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## **Dynamics of thrombin generation and platelet aggregability after mechanical prosthetic valve replacement**

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Mechanical prosthetic valve replacement requires lifelong anticoagulant therapy, although the optimal therapeutic range has been established. In this study, the dynamics of thrombin generation in patients underwent prosthetic valve replacement were monitored over a 2-year period using thrombin-antithrombin III complex (TAT), prothrombin fragment 1+2 (F<sub>1+2</sub>), D-dimer, and other blood coagulation-related factors such as warfarin concentration, vitamin K1-epoxide, and protein C activity. Platelet function was also assessed by maximum aggregation in response to adenosine diphosphate (2 μM), collagen (1 μg/mL) and arachidonic acids (0.6 μM). Blood samples were taken before the operation and 1, 6, 12, 24 months after the operation. The dose of warfarin was started at 3 mg/day and adjusted to control prothrombin time (PT)/international normalized ratio (INR) at around 2.0. After valve replacement, patients were treated with warfarin alone (n=4), warfarin in combination with an antiplatelet agent, ticlopidine (200 mg/day) (n=12) or warfarin and aspirin (81 mg/day) in combination (n=7). Before operation, levels of TAT and F<sub>1+2</sub> and D-dimer were high, indicating enhanced thrombin generation and hyperfibrinolysis. Despite our anticoagulant and antiplatelet therapy, the levels of those parameters remained high during the first year after operation. However, by the end of the second year they decreased significantly and returned to within normal range as compared with those in the first year. Platelet function after the operation was suppressed to a similar degree irrespective of the antiplatelet agent used. Despite the low rate of embolism in our clinical experience, prosthetic valve replacement induces significant activation of the coagulation and fibrinolysis systems during the subsequent first year. However, activation of these systems subsides by the end of the second year, even on a program of low-intensity anticoagulation with low-dose antiplatelet agent.

### **Biography**

Kazuo Nakamura has completed his PhD at the age of 37 years from Kagoshima University and postdoctoral studies from Department of Clinical Pharmacy and Pharmacology, Graduate School of Medical and Dental Sciences, Kagoshima University. He is the Professor of Nihon Pharmaceutical University. He has published more than 25 papers in reputed journals and serving as a counselor of The Japanese Pharmacological Society.

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