Comparison of four methods to assess high-on platelet reactivity under P2Y12 receptor inhibitor

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Résumé en anglais	P2Y12 receptor inhibitors are antiplatelet agents commonly prescribed in the treatment of coronary artery disease. Their efficacy can be limited by high on-treatment platelet reactivity (HPR), which can be evaluated by different biological assays. Most commonly, HPR is evaluated by flow cytometric vasodilator-stimulated phosphoprotein-phosphorylation (VASP-P) assay, which can be time consuming. To evaluate the potential interest of novel technologies, we compared four different assays. Ninety patients receiving P2Y12 inhibitors were included. Four technologies were evaluated: the current standard test measuring VASP-P by flow cytometry, the historical reference test based on light transmittance aggregation (LTA), and two relatively novel techniques: whole blood multiple electrode aggregometry (MEA) and platelet function analyzer (PFA), which are less time consuming. The three latter tests were compared with the VASP-P assay as a reference using receiver operating characteristics (ROC) analysis: LTA has an excellent comparability with the VASP test (ROC AUC > 0.9); the other two tests (multiplate and PFA) have only satisfactory comparability (ROC AUC around 0.7) and therefore may not replace the VASP "gold standard" test, if importance is attached to a quantitative assessment of the substitution parameter of VASP. Nevertheless, if a binary approach of the anti-aggregation result is sought, then one can conclude that the three tests are equivalent since Cohen's kappa coefficients are very close for the three tests (k = 0.548 for LTA; k = 0.554 for MEA; k = 0.570 for PFA/P2Y), and a similar proportion of patients are misclassified (15% for LTA, 14% for MEA, and 13.6% for PFA). Discriminant factor analysis using all the parameters provided by each test did not improve the diagnostic performance of MEA or PFA. In conclusion, only LTA shows a good comparability to the VASP assay using ROC curve analysis, probably because misclassified patients have results close to the cutoff values. All three tests have moderate agreement regarding the classification of patients as responders to P2Y12 inhibition.
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