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EDITORIAL

Death and Destruction in the Intra-Arterial Battle with Acute Ischemic Stroke

The intra-arterial battle with acute ischemic stroke leaves a lot of death and destruction in its wake. Reviewing the casualties of the ongoing battle in the medical literature, we can begin to consider what must be done to reduce the death and disability in patients undergoing intra-arterial therapy. A recent study of the United States National Inpatient Sample[1] is a reasonable place to begin looking for morbidity and mortality results in the "real world." For all patients treated from 2006 to 2008, the rate of discharge to a long-term facility was 51%. The in-hospital mortality rate was 24%.[1] This indicates that in the "real world," a solid majority of 75% of patients that we treat with intra-arterial stroke therapy are having very bad outcomes. Outcomes in patients older than 65 years of age are even worse, with 85% having very bad outcomes.[1] The magnitude of this morbidity and mortality might come as a surprise to some in light of the numerous success stories we hear from our professional colleagues and in the media. Such success stories are meant to inspire us to treat these patients aggressively and also to inspire patients, their families, paramedics, and other health professionals to get these patients to specialized care as fast as possible. While we should continue to be inspired by the good outcomes, the patients with bad outcomes should be teaching us that we have a lot of room for improvement in our treatment paradigm.

One could certainly argue that the outcomes of disabled patients could have been even worse if those patients had not received intra-arterial therapy, but allow me to go out on a limb and assume that patients who were discharged to a long-term nursing home or died were not significantly helped by intra-arterial therapy. It is quite likely that patients who were discharged to a long-term nursing home or died had little or no chance of recovery when intra-arterial treatment was pursued (ie, recanalization was futile). This concept of futile recanalization has recently entered into the dialogue regarding intra-arterial stroke therapies.[2] Hussein et al[3] demonstrated that futile recanalization occurred in 49% percent of cases in their single center study. Nogueira et al[4] demonstrated that in several large registries of patients receiving intra-arterial therapy, outcome was significantly better with recanalization, with a chance of outcome of a modified Rankin Scale score of 0–2 in 29%–49% of those recanalized versus 7%–10% in those not recanalized. This comparison certainly shows improved outcome in patients who were successfully recanalized, but note that, as in the study by Hussein et al,[3] more than half of the patients who were recanalized did not have a good outcome. This situation is reminiscent of the old adage "The operation was a success, but the patient died" (or was permanently disabled). Perhaps half of patients currently undergoing intra-arterial ischemic stroke therapy could be spared futile therapy if we had better patient-selection methods. Treating patients with stroke who have no chance of recovery with intra-arterial therapy is analogous to treating patients with metastatic breast cancer with a lumpectomy. Futile recanalization is also a problem for randomized trials meant to show the efficacy of intra-arterial therapy because it is much more difficult to show a benefit when perhaps half of the patients enrolled in a trial have no chance for a good outcome.

Hussein et al[3] showed that futile recanalization occurs more commonly in patients older than 70 years of age or with an NIHSS score of $\geq$20. The MERCI registry revealed a similar trend with substantial disability or mortality occurring in recanalized patients 70 years of age or older and with an NIHSS score of $\geq$16.[5] The association of bad outcomes with high NIHSS scores is perhaps simply an indicator that patients with the most profound deficits at presentation have the largest areas of ischemic brain and perhaps the worst collateral blood supply. The poor outcomes in the elderly are probably due to an inability to respond to ischemia with collateral supply to the territory at risk. I would not advocate that we abandon intra-arterial therapy in the elderly altogether, but rather we need improved patient selection even more desperately in the elderly.

Using time elapsed since symptom onset as a selection criterion is the weak link in the selection process. Elapsed time is a flawed selection criterion simply because it is based on probabilities of good outcome in a large population rather than in the individual patient being considered for therapy. I have personally recanalized 1 patient at 30 minutes and another at 2 hours after an acute arterial occlusion, and both had large infarctions of the entire revascularized territory. This experience has taught me that for probably many patients, the game is over in well under 8 hours. On the other hand, there are cases of recanalization beyond 8 hours resulting in good clinical outcome, further proving the unreliability of elapsed time in patient selection. Collateral supply is what allows the brain to survive in an individual patient for a given period of time after arterial occlusion, and some patients have it and some do not. To better address the individual differences in collateral supply, we are moving away from elapsed time as a selection criterion and toward imaging to assess the state of the ischemic brain and its circulation (ie, penumbra imaging).

Penumbra imaging is an area of intense research, but no standard approach has yet emerged. We have yet to even reach consensus on whether CT or MR imaging is better, and other questions remain. How much penumbra is enough to be worth saving? How much ischemic core is too much to risk reperfusing? What about the location of core or penumbra in eloquent versus noneloquent brain? At the very least, we are probably reaching a point where imaging can reliably tell us if there is a large ischemic area in a major eloquent territory (such as the all-too-common middle cerebral artery occlusion) with little or no chance for improvement with recanalization. Maybe instead of asking the question whether we can image a penumbra, we should be asking ourselves if we can image a large area of infarcted brain that would be futile to reperfuse.

Perhaps the need for better patient selection has been somewhat obscured by the poor natural history of ischemic stroke due to large-artery occlusion. It has been reasonable in the past to just press on aggressively with intra-arterial therapy and give the patient the benefit of the doubt when faced with a likely terrible outcome without recanalization. However, dur-

ing the past decade, we have acquired more detailed information about patient outcomes and simultaneously developed more advanced imaging techniques, which should allow us to now refine patient selection. We now should face up to what we have learned and begin to recognize the patients for whom recanalization is futile, and perhaps even harmful.

We are gradually acquiring improved devices and techniques that will almost certainly allow us to exceed 90% recanalization in the near future. As we get higher recanalization rates, the poor outcomes due to poor recanalization will drop precipitously, and unless we improve patient selection, most bad outcomes will be related to futile recanalization. Intraarterial ischemic stroke therapy will undoubtedly start to look a lot better in practice and in clinical trials when we start applying it to the most appropriate patients.

Al Gore did not invent the Internet, and I did not invent penumbra imaging. I do not even claim to know the best way to image acute patients with stroke in 2011, but I do feel qualified to call attention to a huge potential improvement in outcomes that imaging could provide by reducing futile recanalization. If we succeed in this endeavor, we will boast of good neurologic outcomes in substantially more than half of the patients undergoing endovascular recanalization for acute ischemic stroke.

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