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Title: Post-Transplant Diabetes Mellitus in Kidney Transplant Recipients: A Multi-Center Study

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Appendix A: Data quality description

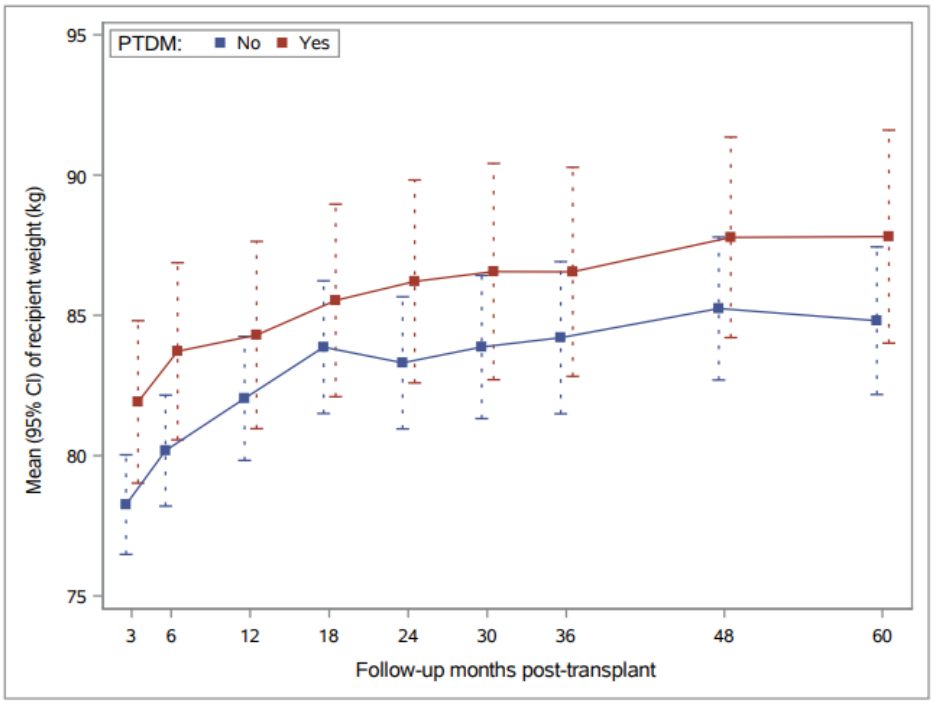
Trained study participants at each site recorded recipient data on standardized case report forms using a secure, online database. Outcomes were adjudicated by site investigators, and extensive data quality control checks were performed by study monitors from the data coordinating center (Yale University at the time of data abstraction, Johns Hopkins University at the time of data analysis). Study monitors validated data abstraction processes via secondary review of submitted paper charts and then continuously reviewed all data points following form completion by site coordinators to confirm data quality and accuracy.

This study utilized various methods such as rigorous study documentation, in-depth coordinator training, independent data monitoring, and principal investigator (PI) involvement to increase the quality of the data collected. A detailed protocol and a manual of operations were created to facilitate consistency in data collection practices across all participating research centers. Coordinators were required to attend two separate web-based trainings provided by a co-investigator, a study monitor (hired from the Yale Center for Clinical Investigation – separate from our department), and a project coordinator. The trainings demonstrated how to use the database (OnCore) and detailed explanation of important data variables and key practices to utilize during chart abstraction.

Research centers were all required to send the first five completed charts to the study monitor for data verification from source documents. All of the remaining charts were validated remotely by following defined guidelines for data quality developed by the Yale Data Coordinating Center. Queries were used for quality control checks to identify potential data anomalies such as missing data or forms, out-of-range or erroneous data, and inconsistent data. The statistician also conducted separate back-end data checks. For instance, if the baseline form indicated a biopsy report was available at 3 month, the statistician would check to see if the biopsy details were provided in the 3-month follow-up form. If it was not, sites would be queried to enter the information. Participants who met the study stopping

