

## Very Early Carotid Endarterectomy After Intravenous Thrombolysis

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### WHAT THIS PAPER ADDS

The timing of carotid endarterectomy (CEA) after intravenous thrombolysis is a controversial issue. Some reports indicate that the surgery soon after thrombolytic therapy is safe. This case series suggests that CEA could be performed very early after thrombolysis, to reduce the risk of recurrence and to save the ischaemic penumbra and improve clinical outcome.

**Objective/Background:** The timing of carotid endarterectomy (CEA) after thrombolysis is still a matter of debate. The aim of this study was to analyse a cohort of patients undergoing urgent endarterectomy after intravenous thrombolysis for acute ischaemic stroke.

**Methods:** This was an observational study. Prospective databases were reviewed and matched to identify patients who underwent CEA early after intravenous thrombolysis (2009–14). The focus was carotid surgery performed within 12 hours of stroke onset in patients with a high grade ( $\geq 70\%$ ) symptomatic carotid stenosis, associated with vulnerable plaques or stroke in evolution, and evidence of a significant salvageable ischaemic penumbra on perfusion computed tomography scan. Demographic and clinical information, as well as data on relevant outcomes were extracted.

**Results:** Thirty four consecutive stroke patients who underwent CEA within 2 weeks of thrombolysis for acute ischaemic stroke and ipsilateral high grade carotid stenosis were identified. In 11 patients the surgical procedure was performed within 12 hours of the onset of symptoms. All patients showed a clinical improvement after combined treatment. The 3 month outcome was favourable (modified Rankin Scale  $\leq 2$ ) in 10 patients. No haemorrhagic complications were registered. There was neither peri-operative stroke nor stroke within 3 months of surgery. One patient died from acute myocardial infarction 3 days after intervention.

**Conclusion:** This experience suggests that very early CEA after thrombolysis, aimed at removing the source of potential embolisation and restoring blood flow, may be safe and can lead to a favourable outcome.

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### INTRODUCTION

Intravenous (IV) thrombolysis for hyperacute ischaemic stroke treatment is accepted worldwide.<sup>1,2</sup> The major risk of IV recombinant tissue plasminogen activator (rtPA) treatment remains intracerebral haemorrhage.<sup>1,2</sup> Although the half-life of rtPA is very short, the effect on the coagulation pathway seems to be prolonged.<sup>3</sup>

The role of carotid endarterectomy (CEA) for severe carotid stenosis is widely established.<sup>4–7</sup> Evidence suggests that the greatest benefit of surgery in reducing the risk of

recurrent stroke is in the first 2 weeks after the index event,<sup>6,7</sup> and the sooner CEA is performed the higher its preventive role.<sup>8</sup> Timely cerebral reperfusion, and the prevention of early recurrent strokes and distal embolism from carotid plaques are key factors in treating patients who have severe ipsilateral internal carotid artery stenosis (CAS). Safety issues, mostly related to the risk of intracerebral haemorrhage and reperfusion injury, are also of great importance for successful interventions.

Although early CEA following thrombolysis seems to be safe,<sup>9–16</sup> the best timing of surgery after IV thrombolysis (IVT) is still a matter of debate. In particular, few data are available on urgent CEA, aimed not only at reducing the risk of recurrence, but also at achieving neurological improvement by reperfusion of the ischaemic penumbra.

The aim of this study was to analyse a cohort of patients with acute ischaemic stroke undergoing CEA within 12 hours of symptoms onset.

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## METHODS

The prospective databases of thrombolysis and carotid surgery of the (Azienda Ospedaliera-Universitaria, Ferrara, Ferrara-Cona, Italy) were reviewed (2009–14) in order to identify patients with stroke and CAS who underwent IVT, and CEA after IVT. All patients were treated with IV rtPA according to national and international guidelines.<sup>17,18</sup> The protocol adopted for IVT is summarised in Table 1. Thereafter, patients with CAS > 50% (North American Symptomatic Carotid Endarterectomy Trial method<sup>5</sup>) on the symptomatic side were considered for CEA within 2 weeks. Of these, patients with high grade symptomatic carotid stenosis ( $\geq 70\%$ ) associated with vulnerable plaques (i.e., soft plaques, intraplaque haemorrhage, or ulcerated surface) and/or patients with stroke in evolution, underwent CEA within 12 h, provided that the neuro-radiological criteria for IVT were fulfilled (no evidence of haemorrhagic transformation and an Alberta Stroke Program Early CT Score [ASPECTS] score > 7). Perfusion computed tomography (CT) scan evidence of a significant salvageable ischaemic penumbra was also a requirement for very early CEA after IVT.

According to protocol, patients with symptomatic carotid stenosis  $\geq 70\%$ , with stable plaques (defined as plaques with a regular and smooth surface, and uniform and homogeneous echogenicity) and neurological status were scheduled to undergo CEA between 12 and 48 h, while patients with carotid stenosis  $\geq 60\%$  and stable plaques were treated within 14 days, according to the current guidelines. Finally, those with stenosis between 50% and 60% associated with uncomplicated plaques ( $n = 7$ ), patients with complete occlusion ( $n = 18$ ), and patients at high operative risk were treated with IVT only ( $n = 3$ ). To exclude haemorrhagic transformation, all patients routinely underwent brain CT after rtPA infusion.

A panel consisting of a neurologist, a neuro-radiologist, and a vascular surgeon discussed the therapeutic approach and the timing of CEA for each patient.

All surgical procedures were performed under general anaesthesia by experienced vascular surgeons. A temporary vascular indwelling *shunt* was used routinely, and a bolus of 5000 units of unfractionated heparin was given before carotid clamping. The longitudinal arteriotomy was closed by primary closure or prosthetic patch. Resection of the vessel,

**Table 1.** Intravenous thrombolysis (IVT) and carotid endarterectomy (CEA) protocol for acute ischaemic stroke.

IVT	
Inclusion criteria	Age 18–80 y Ischaemic stroke with a measurable neurological deficit Onset of symptoms within 4.5 h
Exclusion criteria	Unknown time of symptom onset Minor or rapidly improving symptoms Severe stroke as assessed clinically (stupor or coma, NIHSS score > 25) or ASPECTS $\leq 7$ History or evidence of intracranial haemorrhage, clinical suspicion of subarachnoid haemorrhage Seizure at the onset of stroke Stroke or serious head trauma within the previous 3 months Previous stroke and diabetes mellitus Known intracranial arteriovenous malformation, neoplasm, or aneurysm Major surgery or severe trauma within the previous 3 months Use of heparin within the previous 48 h, with prolonged APTT, oral anticoagulant treatment (INR > 1.7) Platelet count <100,000/mm <sup>3</sup> , disorders associated with an increased risk of bleeding Systolic pressure >185 mmHg or diastolic pressure >110 mmHg, or aggressive treatment necessary to reduce blood pressure to these limits Blood glucose <50 mg/dL or >400 mg/dL Recent (<10 days) traumatic external heart massage, obstetrical delivery, or puncture of a non-compressible blood vessel Manifest or recent severe or dangerous bleeding, bacterial endocarditis, pericarditis, acute pancreatitis, ulcerative gastrointestinal disease during the last 3 months, oesophageal varices, arterial aneurysm, arterial/venous malformation, neoplasm with increased bleeding risk, severe liver disease
Treatment	IV rTPA, 0.9 mg/kg (upper dosage 90 mg), 10% administered as a bolus, the remainder by continuous infusion over 1 h
Early CEA	
General criteria	No evidence of haemorrhagic transformation, and ASPECTS score >7 after IVT
Timing	As soon as possible within 12 h: high grade symptomatic carotid stenosis ( $\geq 70\%$ ), vulnerable plaques and/or stroke in evolution. Evidence of significant ischaemic penumbra on perfusion CT scan Between 12 and 48 h: high grade symptomatic carotid stenosis ( $\geq 70\%$ ), stable plaque, and neurological condition After 48 h and within 14 d: carotid stenosis $\geq 60\%$ and stable plaque

*Note.* NIHSS = National Institutes of Health Stroke Scale; ASPECTS = Alberta Stroke Program Early CT Score; APTT = activated partial thromboplastin time; INR = international normalised ratio; IV = intravenous; rTPA = recombinant tissue plasminogen activator; CT = computed tomography.

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