Most notable research with neurovascular ultrasound in 2005 focused on treatment amplification,\textsuperscript{1–3} identification of high-risk patients with intracranial stenoses,\textsuperscript{4} increased carotid intima-media thickness,\textsuperscript{5,6} monitoring repairs of ascending aorta,\textsuperscript{7} carotid stenting,\textsuperscript{8,9} patient selection and outcomes with percutaneous patent foramen ovale closure,\textsuperscript{10} and acute stroke treatment.\textsuperscript{11–15}

Clopidogrel and Aspirin for Reduction of Emboli in Symptomatic Carotid Stenosis (CARESS) was a randomized, double-blind study in subjects with recently symptomatic ≥50% carotid stenosis. Combination therapy with clopidogrel and aspirin was more effective than aspirin alone in reducing asymptomatic microembolization on transcranial Doppler (TCD) within days of treatment initiation. This controlled trial demonstrated feasibility of TCD emboli detection to evaluate the efficacy of antiplatelet therapy in multicenter studies. Emboli count may become a surrogate marker of stroke risk if validated in future studies,\textsuperscript{16} and this technology could potentially be a part of diagnostic work-up to individualize selection of antiplatelets given documented resistance in some patients.\textsuperscript{17}

Symptomatic intracranial disease remains a global challenge with yet another study showing annual risk of stroke in excess of 12%.\textsuperscript{4} Although ultrasound can be used to identify patients with significant intracranial disease, the challenge remains to find effective secondary prevention strategies.

Preclinical manifestation of high cardiovascular risk can be ascertained with duplex measurement of the intima-media thickness (IMT) in the carotid artery on the neck. Reports demonstrate the ability of IMT to discriminate individuals at low and high 1-year event risk,\textsuperscript{5} and link increased IMT to inflammation as a potential new target in stroke prevention.\textsuperscript{6}

TCD provides real-time monitor to detect hypoperfusion, embolism and thrombosis during surgical and stenting procedures. Most encouraging results were obtained in a cohort of patients undergoing urgent repairs of ascending aortic aneurysms.\textsuperscript{7} TCD detection of successful flow reversal in the middle cerebral arteries (MCA) during brain retroperfusion resulted in decreased perioperative mortality.\textsuperscript{7} Importantly, the authors adjusted pump flow rates and revised surgical procedures to achieve flow reversal on TCD if standard settings failed to do so.\textsuperscript{7}

Several predictors of stroke and transient ischemic attack associated with stenting were demonstrated in a prospective study.\textsuperscript{8} In addition to baseline patients' characteristics, multiple (>5) showers of microemboli at postdilation after stent deployment, particulate macroembolus, and massive air embolism detected by TCD as well as angioplasty-induced asystole and prolonged hypotension with a >70% reduction of MCA flow velocities were independently associated with cerebral deficits.\textsuperscript{8} Another study pointed to the link between MCA flow velocity and likelihood of decreased clearance of cerebral emboli during stenting.\textsuperscript{9} These observations should prompt the use of this technology to help develop safe procedures and train new generation of interventionalists.

On a controversial subject of patent foramen ovale closure and migraine, provocative findings were reported by a group from Seattle\textsuperscript{10} using a new exponential classification of right-to-left shunts,\textsuperscript{18} and power-motion TCD to select patients for cardiac catheterization skipping echocardiography for shunt detection. This single-center experience and classification need to be replicated in a multicenter prospective trial.

Nonimaging 300 KHz ultrasound has been tested in the TRanscranial low-frequency Ultrasound-Mediated thrombolysis in Brain Ischemia (TRUMBI) trial.\textsuperscript{2} The trial was terminated after 26 patients were enrolled because of 36% rate of symptomatic hemorrhage in the target group and no signal of efficacy on early recanalization or clinical outcomes at 3 months.\textsuperscript{2} The trial demonstrated bioeffects of mid-KHz ultrasound that promote bleeding, including brain areas not affected by ischemia.\textsuperscript{2} Further research should determine whether “standing” pressure waves and endothelial disruption may cause these adverse effects. If confirmed in in vivo models, this will have implications on design of future KHz-based or multifrequency systems.

Previously demonstrated safe augmentation of TPA-associated thrombolysis with 2 MHz TCD\textsuperscript{19} can be further enhanced with addition of gaseous microbubbles.\textsuperscript{3,14} Early complete MCA recanalization rate on TCD can be achieved in up to 55% when TPA is given with 2 MHz TCD and microbubbles.\textsuperscript{3} This approach is now tested in a controlled multinational clinical trial of perflutren-containing microbubbles.
Finally, neurovascular ultrasound can be used in multimodal patient selection for thrombolysis at an extended time window to detect and possibly predict arterial reocclusion and, by quickly performing both carotid duplex and TCD, to identify patients with lesions amenable to intervention with excellent agreement with urgent catheter angiography. Recent advances in this field lead to level 1, type A evidence that TCD and carotid duplex are recommended elements of a comprehensive stroke center.

References

Key Words: TPA ■ ultrasonography, Doppler, transcranial ■ stroke ■ thrombolysis ■ outcomes