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In the mechanism of the intramolecular binding of the N-terminal peptide of glu-plasminogen (Glu-pIg) to its kringle, which results in its tight conformation, we synthesized peptides of the N-terminal portion of Glu-pIg molecules and analyzed their effects on the activation of Glu-pIg and its conversion to Lys-plasminogen (Lys-pIg) by plasmin. Three peptides of Ala¹¹-Lys¹², Ala¹¹-Glu¹² and Ala¹¹-Ser¹² were synthesized in order to examine the effect of lysine residue in the peptide. Ala¹¹-Lys¹² and Ala¹¹-Glu¹² enhanced the activation of Glu-pIg by urokinase, whereas the activation of Lys-plasminogen (Lys-pIg) was slightly inhibited. The conversion of Glu-pIg to Lys-pIg by plasmin was also enhanced by these peptides. The results suggest that Ala¹¹-Lys¹² and Ala¹¹-Glu¹² worked on Glu-pIg in a similar manner as lysine analogues by making its conformation looser. The third peptide Ala¹¹-Ser¹² did not have any effect on the activation of Glu-pIg by urokinase or the conversion of Glu-pIg to Lys-pIg by plasmin. Ala¹¹-Lys¹² residue of Glu-pIg is, therefore, strongly implicated as a candidate for the responsible site of the intramolecular binding in Glu-pIg.

Key words: plasminogen, lysine binding site, amino-hexyl side
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transluminal coronary angioplasty is associated with restenosis

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This study examined the role of fibrinolytic components in the process of restenosis after percutaneous transluminal coronary angioplasty (PTCA). Seventy-two patients with single-vessel disease who underwent successful PTCA were prospectively selected. Tissue plasminogen activator (TPA), free plasminogen activator inhibitor-1 (free PAI-1), TPA/PAI-1 complex, and total PAI-1 antigen levels were measured before, at 1 week after, and at 3 months after PTCA. Six months after PTCA, the study patients were divided into two groups: 41 patients without restenosis and 31 patients with restenosis. There were no significant differences with regard to sex, age, coronary risk factors, or morphologic changes in the target lesions between the two groups. There were no significant differences in plasma TPA, TPA/PAI-1 complex, or total PAI-1 levels at each examined period, or in the time course between the two groups, except for total PAI-1 levels at 1 week after PTCA. Although no significant differences in free PAI-1 levels before PTCA were observed, free PAI-1 levels after PTCA in the patients with restenosis were significantly higher than those in the patients without restenosis. In addition, each group had a significant change in the time course of free PAI-1 levels. The results suggest that impaired fibrinolysis early after PTCA might affect the repair process of vascular injury, which leads to restenosis, and also that serial determination of free PAI-1 levels could help predict restenosis. (*Am Heart J* 146: 631-633)

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Restenosis after successful percutaneous transluminal coronary angioplasty (PTCA) remains one of the most important unresolved problems, with an overall incidence of 25% to 50%.¹⁻⁶ Therefore, early detection of prediction of both of patients with developing restenosis has important prognostic and therapeutic implications.

Many studies⁷⁻¹² have focused on investigating the mechanisms of restenosis after PTCA. Recently several reports⁸⁻¹² demonstrated that lesion progression after PTCA was highly correlated with late restenosis, indicating that the process of restenosis begins at least within 1 month of PTCA. According to experimental and clinical studies,⁷⁻¹¹ two major steps involving the mechanisms of resolution or repair of vascular injury after PTCA have been proposed. In the early phase after PTCA (immediately to a few days after PTCA), platelets adhere to the vascular injury site. Subsequently platelets release several factors that cause vascular repair and smooth muscle cell proliferation. At the same time, arterial injury and platelet accumulation can activate the coagulation system and impair the fibrinolytic system, leading to intravascular thrombus formation. In the late phase (a few days to several weeks after PTCA), mitogenic factors released from platelets, monocyte, endothelium and smooth muscle cells stimulate smooth muscle cell proliferation and migration to the area of vascular injury, which finally