

Agnès DELAY<sup>1</sup>, Olivier MORANNE<sup>2</sup>, Nicolas MAILLARD<sup>1</sup>, Eric ALAMARTINE<sup>1</sup> and Christophe MARIAT<sup>1</sup>

1. Service de Néphrologie, Dialyse et Transplantation Rénale, CHU de Saint-Etienne
2. Service de Néphrologie, CHU de Nîmes

## INTRODUCTION:

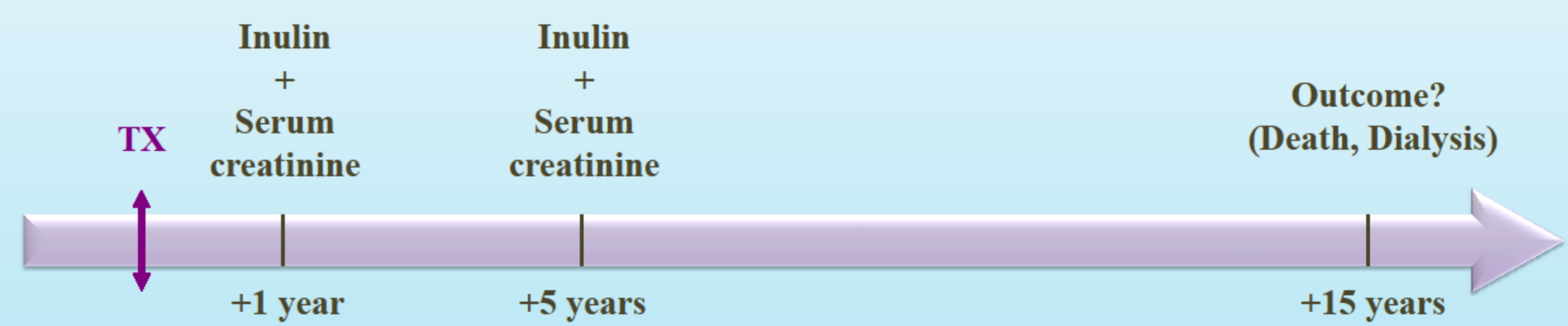
In renal transplantation, GFR decline is strongly associated to graft failure and patient death and thus could be an interesting proxy for clinical research. GFR estimating equations are known to underestimate GFR decline. Consequently, the threshold usually retained for the GFR decline is very high, around 50% (corresponding to a doubling in serum creatinine). Such a decline is a rare and delayed event limiting its relevance as a criterion of judgment. A decline of 30% has recently been proposed as an acceptable alternative in CKD patients with native kidneys.

## OBJECTIVES:

- Evaluate the validity of the 30% threshold in renal transplantation to detect an association between GFR decline and long term outcome
- Evaluate the ability of the CKD-EPI equation to detect this threshold, compared to inulin clearance as a gold standard

