Effectiveness of endovascular therapy in question

Surprise Stroke Study Conclusions Won’t Change Care – Yet

By Todd Neff

Sometimes science seems to contradict common sense. Physicists have proven, for example, that atoms can be in two places at once, spookily entangled in time and space. Now physicians tell us that physically removing blood clots from arteries in a stroke-compromised brain has no obvious impact on the outcomes of those patients.

Endovascular (or intra-arterial) treatment seems to work particularly well for patients with three types of blockages, Kumpe said: in the proximal large arteries, in the middle cerebral artery’s M1 segment, and in the basilar artery at the base of the brain. All are locations for large clots that tPA has a hard time dissolving, he explained. Past studies, though not randomized, and his experience, he said, have shown that using endovascular therapy

Three prominent studies the New England Journal of Medicine published Feb. 8 (Interventional Management of Stroke (IMS) III, SYNTHESIS Expansion, MR RESCUE) all found that the endovascular removal of stroke-causing blockages in concert with an intravenous dose of clot-dissolving tissue plasminogen activator (tPA) was no better for a patient’s recovery at 90 days than using tPA alone.

“It’s frankly surprising that there wasn’t any benefit,” said David Kumpe, MD, the University of Colorado School of Medicine’s chief of neurointerventional radiology, who has performed many endovascular procedures for stroke victims at University of Colorado Hospital.

The numbers. Kumpe and other UCH stroke specialists have watched the procedure restore blood flow to starved brain tissues. But the three studies, which involved more 1,100 patients, found little or no statistical benefit. The largest of them, IMS III, enrolled 656 of a targeted 900 patients at 56 sites. It found the rate of disability-free survival at 90 days to be 40.8 percent among patients who received tPA plus endovascular therapy. That compared with a 38.7 percent rate among those receiving tPA only. Noting the statistically insignificant difference, researchers shut down the study early.

At UCH there were 530 stroke alerts at from January 2012 to mid-February 2013, Kumpe said. Of those, 47 patients received tPA, with 17 of them – or 36 percent— also receiving endovascular treatment, which uses tool-tipped catheters inside an artery to mechanically extract, suck, or squeeze the clot out of the way with a tiny balloon or bust it with doses of directly applied tPA.

Those treatments are reserved for the most serious cases, Kumpe emphasized. “We’re quite selective in whom we treat,” he said. “We treat patients with big artery plugs, and if they don’t have that, we don’t treat them.”

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to clear these blockages works about 80 percent of the time. By comparison, tPA alone clears an M1 occlusion only about 25 percent of the time, he said.

“If you don’t alleviate the block, patients do badly. That has come up in almost every paper that has been published,” Kumpe said. “I don’t for one minute think that patients with these kinds of blockages don’t benefit from intra-arterial therapy.”

William Jones, MD, medical director of the hospital’s Stroke Program, said the study did cast a shadow on intra-arterial (IA) therapy, and that it showed that “just anybody who has a large-vessel clot isn’t necessarily going to do better with IA versus a combination of IA and IV tPA.”

But at the same time, the study lacked the scope to show the difference endovascular treatment makes for patients with, for example, very large distal carotid clots — of which UCH might see one or two a year, Jones said. Kumpe pointed to an analysis of IMS III subgroup data by University of Calgary neurologist Andrew Demchuk, MD, which showed endovascular treatment to improve prospects for those with certain other clots.

Given these sorts of wrinkles, Kumpe said he expects endovascular treatment to remain an option for UCH stroke patients until it’s definitively proven to be of no use.

Timing is everything. In an editorial accompanying the three articles, Medical University of South Carolina neurologist Marc Chimowitz, M.B., Ch.B., suggested that timing of recanalization — the reopening of stroke-blocked arteries in the brain — may have been decisive in the studies’ conclusions. If reopening arteries is critical and endovascular treatment does just that, why was there no benefit in two of the three trials and marginal benefit in the third? It could be that “even a 1-hour delay in the time to treatment negates the benefit of a higher recanalization rate with endovascular treatment,” he wrote. In other words, reopening blood flow to brain tissue that’s already dead does little good.

In the IMS III study, endovascular treatment could start as long as five hours after the stroke, well beyond the UCH Stroke Program goal of 90 minutes, Jones said.

“That’s really much too long — we should be attempting to get these patients into the IA suite much more rapidly,” he said. “The most important thing to keep in mind is if we’re going to continue to offer this to patients, we also have to have a sense of urgency.”

A subgroup analysis in the IMS III trial hinted — though not in a statistically significant way — that if intravenous tPA starts within two hours of a stroke and endovascular treatment happens within 90 minutes of the start of tPA, endovascular treatment may indeed help, Chimowitz added.

To truly get to the root of the question, it might take “a decision by the Centers for Medicare and Medicaid Services (CMS) to place a moratorium on reimbursement for endovascular treatment for acute ischemic stroke” — thus limiting endovascular therapy’s availability to clinical trials, Chimowitz said. That might spur recruitment and enable a clearer understanding of endovascular therapy’s effectiveness, he concluded.

But getting new trials started will be tough because CMS and other insurers do cover endovascular treatment for stroke, and families of stroke victims want no therapeutic stone left unturned. Kumpe said he therefore doesn’t believe conducting trials would win public favor, as it would deny treatment to the “vast majority” of endovascular stroke patients.

There are “few knowledgeable physicians who would subject their son, wife, husband, mother, or father” to a randomized trial when getting rid of the clot by endovascular means is an option, he concluded.