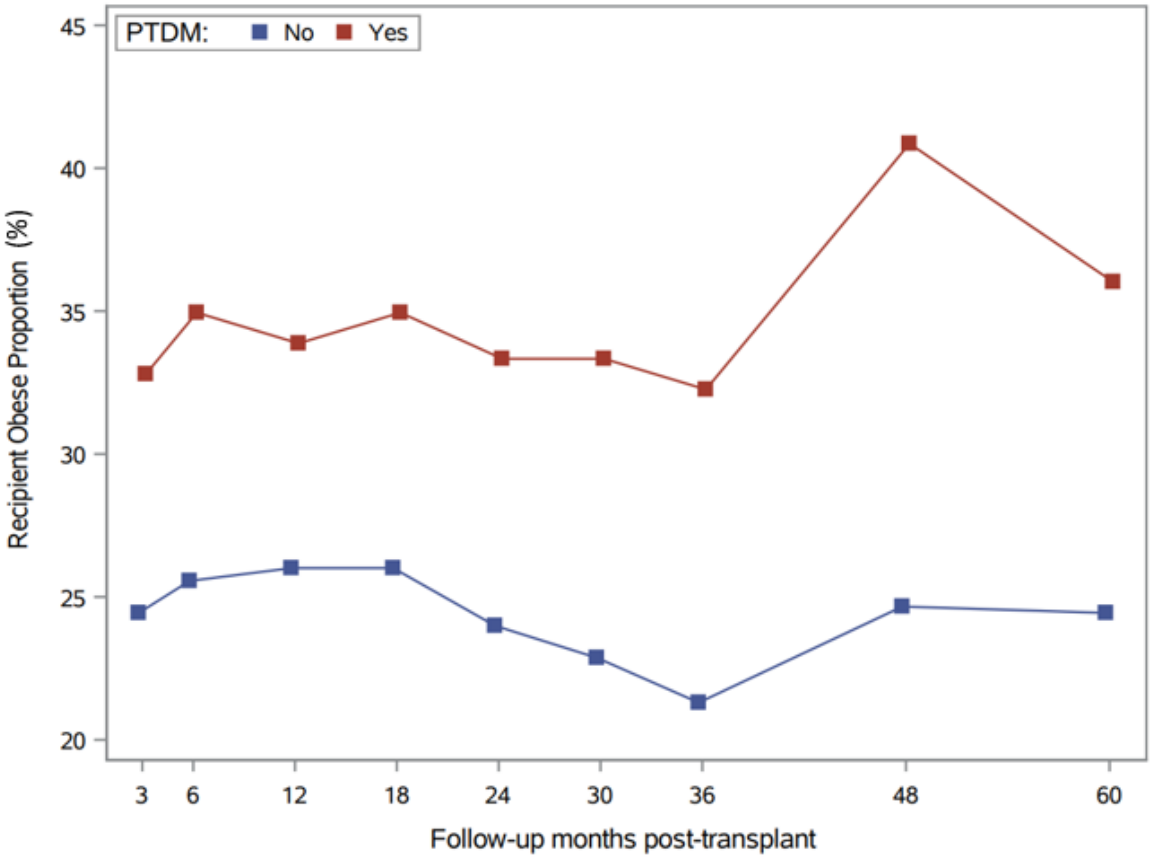
criteria were verified by each site PI. Monthly PI and coordinator calls were utilized to inform sites about timelines and any other updates that required their attention.

Supplementary Figure 1: Comparison of Post-KT Weight over Time between recipients who did and did not develop PTDM



Squares represent the average and whiskers represent the 95% confidence intervals

Supplementary Figure 2: Comparing Proportion of Obese (BMI >30 kg/m^2) Patients between recipients who did and did not develop PTDM



