

Association between tacrolimus levels and antibody-mediated rejection after kidney transplantation

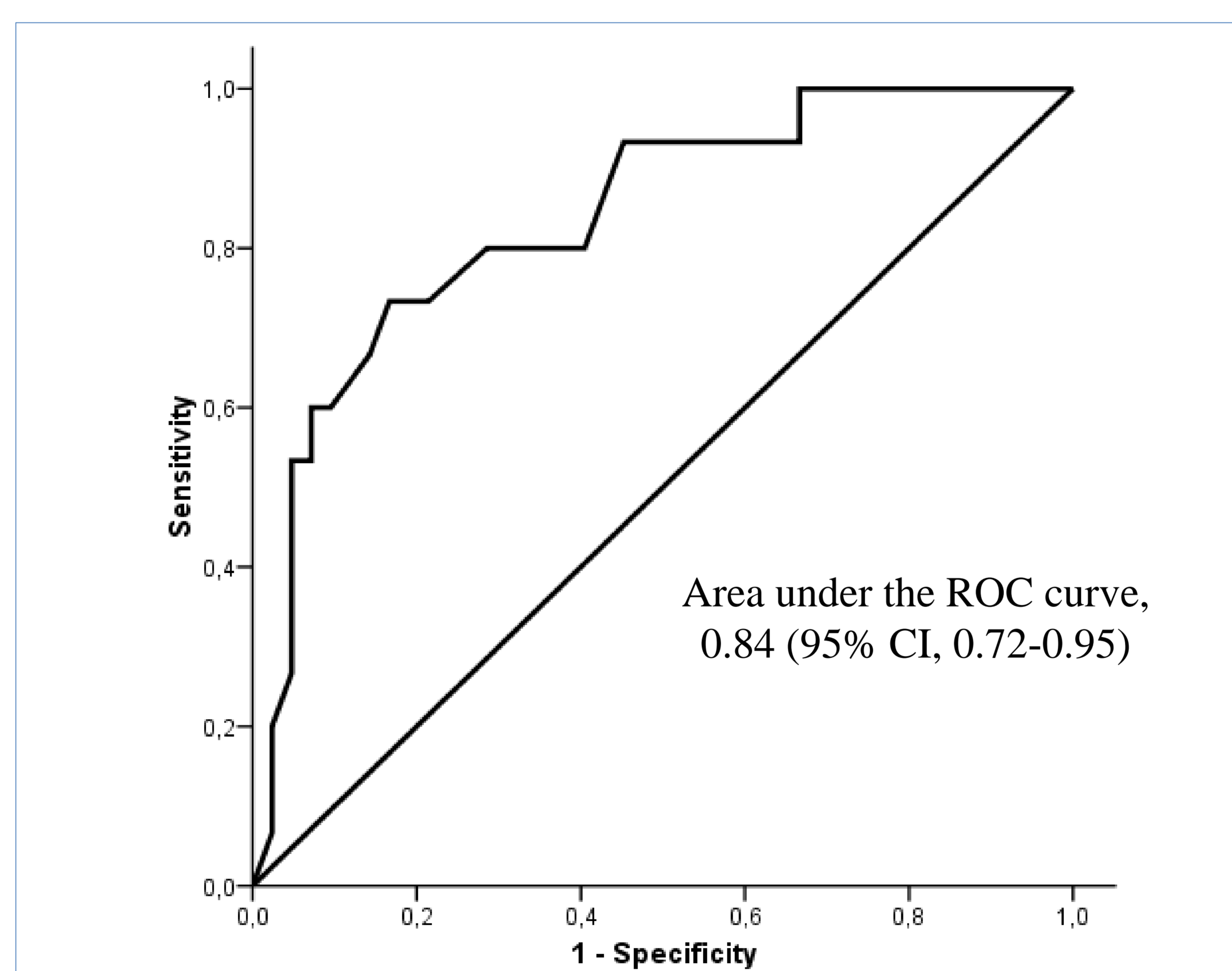
Authors: Ruiz-Esteban P¹, Gonzalez-Molina M¹, Caballero A², Palma E¹, Burgos D¹, Cabello M¹, Alonso-Titos J¹, Duarte A¹, Hernandez D¹.
¹Nephrology and ²Immunology Departments, Regional University Hospital, IBIMA, REDINREN, University of Malaga (Spain).

Introduction. Antibody-mediated rejection (ABMR) is the major cause of allograft failure. We studied whether the coefficient of variability (CV) of blood levels of tacrolimus can predict ABMR.

Material and methods. We studied 591 recipients of a renal transplant (RT) performed between January 2008 and December 2012, followed until June 2014 (median 40 months, interquartile range 26-58). We compared the CV of the blood levels of tacrolimus between the 21 patients who experienced ABMR and a control group (1:2) comprising randomized patients matched for age, gender and transplant year who did not have ABMR. The CV was obtained from the formula $CV (\%) = (SD/\mu) \times 100$, using the 5 last measurements of tacrolimus blood levels before diagnosis of ABMR.

Results. The CV in the ABMR group compared with the controls was 38.3 ± 14.3 vs. $20.7 \pm 11.0\%$ ($p < 0.001$).

Figure 1. ROC curve of the coefficient of variation of tacrolimus blood concentrations in patients with de novo donor specific antibodies for predicting antibody-mediated rejection.



The Youden index showed that a $CV \geq 27.5\%$ was the best predictor of ABMR

Table 1. Relationship between coefficient of variability of the tacrolimus blood concentrations $\geq 27.5\%$ and overall antibody mediated rejection by bivariate and multivariate regression analysis.

Adjusted for	Bivariate analysis		Multivariate analysis*		
	OR (95% CI)	P-value	Variables	OR (95% CI)	P-value
			CV $\geq 27,5$ (%)	9.8(1.1-88.2)	0.042
Pre-transplant antibodies (yes vs. no)	11.6(1.9-71.6)	0.008	Pretransplant antibodies (yes vs. no)	37.2(3.0-461.2)	0.005
Cellular AR (%)	12.4(2.1-73.8)	0.006	Cellular AR (%)	29.4(2.5-345.1)	0.007
Donor age (years)	14.0(3.4-58.7)	<0.001			
Recipient age (years)	13.1(3.0-56.4)	0.001			
Recipient gender	15.9(3.6-67.5)	<0.001			
Retransplantation (%)	18.0(3.3-98.8)	0.001			
DGF (%)	17.8(3.7-86.5)	<0.001			
CIT (hours)	14.1(3.4-58.4)	<0.001			
Time since dialysis (months)	13.4(2.8-64.1)	0.001			
Induction treatment (%)	23.8(4.6-122.5)	<0.001			
Pre-transplant cPRA (%)	11.5(2.4-54.3)	0.002			

OR: Odds ratio; CI: confidence interval; AR: acute rejection; CIT: cold ischemia time; DGF: delayed graft function; cPRA: virtual panel reactive antibodies; CV: coefficient of variability of tacrolimus blood concentrations.

*Because the number of events was few, this analysis was performed entering risk factors two by two.

Conclusion. A CV of 27.5% of tacrolimus levels predicts the risk for ABMR with adequate sensitivity and specificity adjusting for confounding variables.