Advances in minimally invasive treatment of hemorrhagic and ischemic stroke

Cerebrovascular diseases, including ischemic and hemorrhagic strokes, affect more than 6 million US adults annually. Strokes cause high rates of morbidity and mortality due to the central nervous system’s sensitivity to disruptions in blood flow, and are refractory to traditional surgical interventions. A variety of minimally invasive surgical and endovascular approaches have recently been developed to improve patient outcomes following stroke.

Hemorrhagic strokes, also referred to as intracranial hemorrhages (ICH), have clinical outcomes largely dependent on hemorrhage location, size, and secondary peri-hematomal edema (Rennert et al., 2015). In theory, clot evacuation addresses local mass effect and enhances survival of edematous parenchymal tissue (Rennert et al., 2015), however, multiple clinical trials have failed to show a definitive benefit for surgical hematoma evacuation following ICH (Rennert et al., 2015). The largest of these is the 2005 International Surgical Trial in Intracerebral Haemorrhage (STICH) trial (Mendelow et al., 2005), wherein 1,033 patients with spontaneous lobar and/or basal ganglia ICH were randomly selected for surgical evacuation within 24 hours of presentation, or initial conservative treatment. In this study there was no significant difference in favorable outcomes across groups (26% vs. 24%, P = 0.4), yet subgroup analysis revealed that patients with superficial hematomas (≤ 1 cm from the cortical surface) may benefit from surgery, supporting the hypothesis that decreasing secondary neurologic injury from manipulation of injured parenchymal tissue during clot removal critically affects outcomes. Current guidelines thus recommend consideration of open surgical evacuation only in specific clinical scenarios, such as lobar clots > 30 mL and within 1 cm of the cortical surface. In this setting, there has been a recent push to develop minimally invasive approaches for ICH removal.

One such minimally invasive approach is stereotactic surgery (i.e., using an imaging based three dimensional roadmap for surgical localization) combined with intra-clot injection of thrombolytic agents, such as tissue plasminogen activator (tPA). The Minimally Invasive (Stereotactic) Surgery plus tPA for ICH Evaluation (MISTIE) randomized clinical trials have demonstrated the safety and effectiveness of this approach for reducing clot and perihematomal edema (Rennert et al., 2015), with a larger phase III clinical efficacy trial currently ongoing. Stereotactic endoscopic evacuation of intraventricular hemorrhages (IVH) in ICH is also being explored, as is targeted infusion of intraventricular thrombolytics based on pre-clinical and clinical safety data (Gaberel et al., 2014; Rennert et al., 2015).

Endoscopic techniques (i.e., burr hole craniotomy with direct hematoma visualization/removal through a sheath) are similarly appealing due to minimization of secondary neurologic injury from surgical manipulation. Direct hematoma visualization with this approach also allows for identification and real-time treatment of the original bleeding source, and is associated with improved evacuation rates compared to stereotactic aspiration (Stereotactic) surgery. Moreover, this approach is more suited for deeper hematomas, with preliminary data showing improved clot evacuation rates and post-operative neurologic status compared to open surgery in patients with hemorrhage in deeper brain structures such as the putamen and thalamus (Nagasaka et al., 2011).

New technology combining real-time neuronavigation with neuroendoscopy has also been developed and trialed for ICH evacuation (Rennert et al., 2015). The initial multi-center clinical experience with one such system was recently reported, with twenty-nine patients with lobar, basal ganglia, and brainstem hemorrhages (including six with the poor prognostic finding of intraventricular extension) treated with a nearly 92% technical success rate and low morbidity and mortality (Spiotto et al., 2015). While general clinical guidelines for endoscopic ICH evacuation are currently supplanting hemorrhages ≥ 30 mL with a goal of <15 mL post-operative residual, combined neuroendoscopy/neuroendoscopy has already been integrated into the senior

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Figure 1 Endoscopic hematoma evacuation.
Representative pre-operative non-contrast computed tomography (CT) axial (A) and sagittal (B) images of a 63-year-old female with a left basal ganglia hemorrhagic conversion of an ischemic stroke. The patient was treated via navigated neuroendoscopic hematoma evacuation (C) using a frontal craniotomy (trajectory indicated by the red arrow in [B]). Post-operative imaging (D) confirmed a 94% reduction in clot size.

Figure 2 Schematic illustration of the hypothesis that thrombectomy-associated iatrogenic endothelial cell injury can influence stroke outcomes.

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References


Figure 3 In vitro live cell model demonstrating the heterogeneous effects of thrombectomy devices on the endothelium.
(A) Representative 3D reconstructions of full vessel scans post-thrombectomy demonstrating endothelial injury patterns. (B) Correlation between fluorescent whole vessel scans and endothelial cell density, confirming the fidelity of the model. (C) Cumulative in vitro post-thrombectomy cell area comparisons across devices, providing data for future device design. Figure reproduced with permission from Stroke (Teng et al., 2015).


