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There are no conflicts of interest. #MedTwitter #nephtwitter @ISNkidneycare

https://www.kireports.org/article/S2468-0249(25)00103-2/pdf

KI REPORTS
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CLINICAL RESEARCH

Early Determination of Tacrolimus Concentration–Dose Ratio Identifies Risk of Allograft Loss in Kidney Transplantation

Christophe Masset[1,2], Marine Lorent[1], Clarisse Kerleau[1], Claire Garandeau[1], Aurélie Houzet[1], Simon Ville[1,2], Diego Cantarovich[1], Gilles Blancho[1,2], Magali Giral[1,2] and Jacques Dantal[1,2], on behalf of the Nantes DIVAT Consortium[3]

[1]Service de Néphrologie et Immunologie Clinique, Institut de Transplantation Urologie Néphrologie (ITUN), CHU Nantes, Nantes, France; and [2]Center for Research in Transplantation and Translational Immunology, UMR 1064, Nantes Université, INSERM, Institute of Transplantation Urology and Nephrology, CHU Nantes, Nantes, France

3/ 🔆Calcineurin inhibitors (CNIs) are currently the cornerstone of maintenance therapy in kidney transplant recipients (KTR)
📌Tacrolimus(Tac)-metabolized mainly via cytochrome CYP3A5
📌It has narrow therapeutic index-needs strict therapeutic monitoring

https://pubmed.ncbi.nlm.nih.gov/26950724/

4a/⁉️How to assess tacrolimus metabolism?

▶️The ratio between the tac trough level, C0 (in ng/ml) on tacrolimus total daily dose, D (in mg), defined as C0/D, has been described as an efficient and simple tool to assess tacrolimus metabolism

👀https://pubmed.ncbi.nlm.nih.gov/25340655/

5/ ⁉️How does tacrolimus metabolism affect KTR outcomes?
✌️Fast metabolizers-
📌 Associated with ⏬kidney function after KT
🚨They showed ⬇️eGFR at all time points
🔬 More frequent first acute rejection (p = 0.008)

https://www.nature.com/articles/s41598-021-95201-5

6/ 📍Aims of this study
✅Determine the reproducibility of the C0/D ratio after kidney transplantation
✅To define the optimal and earliest time to consider patients as high metabolizers

7/ 📍Study population
🇫🇷France
👨Adult patients who underwent KT between January 1, 2000, and December 31, 2019
💊Functional allograft at 1 month after KT receiving either immediate-release or

extended-release tacrolimus

8a/
🔗C0/D - defined as ratio of blood tac trough level (ng/ml) to the daily total tacrolimus dose (mg)
💊C0 was measured 12 hours (immediate release Tac) or 24 hours (extended release Tac) after drug intake

8b/ 📍Based on C0/D ratio on more than 75% of previous dosages at a defined timepoints, KTRs classified as
✅High tacrolimus metabolizers- High(C0/D ≤ 1.05)
✅low metabolizers- Low(C0/D ≥ 1.05)
✅Variable- patients not corresponding to either high or low

9/📍 Study outcomes
🥇To determine earliest accurate time for the categorization of High patients in first 6 months post KT
🔆Other - patient and allograft survival, occurrence of a first rejection episode, infectious complications and allograft function

10/📍Study population
🌟n=1979 KTRs who were alive with a functional allograft 1 month after KT
🌟During follow-up, 171 return-to-dialysis and 179 deaths were noted

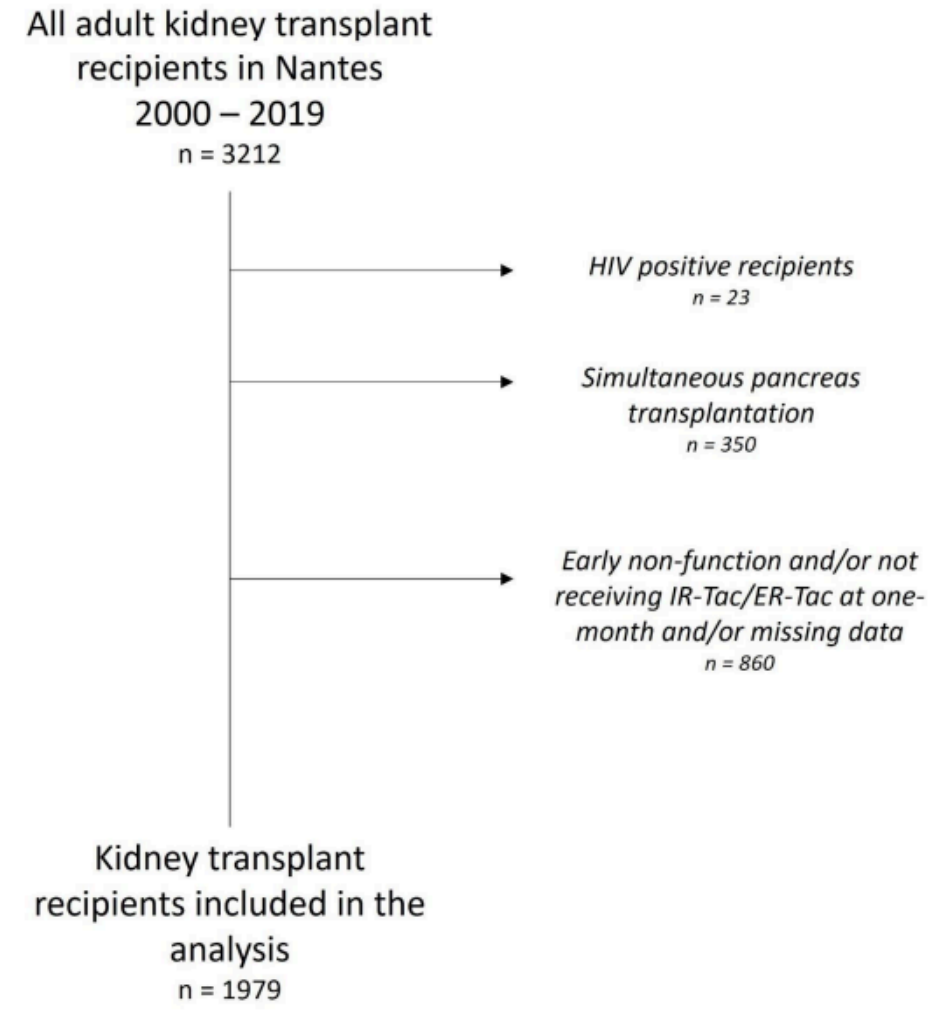

Figure S1. *Flow chart of the study*

11/ 📌At T=1 month post KT, 752 KTRs (38%) were High of which 61% were still considered High at T=6 months

