

## 論 文 要 旨

Cardiovascular risk factors are associated with augmented thrombogenicity in healthy individuals: analysis using the Total Thrombus-formation Analysis System

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Background: Rupture of an atherosclerotic plaque and subsequent exposure of the subendothelial prothrombotic matrix to blood cause arterial thrombosis. Circulating platelets play an indispensable role in the growth of arterial thrombi partially owing to their unique ability to adhere to the subendothelial matrix and to aggregate to each other under flow conditions. Recently, the Total Thrombus-formation Analysis System (T-TAS) was developed for ex vivo analysis of the thrombogenic potential of whole blood samples under flow conditions. Despite the potential clinical utility of the T-TAS in assessing the risk for thrombosis and bleeding, reference intervals for T-TAS analysis in healthy individuals have not been determined.

Methods: In total, 122 whole blood samples were collected from healthy volunteers ranging in age from 25 to 45 years. T-TAS analysis and hematological, physiological, and lifestyle assessments were conducted in these subjects. Whole blood samples anticoagulated with hirudin were perfused into a collagen-coated microchip (PL chip). The time to 10 kPa and the area under the flow pressure curve up to 10 min (AUC10) were analyzed as representative variables for thrombogenic potential.

Reference intervals, which were defined as 2.5–97.5 percentiles, were determined. Additionally,

univariate and multivariate analyses were performed to identify factors associated with the AUC10 in the T-TAS.

Results: The time to 10 kPa and the AUC10 widely varied, even in healthy volunteers. The reference intervals were 1.50–4.02 min and 223.4–456.8, respectively, at a shear rate of  $1,500 \text{ s}^{-1}$ .

Univariate and multivariate analyses showed that platelet counts were most significantly associated with the AUC10 of the T-TAS. The presence of one or more cardiovascular risk factors of a high body mass index, a high pulse pressure, high fasting serum glucose levels, high low-density lipoprotein-cholesterol levels, a history of smoking, and no habitual exercise, had the second largest effect on the AUC10 of the T-TAS.

Conclusions: Healthy volunteers who had any cardiovascular risk factors showed augmented thrombogenicity, even in artificial uniform capillaries, compared with those without any risk factors in the T-TAS.