



Principles, Indications, and Limitations of the Platelet Function Analyzer

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In the past, screening for primary hemostatic disorders, particularly von Willebrand disease (vWD), was performed using the manual bleeding time method. Bleeding time testing has been criticized for being invasive, poorly reproducible and insensitive. Screening tests with a higher sensitivity for platelet dysfunction and von Willebrand disease (vWD) have been unavailable until now. The introduction of the automated platelet function analyzer (PFA-100[®], Dade Behring, Deerfield, Illinois) has provided an alternative to the manual bleeding time method with increased sensitivity for platelet dysfunction, particularly with regard to vWD.

The coagulation cascade in vivo is stimulated by vessel wall injury and continues toward the formation of a platelet plug under the influence of various stimulators of platelet adhesion and aggregation. Well-known stimulators of this process include epinephrine, adenosine diphosphate (ADP), collagen, thrombin and thromboxane A₂. The PFA-100 simulates the conditions following vascular wall injury. Whole blood (citrate anticoagulated) is aspirated from a reservoir through a capillary and a biologically active membrane. The membrane, coated with either collagen/epinephrine or collagen/ADP, contains a central aperture (simulating vessel wall injury). As blood flows through the aperture, platelets begin to adhere and aggregate. The time until the aperture is completely occluded by the platelet/red blood cell thrombus is termed the "closure time."

It has been shown that the PFA-100 is more sensitive for screening patients for vWD (except type 2N) than the manual bleeding time.¹ Since the closure time has been shown to fully correct following desmopressin acetate (DDAVP[®]) treatment, the PFA-100 may also be used for therapeutic monitoring of treated vWD.¹ Abnormal closure times may be seen in various other platelet disorders, however sensitivity and specificity are not high enough to justify use of the PFA-100 as a routine screening tool in these cases.² The closure time in congenital platelet disorders varies depending on the severity of the disease. Severe forms, such as Glanzmann thrombasthenia, Bernard-Soulier syndrome and platelet-type vWD, result in a markedly prolonged closure time. It is currently recommended that platelet aggregation studies be performed in addition to the PFA-100 for a thorough evaluation of platelet function.

While a normal PFA-100 closure time effectively rules out moderate to severe vWD, mild type 1 vWD may not impact the closure time and further testing with ristocetin cofactor activity and von Willebrand factor antigen should be carried out when clinical suspicion is high.³ Prolongation of the closure time must be evaluated within the appropriate clinical context. Thrombocytopenia (platelet count below 150,000/uL) and a decreased hematocrit (<35%) may prolong the closure time because formation of a platelet/red cell thrombus is directly dependent upon these factors. Test results with both the collagen/epinephrine and the collagen/ADP membranes should be prolonged in vWD; however, isolated closure time prolongation with the collagen/epinephrine cartridge occurs in patients taking aspirin. Clopidogrel (Plavix[®]) and ticlopidine (Ticlid[®]) do not cause an abnormal PFA-100 result. Bleeding due to coagulation factor deficiencies cannot be detected using the PFA-100.

In summary, the PFA-100 is a more sensitive screening test than the manual bleeding time for the diagnosis of von Willebrand disease (types 1, 2A, 2B, and 3) and may be useful for other specific platelet function disorders. The test uses stimulators of platelet aggregation and adhesion in an environment that simulates an injured blood vessel wall. The time until complete occlusion of blood flow through an aperture (closure time) is the measured end point. In addition to vWD screening, the PFA-100 is also indicated for monitoring treatment efficacy of DDAVP in vWD patients. False-positive closure time prolongation may be seen with thrombocytopenia (<150,000/uL) or a low hematocrit (<35%). Aspirin therapy will prolong the closure time with the collagen/epinephrine cartridge, a feature that allows the PFA-100 to be used as a screen for coagulopathy due to aspirin effects. Coagulation factor defects or the use of Ticlid and Plavix, do not prolong the closure time. Thorough evaluation of platelet dysfunction should include platelet aggregation studies in addition to the PFA-100.

References

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