📌At T=2 months, 499 KTRs (25%) were High, 84% were considered High at T=6 months

Table 1. Representation of the number of patients that changed group between M* and M6 when defined at 1–3 months posttransplantation

Time of assessment	Categorization at M* posttransplantation	Average number of C0/D used	Categorization at M6 posttransplantation, *n* (%)		
			High	Variable	Low
M1 posttransplantation	High	1.87	458 (60.9%)	281 (37.4%)	13 (1.7%)
	Variable	2.00	31 (8.1%)	180 (47.0%)	172 (44.9%)
	Low	1.86	2 (0.002%)	87 (10.5%)	755 (89.5%)
M2 posttransplantation	High	3.69	420 (84.2%)	79 (15.8%)	0 (0%)
	Variable	3.80	71 (9.8%)	440 (60.5%)	216 (29.7%)
	Low	3.66	0 (0%)	29 (3.8%)	724 (96.2%)
M3 posttransplantation	High	4.62	475 (84.5%)	87 (15.4%)	0 (0%)
	Variable	4.44	16 (3.4%)	407 (87.2%)	44 (9.4%)
	Low	4.61	0 (0%)	54 (5.7%)	896 (94.3%)

C0/D, tacrolimus trough level/dose; M, month.
Among the patients defined as "High" at 2 months posttransplantation, 420 (84.2%) of them remained "High" at 6 months, 79 (15.8%) were defined as "Variable" at 6 months post-transplantation, and 0 (0%) were "Low" at 6 months.

12/ 💥The tacrolimus coefficient variability calculated during the first year postKT was lower in High patients than in Low and Variable patients (27.1 vs. 30.8 vs 32.3, respectively)
👉The complete characteristics of the patients at T= 2 months are described below

Table 2. Description of the 1979 patients with a functioning graft at 2 months posttransplantation according to their fast-metabolizer status

	Whole sample (*N* = 1979)			High patients (*n* = 499)			Variable patients (*n* = 727)			Low patients (*n* = 753)			
	NA	*n*	%	NA	*n*	%	NA	*n*	%	NA	*n*	%	*P*-value
Male recipient	0	1241	62.7	0	300	60.1	0	457	62.7	0	484	64.3	0.3282
Retransplantation	0	509	25.7	0	121	24.2	0	189	26.0	0	199	26.4	0.6729
Preemptive	0	379	19.1	0	97	19.4	0	143	19.7	0	139	18.5	0.8246
History of diabetes	0	342	17.3	0	80	16.0	0	118	16.2	0	144	19.1	0.2354
History of dyslipidemia	0	917	46.3	0	203	40.7	0	338	46.5	0	376	49.9	0.0057
History of hypertension	0	1796	90.7	0	443	88.8	0	663	91.2	0	690	91.6	0.2033
History of cardiac disease	0	611	30.9	0	133	26.6	0	216	29.7	0	262	34.8	0.0066
Male donor		1153	58.3		298	59.7		430	59.1		425	56.4	0.4280
Donor type	0			0			0			0			
Living		328	16.6		90	18.0		124	17.1		114	15.1	0.3652
SCD		904	45.7		263	52.7		328	45.1		313	41.6	0.0005
ECD		747	37.7		146	29.2		275	37.8		326	43.3	<0.0001
HLA-A-B-DR incompatibilities > 4	0	374	18.9	0	108	21.6	0	129	17.7	0	137	18.2	0.1893
Depleting induction	0	999	50.5	0	299	59.9	0	366	50.3	0	334	44.4	<0.0001
Machine perfusion	185	479	26.7	31	143	30.5	53	177	26.3	101	159	24.4	0.0671
Delayed graft function	24	624	31.9	8	175	35.6	10	216	30.1	6	233	31.2	0.1122
BPAR in the first 2 mos	0	84	4.2	0	30	6.0	0	31	4.3	0	23	3.0	0.0396
Tacrolimus at 2 mos	1			1			0			0			
Extended release		736	37.2		260	52.2		284	39.0		192	25.5	<0.0001
Immediate release		1242	62.7		238	47.8		443	61.0		561	75.5	< 0.0001

	NA	m	SD	NA	m	SD	NA	m	SD	NA	m	SD	*P*-value
Recipient age (yrs)	0	52.0	14.5	0	48	14.3	0	51.8	14.7	0	54.9	13.8	< 0.0001
Recipient BMI (kg/m^2)	0	24.5	4.4	0	24.2	4.5	0	24.4	4.2	0	24.8	4.4	0.0414
Donor age (yrs)	1	53.3	15.9	0	50.4	15.6	1	53.3	16.1	0	55.2	15.7	< 0.0001
Donor creatinine (ml/min/m^2)	4	86.8	49.2	2	89.9	54.8	0	86.5	48.0	2	85.0	46.2	0.2235
Cold ischemia time (h)	0	15.8	9.9	0	13.9	8.8	0	15.5	9.9	0	17.3	10.4	< 0.0001
eGFR at 2 mo (ml/min/m^2)	162	48.4	19.4	49	46.1	18.9	41	48.5	19.9	72	50.0	18.9	0.0014
Tac dose (2 mos, mg/d)	0	8.1	4.9	0	14.3	4.9	0	7.6	2.4	0	4.6	1.7	< 0.0001
Tac trough level (2 mos, ng/ml)	0	9.6	3.3	0	8.8	2.3	0	9.8	3.7	0	9.8	3.4	< 0.0001
C0/D ratio at 2 mos	0	1.65	1.41	0	0.66	0.20	0	1.39	0.70	0	2.55	1.79	< 0.0001
Tacrolimus CV during first yr (%)	0	30.4	16.8	0	27.1	14.9	0	32.3	15.6	0	30.8	18.8	< 0.0001

