Supplemental Materials

Androgens and Development of Post-Transplantation Diabetes Mellitus in Male Kidney Transplant Recipients: A post-hoc analysis of a prospective study

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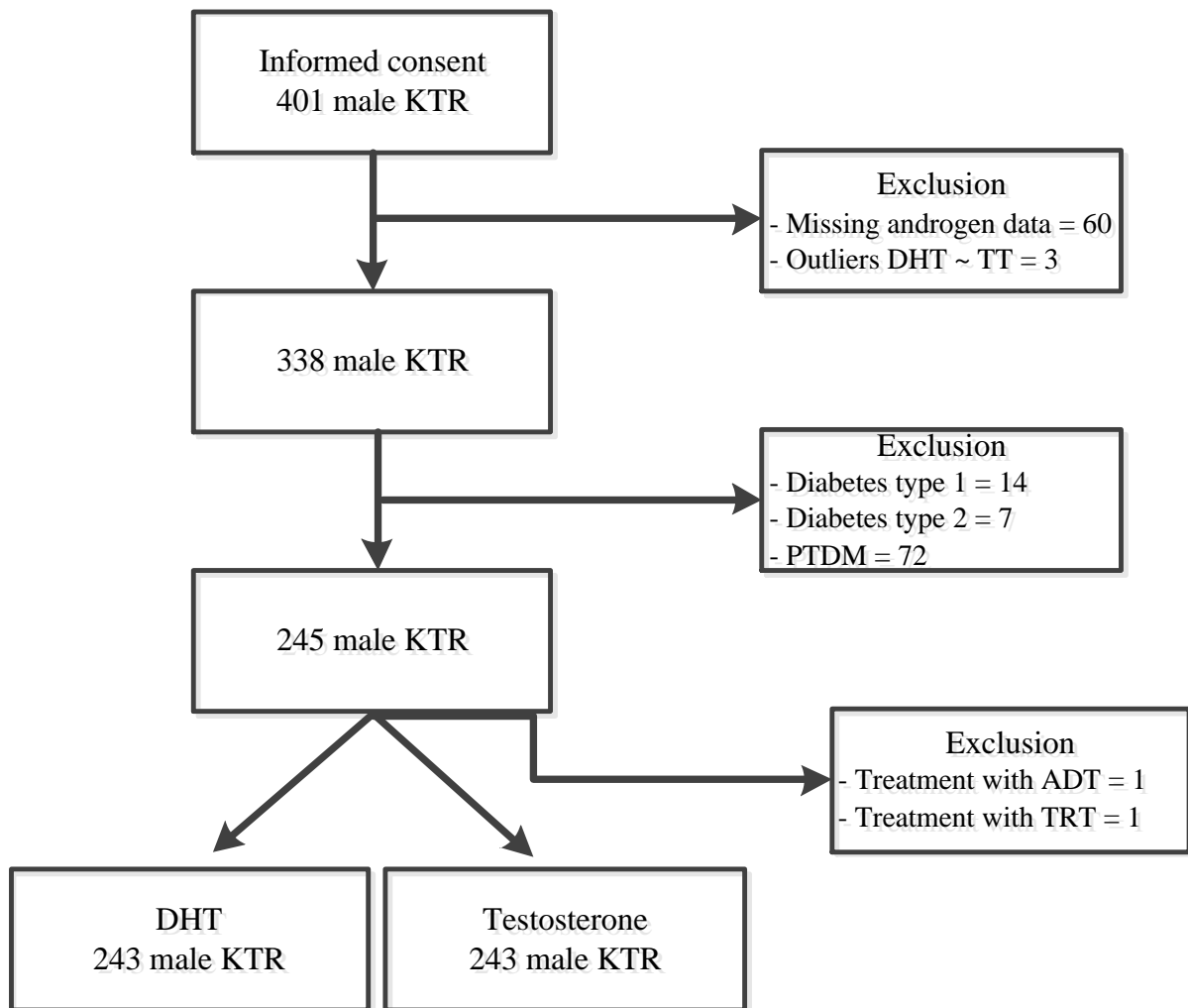
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Informed consent
401 male KTR

Exclusion
- Missing androgen data = 60
- Outliers DHT ~ TT = 3

338 male KTR

Exclusion
- Diabetes type 1 = 14
- Diabetes type 2 = 7
- PTDM = 72

245 male KTR

Exclusion
- Treatment with ADT = 1
- Treatment with TRT = 1

DHT
243 male KTR

Testosterone
243 male KTR

Supplemental figure S1. STROBE flow diagram. ADT, androgen deprivation therapy; DHT, dihydrotestosterone; KTR, kidney transplant recipients; PTDM, post-transplantation diabetes mellitus; TT, total testosterone; TRT, testosterone replacement therapy.

Supplemental figure S2.

