nephropathy [*n* (%)]	1 (2%)	4 (2%)	0.590
Cystic degeneration [*n* (%)]	3 (6%)	35 (14%)	0.099
Others [*n* (%)]	20 (40%)	81 (31%)	0.303

Table 2. Immunosuppressive drugs used during the follow-up

Patients	With diabetes mellitus (*n* = 49)	Without diabetes mellitus (*n* = 253)	*P*-value
Steroids [*n* (%)]	27 (55%)	158 (62%)	0.420
Cyclosporin A [*n* (%)]	21 (43%)	126 (50%)	0.463
Tacrolimus [*n* (%)]	13 (27%)	70 (28%)	0.990
Azathioprin [*n* (%)]	20 (41%)	114 (45%)	0.696
Cellcept [*n* (%)]	24 (49%)	149 (59%)	0.260
Sirolimus [*n* (%)]	1 (2%)	0 (0%)	0.162

increase in HbA1c (up to 5.46 ± 0.92%; *P* = 0.048). Out of this group, a total of 44 patients (17%) developed new-onset diabetes mellitus after transplantation.

Immunosuppressive treatment

Following kidney transplantation, various types of initial immunosuppressive protocols were used in all the patients. The absolutely dominant regimen comprised one of three available forms of cyclosporin A (during recent years, more and more often tacrolimus) with azathioprine and prednisone (> 95% in both groups). However, despite this heterogeneity, initially and during the follow-up period in both groups, in patients with and without diabetes mellitus, statistically comparable types of immunosuppressive protocols were used (Table 2). There were no significant differences with respect to both patient and graft survivals between the patients with and without diabetes who received steroids, likewise with respect to the choice of calcineurin inhibitor (cyclopsorin or tacrolimus).

Patients' outcomes

Death and cardiovascular events. Before the end of the trial, out of the group of 49 patients who had diabetes mellitus before kidney transplantation, three patients died (6%), 5.1, 5.6 and 7.0 years following transplantation. All deaths were due to cardiovascular complications [two patients with myocardial infarction (aged 69 and 75 years) and one patient with stroke (aged 72 years)]. In the group of 253 patients without diabetes mellitus before transplantation, the total number of patients who died during the follow-up period was also three (1%, *P* = 0.032 *vs* patients with diabetes before transplantation). The deaths in this group of patients occurred at the ages of 42 (car accident), 45 (myocardial infarction) and 69 (prostate carcinoma) years, at 0.8, 10.8 and 0.4 years after renal transplantation, respectively. Additional cardiovascular disease events occurred in three patients with diabetes (6%) and in six patients without diabetes mellitus (2%) (*P* = 0.165)

Diabetes-related long-term complications. Prior to transplantation, eight out of 49 patients (16%) with diabetes mellitus had pre-proliferative retinopathy (according to the ETDRS-criteria [16]); in five out of 49 patients (10%) peripheral neuropathy was diagnosed (according to Young *et al.* [17]). During the follow-up period, one patient with pre-proliferative retinopathy at the beginning of the trial developed proliferative retinopathy requiring laser coagulation. No patient developed foot complications or required an amputation.

Renal function and allograft rejection. At the end of the trial, there were no differences between the

groups with respect to blood pressure control (patients with diabetes $135.3 \pm 28.2/79.6 \pm 17.2$ mmHg vs non-diabetic patients $130.9 \pm 28.7/78.8 \pm 17.1$ mmHg, $P = 0.33/0.78$) and renal function (creatinine, 142.9 ± 61.6 vs 151.8 ± 68.2 µmol/l, $P = 0.38$; glomerular filtration rate, 63.1 ± 23.3 vs 59.1 ± 24.0 ml/min/1.73 m^2, respectively, $P = 0.30$). In total, 26 patients showed transplant rejections [eight patients with diabetes (prevalence 16.3%) vs 18 non-diabetic patients (prevalence 7.1%), $P = 0.11$; Banff grading: borderline, $n = 1$; acute rejection grade I (AR I), $n = 19$; AR IIA, $n = 1$; AR III, $n = 5$]. Rejections were mostly classified as mild (AR I) to moderate (AR II) in 19 out of 26 patients. In five patients, severe acute rejections (AR III) and in one patient a borderline change were diagnosed, without differences between patients with and without diabetes mellitus. In no patient was a recurrent diabetic nephropathy diagnosed.

