Supplementary Information

Table S1. Univariable and multivariable associations of serum T_{50} with clinical parameters in stable renal transplant recipients (RTR).

	T_{50}			
	Univariable		**Multivariable**	
	St. Beta	**P-value**	**St. Beta**	**P-value**
Demographics				
Age, years	-0.05	0.21		
Male gender	0.02	0.56		
Current smoker	-0.03	0.43		
Current diabetes	-0.08	**0.04**		
BMI, kg/m^2	-0.03	0.41		
Systolic blood pressure, mmHg	-0.05	0.17		
Diastolic blood pressure, mmHg	-0.05	0.22		
Heart rate, bpm	-0.07	0.06		
Renal transplantation				
Ln transplant vintage, years	-0.02	0.52		
Living donor	0.16	**<0.001**		
Pre-emptive KTx	0.07	0.07		
Ln dialysis vintage, months	-0.08	**0.05**		
HLA mismatches, number	-0.03	0.47		
Age donor, years	0.04	0.35		
Acute rejection	-0.10	**0.01**		
Laboratory measurements				
Hemoglobin, mmol/L	0.21	**<0.001**	-0.07	**0.04**
HbA1C, %	-0.06	0.15		
eGFR, CKD-EPI ($mL/min/1.73m^2$)	0.27	**<0.001**		
Corrected calcium mmol/L	0.20	**<0.001**		
Phosphate, mmol/L	-0.48	**<0.001**	-0.42	**<0.001**
Magnesium, mmol/L	0.19	**<0.001**	0.22	**<0.001**
Ln PTH, pmol/L	0.09	**0.02**	0.07	**0.03**
Venous pH	0.14	**<0.001**		
Venous HCO_3^-, mmol/L	0.36	**<0.001**	0.30	**<0.001**
Ln hsCRP, mg/L	-0.17	**<0.001**		

Albumin, g/L	0.26	**<0.001**	0.17	**<0.001**
Ln alkaline phosphatase, U/L	0.00	0.93		
Total cholesterol, mmol/L	0.07	0.08		
HDL cholesterol, mmol/L	0.07	0.06		
LDL cholesterol mmol/L	0.07	0.06		
Ln triglycerides, mmol/L	-0.08	**0.03**		
Ln albuminuria, mg/24h	-0.17	**<0.001**		
Medication				
Anti-hypertensives	-0.05	0.22		
Statins	-0.11	**0.005**		
Calcium supplements	-0.18	**<0.001**		
Vitamin D supplements	-0.11	**0.005**		
Vitamin K antagonists	-0.10	**0.01**	-0.12	**<0.001**
Prednisone, mg/d	-0.07	0.06		
Calcineurin inhibitors	-0.19	**<0.001**	-0.07	**0.03**
Proliferation inhibitors	0.09	**0.02**		
Sirolimus	0.06	0.15		

Data are presented as standardized beta coefficient (β) with corresponding P-value. Bold letters indicate a *P*-value < 0.05.

Abbreviations: BMI, body mass index; eGFR, estimated glomerular filtration rate; HbA1c, glycated hemoglobin; HCO3-, bicarbonate; HDL, high-density lipoprotein; HLA, human leukocyte antigen; hsCRP, high-sensitivity C-reactive protein; KTx, kidney transplantation; LDL, low-density lipoprotein; PTH, parathyroid hormone.

Table S2. Additive value of serum T_{50} for the prediction risk of all-cause mortality.

Model	**C-statistic (95% CI)**	**Change (95% CI)***	**IDI (%), P-values**
Age, gender, eGFR	0.72 (0.66 - 0.78)	NA	NA
Age, gender, eGFR plus *Framingham risk factors*	0.73 (0.67 - 0.79)	0.011 (-0.014 - 0.036)	0.8, 0.28
Age, gender, eGFR plus *Ca x Pi product*	0.72 (0.66 - 0.78)	0.003 (-0.006 - 0.012)	0.2, 0.42
Age, gender, eGFR plus *serum T_{50}*	0.75 (0.70 - 0.80)	0.030 (0.004 - 0.056)	1.6, 0.03

Data are presented as Harrell's concordance statistic (C-statistic) with 95% confidence interval (CI) and integrated discrimination improvement (IDI) with P-value. NA, not applicable. * Change in C-statistics compared to model of age, gender and eGFR.

