PREDICTORS OF NEW-ONSET DIABETES IN KIDNEY TRANSPLANT RECIPIENTS

Bogdan Marian SOROHAN[1], Cristina BUCȘA[2] , Dorina TACU[2], Bogdan OBRISCA[1], Gener ISMAIL[1,3] ,Ioanel SINESCU [2,3]

[1]Department of Nephrology, Fundeni Clinical Institute, Bucharest, Romania

[2]Center for Uronephrology and Renal Transplantation, Fundeni Clinical Institute, Bucharest, Romania

[3]'Carol Davila' University of Medicine and Pharmacy, Bucharest, Romania

Objectives:

New onset diabetes after transplantation (NODAT) is a serious, yet common complication following kidney transplantation, associated with an increased risk of graft failure, cardiovascular complications, death and important healthcare costs.

The main end-point of this study was to evaluate the predictors associated with NODAT development.

Secondary end-point was to determine the incidence of NODAT among kidney transplant recipients.

Methods:

We performed a single-center, retrospective, observational study that included 219 patients who underwent consecutive kidney tranplantations between 2007 and 2010. The follow-up period was of 36 months after transplant. NODAT was defined according to American Diabetes Association criteria. Data collected included demographic characteristics of recipients and donors, comorbidities, treatment , transplant features and creatinine levels.

Exclusion criteria: pre-transplant diagnosis of diabetes and recipient age <18 years.

Statistic analysis: To investigate the predictors of NODAT, a logistic regression analysis was performed. Variables that had a p-value ≤0.30 after group comparison were selected in logistic regression predictive model.

Table 1. Baseline characteristics of recipients and donors

Baseline recipient and donor characteristics	Mean±SD/Median + IQR/ Percentages
Recipient age (years)	39 (31-49)
Recipient age group	
18-25 years	13.7%
26-39 years	37.4%
≥40 years	48.9%
Recipient gender (male)	62.1%
Hemodialysis	71.2%
Peritoneal dialysis	11.9%
Preemptive	16%
Duration of dialysis (months)	24 (5-53)
Primary disease for transplantation	
Glomerulonephritis	58.9%
Polycystic kidney disease	11%
Others	7.3%
NODAT	8.2%
Pre-transplant BMI (kg/m^2)	23.1(21.5-24.8)
Pre-transplant BMI category(%)	
<18.5 kg/m^2	10%
18.5-24.9 kg/m^2	66.2%
25-29.9 kg/m^2	19.2%
≥30 kg/m^2	4.6%
Pre-transplant hypertension %	71.7%
Pre-transplant smoking status(yes) %	7.8%
Pre-transplant hypercholesterolemia %	47.9%
Urinary tract infections %	53.2%
Cardiovascular events %	12.3%
Viral serological status	
CMV-positive	29.2%
BKV-positive	9.5%
HBV-positive	7.3%
HCV-positive	11%

Table 1. Baseline characteristics of recipients and donors- continued

Baseline recipient and donor characteristics	Mean±SD/Median + IQR/ Percentages
Acute rejection	31.3%
Allograft failure	5.5%
Immunosuppressive treatment %	
TAC+MMF	46.6%
CSA+MMF	18.7%
RAPA+TAC	11.4%
RAPA+MMF	22.8%
eGFR, 6 months (mL/min/1.73 m2)	49 (38-59.8)
eGFR, 1 year (mL/min/1.73 m2)	52 (40.7-66.6)
eGFR, 3 years (mL/min/1.73 m2)	55.1 (40.4-69.4)
Donor age (years)	43.3 ±15
Donor age group (%)	
18 -29 years	14%
30-39 years	19.8%
40-49 years	27.5%
50-59 years	24.2%
≥60 years	14.5%
Donor type	
Living donor	57.1%
Donor gender (male)	49.3%

