Personalized Medicine Corner

Genetic Test Shows Promise for Improved Cardiovascular Outcomes Post-PCI

Clopidogrel is an antiplatelet medication used post-percutaneous coronary intervention (PCI) to prevent major adverse cardiovascular events (MACE).[1] Clopidogrel is activated by the *CYP2C19* enzyme, whereas other P2Y12 inhibitors (i.e., ticagrelor, prasugrel) are not dependent on *CYP2C19* for activation. Clopidogrel activation and effectiveness after PCI are reduced in patients with a *CYP2C19* genetic polymorphism that decreases enzyme activity, also referred to as a loss-of-function (LOF) allele.[2] Post-hoc analyses of randomized controlled trials and patient registries have shown a higher risk for MACE in clopidogrel-treated patients with a *CYP2C19* LOF allele.[3]

Results of a collaboration among 7 U.S. institutions that implemented *CYP2C19* genotype-guided therapy post-PCI as part of clinical care and examined outcomes with this approach were presented at the November 2016 American Heart Association Scientific Sessions.[4] Alternative antiplatelet therapy (i.e., prasugrel, ticagrelor) was recommended in patients at each institution with a *CYP2C19* LOF allele.

Of 1,815 total patients, 572 (31.5%) carried a *CYP2C19* LOF allele, with 346 of these patients (60.5%) prescribed an alternative to clopidogrel. Clinicians received genotype test results and implemented alternative therapy at a median of 1 day (interquartile range 1–6 days) after PCI across all sites. Patients with a *CYP2C19* LOF allele who received clopidogrel were more likely to experience MACE in the 12 months post-PCI than those who received alternative therapy (adjusted hazard ratio [HR] 2.21, 95% confidence interval [CI] 1.13–4.33; p=0.021). The risk of MACE was similar in patients with a *CYP2C19* LOF allele who received alternative therapy and those without a LOF allele (adjusted HR 0.81, 95% CI 0.48–1.35; p=0.41).

These data show that use of pharmacogenetic testing to guide antiplatelet drug therapy decisions post-PCI is feasible in a real-world environment across multiple institutions. Study findings also suggest that a genotype-guided approach can lead to improved outcomes when genotype is made available early after PCI and alternative antiplatelet therapy is started in patients with a *CYP2C19* LOF allele.

For questions about these data, or ordering and interpreting a pharmacogenetic test, contact the UF Health Personalized Medicine Program (PMP-HELP@ctsi.ufl.edu).

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4. Cavallari LH, et al. Prospective Implementation of *CYP2C19* -Genotype Guided Antiplatelet Therapy after PCI: a Multi-Site Investigation of MACE Outcomes in a Real-World Setting. *Circulation* 2016;134:e711-712. Presented as a Late-Breaking Abstract at the American Heart Association's Scientific Session 2016. New Orleans, LA. November 15, 2016.

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