Worsening in Ischemic Stroke Patients: Supplementary Activation of Cerebral Hemodynamic With EC/IC Bypass

To the Editor:

In a recently published editorial, Caplan propounded a question for new therapy strategy in ischemic stroke patients. He pointed out 3 main factors that are responsible for progression and worsening of neurological deficits in patients with noncardioembolic stroke. According to Steinke and Ley, one of these factors concerns reduced blood flow in the ischemic zone following occlusive disease of the supplying arteries. In respect of discussed facts, Caplan concluded that the only efficient therapy for worsening in stroke patients is an augmentation, ie, improvement in cerebral blood supply.

In addition to his proposal about either pharmacological or surgical management (eg, by established carotid endarterectomy), there is, in our opinion, a method of extracranial-intracranial bypass (EC/IC bypass), which should be considered in selected patients for improving circulation in the brain, if reopening of carotid obstructive lesion is impossible.

Caplan himself commented that there is a group of patients in whom the long-occluded vessels could not be reopened, by neither surgical methods nor thrombolysis.

We have experience with such patients, when progression of brain ischemia occurred despite established management procedures (such as sufficient anticoagulating therapy, among others) in conformity with the recommendations and guidelines of scientific societies, eg, the American Heart Association.

Various studies have been published in the past 30 years—including the experiences of the senior authors (S.P., H.W.)—on microsurgical brain revascularization (eg, EC/IC bypass) of occlusive diseases, confirming regression of the clinical symptoms after this surgical procedure, even in noncardioembolic stroke patients with progression of deficit. Who among these patients with extracranial or intracranial artery occlusive disease are definitely proper candidates for such a revascularization is still not established. Unfortunately, since the 1985 publication of the data of the EC/IC Bypass Study Group, which did not consider a subgroup of patients with recurrent ischemic attacks based on occluded internal carotid artery and reduced cerebral vascular reserve, the research of surgical management of brain ischemia has not been generally of intensive interest. The problem of rational management, including neurosurgical procedures, for more benefit to the stroke patient should again be brought to the forefront, as Caplan suggested.

Still, there are not convincing data on whether ischemic brain attacks are of hemodynamic or thromboembolic origin. This matter should also be clarified in the future, using modern imaging techniques for more understanding and elucidation of cerebral hemodynamic pattern. In almost the same manner as other cerebrovascular diseases, an ischemic stroke presents a multidisciplinary therapeutic problem as well, which can only be solved by multidisciplinary cooperation, including neurosurgical revascularization procedures, if indicated.

In conclusion, the surgical treatment with EC/IC bypass can be of benefit for prevention of stroke. Nevertheless, further studies must clarify this matter, as recommended by the Carotid Occlusion Surgery Study.

Bernhard Fischer, MD
Stefan Palkovic, MD, PhD
Hansdettel Wassmann, MD, PhD
Department of Neurosurgery
University of Muenster (UKM)
Muenster, Germany


Response

Anecdotal reports before the EC/IC Bypass Study attested to the utility of bypass procedures, but the trial showed that the procedure as then performed was not effective. I agree with Fischer et al that there are some circumstances when bypass might be useful. A discussion at a Princeton conference focused on the issue of conducting a trial that studied the utility of bypass in patients with chronic hypoperfusion distal to a large-artery occlusion documented by modern neuroimaging techniques. Most attendees thought that the project was worthwhile. I do think that such a trial is now feasible.

Louis R. Caplan, MD
Department of Neurology
Beth Israel Deaconess Medical Center
Boston, Massachusetts
Progressive Stroke, Lacunae, and Systemic Blood Pressure

To the Editor:

We read with great interest the article by Steinke and Ley and the editorial by Caplan in the June issue of Stroke. Among 941 patients with stroke, Steinke and Ley identified 92 patients with prevalent motor deficit; motor performances further deteriorated in 22 of these patients, and a prevalence of deep (lacunar) lesions was found on these latter patients. The conclusion, which gives the title to the article, is that lacunar stroke is the major cause of progressive motor deficits. Some observations could be made. The strict inclusion criteria of Steinke and Ley allowed selection of only a minimal number of the screened patients. Such a situation is highly “at risk” for selection biases; for example, the exclusion of patients with “minor motor or predominantly other deficits” may rule out the whole population of patients with embolic occlusion of small pial branches of the middle cerebral artery, or may overestimate relatively rare conditions such as basal ganglia infarctions as a major consequence of an embolic occlusion of the main trunk of the middle cerebral artery, with an efficient leptomeningeal collateral circulation. Moreover, the European Stroke Scale baseline is different between groups: the 22 patients with progressive courses had more limited neurological deficits and less frequent consciousness impairment, due to smaller infarctions as demonstrated on neuroimaging studies. In this setting, a worsening clinical course is more easily appreciated in the less severely affected patients, because of the “saturation effect” of the upper end of the scale.

