PGx and functional markers in antiaggregating and anticoagulation therapies – Everything clear?

Alexander C. Haushofer
Medilab Dr. Mustafa, Dr. Richter Labor für medizinisch-chemische und mikrobiologische Diagnostik GmbH, 5020 Salzburg, Austria

Pharmacogenetics (PGx) and functional biomarkers are emerging as key tools to individualize antiplatelet and anticoagulant therapy, aiming to balance thrombotic risk against bleeding complications. In antiplatelet therapy, CYP2C19 variants are well established for clopidogrel. However, there are no robust PGx data for prasugrel, which is also a prodrug but provides more consistent platelet inhibition, or for ticagrelor, for which no evidence supporting PGx-guided therapy has been published or seems to be necessary until now because of very good antiaggregating effect. Platelet function testing (e.g., light transmission aggregometry, VerifyNow, Multiplate) helps to identify high on-treatment platelet reactivity and low responders, providing a functional correlate to PGx profiles, especially in clopidogrel therapy. In anticoagulation, VKORC1 and CYP2C9 polymorphisms significantly affect warfarin sensitivity and dose requirements, due to the high risk of bleeding complications at therapy initiation. For phenprocoumon (Marcoumar©, 4-hydroxycoumarin derivate), PGx analysis is not commonly established because of its delayed onset of anticoagulant effect. For direct oral anticoagulants (FIIa and FXa inhibitors), variants in genes related to drug transport and metabolism may modulate drug exposure. Global coagulation assays and specific activity measurements (e.g., anti-Xa levels, thrombin generation tests) offer complementary information on the achieved anticoagulant effect. In the future, integrating PGx data with functional markers may enable more precise patient stratification, optimized drug and dose selection, and dynamic therapy adjustment. However, implementation in routine care is still limited by heterogeneous evidence, variable assay standardization, cost, turnaround time, and uncertainty regarding which combinations of genetic and functional tests offer the greatest clinical utility. This review provides a brief overview of PGx variants and functional markers relevant to antiplatelet therapy, as well as a short summary of guidance for anticoagulant therapies.