Supplementary Material

List of participating institutions

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6. Department of Neurology, Sana Hospital Lubeck, Lübeck, Germany
7. Neurology Department and International Clinical Research Center, St. Anne's Hospital, Brno, Czech Republic
8. Department of Neurology, University Hospital of Alexandroupolis, Democritus University of Thrace, Alexandroupolis, Greece
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Supplementary methods

Per study protocol, we excluded from further evaluation patients with: (1) hypodensity on computed tomography (CT) scan with unknown stroke onset time; (2) acute intracranial hemorrhage (ICH) on baseline CT examination; (3) history of ICH or subarachnoid hemorrhage; (4) history of intracerebral malignancy; (5) absent temporal windows on pre-bolus transcranial Doppler (TCD) examination; (6) pre-treatment systolic blood pressure equal or more than 185 mm Hg or diastolic blood pressure equal or more than 110 mm Hg not responding to antihypertensive therapy; (7) other standard institutional or regional contra-indications to intravenous thrombolysis (IVT); (8) patient or substitute decision-maker refusal to give informed consent to participate in the study; (9) patients treated directly with endovascular therapies (without receiving tissue plasminogen activator [tPA] preatreament); and (10) patients in whom tPA was initiated in other settings before being transferred to the participating in the current study institutions ("drip and ship" patients). Concomitant severe stenosis or occlusion of the proximal internal carotid artery (ICA), established by either carotid duplex ultrasonography, magnetic resonance angiography, CT angiography, or digital subtraction angiography of the neck vessels was not an exclusion criterion and did not preclude patient enrollment into the study as long as patient has proximal intracranial occlusion on their baseline diagnostic TCD.

Arterial occlusion at baseline TCD assessment was defined as residual thrombolysis in brain ischemia (TIBI) flow grades 0–3, complete recanalization was diagnosed if flow improved to TIBI grades 4–5 and partial recanalization was identified if flow improved by one grade or more from the baseline but not to grades 4–5 on the TIBI scale. Patients with re-occlusion following IVT were diagnosed, if after an improvement by at least one TIBI flow grade during TCD monitoring the residual flow worsens and an arterial occlusion is diagnosed at the end of monitoring with TIBI grades 0–3. In patients with concomitant and persisting severe stenosis or occlusion of the proximal ICA, complete recanalization of the middle cerebral artery (MCA) was considered if TCD showed low-resistance waveforms (TIBI 2 or greater) over both M1 and M2 segments, with an improvement in mean flow velocity to more than 20 cm/seconds.

The following baseline characteristics were included as candidate variables in logistic regression models: age (per 1-year increase), male sex, National Institutes of Health Stroke Scale score (per 1-point increase), hypertension, diabetes mellitus, atrial fibrillation, hypercholesterolemia, coronary artery disease, baseline TIBI score 0–1, isolated ICA or tandem ICA/MCA occlusion, systolic blood pressure before tPA-bolus (per 10 mm Hg increase), diastolic blood pressure before tPA-bolus (per 10 mm Hg increase), mean serum glucose before tPA-bolus (per 10 mg/dL increase), endovascular reperfusion therapies (intra-arterial thrombolysis and/or mechanical thrombectomy), time from symptom onset to tPA-bolus (per 10-minute increase), and early (within 1-hour from tPA-bolus) recanalization. The variables that were significantly ($P<0.05$) associated with the outcome events in the univariable analyses were selected for inclusion in the multivariable models.