Framingham risk factors included current smoking status, diabetes mellitus, body mass index, systolic blood pressure, and plasma LDL cholesterol. For the calcium-phosphate (Ca x Pi) product, calcium was corrected for hypoalbuminemia (<40 g/L).

Table S3. Associations of calcification propensity, serum T_{50}, with death-censored graft failure in stable renal transplant recipients (n_{events}/n_{total} = 45/699). Data are presented as hazard ratio (HR) plus 95% confidence interval (CI) according to tertiles of serum T_{50} and per standard deviation (SD) serum T_{50} decrease.

	High	**Intermediate**	**Low**		**Serum T_{50} continuous**	
		HR (95% CI)	**HR (95% CI)**	**P (trend)**	**HR (95% CI) per SD**	**P**
Model 1	1.0 (Ref)	2.05 (0.76 - 5.54)	6.38 (2.63 - 15.48)	<0.001	2.61 (1.94 – 3.50)	<0.001
Model 2	1.0 (Ref)	2.11 (0.78 - 5.70)	6.67 (2.75 - 16.22)	<0.001	2.62 (1.96 – 3.51)	<0.001
Model 3	1.0 (Ref)	1.71 (0.63 - 4.63)	2.46 (0.99 - 6.06)	0.04	1.64 (1.19 – 2.27)	0.003
Model 4	1.0 (Ref)	1.97 (0.72 - 5.35)	5.44 (2.21 - 13.44)	<0.001	2.48 (1.82 – 3.37)	<0.001

Model 1: crude.

Model 2: adjusted for age and gender.

Model 3: adjusted for model 2 plus eGFR (CKD-EPI) and albuminuria.

Model 4: adjusted for model 2 plus CNI use, dialysis vintage and type of KTx (living vs. deceased).

Abbreviations: CI, confidence interval; eGFR, estimated glomerular filtration rate; HR, hazard ratio; KTx, kidney transplantation; Ref, referent; SD, standard deviation.

Mean ± SD T_{50}: 286 ± 62 minutes.

Supplementary figure legends

Supplementary Figure S1. Histogram of serum T_{50} showing a normal distribution in renal transplant recipients.

Supplementary Figure S2. Possible mediation by FGF23 or NT-proBNP on the association between T_{50} and all-cause mortality. a, b and c are the standardized regression coefficients between variables. The indirect effect (through FGF23 or NT-proBNP) is calculated as a*b. The total effect is a*b + c.

Supplementary Figure S3. Comparative analysis of serum T_{50} with serum-corrected calcium (Ca), phosphate (Pi), magnesium (Mg), parathyroid hormone (PTH), and calcium-phosphate (Ca x Pi) product, displayed per tertile, as independent risk factors for death-censored graft failure. Bars represent hazard ratio with 95% CI. A) Crude analyses. B) Adjusted for age, gender, eGFR, albuminuria, and type of kidney transplantation (KTx, living vs. deceased). Tertile with the lowest risk on graft failure served as reference group (R).