Table 2. Characteristics of patients with and without NODAT

Variable	Non-NODAT (n=201)	NODAT (n=18)	P value
Recipient age (years)	39(31-49)	41.5(36-49.2)	0.25
Recipient age group (%)			
≥40 years	47.8%	61.1%	0.27
Recipient gender (male)	61.2%	72.2%	0.3
Dialysis (%)			
Hemodialysis	70.6%	77.8%	0.52
Peritoneal dialysis	11.4%	16.7%	0.53
Preemptive transplant	17.9%	5.6%	0.13
Duration of dialysis (months)	22(4.5-52)	33(11.5-73.2)	0.13
Primary disease for transplantation			0.57
Glomerulonephritis	58.7%	61.1%	
Polycystic kidney disease	10.9%	11.1%	
Obstructive nephropathy	7%	11.1%	
Others	8%	0%	
Pre-transplant BMI (kg/m^2)	23.1(21.3-24.8)	23.6(21.8-25.3)	0.35
Pre-transplant BMI category (%)			
≥25 kg/m2	23.4%	27.8%	0.68
Pre-transplant hypertension (%)	77.1%	77.8%	0.55
Pre-transplant hypercholesterolemia (%)	46.8%	61.1%	0.24
Cardiovascular events (%)	12.4%	11.1%	0.86
Viral serological status			
CMV-positive	29.9%	22.2%	0.49
BKV-positive	8.5%	22.2%	0.09
HBV-positive	7%	11.1%	0.54
HCV-positive	10%	22.2%	0.14
Acute rejection	31.3%	27.8%	0.75
Immunosuppressive treatment (%)			
TAC+MMF	45.8%	55.6%	0.42
CSA+MMF	**16.9%**	**38.9%**	**0.03***
RAPA+TAC	12.4%	0%	0.11
RAPA+MMF	**24.4%**	**5.6%**	**0.03***
Donor age (years)	43.2±15	45.2±15.3	0.58
Donor age ≥40 years	61.2%	77.8%	0.16
Deceased donor	42.3%	50%	0.52
Donor gender (male) (%)	48.8%	55.6%	0.58

Table 3. Binary logistic regression of risk factors associated with NODAT

Variable	Univariate logistic regression			Multivariate logistic regression		
	OR	95%CI	P-value	OR	95%CI	P-value
Recipient age > 40 years	1.71	0.64-4.61	0.28	1.99	0.66-5.94	0.21
Donor age > 40 years	2.22	0.70-6.98	0.17	2.54	0.70-9.15	0.15
HCV infection	**2.58**	**0.77-8.61**	**0.12**	**5.08**	**1.19-21.60**	**0.02***
BKV infection	3.09	0.91-10.44	0.06	2.35	0.61-9.08	0.21
CSA+MMF regimen	**3.12**	**1.13-8.64**	**0.02***	**3.37**	**1.02-11.14**	**0.04***
RAPA+MMF regimen	0.18	0.02-1.40	0.10	0.18	0.02-1.65	0.13
Hypercholesterolemia	1.78	0.66-4.80	0.24	1.55	0.52-4.61	0.42
Preemptive transplant	0.27	0.03-2.09	0.21	0.25	0.03-2.19	0.21
Recipient male gender	1.64	0.56-4.80	0.30	2.26	0.68-7-45	0.17

Results:

The median age at the time of transplantation was 39 years (IQR:31-49), 48.9% of recipients were ≥ 40 years and 62.1% were males. The majority of donors were females, mean age of donors was 43.3 ±15 years and living donor was the predominant donor type. Hemodyalisis was the most frequent pre-transplant dialysis type. Patients were characterized by normoponderality (median BMI: 23.1, IQR:21.5-24.8 kg/m^2), but 23.8% of recipients were overweight and obese at the moment of transplantation. Chronic glomerulonephritis and polycystic kidney disease were the main causes that lead to ESRD. Pre-transplant hepatitis C virus infection was present in 11% of kidney recipients. The association of tacrolimus with mycophenolate mofetil was the predominant immunosuppressive regimen. Eighteen patients (8.2%) developed NODAT during the 3 years of follow-up **(Tabel 1).** The group that developed NODAT was older, but without statistical significance [39(31-49) vs 41.5(36-49.2), p=0.25]. No significant differences were observed between the two groups in BMI, pre-trasnplant hypertension, hypercholesterolemia, hepatitis C virus infection, donor type and age. Use of cyclosporine with mycophenolate mofetil (16.9% vs 38.9%, p=0.03) and rapamycin with mycophenolate mofetil (24.4% vs 5.6%, p= 0.03) as immunosuppression regimens presented significant differences between the two groups **(Table 2).** By multivariate analysis, predictors that we found to be associated with NODAT were pre-transplant infection with hepatitis C virus (OR: 5.08; 95% CI: 1.19-21.60; p= 0.02) and use of cyclosporine with mycophenolate mofetil regimen (OR: 3.37;95% CI: 1.02-11.14, p= 0.04) **(Tabel3).**

Conclusions:

In summary, the incidence of NODAT in our study was of 8,2%. The use of cyclosporine with mycophenolate mofetil immunossuppresion regimen and pre-transplant infection with hepatitis C virus were predictors of new-onset diabetes after kidney transplantation.

References:

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