BMI, body mass index; BPAR, biopsy-proven acute rejection; C0/D, tacrolimus trough level/dose; ECD, expanded criteria donor; eGFR, estimated glomerular filtration rate; HLA, human leukocyte antigen; NA, not available (missing); SCD, standard criteria donor; Tac, tacrolimus.
P-values are obtained using Chi-square test for categorical variables and ANOVA for continuous variables.

13/ 📊Despite similar trough levels between groups over time, the mean C0/D remained <1.05 in High patients, during complete follow up
📌The density plot of all C0/D values among groups, defined at the second month post KT, confirmed good reproducibility over time from this time point

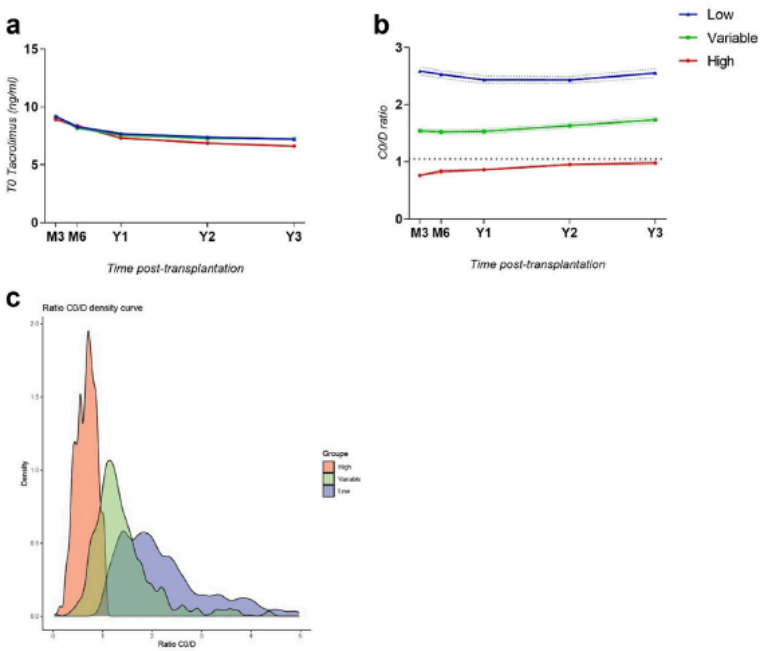

Figure 1. (a) Evaluation of tacrolimus trough level among groups defined from T = 2-months during the first 3 years posttransplantation. (b) Evaluation of C0/D ratio among groups defined from T = 2 months during the first 3 years posttransplantation. (c) Density plot of all measured C0/D values among groups defined from the second month posttransplantation. C0/D, tacrolimus trough-level / total daily dose.

14/
📌High patients had a significantly ↩️eGFR at 2 months than Variable and Low patients (46.1 ml/min vs. 48.5 and 50.0 ml/min)
⏩Higher rejection episodes during the first 2 months (6% vs. 4.3 and 3%) and
⏩Higher CNI total dose (14.3 mg/d vs. 7.6 and 4.6 mg/day)

15/ 👀Let's look at the graft survival
📍 The confounder-adjusted death-censored graft survival rates at 5 and 10 years postKT were 💊83% and 70% for High patients, 89% and 73% for Variable patients, and 93% and 81% for Low patients, respectively(P <0.0001)

