Genetic Test Shows Promise for Improved Cardiovascular Outcomes Post-PCI

Clopidoğrel is an antiplatelet medication used post-percutaneous coronary intervention (PCI) to prevent major adverse cardiovascular events (MACE). Clopidoğrel is activated by the CYP2C19 enzyme, whereas other P2Y12 inhibitors (i.e., ticagrelor, prasugrel) are not dependent on CYP2C19 for activation. Clopidoğrel 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. Post-hoc analyses of randomized controlled trials and patient registries have shown a higher risk for MACE in clopidoğrel-treated patients with a CYP2C19 LOF allele.

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. 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 clopidoğrel. 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 clopidoğrel 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).

References: