

# Systemic Thrombolysis in Acute Stroke After Protamine-Reversal of Anticoagulation with Low-Molecular-Weight Heparin

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## Abstract

**Introduction:** Intravenous thrombolysis may be withheld due to current exclusion criteria even if the patient arrives at hospital in time. However, under certain circumstances, some of these contraindications could be eliminated.

**Case Presentation:** We report a systemic thrombolysis after reversal of anticoagulation with protamine sulfate in an acute stroke patient with suspected subacute non-ST-segment elevation myocardial infarction (NSTEMI) receiving full-dose low-molecular-weight heparin (LMWH).

**Conclusions:** Considering the fact that only less than 10% of all acute strokes are eligible for intravenous thrombolysis, in particular circumstances and weighing a risk-benefit ratio, elimination of certain exclusion criteria could be a reasonable method to decrease the number of patients who currently fail to receive adequate treatment.

**Keywords:** Thrombolytic Therapy, Stroke, Low-Molecular-Weight Heparin, Protamine Sulfate

## 1. Introduction

Although latest guidelines (1) endorse endovascular intervention in highly selected patients, since its US FDA approval in 1996, intravenous recombinant tissue-type plasminogen activator (rtPA, alteplase) remains the mainstay of acute ischemic stroke treatment within 3 - 4.5 hours after symptom onset. However, exclusion criteria may preclude systemic thrombolysis in acute stroke even if the patient arrives at hospital in time. Nonetheless, under certain circumstances, with adequate medical interventions and weighing a risk-benefit ratio some of these contraindications could be eliminated.

## 2. Case Presentation

A 70-year-old male patient was admitted to hospital due to progressive circulatory decompensation starting two weeks earlier. As blood tests (slightly elevated cardiac necroenzymes), echocardiogram (new atrial fibrillation [AF]) and echocardiography (diffuse hypokinesis with inferoseptal akinesis) suggested subacute non-ST segment elevation myocardial infarction (NSTEMI), coronarography was performed showing normal coronary circulation. In consequence of the previously unknown AF, anticoagulation with therapeutic doses of low-molecular-weight heparin (LMWH; 1 mg/kg enoxaparin sodium twice daily) was

initiated subcutaneously. During hospitalization, the patient was noticed with somnolency, dysarthria, severe left-sided hemiparesis and neglect early in the morning (national institutes of health stroke scale [NIHSS] Score: 9). The last time he was seen symptom-free had been 3 hours earlier. An urgent noncontrast CT scan of the brain did not contraindicate systemic thrombolysis. As approximately 12 hours since the last LMWH application had already passed, 6000 IU protamine sulfate was administered intravenously to reverse previous anticoagulation. After obtaining informed consent, systemic thrombolysis with 0.9 mg/kg rtPA (70 mg alteplase) was initiated. After the procedure only left-sided central facial palsy and mild paresis of the left upper limb were present (NIHSS Score: 3). A 24-hour control CT scan showed no new lesions. Cardiac embolization was assumed as the etiology of stroke. After two weeks spent in hospital, the patient was transmitted to a cardiac rehabilitation facility, which he left three weeks later with a modified Rankin Score (mRS) 1. Acenocoumarol and clopidogrel were administered as antithrombotic therapy.

## 3. Discussion

Myocardial infarctions (MI) are followed by an increased risk of stroke (2). As acute stroke patients with recent myocardial ischemia pose a risk for hemoperi-

cardium after treatment with thrombolytic drugs, current thrombolysis guidelines rate recent MI (within previous 3 months) as a relative exclusion criterion (3). Fibrinolytic therapy during heparin anticoagulation is followed by an increased risk of bleeding (4). Nevertheless, guidelines do not declare the opportunity of systemic thrombolysis after certain premedication. Enoxaparin has a half-life of roughly 4.5 hours. In our case, 12 hours have already passed since the last enoxaparin dosage, which means the administered antidote could effectively reverse the remaining LMWH activity. Considering the possibility that prevention of bleeding or hemopericardium had no correlation with the reversal of anticoagulation, such treatment should only be applied on a case-by-case basis with individual decision making. Successfully performed thrombolysis preceded by protamine sulfate administration after unfractionated heparin (UFH) anticoagulation has already been reported (5). However, this is the first case with prior full-dose LMWH treatment. Considering the fact that only less than 10% of all acute strokes are eligible for systemic thrombolysis (6), elimination of certain contraindications at least in particular situations could be a reasonable method to decrease the number of patients who fail to receive adequate treatment due to current exclusion criteria.

#### Footnote

**Authors' Contribution:** All authors contributed sufficiently to the content of the manuscript.

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