News and Views From the Literature

Antiplatelet Agents

Cardiovascular Mortality in Chronic Kidney Disease Patients Undergoing Percutaneous Coronary Intervention

Reviewed by Norman E. Lepor, MD, FACC, FAHA, FSCAI

Department of Medicine, Division of Cardiology, Cedars-Sinai Medical Center, Los Angeles, CA

[*Rev Cardiovasc Med.* 2011;12(3):168-169 doi: 10.3909/ricm0599]

Cardiovascular Mortality in Chronic Kidney Disease Patients Undergoing Percutaneous Coronary Intervention is Mainly Related to Impaired $P2Y_{12}$ Inhibition by Clopidogrel

Morel O, El-Ghannudi S, Jesel L, et al.

J Am Coll Cardiol. 2011;57:399-408.

It is estimated that 26 million Americans have chronic kidney disease (CKD). Patients with CKD are more likely to develop accelerated coronary atherosclerosis and its associated complications. This may be related to pathophysiologic changes associated with CKD, including heightened platelet activation, greater oxidative potential, endothelial dysfunction, inflammation, and abnormalities of lipid and calcium/phosphate metabolism. Little is known about how patients with CKD respond to oral antiplatelet therapy with clopidogrel and how this response may affect thrombotic complications in patients undergoing percutaneous coronary interventions (PCI).

In this study, 440 patients undergoing urgent or planned PCI were prospectively enrolled; 126 of these patients had an estimated glomerular filtration rate < 60 mL/min/1.73 m^2. The study was designed to test the hypothesis that low platelet responsiveness to clopidogrel as assessed by vasodilator stimulated phosphorylation-flow cytometry test (VASP-FCT) is independently associated with thrombotic events following PCI in patients with CKD. The VASP assay selectively assesses for activity of the $P2Y_{12}$ receptor. All patients received dual oral antiplatelet therapy following PCI and were followed for a mean of 9 months. Patients were classified as low responders if the platelet reactivity index as assessed by the VASP-FCT $> 61\%$. Of patients with CKD, 58% were classified as low responders. Patients with CKD and low response to clopidogrel had a higher all-cause mortality rate (25.5% vs 2.8%; $P < .001$), cardiac death rate (23.5% vs 2.8%; $P < .001$), and all stent thrombosis rate (19.6% vs 2.7%; $P = .003$) than those who were not low responders (Table 1).

In conclusion, low response to clopidogrel therapy is common among patients with CKD who undergo PCI.

Table 1
Outcomes According to Renal Function and Platelet Responsiveness to Clopidogrel

	No CKD (n = 309)			CKD (n = 124)		
	Responder (n = 187)	Low responder (n = 122)	*P*	Responder (n = 73)	Low responder (n = 51)	*P*
All-cause mortality	7 (3.7)	3 (2.5)	.745	2 (2.8)	13 (25.5)	< .001
Cardiac death	4 (2.1)	2 (1.6)	1.00	2 (2.8)	12 (23.5)	< .001
STEMI	3 (1.6)	1 (0.8)	1.00	2 (2.8)	2 (3.9)	1.00
NSTEMI	10 (5.3)	8 (6.6)	.804	2 (2.8)	3 (5.9)	.640
TLR	19 (10.2)	14 (11.5)	.711	5 (6.9)	4 (7.8)	1.00
Definite stent thrombosis	3 (1.6)	4 (3.2)	.443	1 (1.4)	1 (1.9)	1.00
Probable stent thrombosis	2 (1.1)	1 (0.8)	1.00	1 (1.4)	4 (7.8)	.158
Definite/probable stent thrombosis	5 (2.7)	5 (4)	.527	2 (2.7)	5 (9.8)	.123
Possible stent thrombosis	1 (0.5)	0 (0)	1.00	0 (0)	5 (9.8)	.010
All stent thrombosis	6 (3.2)	5 (4)	.759	2 (2.7)	10 (19.6)	.003
MACE	27 (14.4)	18 (14.8)	1.00	9 (12.3)	17 (33.3)	.007

Data are expressed as n (%) unless specified otherwise.

CKD, chronic kidney disease; MACE, major adverse cardiac events; NSTEMI, non–ST-segment elevation myocardial infarction; STEMI, ST-segment elevation myocardial infarction; TLR, target lesion revascularization.

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Suboptimal $P2Y_{12}$ receptor blockade is associated with greater major adverse cardiac event (MACE) rates, including mortality and stent thrombosis in patients with CKD. In patients with normal renal function, there was no association between suboptimal platelet inhibition and MACE.

Whether low response to clopidogrel is the direct cause of thrombotic complications in patients with CKD or a marker for other, unmeasured patient comorbidities is unclear. Although patients presenting with acute coronary syndromes undergoing PCI have lower thrombotic complications when treated with the third-generation thienopyridine, prasugrel, compared with clopidogrel,[1] whether patients with CKD undergoing PCI could benefit from more aggressive platelet inhibition with prasugrel remains to be determined, and should be examined prospectively in clinical trials. Future studies should also evaluate the utility of testing platelet reactivity (using point of care systems such as VerifyNow® [Accumetrics, San Diego, CA] or VASP) to guide therapy in patients with CKD undergoing PCI, and should include the entire range of CKD severity. ■

Reference

1. Wiviott SD, Braunwald E, McCabe CH, et al; TRITON-TIMI 38 Investigators. Prasugrel versus clopidogrel in patients with acute coronary syndromes. *N Engl J Med*. 2007;357:2001-2015.