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The 14th International Symposium on Thrombolysis, Thrombectomy and Acute Stroke Therapy (TTST) took place in Houston, Texas on October 21st and 22nd, 2018. Attended by over 150 invited global experts, the objective of TTST 2018 was to explore the changing landscape of acute ischemic stroke therapy and address current controversies in thrombolysis and thrombectomy including expanding access and systems of care with global relevance. This manuscript summarizes the proceedings of TTST 2018. The key points of each session are listed below, and the full text of presentations and discussion in the on-line supplement.

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Changing demographics of stroke and impact on thrombolysis and thrombectomy

Stroke incidence is predicted to increase by two-fold in the world population, particularly in the elderly, and the current racial profile is changing with Hispanics affected more than Whites. Despite continuous efforts in controlling cardiovascular risk factors, the growth and aging of the world population, coupled with the socioeconomic inequality, are likely to lead to an increase in large vessel occlusion (LVO) stroke. Unfortunately, thrombolysis and thrombectomy rates worldwide are unmatched to the burden of stroke.

Thrombolysis—where, when, and who?

As thrombolysis remains a viable treatment for patients, there is an urgent demand to extend the available neurology expertise to physicians, and other advanced providers, involved in stroke care. Restructuring minimal requirements for thrombolysis may help in extending this treatment modality outside specialized centers through Mobile Stroke Units (MSUs) and Telemedicine.

Thrombectomy—where, when, and who?

The limited access to high-quality endovascular therapy (EVT), in both developed and developing nations, represents an issue for stroke systems of care and thrombectomy providers. Standardization of pre-hospital notifications and pre- and inter-hospital routing systems may increase access to thrombectomy. Restructuring hospital certification and training standards on neurointervention will likely ensure that patients are treated by competent providers and capable hospitals, but data to evaluate the effect of inter-operator variability and hospital volume on patient outcomes is missing.

Structuring Stroke Systems of Care

Stroke systems of care need to be revolutionized to increase availability to EVT by enhancing access to care in the pre-hospital environment, developing clinical tools for evaluating the presence of LVO, and by decreasing the gap between patient and provider through the use of telemedicine and MSUs.

Summary of new data from clinical trials of thrombolysis
The WAKE-UP trial compared the likelihood of excellent functional outcome for tPA vs no tPA in patients presenting with unknown stroke onset and a DWI/FLAIR mismatch on MRI. Better outcome was observed with tPA (mRS 0-1 in 53% vs 42%, P = 0.02), with no significant increase in symptomatic ICH (2%).

The EXTEND trial evaluated patients presenting within 4.5-9 hours from stroke onset, including those presenting with a wake-up stroke, selected based on the penumbra calculated by automated CT perfusion imaging software. The group treated with tPA achieved a significantly better functional outcome at three months.

Future of thrombolysis

With the surge of tenecteplase and the use of low-dose tPA, thrombolysis is being tested for preserved safety and efficacy in additional patient cohorts. Novel lytic, anticoagulant and cytoprotective therapies show promising results in enhancing thrombolytic treatments, minimizing brain injury, and improving recanalization rates while reducing the risk of intracranial hemorrhage.

Summary of new data from clinical trials of thrombectomy

The BEST trial demonstrated no clear benefit of mechanical thrombectomy over medical therapy alone in the treatment of basilar artery occlusion within 8 hours of stroke onset. Significantly better outcomes were found after adjusted analysis in the thrombectomy group, but results may have been confounded by high cross-over rates.

The AURORA Consortium has challenged the “time is brain” concept to allow patients with favorable collaterals and slow infarct growth to receive reperfusion therapy even in very late time windows, as recent data from DEFUSE3 suggest that in around 20% of patients, a favorable imaging profile persists for up to 40 hours after the time of last known well.

Future of thrombectomy

Recent data and clinical trials may show benefit in including patients with a large core and those presenting in the late time window for thrombectomy. Meanwhile, the capacity to revascularize occluded vessels and reduce core and penumbra progression becomes more relevant by the development of neuroprotective strategies, including NA-1, uric acid, and hypothermia. New devices for thrombectomy should focus on achieving effective reperfusion on the first pass for clot retrieval, and improve treatment of intracranial atherosclerotic disease.

Imaging selection

Determining the optimal neuroimaging protocol to assess for thrombolytic and endovascular therapy is challenging, and large imaging databases to define target patient profiles is required. Practical consideration in terms of availability and expertise may be the greatest deciding factor for imaging protocols.

Other new approaches
Ongoing approaches to improve functional outcome and treatment availability of thrombolysis and thrombectomy include remote ischemic preconditioning, enhancing collaterals through oxygen carriers, sonothrombolysis, targeting the multiplicity of the neurovascular unit, stem cells, and a better understanding of clot composition.