László Csiba (Department of Neurology, Debrecen University, Hungary): Endovascular therapy: Start with IV tPA or go directly to the catheter lab?

Large vessel occlusions represent ca.10-15% of all ischemic stroke. There is strong evidence for efficacy for thrombectomy in adjunct to i.v. fibrinolysis, when compared with i.v. fibrinolysis alone. Recently, 5 multicenter, prospective studies have confirmed the benefit of mechanical thrombectomy (MET).

The results of recent studies comparing the efficacy of combined intervention (intravenous + endovascular therapy versus intravenous only) are as follow (we focus only on those studies that included 100% iv. thrombolysis patients as control group): The IMS-III included patients with intravenous t-PA and additional endovascular therapy or intravenous t-PA alone, in a 2:1 ratio. The primary outcome measure was a modified Rankin scale score of 2 or less. Unfortunately, The IMS trial had inhomogenous MET group using four endovascular interventions: intraarterial t-PA (51 patients), MicroSonic SV infusion system with intraarterial t-PA (14 patients), Merci retriever (77 patients), Penumbra System (39 patients), and Solitaire FR revascularization device (4 patients). There was no significant difference between the endovascular-therapy and intravenous t-PA groups in the overall proportion of participants with a modified Rankin score of 2 or less (40.8% and 38.7%, respectively. The trial showed similar safety outcomes and no significant difference in functional independence with endovascular therapy after intravenous t-PA, as compared with intravenous t-PA alone. (1)

EXtend-IA investigators applied 0.9 mg/kg of t-PA in less than 4.5 hours after the onset of ischemic stroke either to undergo endovascular thrombectomy with the Solitaire FR or to continue receiving alteplase alone. All the patients had occlusion of the internal carotid or middle

cerebral artery and evidence of salvageable brain tissue and ischemic core of less than 70 ml on computed tomographic (CT) perfusion imaging.
All patients received alteplase at a dose of 0.9 mg per kilogram as standard care. Endovascular therapy improved the functional outcome at 90 days, with more patients achieving functional independence (score of 0 to 2 on the modified Rankin scale, 71% vs. 40%; P=0.01). There were no significant differences in rates of death or symptomatic intracerebral hemorrhage. (2)

The SWIFT PRIME Investigators assigned stroke patients to t-PA alone (control group) or to undergo endovascular thrombectomy with the use of a stent retriever within 6 hours after symptom onset. Patients had confirmed occlusions in the proximal anterior intracranial circulation and an absence of large ischemic-core lesions. The rate of functional independence (modified Rankin scale score, 0 to 2) was higher in the intervention group than in the control group (60% vs. 35%, P<0.001). There were no significant between-group differences in 90-day mortality (9% vs. 12%, P=0.50) or symptomatic intracranial hemorrhage (0% vs. 3%, P=0.12) (3)
The other studies (McClean, REVASCAT, Escape etc) have also confirmed the beneficial effect of mechanical intervention (4).
The recent positive RCTs share same common features: patients with a high NIHSS and ASPECT score of 8–10 were included, and most commonly in the control group there was proof of vessel occlusion required. In general the time to endovascular treatment was below 4.5h and cotreatment with rtPA occurred in more than 90% of all cases. (5).

The recently published Karolinska guideline summarizes: " Mechanical thrombectomy, in addition to intravenous thrombolysis within 4.5 h when eligible, is recommended to treat acute stroke patients with large artery occlusions in the anterior circulation up to 6 h after symptom onset (Grade A, Level 1a, KSU Grade A).

Mechanical thrombectomy should not prevent the initiation of intravenous thrombolysis where this is indicated, and intravenous thrombolysis should not delay mechanical thrombectomy (Grade A, Level 1a, KSU Grade A). (6)

Similar statement has been formulated in the American guideline:

"Patients eligible for intravenous r-tPA should receive intravenous r-tPA even if endovascular treatments are being considered *(Class I; Level of Evidence A)*. (7)

But recently Kass-Hout T et al. analysed patients with acute large artery occlusion. Forty-two received endovascular therapy in combination with IV thrombolysis (bridging group), and 62 received endovascular therapy only. The Favorable outcome (mRankin <2 at 90 days), did not differ between the bridging group and the endovascular-only group (37.5% and 32.76%; P=0.643). There was no difference in mortality rate (19.04% and 29.03%; P=0.5618) and sICH rate (11.9% and 9.68%; P=0.734). A significant difference was found in mean time from symptom onset to treatment in the bridging group and the endovascular-only group (227±88 min vs. 125±40 min; P<0.0001). They concluded, that Combining IV thrombolysis with endovascular therapy resulted in similar outcome, revascularization, sICH, and mortality rates compared with endovascular therapy alone. (8)
So, the iv. part could be omitted and the patients should go directly to the catheter lab.
but the final answer could be given by a prospective, randomized, multicenter trial with the following criteria.

1. Acute ischemic stroke patients 4,5 hours after stroke.
2. All patients should undergo CT or MR angiography.
3. Only patients with large vessel occlusion (ICA, MCA occlusion) should be randomized.

4. One group of patients should be treated only with mechanical thrombectomy as soon as possible.
5. The other group of patients should receive first iv. thrombolysis with additional mechanical thrombectomy.
6. mRankin scale after 3 months and complications should be compared.

This study will finally answer the question if a large vessel occlusion patient should be transferred directly to the catheter lab or start first with iv. thrombolysis.

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