A

PTDM; unadjusted models

B

PTDM; adjusted models
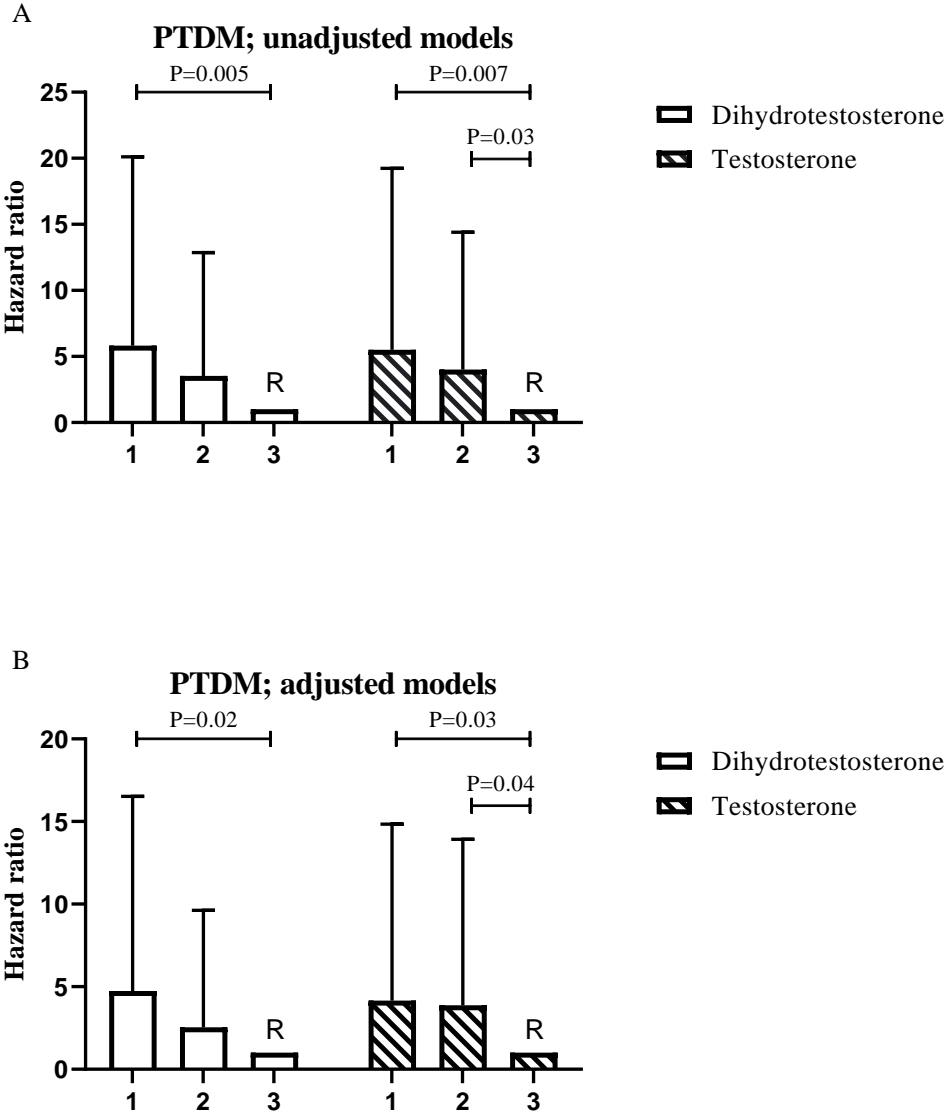
Supplemental Figure S2. Bars represent hazard ratio with 95%CI. (A) Crude analysis. (B) Model 6, adjustment for baseline fasting plasma glucose levels and HbA$_{1c}$ levels. The 3rd tertile served as a reference point. PTDM, post-transplantation diabetes mellitus

Supplemental Figure S3.

STROBE Statement

	Item	Recommendation	Reported on manuscript page
Title and abstract			
	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1(a) p. 1,4
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	1(b) p. 4
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	2 p. 5
Objectives	3	State specific objectives, including any prespecified hypotheses	3 p. 5,6
Methods			
Study design	4	Present key elements of study design early in the paper	4 p. 7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5 p. 7(FU p.9)
Participants	6	(a) Cohort study—give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up. Case-control study—give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls. Cross-sectional study—give the eligibility criteria, and the sources and methods of selection of participants	6(a) p. 7 6(b) N.A.
		(b) Cohort study—for matched studies, give matching criteria and number of exposed and unexposed. Case-control study—for matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7 p. 9-10
Data sources/ measurement	8*	For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8 p. 7-9 9 p. 10 10 p.7, supplemental material
Bias	9	Describe any efforts to address potential sources of bias	
Study size	10	Explain how the study size was arrived at	11 p. 9,10
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	12(a) p. 9,10
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	
		(b) Describe any methods used to examine subgroups and interactions	12(b) p. 10,14 12(c) p. 7
		(c) Explain how missing data were addressed	
		(d) Cohort study—if applicable, explain how loss to follow-up was addressed Case-control study—if applicable, explain how matching of cases and controls was addressed Cross-sectional study—if applicable, describe analytical methods taking account of sampling strategy	12(d) p. N.A. 12(e) p. 10,14
		(e) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report the numbers of individuals at each stage of the study—eg, numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	13(a) p. 7 supplemental material
		(b) Give reasons for non-participation at each stage	13(b) p. 7
		(c) Consider use of a flow diagram	13(c) supplemental material
Descriptive data	14*	(a) Give characteristics of study participants (eg, demographic, clinical, social) and information on exposures and potential confounders	14(a) p.11,23
		(b) Indicate the number of participants with missing data for each variable of interest	14(b) p. 7
		(c) Cohort study—summarise follow-up time (eg, average and total amount)	14(c) p. 11
Outcome data	15*	Cohort study—report numbers of outcome events or summary measures over time Case-control study—report numbers in each exposure category, or summary measures of exposure Cross-sectional study—report numbers of outcome events or summary measures	15 p. 11
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	16(a) p.11-13 + p. 24,25
		(b) Report category boundaries when continuous variables were categorised	16(c) N.A.
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg, analyses of subgroups and interactions, and sensitivity analyses	17 p.13
Discussion			
Key results	18	Summarise key results with reference to study objectives	18 p. 14,17
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	19 p. 17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	20 p. 14-17
Generalisability	21	Discuss the generalisability (external validity) of the study results	21 p. 17
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	22 p. 18