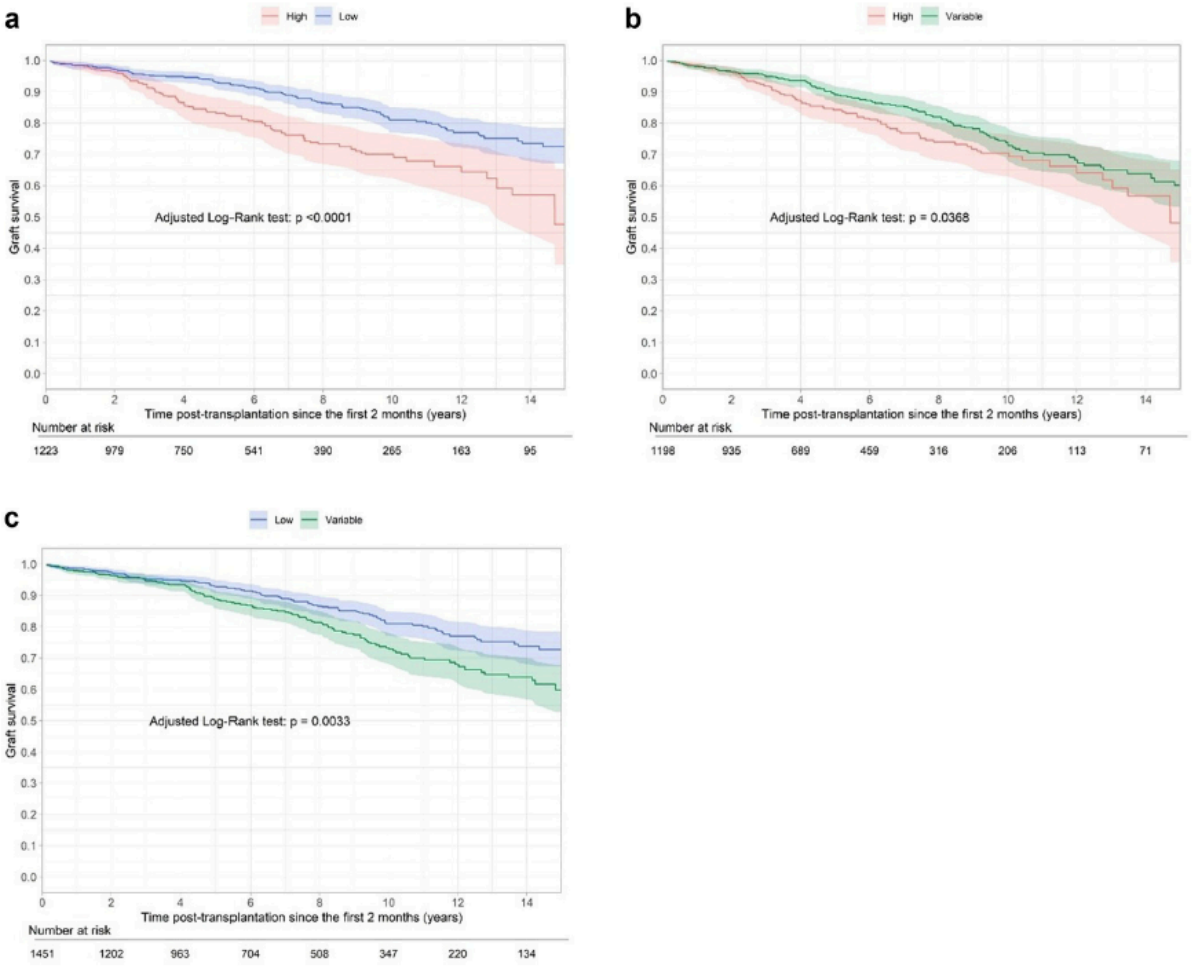

Figure 2. (a) Long-term confounder-adjusted graft survival from T = 2 months posttransplantation according to the patient's status (High vs. Low) estimated from the weighted Kaplan-Meier estimator. (b) Long-term confounder-adjusted graft survival from T = 2 months post-transplantation according to the patient's status (High vs. Variable) estimated from the weighted Kaplan-Meier estimator. (c) Long-term confounder-adjusted graft survival from T = 2 months posttransplantation according to the patient's status (Variable vs. Low) estimated from the weighted Kaplan-Meier estimator.

Table 2. Description of the 1979 patients with a functioning graft at 2 months posttransplantation according to their fast-metabolizer status

	Whole sample (N = 1979)			High patients (n = 499)			Variable patients (n = 727)			Low patients (n = 753)			
	NA	n	%	NA	n	%	NA	n	%	NA	n	%	P-value
Male recipient	0	1241	62.7	0	300	60.1	0	457	62.7	0	484	64.3	0.3282
Retransplantation	0	509	25.7	0	121	24.2	0	189	26.0	0	199	26.4	0.6729
Preemptive	0	379	19.1	0	97	19.4	0	143	19.7	0	139	18.5	0.8246
History of diabetes	0	342	17.3	0	80	16.0	0	118	16.2	0	144	19.1	0.2354
History of dyslipidemia	0	917	46.3	0	203	40.7	0	338	46.5	0	376	49.9	0.0057
History of hypertension	0	1796	90.7	0	443	88.8	0	663	91.2	0	690	91.6	0.2033
History of cardiac disease	0	611	30.9	0	133	26.6	0	216	29.7	0	262	34.8	0.0066
Male donor		1153	58.3		298	59.7		430	59.1		425	56.4	0.4280
Donor type	0			0			0			0			
Living		328	16.6		90	18.0		124	17.1		114	15.1	0.3652
SCD		904	45.7		263	52.7		328	45.1		313	41.6	0.0005
ECD		747	37.7		146	29.2		275	37.8		326	43.3	<0.0001
HLA-A-B-DR incompatibilities > 4	0	374	18.9	0	108	21.6	0	129	17.7	0	137	18.2	0.1893
Depleting induction	0	999	50.5	0	299	59.9	0	366	50.3	0	334	44.4	<0.0001
Machine perfusion	185	479	26.7	31	143	30.5	53	177	26.3	101	159	24.4	0.0671
Delayed graft function	24	624	31.9	8	175	35.6	10	216	30.1	6	233	31.2	0.1122
BPAR in the first 2 mos	0	84	4.2	0	30	6.0	0	31	4.3	0	23	3.0	0.0396
Tacrolimus at 2 mos	1			1			0			0			
Extended release		736	37.2		260	52.2		284	39.0		192	25.5	<0.0001
Immediate release		1242	62.7		238	47.8		443	61.0		561	75.5	< 0.0001
	NA	m	SD	NA	m	SD	NA	m	SD	NA	m	SD	P-value
Recipient age (yrs)	0	52.0	14.5	0	48	14.3	0	51.8	14.7	0	54.9	13.8	< 0.0001
Recipient BMI (kg/m^2)	0	24.5	4.4	0	24.2	4.5	0	24.4	4.2	0	24.8	4.4	0.0414
Donor age (yrs)	1	53.3	15.9	0	50.4	15.6	1	53.3	16.1	0	55.2	15.7	< 0.0001
Donor creatinine (ml/min/m^2)	4	86.8	49.2	2	89.9	54.8	0	86.5	48.0	2	85.0	46.2	0.2235
Cold ischemia time (h)	0	15.8	9.9	0	13.9	8.8	0	15.5	9.9	0	17.3	10.4	< 0.0001
eGFR at 2 mo (ml/min/m^2)	162	48.4	19.4	49	46.1	18.9	41	48.5	19.9	72	50.0	18.9	0.0014
Tac dose (2 mos, mg/d)	0	8.1	4.9	0	14.3	4.9	0	7.6	2.4	0	4.6	1.7	< 0.0001
Tac trough level (2 mos, ng/ml)	0	9.6	3.3	0	8.8	2.3	0	9.8	3.7	0	9.8	3.4	< 0.0001
C0/D ratio at 2 mos	0	1.65	1.41	0	0.66	0.20	0	1.39	0.70	0	2.55	1.79	< 0.0001
Tacrolimus CV during first yr (%)	0	30.4	16.8	0	27.1	14.9	0	32.3	15.6	0	30.8	18.8	< 0.0001

BMI, body mass index; BPAR, biopsy-proven acute rejection; C0/D, tacrolimus trough level/dose; ECD, expanded criteria donor; eGFR, estimated glomerular filtration rate; HLA, human leukocyte antigen; NA, not available (missing); SCD, standard criteria donor; Tac, tacrolimus.
P-values are obtained using Chi-square test for categorical variables and ANOVA for continuous variables.