Figure S1

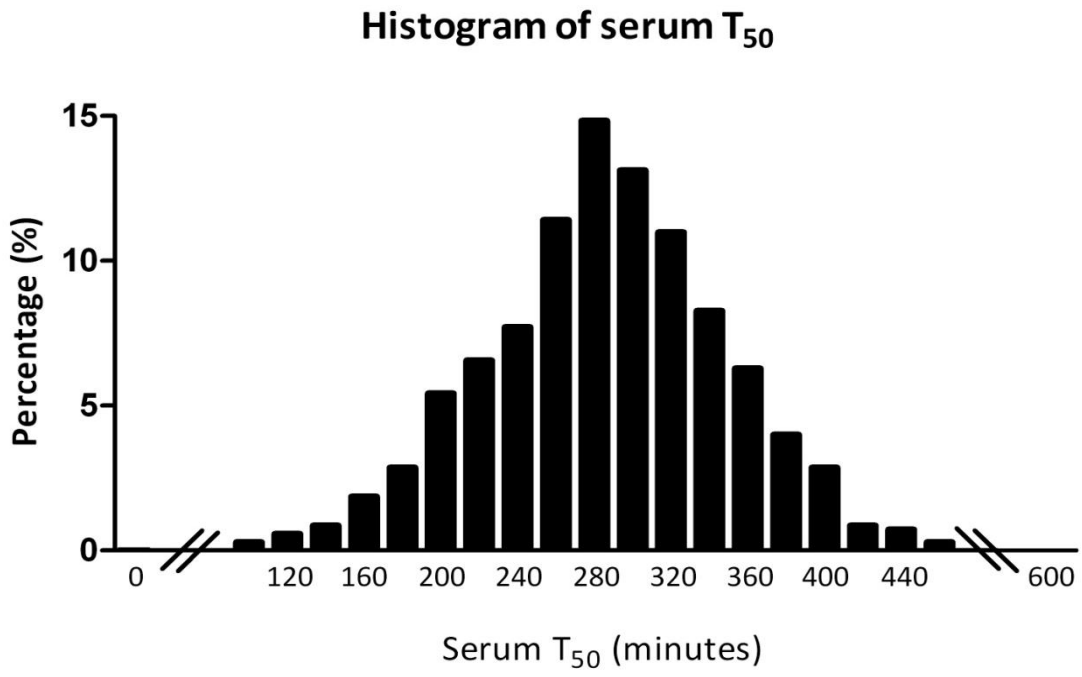

Histogram of serum T_{50}
Percentage (%)
15
10
5
0
0
120
160
200
240
280
320
360
400
440
600
Serum T_{50} (minutes)