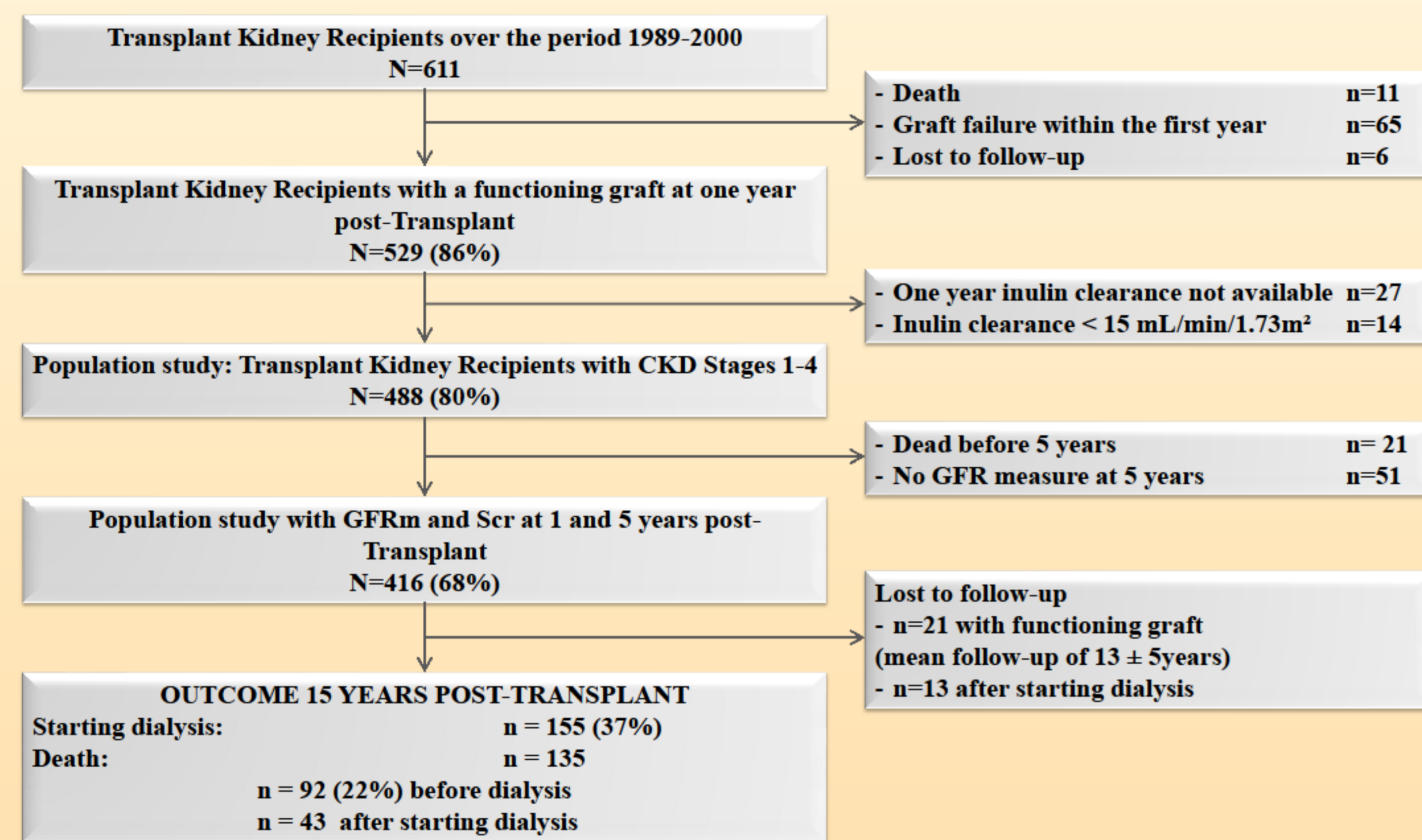
## METHODS:

- Monocentric analysis of patients transplanted from 1989 to 2000 at the CHU of Saint-Etienne (France) with a functioning graft 5 years post-transplantation and an evaluation of GFR with inulin and CKD-EPI equation available at 1 and 5 years post-transplantation.
- Association between GFR decline and graft failure and patient death was analysed with a competing-risk COX model.



## RESULTS:

### Flow chart:



### Population Characteristics:

Characteristics	Whole Cohort	DFG at 1 yr and at 5 yrs
<b>RECIPIENTS (n) At the time of transplant</b>	<b>488</b>	<b>416</b>
Age (yr; mean ± SD)	45.4 ± 12.9	56.2 ± 12.9
Male gender - n (%)	339 (69%)	289 (69%)
Cause of renal disease - n(%)		
Glomerulopathy	160 (33%)	140 (34%)
Diabetes	5 (1%)	4 (1%)
Polycystic kidney disease	68 (14%)	59 (14%)
Hypertension	38 (8%)	30 (7%)
Interstitial nephritis	37 (8%)	30 (7%)
other	121 (25%)	52 (13%)
Unknown	59 (12%)	101 (24%)
Preemptive transplantation - n (%)	43 (9%)	37 (9%)
Retransplantation - n (%)	76 (16%)	64 (15%)
<b>DONORS</b>		
Age (yr; mean ± SD)	37.8 ± 13.8	38.0 ± 13.8
Living donor - n(%)	18 (4%)	13 (3%)
<b>TRANSPLANTATION-baseline &amp; 1 yr of transplantation</b>		
HLA mismatch > 3 - n (%)	323 (66%)	279 (67%)
PRA > 80%	39 (9%)	37 (9%)
Delayed graft function - n (%)	127 (26%)	101 (24%)
1 year-rejection - n (%)	202 (41%)	169 (41%)
<b>RECIPIENTS- 1 year post-transplantation</b>		
≥ 1 anti-hypertensive medication	387 (80%)	327 (79%)
Inulin Clearance(mL/min/1.73m²; Mean ± SD)	47.2 ± 19.2	42.4 ± 21.3
Urinary Protein Creatinine Ratio (mg/g; Mean ± SD)	233 ± 665	170 ± 490
Immunosuppressive Regimen:		
- without CNI	15 (3%)	12 (3%)
- with CNI	473 (97%)	404 (97%)