*Give such information separately for cases and controls in case-control studies, and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies. An explanation and elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the websites of PLoS Medicine, Annals of Internal Medicine, and Epidemiology). Separate versions of the checklist for cohort, case-control, and cross-sectional studies are available on the STROBE website.

Table: The STROBE statement—checklist of items that should be addressed in reports of observational studies

Supplemental table S4. Characteristics of kidney transplant recipients who develop post-transplantation diabetes mellitus and non-developers

	PTDM	No PTDM	*P*-value
Men, (n)	28	215	
Dihydrotestosterone, nmol/L	0.8 (0.5 – 0.9)	1.0 (0.74 – 1.3)	<0.001
Testosterone, nmol/L	10.2 (8.6 – 12.7)	12.4 (9.6 – 16.0)	0.002
Age, years	52.0 ± 11.8	50.6 ± 13.8	0.60
Weight, kg	87.8 ± 10.7	82.5 ± 14.4	0.06
BMI, kg/m^2	26.8 ± 2.5	25.6 ± 3.8	0.03
Cardiovascular history, n (%)	4 (14.3)	18 (8.4)	0.30
SBP, mmHg	139.4 ± 14.3	135.8 ± 15.9	0.25
eGFR, ml/min per 1.73 m^2	49.2 ± 16.8	53.2 ± 20.0	0.32
Glucose, mmol/L	5.5 ± 0.7	5.2 ± 0.6	0.05
HbA$_{1C}$, %	6.0 ± 0.3	5.6 ± 0.3	<0.001
HbA$_{1C}$, mmol/mol	42.5 ± 3.2	38.2 ± 3.7	<0.001
hsCRP, mg/L	1.6 (1.0 – 3.2)	1.1 (0.5 – 3.3)	0.19
Transplantation vintage, years	3.7 (1.3 – 13.8)	5.1 (2.0 – 12.1)	0.40
Steroid treated acute rejection, n (%)	7 (25.0)	50 (23.3)	0.82
Calcineurin inhibitor, n (%)	22 (78.6)	121 (56.3)	0.03
Tacrolimus	7 (25.0)	39 (18.1)	0.44
Proliferation inhibitor, n (%)	20 (71.4)	180 (83.7)	0.12
Cumulative prednisolone dose, g	15.5 (4.7 – 43.0)	18.5 (7.5 – 40.1)	0.41

Data are represented as mean ± SD, median (interquartile range) or n (%). Differences between kidney transplant recipients who developed post-transplantation diabetes mellitus and those who did not were tested with independent sample t-test when variables were normally distributed, Mann-Whitney U test for skewed variables, and with Fishers exact test for categorical variables. SBP, systolic blood pressure; eGFR, estimated glomerular filtration rate; hsCRP, high-sensitivity C-reactive Protein; PTDM, post-transplantation diabetes mellitus; Cardiovascular history was defined as a history of cerebrovascular accident, myocardial infarction, and/or peripheral arterial disease; Transplantation vintage was defined as the time between transplantation and baseline

Supplemental table S5. Association of log2 dihydrotestosterone with post-transplantation diabetes mellitus

	Dihydrotestosterone – no prediabetes		Dihydrotestosterone - prediabetes	
	HR (95% CI)	P-value	HR (95% CI)	P-value
Events, no.	5		23	
Model 1	0.03 (0.003 – 0.34)	0.005	0.43 (0.22 – 0.83)	0.01

Model 1: crude analysis

Supplemental table S6. Association of log2 total testosterone with post-transplantation diabetes mellitus

	Dihydrotestosterone – no prediabetes		Dihydrotestosterone - prediabetes	
	HR (95% CI)	P-value	HR (95% CI)	P-value
Events, no.	5		23	
Model 1	0.02 (0.002 – 0.19)	0.001	0.56 (0.24 – 1.29)	0.17

Model 1: crude analysis