Multivariate analysis

In multivariate analysis, and after adjustment for age, the most important parameter associated with the incidence of transplant rejections (dependent variable) turned out to be fasting blood glucose, assessed 6–8 weeks after transplantation and at the beginning of each of the following trimesters, during the times patients were free of symptoms of a rejection episode ($R^2 = 0.044$, $\beta = 0.21$, $P = 0.009$). All other parameters included in the model [BMI, interval since transplantation, duration of diabetes, immunosuppressive therapy, HbA1c and HLA mismatch (independent variables)] revealed no associations.

Time course

Figures 1–3 show the course of HbA1c, fasting blood glucose and creatinine clearance during the follow-up period of 4 years. HbA1c levels at baseline ($P = 0.031$), 1 year ($P = 0.017$), 2 years ($P = 0.027$) and 3 years ($P = 0.031$) following renal transplantation were significantly higher in the patients with diabetes mellitus compared with those without diabetes mellitus. The differences did not reach significance at 0.5 ($P = 0.073$) and 4 years ($P = 0.283$) after renal transplantation. The same tendency was apparent with respect to fasting blood glucose values: the values in patients with diabetes mellitus were significantly higher at baseline ($P < 0.001$) and 0.5 ($P = 0.019$), 1 ($P = 0.020$), 2 ($P = 0.003$), 3 ($P < 0.001$) and 4 years ($P = 0.040$) following renal transplantation. Similarly, patients with diabetes mellitus had significantly lower creatinine clearances ($P < 0.001$) at all examination points, stably and starting from the beginning of the trial.

Discussion

The proportion of type 2 diabetic patients requiring renal replacement therapy has drastically increased over recent decades [1–6]. Their ideal treatment is still a matter of dispute [18]. In comparison with non-diabetic patients, patients with type 2 diabetes mellitus and ESRD still have a worse prognosis. Their main causes of death are myocardial infarction and sepsis. A history of severe vascular complications is an additional independent factor of decreased survival in patients with type 2 diabetes mellitus [9,10,18]. In a Scandinavian study of a cohort of 27 patients with type 2 diabetes mellitus on insulin therapy who had renal transplantation between 1985 and 1993, the authors found a significantly worse outcome in the cohort in comparison with non-diabetic subjects. However, although graft survival rates in both groups were comparable, the recommendation of the authors for patients with type 2 diabetes mellitus was a 'continued restriction in the acceptance rate for transplantation' [19]. In contrast, in a retrospective analysis of data on all renal transplants performed at the University of Minnesota since 1984, Kronson et al. found that kidney transplantation is a 'relatively safe, viable option' for patients with type 2 diabetes mellitus. In this trial, there were no significant differences between diabetic and non-diabetic subjects with respect to 5-year patient as well as graft survivals, though there still was a tendency to a poorer outcome [20]. More encouraging results were reported by Mieghem et al. in 2001 [21] and Boucek et al. in 2002 [12]. Moreover, a case–control study of patients with type 1 diabetes mellitus, published in 2003 by Brunkhorst et al., even showed an improved survival after renal transplantation compared with haemodialysis [22].

Further supporting kidney transplantation in patients with diabetes mellitus are some trials that demonstrate an improvement in health-related quality of life. The overall improvement in functional performance after kidney transplantation, the positive effect of time after transplantation and the negative effects of cadaveric organs and diabetes on post-transplant health-related quality of life are indirect, and they are mediated by the direct effects of these variables on post-transplant functional performance.

