Intra-Arterial Thrombolysis for Basilar Artery Thrombosis and Stenting for Asymptomatic Carotid Disease

Implications and Future Directions

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Where knowledge fails controversies thrive. This applies particularly to techniques in evolution. Intra-arterial thrombolysis (IAT) for basilar artery thrombosis and stenting for asymptomatic carotid disease share 3 characteristics: they are operator-dependent, technology-intensive and expensive. Although IAT and stenting imply a similar approach, the clinical problems that they address differ radically. IAT is unscheduled and dramatic, the interventionalist hoping for something to happen, namely recanalization and improvement, whereas stenting for asymptomatic carotid disease is scheduled and undramatic, the interventionalist hopes that nothing happens, either during the procedure, or thereafter (ie, no stroke).

IAT for Basilar Artery Thrombosis

We have no accurate data on the natural history of basilar thrombosis, but from the published literature, a perception persists that the usual prognosis appears so dismal that almost any intervention can be justified.1

The natural history of asymptomatic carotid disease is much better known,2 being benign enough to call into question the need for any invasive procedure.

Basilar thrombosis can lead to desperate situations, calling for desperate measures. One is justified in trying to do something about the natural history, but only if it can be done systematically. Otherwise, we are performing a potentially harmful, costly procedure with no evidence of benefit, and with the potential for harm. By not evaluating what we do, we perpetuate and inflict our dangerous ignorance on future patients.

A rationale can be made for using thrombolysis in basilar occlusion. It may be life-saving and decrease disability. The complications can be predicted, generically but not individually. The treatment could make the patient worse, converting certain death into a living death. Moreover, subgroups of patients may not benefit. Conceivably, a young individual undergoing a cardiac investigative procedure could have an embolus to the basilar artery, but with good collaterals and an active fibrinolytic system, the natural outcome could be benign. In fact, prospectively collected data on consecutive patients with posterior circulation strokes suggests that a favorable outcome can occur in 59% of the patients.3

Future Directions

Patients still typically arrive at hospitals many hours after the onset of their stroke. Enormous gains can still be made by decreasing the mean time of patient arrival. The magnitude of the benefit of having patients arrive 1 or 2 hours earlier would qualify many more patients not only for intravenous thrombolysis, but IAT and perhaps mechanical disruption or retrieval of clots.

Every stroke patient should be looked at as a potential candidate for a broad range of interventions, beginning in the ambulance with the administration of a histoprotective agent and continuing with the potential for administration of intravenous or intra-arterial thrombolysis or clot dissolution or retrieval by the use of devices.

Telemedicine offers an opportunity for expanding the use of this broad approach by identifying, from the beginning, potential candidates for invasive interventions.

Convergent Step-Wise Studies: A Proposal

We have weak data breed strong opinions. At times an inverse relationship appears between the strength of the data and the vehemence of people’s convictions. This holds true for the use of thrombolysis for basilar thrombosis. Nevertheless, some patients with basilar thrombosis most physicians, surgeons or interventionalists would consider ineligible for an intervention (eg, a patient who had been in a coma for 24 hours). Conversely, some patients may not be considered candidates because of a probable favorable prognosis, such as patients with a basilar thrombosis who are beginning to recover spontaneously.

A study could be designed whereby each center would define “a priori” which patients they would be willing and unwilling to treat, and then treat the rest according to their convictions. Data and outcomes on all the patients would be kept. If enough centers participated, an external monitoring committee could determine which patient categories are not benefiting judged by death and severe disability and which have such a benign outcome that no intervention would be justified.

This would be a reiterative process, whereby the categories of patients where treatment is demonstrably useless, harmful
or unnecessary would be reduced in a stepwise, convergent fashion. A randomized clinical trial could then be justified in the group where the treatment remained uncertain.

Carotid Stenting for Asymptomatic Carotid Disease

No appropriate controlled data of the effect of carotid stenting in asymptomatic carotid disease exists. We have good indirect evidence about the natural history of asymptomatic carotid disease and of carotid endarterectomy, as a result of 2 randomized clinical trials. Carotid endarterectomy benefits mainly relatively healthy men, women having a higher risk and lesser benefit from the operation. The overall absolute yearly stroke reduction is only about 1%.6

The 2 trials of carotid endarterectomy are remarkable in the similarity of the results and an unusually low complication rate of surgery, which was 3.4% for the Asymptomatic Carotid Atherosclerosis Study and 3.5% for the Medical Research Council trial. This is contrary to the results of the Aspirin and Carotid Endarterectomy study,7 that included asymptomatic and symptomatic carotid disease patients and which was performed by many of the same surgeons who carried out the ACAS study. The ACE study perioperative stroke and death rate for asymptomatic and symptomatic disease was 4.6%. It is probably higher outside of a clinical trial. These results parallel those of the Yadav et al study of stenting, that included mainly asymptomatic patients, in which the complication rate was similarly high, 5.4%.8 Although in fairness, the patients in the stenting study had greater medical and surgical comorbidities.

Local Attack on a Generalized Condition: The Need for Global Risk Stratification

Carotid stenting represents a local attack on a generalized condition, atherosclerosis. Therefore, it makes sense to evaluate what the global risk for stroke, myocardial infarction and vascular death the patient carries as a result of generalized atherosclerosis and its attendant risk factors and what difference the intervention makes to the overall risk. Although randomized clinical trials control for risk factors, they seldom evaluate the overall risk of the patients having a vascular outcome. In the published evidence with asymptomatic carotid disease, a patient is more likely to have a myocardial infarction than a stroke in the distribution of the intervened carotid. If one adds the fact that the local intervention is not likely to change the overall disease, the question arises as to the cost effectiveness of doing a procedure at all, as compared with an aggressive approach at risk factor control and vascular outcome risk reduction. In theory both should be done. The reality is that the results of the trials convey the overall impression that the risk of stroke has been “cut in half”, whereas almost half of subsequent strokes are attributable to other mechanisms (lacunar occlusions and cardioembolism), unrelated to the carotid artery stenosis.9 Certainly, when discussing a possible intervention with a patient, the absolute risk of all vascular events should be discussed and the fact that carotid endarterectomy has been tested in appropriately controlled trials and stenting has not.

New Techniques: Try Them or Trial Them?
The adjectives “aggressive” and “conservative” are used either to criticize or justify opinions. What really matters is an appropriately aggressive or conservative stance. In the case of basilar thrombosis, an aggressive attitude would seem justified because the prognosis appears poor. Contrarily, a conservative stance regarding stenting for symptomatic disease makes an appropriate departure standpoint, given the relatively benign natural history of asymptomatic disease.

For both IAT and stenting, no intervention should be planned unless it is part of a systematic evaluation. In the case of basilar thrombosis the convergent stepwise approach could be justified, whereas with a symptomatic carotid stenosis a direct comparison between best medical management and best medical management plus stenting may be warranted.

Randomized clinical trials, which evaluate the efficiency of treatments probably should be followed by selected efficacy trials, in which the procedure continues to be assessed in the real world, the data-recording incentivized by reimbursement or premium payments.

Some individuals try the new without evaluating it, others insist that it be evaluated before trying it. Both are right. Without pioneers we would have no progress and without trialists we would have no proof. We need pioneers and trialists, preferably as the same person.

Disclosures

None.

References


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