16/👀What about graft loss?

🚨The adjusted risk of death-censored graft loss was significantly higher in High patients (CS-HR 2.00, 95% CI=1.48–2.69) and Variable patients (CS-HR 1.51, 95% CI=1.17–1.97, P < 0.0001) than in Low patients

Table 3. Results of the univariate and multivariate cox model ($n = 1936$) studying the risk of graft failure from the second month posttransplantation

	Univariate Analysis			Multivariate analysis			
	CS-HR	95% CI	*P*-value	CS-HR	95% CI	*P*-value	Adjusted *P*-value
Metabolizer status (ref: low)			0.0119			< 0.0001	< 0.0001
High	1.87	[1.41–2.47]		2.00	[1.48–2.69]		
Variable	1.39	[1.08–1.79]		1.51	[1.17–1.97]		
Retransplantation	1.57	[1.25–1.96]	<0.0001	1.54	[1.21–1.97]	0.0005	0.0016
Delayed graft function	1.85	[1.48–2.30]	< 0.0001	1.22	[0.96–1.56]	0.1029	0.1132
History of diabetes	1.48	[1.11–1.99]	0.0087	1.35	[0.99–1.84]	0.0593	0.0725
History of cardiac disease	1.59	[1.27–1.99]	< 0.0001	1.28	[1.01–1.64]	0.0428	0.0673
Donor type (ref: Living)			< 0.0001			< 0.0001	< 0.0001
SCD	1.83	[1.23–2.72]		1.16	[0.76–1.76]		
ECD	2.57	[1.71–3.84]		1.55	[1.00–2.41]		
Rejection episode in the first 2 mos posttransplantation	2.07	[1.40–3.07]	0.0003	1.99	[1.33–2.98]	0.0007	0.0016
Immediate release Tacrolimus	1.41	[1.05–1.90]	0.0223	1.71	[1.25–2.33]	0.0007	0.0016
MDRD	0.97	[0.97–0.98]	< 0.0001	0.98	[0.97–0.99]	< 0.0001	< 0.0001
Recipient age (yrs)	1.00	[0.99–1.01]	0.8103				
Male recipient	0.86	[0.69–1.07]	0.1715				
Recipient BMI (kg/m^2)	0.99	[0.97–1.02]	0.4861				
Preemptive transplantation	0.67	[0.48–0.93]	0.0173				
Hypothermic machine perfusion	1.39	[0.98–1.97]	0.0625				
Cold ischemia time (h)	1.02	[1.01–1.03]	0.0017				
History of dyslipidemia	1.09	[0.87–1.36]	0.4456				
History of hypertension	0.91	[0.63–1.31]	0.6014				
Donor age (yrs)	1.01	[1.01–1.02]	0.0006				
Male donor	0.93	[0.75–1.16]	0.5178				
HLA-A-B-DR incompatibilities >4	1.16	[0.93–1.44]	0.1922				
Depleting induction	1.46	[1.17–1.81]	0.0007				

BMI, body mass index; CI, confidence interval; CS-HR, cause-specific hazard ratio; ECD, expanded criteria donor; HLA, human leukocyte antigen; MDRD, Modification of Diet in Renal Disease; SCD, standard criteria donor.
318 events observed during the follow-up; 43 patients were excluded because of missing data.

17/ ⚡What is significant at T=2 months?
👉From T=2 months, the occurrence of allograft rejection was significantly higher in High patients (CS-HR 1.71, 95% CI=1.15–2.54) and Variable patients (CS-HR 1.55, 95% CI 1.07–2.54], P=0.0151) than in Low patients

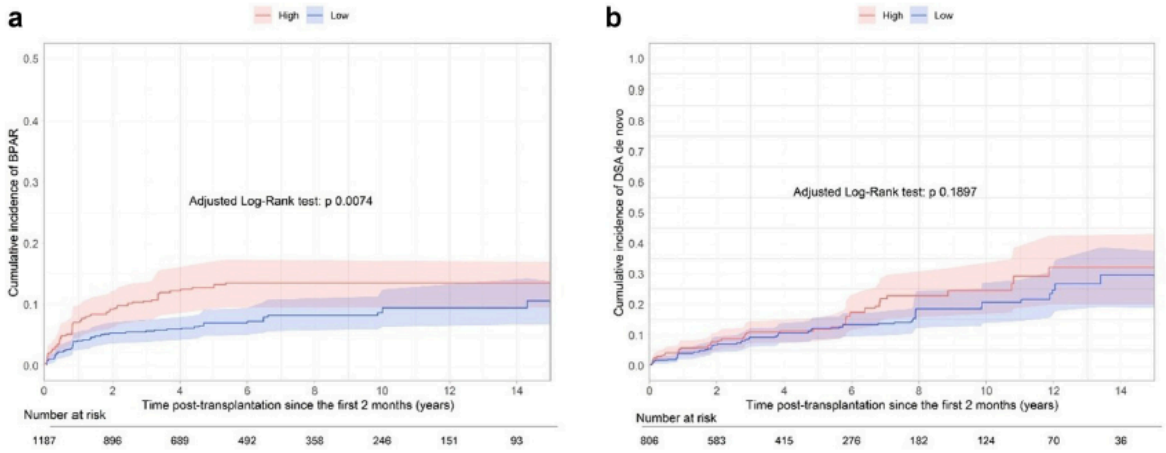

Figure 3. (a) Long-term confounder-adjusted death-censored occurrence of rejection from T = 2 months posttransplantation according to the patient's status (High vs. Low) estimated from the weighted Kaplan-Meier estimator. (b) Long-term confounder-adjusted occurrence of de novo DSA from T = 2 months posttransplantation according to the patient's status (High vs. Low) estimated from the weighted Kaplan-Meier estimator. DSA, donor-specific antibody.