Supplementary Table 1: Summary of PTDM Definitions from Literature, 2009-2019

Title	First Author	Year of Publication	Single-center or Multi-center	PTDM definition
High Density Lipoprotein Cholesterol Efflux Predicts Incident New Onset Diabetes After Transplantation (NODAT) in Renal Transplant Recipients Independent of High Density Lipoprotein Cholesterol Levels[2]	Szili-Torok, T et al.	2019	single-center	2003 International Consensus Guidelines based on American Diabetes Association Criteria[A]
Plasma Malondialdehyde and Risk of New-Onset Diabetes after Transplantation in Renal Transplant Recipients: A Prospective Cohort Study[36]	Yepes-Calderón, M et al.	2019	single-center	2003 International Consensus Guidelines based on American Diabetes Association Criteria[A] and the HBa1c criterion added by the International Expert Panel in 2014
Fruit and Vegetable Intake and Risk of Posttransplantation Diabetes in Renal Transplant Recipients[37]	Gomes-Neto, A et al.	2019	single-center	2003 International Consensus Guidelines based on American Diabetes Association Criteria[A], the start of antidiabetes medication, *or* the HBa1c criterion added by the International Expert Panel in 2014
Serum magnesium, hepatocyte nuclear factor 1β genotype and post-transplant diabetes mellitus: a prospective study[3]	van der Burgh, A et al.	2019	single-center	Fasting blood glucose >7.0 mmol/L *or* Non-fasting blood glucose >11.1 mmol/L *or* Patients who were started on glucose-lowering drugs after KT
Validation of diagnostic utility of fasting plasma glucose and HbA1c in stable renal transplant recipients one year after transplantation[38]	Ussif, A et al.	2019	single-center	Fasting plasma glucose ≥7.0 mmol/L *or* 2-hr plasma glucose ≥11.1 mmol/L after an oral glucose tolerance test
Human Immunology Immune phenotype predicts new onset diabetes after kidney transplantation[47]	Ducloux, D et al.	2019	multi-center	2014 International Expert Panel from the international consensus meeting on PTDM[B]
Regulatory T Cells in the Context of New-Onset Diabetes After Renal Transplant: A Single-Center Experience[39]	Biró, B et al.	2019	single-center	2014 International Expert Panel from the international consensus meeting on PTDM[B]
Incidence and Risk Factors of Posttransplantation Diabetes Mellitus in Living Donor Kidney Transplantation: A Single-Center Retrospective Study in China[40]	Xu, J et al.	2018	single-center	2014 International Expert Panel from the international consensus meeting on PTDM[B]
New-onset diabetes after kidney transplantation: Incidence and associated factors[41]	Gomes, V et al.	2018	single-center	2003 International Consensus Guidelines based on American Diabetes Association Criteria[A]

Inflammatory and related biomarkers are associated with post-transplant diabetes mellitus in kidney recipients: a retrospective study[42]	Heldal, T et al.	2018	single-center	Modified ADA criteria (Fasting plasma glucose ≥7.0 mmol/L, and/or two-hour plasma glucose concentration ≥ 11.1 mmol/L)
High serum PCSK9 is associated with increased risk of new-onset diabetes after transplantation in renal transplant recipients[21]	Eisenga, M et al.	2017	single-center	2003 International Consensus Guidelines based on American Diabetes Association Criteria[A]
Post-transplant diabetes mellitus after kidney transplant in hispanics and caucasians treated with tacrolimus-based immunosuppression[43]	Baron, P et al.	2017	single-center	2003 International Consensus Guidelines based on American Diabetes Association Criteria[A]
Visceral fat is strongly associated with post-transplant diabetes mellitus and glucose metabolism 1 year after kidney transplantation[15]	von Düring, M et al.	2017	single-center	Modified ADA criteria (Fasting plasma glucose ≥7.0 mmol/L, and/or two-hour plasma glucose concentration ≥ 11.1 mmol/L)
Risk of post-transplantation diabetes mellitus is greater in South Asian versus Caucasian kidney allograft recipients[13]	Peracha, J et al.	2016	single-center	2014 International Expert Panel from the international consensus meeting on PTDM[B]
The role of TCF7L2 rs7903146 in diabetes after kidney transplant: Results from a single-center cohort and meta-analysis of the literature[11]	Quaglia, M et al.	2016	single-center	2013 American Diabetes Association criteria[C]
Long-term patient survival and kidney allograft survival in post-transplant diabetes mellitus: a single-center retrospective study[44]	Dienemann, T et al.	2016	single-center	2003 International Consensus Guidelines based on American Diabetes Association Criteria[A]
Mortality risk in post-transplantation diabetes mellitus based on glucose and HbA1c diagnostic criteria[45]	Eide, I et al.	2016	single-center	Chronic hyperglycemia (recurrent fasting plasma glucose ≥7.0 mmol that fails to normalize within 10 weeks after KT *or* Fasting plasma glucose ≥7.0 mmol and/or 2-hr plasma glucose ≥11.1 mmol during an oral glucose tolerance test at 1 weeks post-KT *or* HbA1c > 6.5%
Genetics of new-onset diabetes after transplantation[10]	McCaughan, J et al.	2014	single-center	New requirement for oral hypoglycemic agents or insulin for management of hyperglycemia after transplantation
Prediction at first year of incident new-onset diabetes after kidney transplantation by risk prediction models[46]	Rodrigo, E et al.	2012	single-center	2003 International Consensus Guidelines based on American Diabetes Association Criteria[A]
Pretransplant risk score for new-onset diabetes after kidney transplantation[20]	Chakkera, H et al	2011	single-center	HbA1c (HbA1c) > 6.5% *or* fasting plasma glucose ≥7.0 mmol *or* prescribed therapy for diabetes within 1 year post-KT

