



IMPORTANCE OF PLATELET FUNCTION TESTING WITH THE AGGREGUIDE AMID THE COVID-19 OUTBREAK

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SUMMARY

COVID-19 can cause dangerous blood clots in some patients and can also significantly prolong the duration for which critically ill patients are reliant on ventilators. Platelets may play a critical role in exacerbating these conditions and antiplatelet drugs (a type of 'blood thinner') may help mitigate these problems. Careful application of these drugs is important due to the potential risk of bleeding in some patients. The AggreGuide is a blood test that can enable optimal use of these drugs for each individual COVID-19 patient to reduce the deleterious effects of platelets without increasing bleeding risk. Thus, the AggreGuide can facilitate precision medicine to improve outcomes in COVID-19 patients.

Platelets and Infectious Disease

Infectious diseases such as COVID-19 can evoke an uncontrolled immune response in some patients¹. Both the pathogen and the stimulated immune system (e.g. white cells) can cause activation and aggregation of platelets in the blood stream. This can lead to thromboembolic events such as ischemic stroke, disseminated intravascular coagulation, venous thromboembolism, myocardial infarction, and death. Recently published clinical studies and several anecdotal reports indeed suggest that COVID-19 patients show signs of platelet aggregation (e.g. 'COVID toes') and serious thrombotic events^{2,3}. Further, the mortality rate of COVID-19 patients with pre-existing cardiovascular conditions is high. These evolving observations underscore the significance of the platelet pathway in COVID-19 pathology.

Antiplatelet therapy, Cardiovascular Disease, and COVID-19⁴

Aspirin and platelet P2Y₁₂ inhibitors such as clopidogrel are routinely administered to cardiovascular disease patients with the intent of reducing platelet-mediated thrombotic events. However, it has been recognized for over a decade that some of these antiplatelet agents may not be consistently inhibiting platelet aggregation in all patients. This inter-individual variability in antiplatelet therapy assumes critical importance during the COVID-19 outbreak since this infectious disease appears to be exacerbating platelet activation as noted above. Further, administration of other therapeutic drug candidates (e.g. Lopinavir/Ritonavir) seem to reduce the efficacy of clopidogrel². Thus, ensuring that appropriate platelet inhibition is being achieved in each vulnerable cardiovascular disease patient during the COVID-19 outbreak merits urgent attention.



Monitoring Antiplatelet Therapy with the AggreGuide during COVID-19

The AggreGuide is a rapid (<5min) and cost-effective blood test which measures platelet aggregation in a manner that closely resembles how platelets aggregate in blood vessels in the body. Clinical studies with the AggreGuide have determined a cut-off Platelet Activity Index (PAI) below which platelet aggregation may be considered inhibited. Measuring the platelet function of patients on antiplatelet therapy during this COVID-19 outbreak using the AggreGuide will help physicians ascertain if the current therapy is providing appropriate platelet inhibition for each patient or if an alternate therapy (e.g. guided escalation to more potent antiplatelet agents) is warranted to counter drug-drug interactions, immune-thrombotic state, etc. for some patients during this high-risk period.

Guided Antiplatelet Therapy to Improve Outcomes in COVID-19 Patients

In addition to the challenges associated with cardiovascular disease patients discussed above, infection-induced platelet activation can also compromise the ability of platelets to maintain optimal permeability of the blood vessel wall and the small airways in the lung¹. This can in turn exacerbate the respiratory distress in some patients and may prolong their dependence on mechanical ventilators. Considering this association between platelet function and infectious lung disease, antiplatelet therapy has been successfully used in past studies to improve the condition of pneumonia patients on mechanical ventilators. Randomized controlled clinical trials as well as large observational clinical studies indicate that P2Y12 inhibitors help reduce the patients' dependence on ventilators and alleviate the underlying inflammation during pathogen-induced acute lung injury^{5,6}.

It is noteworthy that physicians are currently using anticoagulants (heparin) and thrombolytic agents (tPA) to treat COVID-19 patients with thrombotic events such as stroke and venous thromboembolism⁷. While this reactive strategy is understandable at this early stage in our experience with COVID-19, it may be prudent to consider a more proactive, individualized approach using antiplatelet therapy in some patients. Since platelet activation appears to be one of the early responses to the pathogen, it may be more effective to mitigate the process early in the thrombotic cascade using antiplatelet therapy rather than wait for activated platelets to trigger coagulation and then treat that with anticoagulants/thrombolytics subsequently. Also, antiplatelet therapy has proven to improve the condition of pneumonia patients as noted above. Such an application of antiplatelet therapy should be guided by platelet function testing in each patient to minimize the bleeding risk. In fact, American College of Cardiology (ACC) guidelines suggest that using platelet function testing to dynamically select the antiplatelet agent for each patient's prevailing need can be useful to reduce the risk of thrombotic events without increasing the risk of bleeding⁸.

This type of risk stratification and personalized antiplatelet therapy can be effectively achieved using the AggreGuide as noted above. Clinical studies have demonstrated that the AggreGuide is able to stratify platelet aggregation across subjects and is able to differentiate the efficacy of various antiplatelet agents. Thus, rather than a broad, one-type-fits-all application of these drugs, the AggreGuide can individualize antiplatelet therapy to address the most dangerous and debilitating consequences of COVID-19, i.e. extended ventilator needs and thromboembolic events such as heart attack/stroke.

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