18/ 🔬What are the histopathologic findings?

🚩High patients presented with a significantly higher occurrence of T-cell–mediated rejection and borderline lesions

🚩The occurrence of antibody-mediated rejection did not differ between the groups

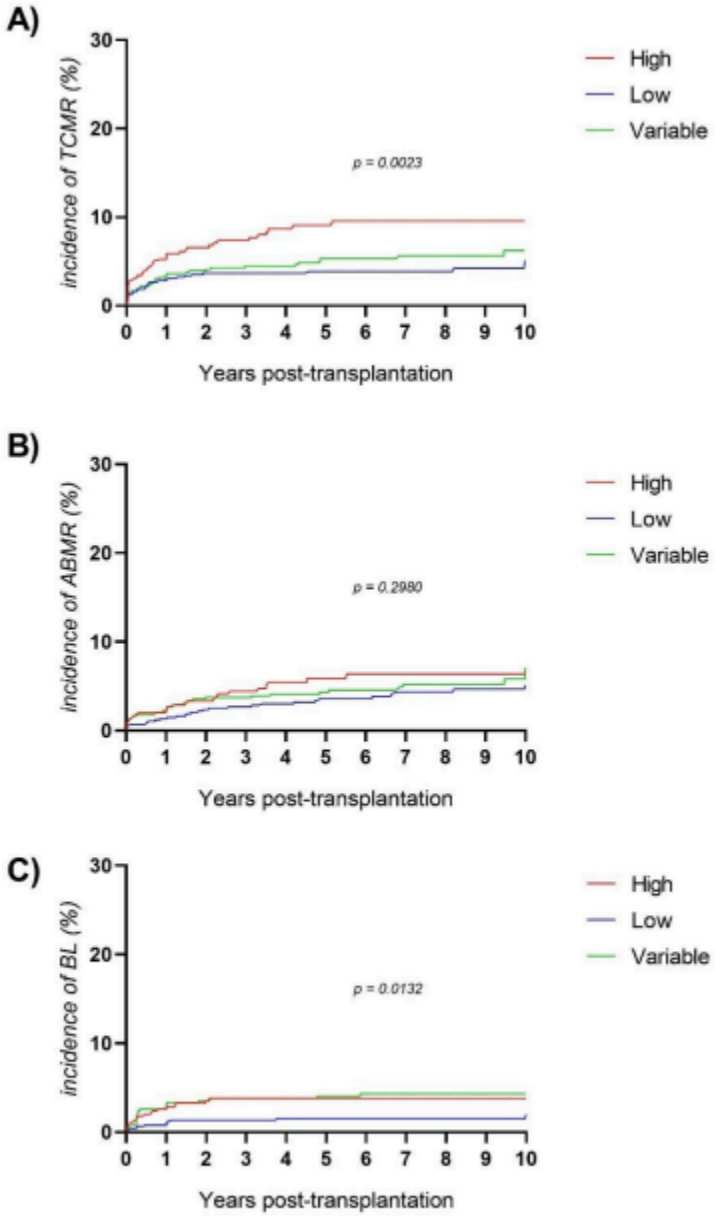

***Figure S2**. Panel A. Incidence of TCMR among groups (censored at 10 years post-transplantation). Panel B. Incidence of ABMR among groups (censored at 10 years post-transplantation). Panel C. Incidence of Borderline Lesions among groups (censored at 10 years post-transplantation).*

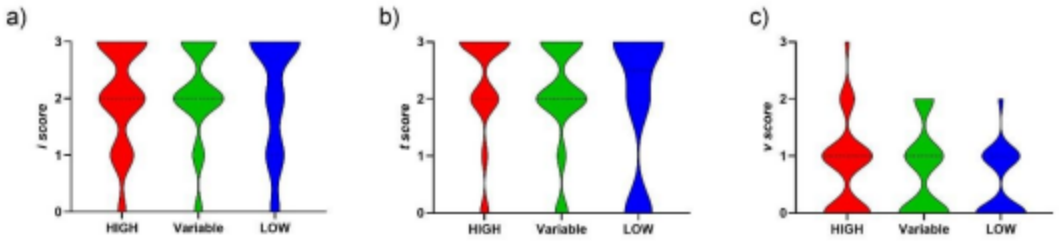

Figure S3. Histological severity of TCMR episodes represented by i (Panel A), t (Panel B) and v (Panel C) scores from the Banff Classification among HIGH, Variable and LOW patients.

19/ 🦠Infectious complications, anyone?

