Minimizing the "Aggravation" of Platelet Aggregation: The Need for Improved Assessments of Platelet Function

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Light transmission aggregometry (LTA) is the "gold standard" assay for studying platelet function, yet its standardization in the clinical laboratories is challenging.

In this volume of *Thrombosis and Haemostasis*, the THROMKID-Plus Group presents a survey among laboratories from Germany and Austria.[1] They studied five agonists following the Scientific and Standardization Committee/International Society on Thrombosis and Haemostasis recommendations including three different sets, including one simulating a healthy control and other two simulating platelet disorders. Fifteen expert laboratories in Germany and Austria studied platelet function using the above agonists applying LTA. Laboratory-internal agonists were tested as well. The results revealed consistent data regarding the maximum percentage of aggregation and identified the diagnosis of the simulated platelet function disorders. However, significant variability in laboratory-internal agonists including reagent type, concentrations, and pathological cut-off values was observed.

The authors concluded that centrally shipment of standardized agonists may be used for interlaboratory quality assurance of LTA, and yet there is a need for standardization of agonist reagents and their concentration as well as for definition of reference ranges.

Platelet function testing presents several limitations including the need for a fresh blood sample, the need for a gentle handling of the sample due to the very high sensitivity of platelets to ambient conditions (temperature, tilting of the tube), and many others. That may explain the inconsistent results even with the same patient's blood sample. Moreover, different methods and devices which are in use at the clinical laboratories may yield different results.

One major obstacle in achieving a "common denominator" basis in this field is the different methods which are used, including LTA, impedance aggregometry, and fax analysis of platelet's expression of activation markers.

The above study together with different societies' recommendations is promoting our ability to apply LTA as a gold standard test for platelet function abnormalities as well as the response to different platelet's antagonists.[2–4] Despite the long time since its development,[5] LTA probably remains the best assay for these studies, but due to its inter- and intraoperator dependence, there is a need for standardization of all the components, including reagents, blood drawing, procedure's protocol, etc.

Recently, several devices were developed in an effort to allow platelet function testing at the "point-of-care" environment, employing automated approach, including the "VerifyNow,"[6] the PFA 100,[7] Multiplate,[8] as well as the thromboelastography devices.[9] These methods are testing platelet function in the acute care setting yielding a general impression (usually a "yes-no" output) but not necessarily a more detailed evaluation of platelet function, thus lacking the flexibility of the LTA as a more diverse system for different applications. Assessments using flow cytometry are also limited by the lack of inter- and intra-assay reproducibility, or lower limits of detection. Perhaps we should even consider scrutiny of assay validation studies that include looking at diurnal variation, exercise, time since sample was taken or processed, body weight, etc., as all these aspects may affect the data when assessing a "labile" parameter such as platelet activation.[10,11] This is needed given the interest into platelet indices in the clinical setting, especially in relation to interventions and decision-making for antiplatelet drugs use.[12–17] As new platelet indices and protocols are developed and proposed as biomarkers of platelet function,[18–20] clear assay validation and reproducibility data are needed.

The paper from the THROMKID-Plus Group[1] contributes to the standardization of reagent used with LTA yet there remains a need for further standardizing other assessments of platelet function as well. Things can only get better.

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Conflict of Interest
None declared.

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