Scientists propose a new approach to assessing platelet activation risk

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A novel approach for thrombosis risk assessment Credit: Daria Sokol, MIPT

Researchers from Moscow Institute of Physics and Technology together with their colleagues from National Research Center for Hematology have developed a new method for assessing individual risks of intravascular platelet activation. The latter plays a crucial role in the development of various serious clinical situations such as heart attacks and strokes. The range of circumstances that may be associated with the development of intravascular coagulation is currently actively investigated worldwide. In particular, the onset of intravascular

coagulation may be triggered by temporary spikes in blood pressure.

The suggested approach enables calculating the probability of a hydrodynamic shear-induced activation of platelets—blood cells that initiate formation of the blood clot. It will allow physicians to evaluate the critical level of systolic pressure for individual patients. Above this level, shear-induced platelet activation becomes the leading factor of intravascular coagulation. The study has been published in *PLOS ONE*.

In clinical practice, risks of blood clotting are usually assessed based on laboratory blood tests such as thromboelastography, APPT, thrombin generation test. Those give a general picture of how stable the liquid state of blood is. The tests enable detecting increased blood clotting tendency and, therefore, higher risks of coagulation. Traditional methods of intravascular coagulation risk assessment are based on in vitro analysis of small blood samples drawn from a vein. Such analysis does not, however, take into account individual characteristics of the patient's blood circulation such as the intensity of blood flow, cardiac output, etc.

Therefore, until recently intravascular coagulation risk assessments for stress situations accompanied by blood pressure spikes were based on methodologies that could hardly be called evidence-based. Development of the new approach to shear-induced intravascular thrombosis risk assessment is important at least for vessels at the highest risk of coagulation.

Hydrodynamic shear-induced activation of platelets in a vessel starts when cumulative shear stress reaches a critical level. The critical level of cumulative shear stress is a parameter that depends on both the amplitude and the duration of elevated shear stress affecting the platelets in the blood stream. The shear stress characterizes the force between adjacent blood flows moving at different speeds. The problem is, the critical cumulative shear stress value is patient-specific and may vary

greatly from patient to patient.

"We have studied the way critical cumulative shear stress value may depend on the length of von Willebrand factor molecules. These molecules attach to GP1b receptors on platelets' surface, acting as a sort of sensors for the hydrodynamic environment the platelets find themselves in. Analyzing conformational dynamics of the VWF molecules on the surface of platelets enabled us to find an analytical expression that links their length to the critical cumulative shear stress value," says Denis Pushin, postgraduate student at MIPT.

The cumulative shear stress value in a certain artery directly depends on the patient's arterial blood pressure. The expression discovered in the study makes it possible to determine a given patient's safe limit of upper arterial blood pressure.

"We believe that knowing a patient's individual systolic blood pressure limit will allow doctors to plan a more effective strategy of personalized antithrombotic treatment," comments Georgy Guria, professor at MIPT.

More information: Denis M. Pushin et al. Platelet activation via dynamic conformational changes of von Willebrand factor under shear, *PLOS ONE* (2020). DOI: 10.1371/journal.pone.0234501

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