🚩Severe infectious complications were more frequent in High patients than in Low patients (CS-HR=1.27, 95% CI=1.06–1.52, P=0.0274)

🦠Though, the risk of CMV or BKV viremia was not significantly increased in high patients

Table S3. Results of the multivariate cox model (n = 1,725) studying the risk of severe infection (857 events observed during the follow-up, 254 patients were excluded due to missing data)

	Univariate Analysis			Multivariate analysis			
	CS-HR	95% CI	p-value	CS-HR	95% CI	p-value	Adjusted p-value
Metabolizer status (ref: Low)			0.2083			0.0274	0.0382
High	1.18	[0.99 ; 1.40]		1.27	[1.06 ; 1.52]		
Variable	1.10	[0.94 ; 1.29]		1.14	[0.97 ; 1.33]		
Recipient age (years)	1.02	[1.01 ; 1.02]	<0.0001	1.01	[1.00 ; 1.02]	0.0265	0.0376
Male recipient	0.75	[0.66 ; 0.86]	<0.0001	0.76	[0.66 ; 0.88]	0.0001	0.0007
Male donor	0.85	[0.74 ; 0.97]	0.0186	0.86	[0.75 ; 0.99]	0.0301	0.0398
Donor type (ref: Living)			<0.0001			0.0004	0.0012
SCD	1.36	[1.10 ; 1.69]		1.31	[1.05 ; 1.64]		
ECD	2.21	[1.78 ; 2.74]		1.84	[1.44 ; 2.35]		
History of diabetes	1.47	[1.24 ; 1.74]	<0.0001	1.30	[1.09 ; 1.55]	0.0038	0.0125
History of cardiac disease	1.23	[1.07 ; 1.42]	0.0047	1.12	[0.96 ; 1.30]	0.1397	0.1436
Depleting induction	1.28	[1.12 ; 1.47]	0.0003	1.22	[1.06 ; 1.40]	0.0057	0.0142
Re-transplantation	1.13	[0.97 ; 1.32]	0.1065				
Recipient BMI (kg/m²)	1.01	[0.99 ; 1.02]	0.2942				
Pre-emptive transplantation	0.80	[0.67 ; 0.96]	0.0178				
Hypothermic machine perfusion	1.52	[1.29 ; 1.78]	<0.0001				
Delayed graft function	1.18	[1.03 ; 1.37]	0.0193				
Cold ischemia time (hours)	1.01	[1.00 ; 1.02]	0.0707				
History of dyslipidemia	1.24	[1.09 ; 1.42]	0.0016				
History of hypertension	1.04	[0.82 ; 1.31]	0.7570				
Donor age (years)	1.02	[1.01 ; 1.02]	<0.0001				
HLA-A-B-DR incompatibilities > 4	1.10	[0.96 ; 1.26]	0.1887				
Rejection episode in the first 2 months post-transplantation	1.16	[0.83 ; 1.61]	0.3890				
Immediate release Tacrolimus	0.82	[0.71 ; 0.95]	0.0074				
MDRD	0.99	[0.98 ; 1.00]	<0.0001				

CI, confidence interval; DGF, Delayed Graft Function CS-HR : Cause specific hazard ratio; MDRD, Modification of Diet in Renal Disease.

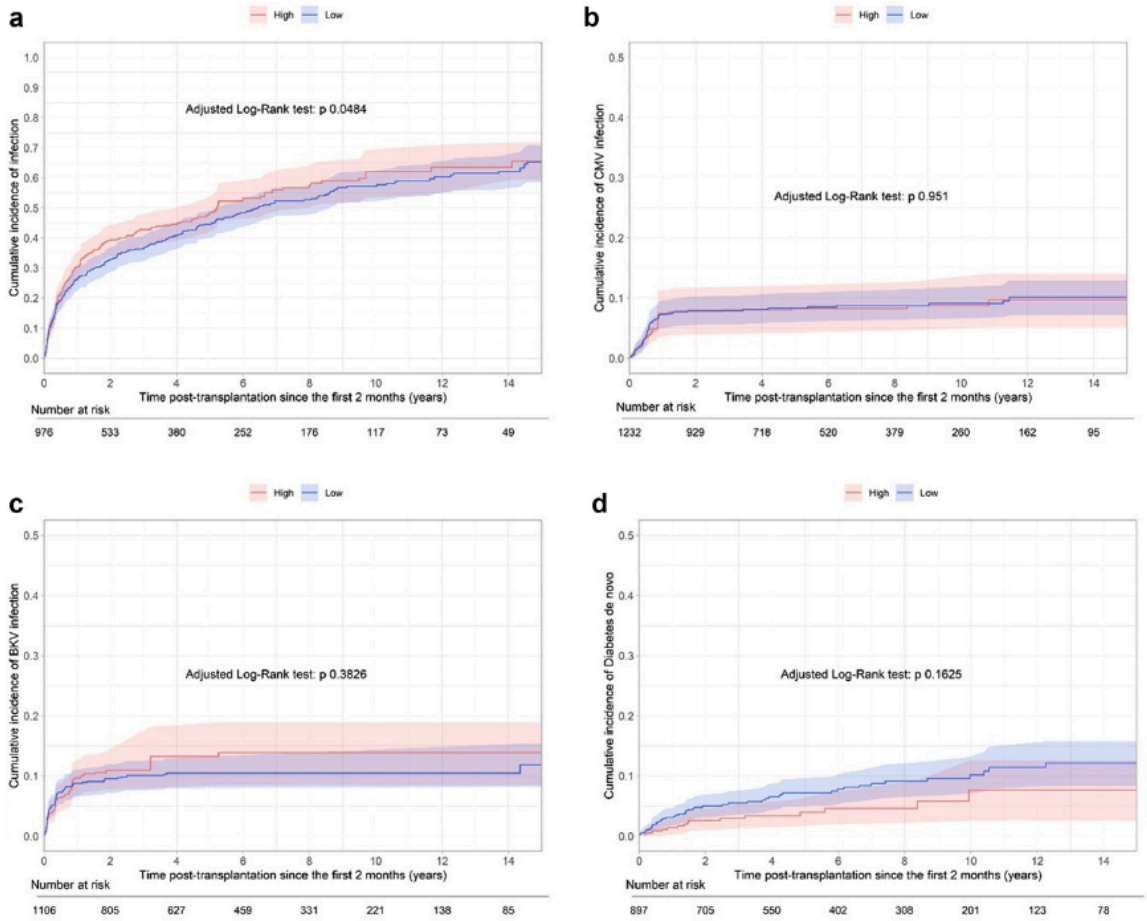

Figure 4. (a) Long-term confounder-adjusted occurrence of severe infectious complications from T = 2 months posttransplantation according to the patient's status (High vs. Low) estimated from the weighted Kaplan-Meier estimator. (b) Long-term confounder-adjusted occurrence of CMV viremia from T = 2 months posttransplantation according to the patient's status (High vs. Low) estimated from the weighted Kaplan-Meier estimator. (c) Long-term confounder-adjusted occurrence of BKV infection from T = 2 months posttransplantation according to the patient's status (High vs. Low) estimated from the weighted Kaplan-Meier estimator. (d) Long-term confounder-adjusted occurrence of posttransplant diabetes mellitus from T = 2 months posttransplantation according to the patient's status (High vs. Low) estimated from the weighted Kaplan-Meier estimator. BKV, BK polyomavirus; CMV, cytomegalovirus.

