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INFLUENCE OF THE GENETIC POLYMORPHISMS ON THE RESPONSE TO CLOPIDOGREL IN PERIPHERAL ARTERY DISEASE PATIENTS FOLLOWING PERCUTANEOUS TRANSLUMINAL ANGIOPLASTY

Xando Díaz Villamarín*[1], Cristina Lucía Dávila-Fajardo*[1], Luis Javier Martínez-González[2], Pedro Carmona-Saez[3], Jesús Sánchez Ramos[4], Luis Miguel Salmerón-Febres[5], Jose Cabeza Barrera[1], Fidel Fernández-Quesada[5], Inmaculada Casas Hidalgo[1], Margarita Valle Corpas[1]

[1]Department of Clinical Pharmacy, Instituto de Investigación Biosanitaria de Granada Hospital Universitario San Cecilio, Granada, Spain.

[2]Genomics Unit, Centre for Genomics and Oncological Research (GENYO), Pfizer-University of Granada-Andalusian Regional Government, Health Sciences Technology Park, Granada, Spain

[3]Bioinformatics Unit, Centre for Genomics and Oncological Research (GENYO), Pfizer-University of Granada-Andalusian Regional Government, Health Sciences Technology Park, Granada, Spain

[4] Cardiology, Instituto de Investigación Biosanitaria de Granada Hospital Universitario San Cecilio, Granada, Spain.

[5]Vascular Surgery, Instituto de Investigación Biosanitaria de Granada, Hospital Universitario San Cecilio, Granada, Spain.

BACKGROUND Clopidogrel has provided significant reduction in major vascular events in patients with peripheral artery disease in general. At present it is not possible to predict which patients will develop restenosis, amputation, thrombosis or reoperation for lower limb following percutaneous transluminal balloon angioplasty. However, different polymorphisms have been associated with differences in clopidogrel response in acute coronary syndrome patients.

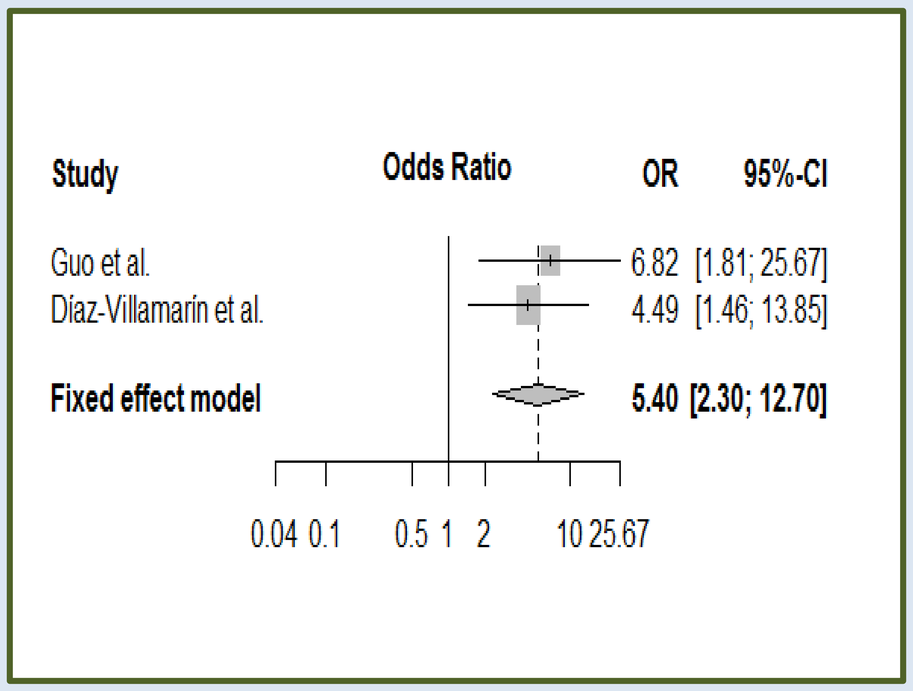
OBJECTIVES The aim of this article is to study the association of theses genetic variations with the clopidogrel response in a cohort of Spanish peripheral artery disease patients and performed a meta-analysis combining these data with another published previously.

MATERIAL AND METHODS 72 patients with lower limb atherosclerotic disease following percutaneous transluminal balloon angioplasty and treated with clopidogrel were recruited. We evaluated the effect of *ABCB1* 3435 C>T genotype, *CYP2C19*2* and *CYP2C19*3* genotypes and rates of the primary efficacy endpoint including atherotrombotic ischemic events. Other clinical parameters used to evaluate the clinical evolution of the patients (intermittent claudication, toe-brachial pressure index, arterial PVR test, Fontaine/Routherford degree) were measured at baseline and at 12 months after the first day with clopidogrel, then we classified our patients into 2 groups (GOOD or BAD evolution).

RESULTS

	CYP2C19*2+ABCB1 TT		CYP2C19*2		ABCB1 TT	
	OR (IC95%)	p-value	OR (IC95%)	p-value	OR (IC95%)	p-value
Fontaine bad evolution	13.96 (4.44-43.80)	<0.0001	8.31 (2.36 – 29.16)	0.001	4.75 (1.32-17.07)	0.017
TBPI bad evolution	2,75 (0.64-11.69)	0.171	2.16 (0.48-9.64)	0.310	1.87 (0.29-12.14)	0.510
PVR bad evolution	4.35 (1.14-16.49)	0.031	2.91 (0.79-10.67)	0.106	3.46 (0.77-15.55)	0.10
IC bad evolution	6.28 (1.60-24.56)	0.008	6.22 (1.31-29.44)	0.021	1.91 (0.40-9.04)	0.41

Associations between genetic polymorphisms and TBPI, PVR, IC and Fontaine evolution. PVR: arterial PVR test, IC: intermittent claudication, TBPI: toe brachial pressure index



	CYP2C19 *1/*2 or *2/*2	CYP2C19 *1/*1	OR (95% CI)	P-value	CYP2C19 *1/*2; *2/*2 + ABCB1 TT	CYP2C19 *1/*1 or ABCB1 CC; CT	OR (95% CI)	P-value
Primary endpoint (n=25, 34.7%)	11 (44%)	14 (56%)	4.49 (1.45 – 13.84)	0.009	17 (68%)	8 (32%)	5.00 (1.75-14.27)	0.003
Non-primary endpoint (n=47, 65.3%)	7 (15%)	40 (85%)			14 (30%)	33 (70%)		

Primary endpoint: atherotrombotic ischemic events diagnosed by ultrasound of the affected limb.

CONCLUSION

Our results support the role of the *CYP2C19* and *ABCB1* polymorphisms as a genetic marker of cardiovascular events in atherosclerotic of the arteries of the lower limb disease patients following PTA treated with clopidogrel.