### Distribution of patients according to their GFR change:

	[Min ; -50%]	[-50% ; -30%]	[-30% ; 0]	[0 ; Max]
mGFR	23	47	109	237
CKD-EPI	23	39	149	205

A GFR decline of almost 30% was an event three times more frequent than one of almost 50%.

### Concordance of patients according to their class of GFR change percentage between inulin and CKD-EPI evaluation:

At the 30%-threshold of GFR decline, concordance between inulin and CKD-EPI was 53% (37/70 patients).

CKD-EPI %	mGFR %			
	-85 ; -30%	-30% ; 0	> 0 %	
-83 ; -30%	37	13	12	
-30% ; 0	25	54	70	
> 0%	8	42	155	

### Association between GFR change over 4 years and long term outcome at 15 years:

GFR Change over 4 years (%)	N = 416	Death N=92	Dialysis N=155	Association to Death (Censored for Dialysis)	Association to Dialysis (Censored for Death)		
				HR [95% CI]	p	HR [95% CI]	p
<b>mGFR slope</b>							
<b>Threshold 30%</b>					0.02		<0.0001
[-85;-30]	70	19	35	1.907 [1.078;3.373]	0.027	2.473 [1.593;3.841]	<0.0001
]-30;0]	109	18	34	0.702 [0.394;1.251]	0.23	0.893 [0.575;1.386]	0.61
[0;+30]	136	32	48	Ref		Ref	
<b>mGFR slope</b>					<b>0.83</b>		<b>&lt;0.0001</b>
<b>Threshold 50%</b>							
[-85;-50]	23	3	17	1.550 [0.479;5.023]	0.47	5.811 [3.377;9.999]	<0.0001
]-50;0]	156	34	52	1.046 [0.663;1.649]	0.85	1.047 [0.726;1.511]	0.81
[0;+50]	181	41	64	Ref		Ref	
<b>CKD-EPI slope</b>					<b>0.023</b>		<b>&lt;0.0001</b>
<b>Threshold 30%</b>							
[-82;-30]	62	16	31	1.858 [1.023;3.366]	0.04	3.092 [1.940;4.928]	<0.0001
]-30;0]	149	24	59	0.693 [0.412;1.166]	0.17	1.387 [0.936;2.056]	0.10
[0;+30]	139	35	43	Ref		Ref	
<b>CKD-EPI slope</b>					<b>0.03</b>		<b>&lt;0.0001</b>
<b>Threshold 50%</b>							
[-82;-50]	23	4	16	2.007 [0.715;5.631]	0.19	6.433 [3.464;11.350]	<0.0001
]-50;0]	188	36	74	0.962 [0.614;1.505]	0.86	1.501 [1.058;2.129]	0.023
[0;+50]	177	41	55	Ref		Ref	

- Association between mGFR decline and graft failure or death remained significant regardless of the considered threshold.

- CKD-EPI GFR decline was similarly associated to these events.

## CONCLUSIONS:

- A GFR decline of 30% between 1 and 5 years post-transplantation is significantly associated with all cause mortality and graft loss. So it might be a valid surrogate for long term outcome in renal transplantation.

- Despite a poor concordance between inulin and CKD-EPI, utilization of CKD-EPI equation does not seem to impair the association between GFR decline and graft/patient survival.

## REFERENCES:

- O.Moranne et al. "Rate of Renal Graft Function Decline After One Year Is a Strong Predictor of All Cause Mortality". American Journal of Transplantation 2013; 13: 695-706
- M.Gera et al. "Assessment of Changes in Kidney Allograft Function Using Creatinine-Based Estimates of Glomerular Filtration Rate". American Journal of Transplantation 2007; 7: 880-887
- J.Coresh et al. "Decline in Estimated Glomerular Filtration Rate and Subsequent Risk of End-Stage Renal Disease and Mortality". JAMA 2014; 311(24): 2518-2531