All in all, in agreement with the studies published during recent years, the present trial also shows that in patients with diabetes mellitus, the outcome of kidney transplantation may almost be matched by that in non-diabetic subjects. Patient and graft survival in our diabetic group were not significantly different from those in the non-diabetic patients, although patients with diabetes were older, and had higher HbA1c and fasting blood glucose levels. However, according to the results of our trial, there was a tendency to a higher prevalence of transplant rejections in patients with diabetes mellitus. Similarly, although they concluded that renal transplantation in patients with type 2 diabetes mellitus is a safe, viable option, Kronson et al. still found the relatively low 5-year survival of 53% for grafts in patients with type 2 diabetes. This was worse, and was accompanied by a higher mortality rate, in comparison with the results obtained in the cohort

of patients with type 1 diabetes or in non-diabetic subjects [20]. When considering these controversial results, there are some striking differences between the groups analysed in the literature and our present cohort: since the reports of Nyberg *et al.* [19], and Kronson *et al.* [20] there has been a striking improvement in the strategies for the management of post-transplant complications such as rejection and sepsis. Moreover, in contrast to the trial of Boucek *et al.* [17], in most of the preceding trials controls are far less rigorously matched for age, duration of diabetes, quality of diabetes control, long-term complications of diabetes or the prevalence of cardiovascular diseases.

In multivariate analysis, the only and most important parameter associated with the incidence of transplant rejections was fasting blood glucose. However, the relationship revealed no threshold value. Hence, these results provide striking evidence not only for a strict mean-day diabetes quality control, reflected in an HbA1c as close to the normal range as possible, but also for fasting blood glucose levels as close to the normal range as possible. Perhaps elevated blood glucose levels, having direct glucotoxic effects, are associated with underlying inflammation or specific immune defects. In principle, the findings of our trial are in agreement with the results that Sato *et al.* obtained from a cohort of 48 patients with renal transplantation. In this group, the authors found that it was not age, duration of pre-transplant dialysis or BMI that were relevant parameters and important predictors of outcome, but pre- and post-transplant abnormalities of insulin secretion and sensitivity. Moreover, in their study, the cumulative doses of corticosteroids clearly affected the incidence of post-transplant diabetes mellitus, cyclosporin A treatment influenced insulin secretion, and both drugs were identified as risk factors for adverse patient outcomes [23]. In some respects, the positive outcome of the patients with diabetes mellitus in our study may have contributed to correct this tendency of avoiding diabetogenic drugs such as steroids, cyclosporin A or tacrolimus.

Further risk factors, mostly associated with higher insulin levels, that impair insulin sensitivity and often elevate blood glucose levels, are overweight and obesity [24]. In the USA, Friedman *et al.* [24] found that the majority (60%) of subjects at the time of transplantation are overweight or obese. Between 1987 and 2001, the proportion of obese transplant recipients rose by 116%. Furthermore, since overweight and obesity are very prevalent at the time of kidney transplantation, and they eclipse protein-energy malnutrition as the more common nutritional illness, the authors postulated a negative effect of overweight and obesity on graft survival [24]. In our present trial, the mean BMI of patients with diabetes mellitus was $25.2 \, \text{kg/m}^2$ with a wide standard deviation of $3.6 \, \text{kg/m}^2$, but it was substantially lower than in the general population of insulin-treated patients with type 2 diabetes mellitus in the same geographical area ($>28 \, \text{kg/m}^2$) [25], and it

was comparable with the BMI of non-diabetic renal transplant recipients.

This trial of 302 patients, all of whom received kidney transplantation at a single centre since 1992, provides important additional evidence for the substantial improvement that has occurred in recent years in the outcomes (morbidity and mortality) of patients with diabetes mellitus (in particular of those with type 2 diabetes and end-stage renal failure). The most important parameters associated with this improvement seem to be not only a more rigorous pre-transplant screening and effective treatment of cardiovascular complications before performing renal transplantation, but also new types and regimens of immunosuppressive therapy with better care of complications and a metabolic control as close as possible to normoglycaemia. According to our results, it is of special importance to focus on the quality of the patients' diabetes control—not only on an optimal HbA1c, but also on lower fasting blood glucose levels. Hence, although in some respects the presence of diabetes mellitus still constitutes an important risk factor, the results of our trial no longer support the restriction of the access to kidney transplantation of patients with diabetes mellitus.

Conflict of interest statement. None declared.

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