TCF7L2 polymorphism associates with new-onset diabetes after transplantation[9]	Ghisdal, L et al.	2009	multi-center	2003 International Consensus Guidelines based on American Diabetes Association Criteria[A]

[A] **2003 International Consensus Guidelines based on American Diabetes Association Criteria:** Symptoms of diabetes plus casual plasma glucose concentrations ≥200 mg/dL (11.1 mM) (casual is defined as any time of day without regard to time since last meal; the classic symptoms of diabetes include polyuria, polydypsia, and unexplained weight loss) *or* fasting plasma glucose ≥126 mg/dL (7.0 mM) (fasting is defined as no caloric intake for at least 8 hr) *or* 2-hr plasma glucose ≥200 mg/dL (11.1 mM) during an oral glucose tolerance test[50]

[B] **2014 International Expert Panel from the international consensus meeting on PTDM:** Symptoms of diabetes plus resting plasma glucose ≥200 mg/dL (11.1 mmol/L) OR fasting plasma glucose ≥126 mg/dL (7.0 mmol/L) OR 2-hr plasma glucose ≥200 mg/dL (11.1 mmol/L) during an OGTT OR HbA1c ≥6.5%[51]

[C] **2013 American Diabetes Association Criteria:** HbA1c > 6.5% or fasting plasma glucose ≥7.0 mmol/L or 2-hr plasma glucose ≥11.1 mmol/L during an oral glucose tolerance tests in two 30-day apart samples or fasting plasma glucose ≥11.1 mmol/L with symptoms of hyperglycemia or use of hypoglycemic agent for at least 30 days[52]

Supplementary Table 2. Association of BMI/Weight Trajectory and PTDM

	PTDM		
	No (n=446)	Yes (n=186)	P-value
	Median (IQR)	Median (IQR)	
Mean increase from 3mo post-KT to 1 yr post-KT			
Weight (kg)	3.7 (0, 7.4)	3.2 (0, 7)	0.79
BMI (kg/m^2)	1.3 (0, 2.5)	1.1 (0, 2.6)	0.84
Mean increase after 1 year (from 12 months)			
Weight (kg)	1.7 (-1.3, 4.8)	0.9 (-2.1, 4.6)	0.20
BMI (kg/m^2)	0.5 (-0.5, 1.8)	0.3 (-0.7, 1.7)	0.19

Values presented are median (IQR)

Supplementary Table 3: Association of Biopsy-Proven Acute Rejection (time to first biopsy proven rejection) and PTDM

Exposure		Biopsy proven acute rejection			
		n (%)	Event rate per 1000py	Unadjusted HR (95%)	Adjusted* HR (95%)
A)	No PTDM (n=446)	65 (15%)	29 (23, 37)	1 (ref)	1 (ref)
	PTDM (n=186)	32 (17%)	48 (34, 68)	3.65 (2.27, 5.87)	4.38 (2.67, 7.18)

*Adjusted models include donor KDPI, cold ischemia time and the following recipient variables: age (years), black race, sex, previous kidney transplant, number of human leukocyte antigen mismatches, panel reactive antibody (%), body mass index (kg/m2), preemptive transplant and transplant center.

Supplementary Table 4: Methylprednisolone Administration and PTDM Development among Patients with Biopsy-Proven Acute Rejection

	Developed PTDM		P-value
	No (n=65)	**Yes(n=32)**	
Received methylprednisolone (n=63)	42 (67%)	21 (33%)	0.92
Did not receive methylprednisolone (n=34)	23 (68%)	11 (32%)	