20/
📅On follow up, authors observed that the eGFR at 3 years was significantly lower in High patients than in Variable/Low patients (46.7 ml/min vs. 49.7 and 52.9 ml/min, respectively; P<0.0001)
🔬Similarly arteriolar hyalinosis (ah>2) @1 year was significantly higher in High patients

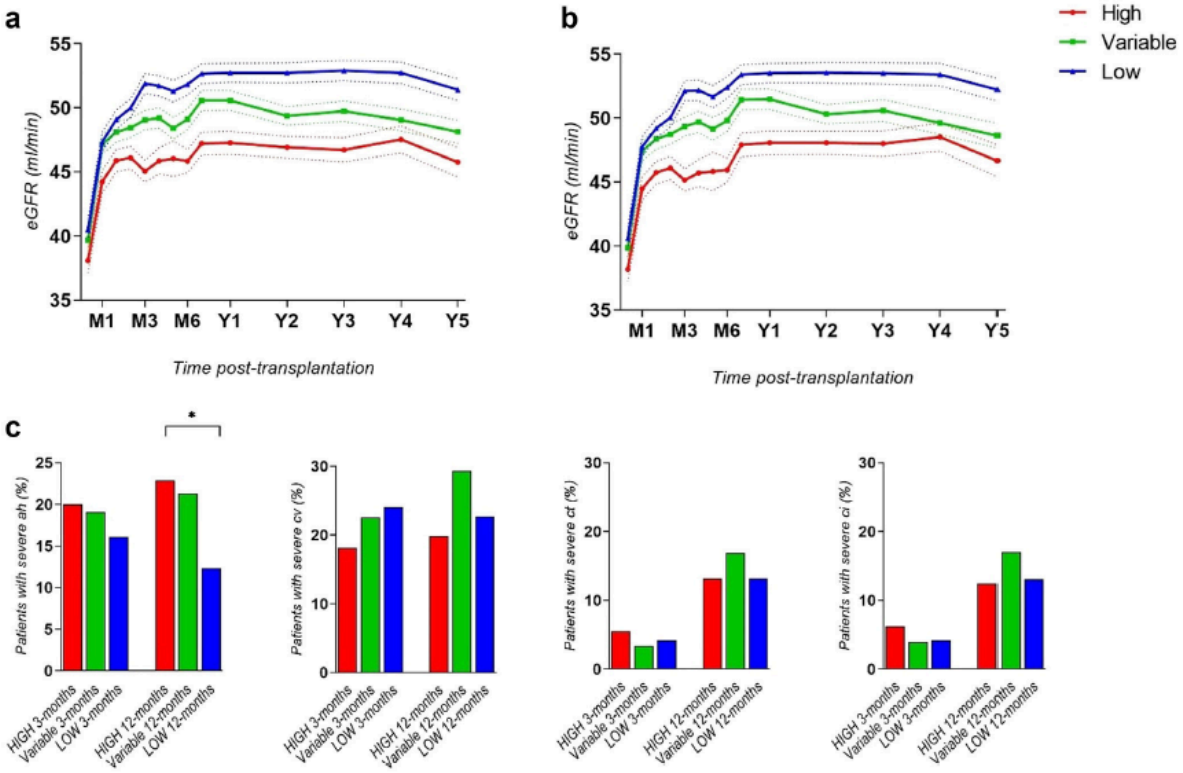

Figure 5. (a) Evaluation of allograft function estimated by eGFR (MDRD) among groups during the first years censored by allograft failure. *(b)* Evaluation of allograft function estimated by eGFR (MDRD) among groups during the first years censored by allograft failure and occurrence of a rejection episode. *(c)* Occurrence of severe chronic injuries in patients from High, Variable, and Low groups defined from the second month posttransplantation, in for cause and protocolar biopsies at 3 and 12 months posttransplantation. eGFR, estimated glomerular filtration rate; MDRD, modification of diet in renal disease.

21/
🌟To conclude, this study showed that patients with C0/D<1.05 for at least 75% of the time can be accurately categorized as high metabolizers (from 2nd month postKT)
📌C0/D ratio is a simple tool, can be used in routine practice to identify patients at risk of allograft failure and rejection

22/ 💣High patients defined as soon as the 2nd month carried significant worse outcomes than others
⏫ Risk of allograft rejection (mainly TCMR)
🚨Significant worse allograft survival and function
⏫Burden of chronic vascular injuries
⏫Greater nephrotoxicity

23/ 📌High patients had greater nephrotoxicity with consequent impact on allograft survival

🚩Most of them needed ⏫ CNI doses to reach the target trough levels, leading to ⏫tacrolimus peak levels- important initiators of nephrotoxicity
https://pubmed.ncbi.nlm.nih.gov/29162334/

24/ 📌Limitations:
📍Observational study- possible unobserved confounders cannot be excluded
✂The lack of measures of tacrolimus AUC prevents definitive conclusion regarding the real exposure to CNI among High patients

25/ 🏆Thank you! Please share this #skeetorial with your followers and friends

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the opportunity and @mchanmd.bsky.social @brianrifkin.bsky.social for feedback!