Figure S2

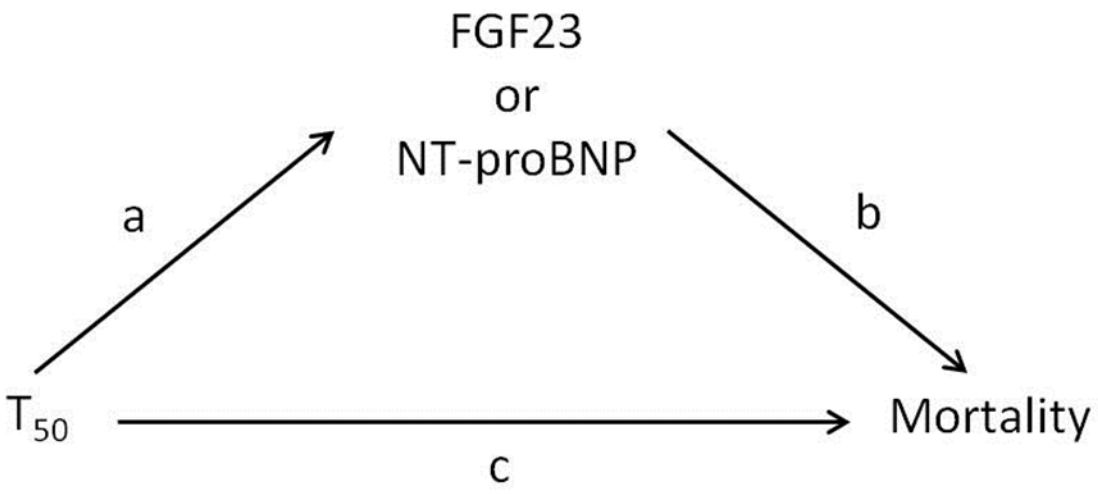
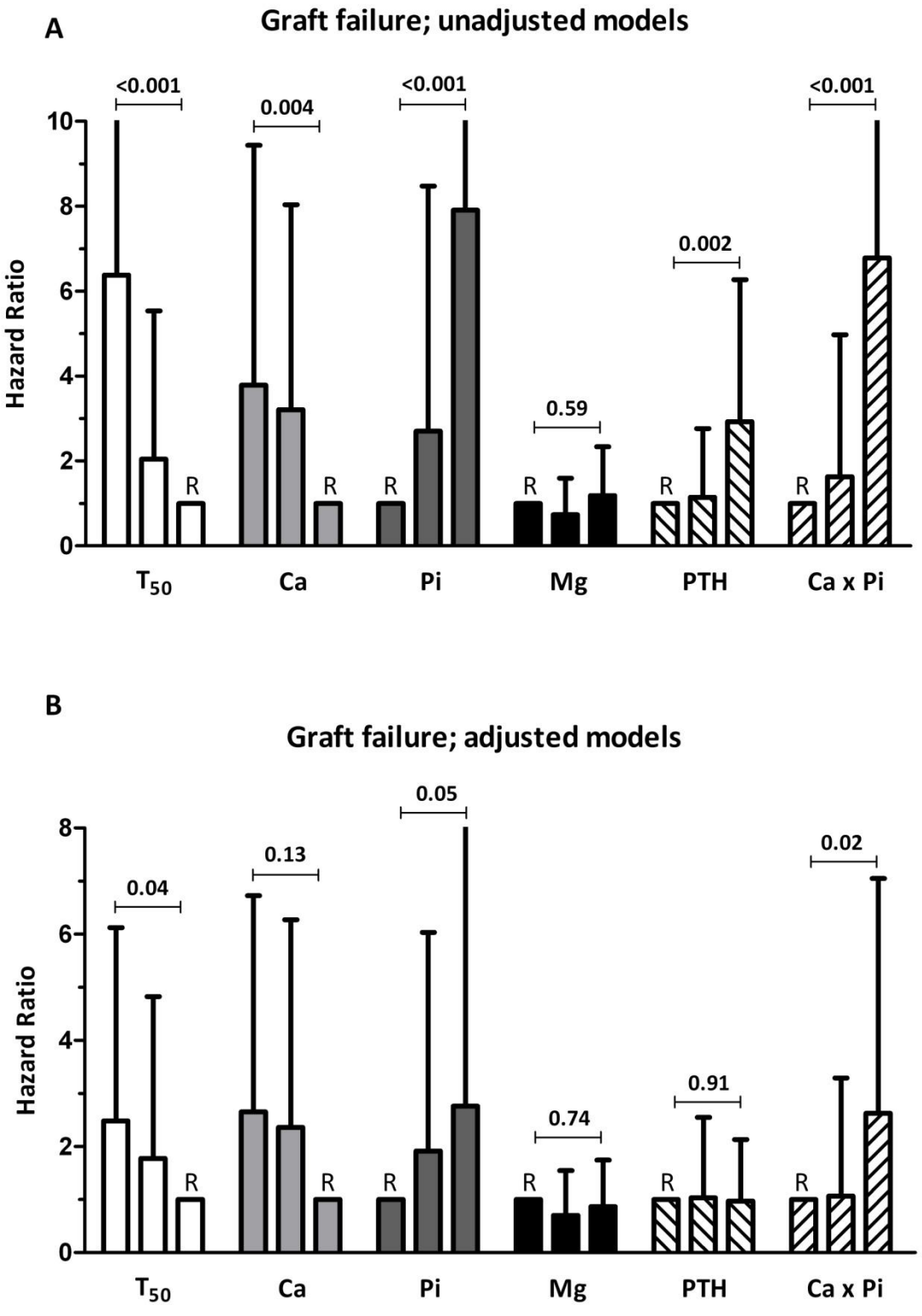


Figure S3



Adjustment for age, gender, eGFR, albuminuria, and type of NKx (living vs. deceased).