The possibility of these biases is not avoidable in such a work but must be discussed. While considering these criticisms, the conclusions drawn by Steinke and Ley are correct in the sense that patients with progressive motor deficits caused by stroke typically have mild deficits at the admission and develop prevalently deep lesions. What is to be noticed is that, because of the already mentioned biases, this population does not necessarily match the “canonical” definition of patients with lacunar infarctions.

These criticisms extend in part to the editorial. In the comments, Caplan focuses some critical point on the meaning and the physiopathology of the “progressing stroke” in a fascinating, global vision of the problem. Apart from systemic disease, such as febrile diseases —perforators or pial vessels. This effect is more easily demonstrated on the particular subtype of deep infarctions that causes a clinical worsening. Those infarctions, whose physiopathology is not yet known, appear as lacunae on neuroimaging studies.

Mauro Bergui, MD
Gianni Boris Bradcac, MD
Department of Neuroradiology
University of Turin
Turin, Italy


Response

We appreciate the comments of Drs Bergui and Bradac regarding our article on progressive motor deficits in acute stroke. We agree that the application of strict inclusion criteria for the study population may have introduced a certain selection bias. However, in order to study the pathogenesis of further worsening of a relevant initial hemiparesis, it seemed methodologically adequate to exclude hemiplegic and comatose stroke patients as well as those with minimal motor or predominantly other neurological deficits. This approach provided a relatively homogeneous patient population for the investigation of stroke types in progressive motor deficits. Although we restricted the analysis to patients with a distinct clinical syndrome and course according to predefined criteria, all types of strokes were included in the final study population without selection bias. In contrast, definitions of stroke progression including decreasing level of consciousness and non-neurological causes of deterioration lead to more heterogeneous study populations in other recent studies, although with a main focus on large middle cerebral artery infarctions. Our study indicated lacunar infarction as the predominant stroke type in patients with worsening of motor hemiparesis. However, adequate interpretation of this result requires consideration of the inclusion criteria for our study population.

Drs Bergui and Bradac found a “saturation effect” in our study leading to easier assessment of worsening of the hemiparesis, if the initial deficit was less severe. Although our patients with progres-
CT or MRI for Imaging Patients with Acute Stroke: Visualization of “Tissue at Risk”?  

To the Editor:

In a recent Stroke editorial weighing the relative merits of CT versus MRI for imaging patients with acute stroke, Tatlisumak raises a number of important and compelling points.1 Among these, however, is the statement—with regard to using MR perfusion-diffusion mismatch in order to identify treatable “tissue at risk”—that a “similar approach does not yet exist for CT imaging.” We wish to call attention to preliminary results suggesting that such an approach may, indeed, currently exist using CT perfusion imaging.2,3 Specifically, pilot studies in patients with middle cerebral artery stroke have revealed that, like diffusion-weighted imaging, CT cerebral blood volume maps may delineate ischemic regions with a high probability of being already infarcted by the time of image acquisition.4–6 Quantitation of cerebral blood flow (CBF) and mean transit time with the bolus tracking technique should be more accurate using CT, rather than MR methodology, because signal change is linearly proportional to dye concentration with CT, but not with MR, and because CT images typically have higher signal change is linearly proportional to dye concentration with CT, and mean transit time with the bolus tracking technique should be

correspondence, and some very limited personal experience, and suggested the development of a “stroke CT package” including conventional CT images, perfusion CT, and CT angiography.2 This is a good (and a very delightful) example of how rapidly stroke research is progressing before our eyes, and our statements are becoming obsolete before they are even published. It took only few years for diffusion-weighted and perfusion-weighted MRI to become generalized after the early milestone reports,9,10 and this may be the case for CT perfusion studies.11 A “stroke CT package” will increase the dose of radiation to which the patient is exposed by 3-fold or more. However, the disadvantages of radiation exposure are likely to be overstated unless the same patient is imaged repeatedly in a short period of time.

CT perfusion imaging may deliver more accurate information than MR perfusion imaging, but it is limited to a lesser number of slices and requires extensive postprocessing. Currently, whole brain perfusion CT imaging requires abundant doses of radiation and contrast agent, and if the lesion cannot be visualized by conventional CT imaging, placement of the perfusion CT slice to the correct region of interest relies on clinical judgment only, and furthermore, perfusion CT cannot yet be used for volumetric measurements, but

Response

I thank Dr Lev et al for their interest and constructive criticism1 on my editorial.2 Unfortunately, at the time I processed the editorial, the most recent articles cited by Dr Lev and his colleagues3–5 were yet not available to me, and the rest I considered preliminary.6–8 Indeed, I have anticipated this development on the basis of preliminary publications, personal communications, and some very limited personal experience, and suggested the development of a “stroke CT package” including conventional CT images, perfusion CT, and CT angiography.2 This is a good (and a very delightful) example of how rapidly stroke research is progressing before our eyes, and our statements are becoming obsolete before they are even published. It took only few years for diffusion-weighted and perfusion-weighted MRI to become generalized after the early milestone reports,9,10 and this may be the case for CT perfusion studies.11 A “stroke CT package” will increase the dose of radiation to which the patient is exposed by 3-fold or more. However, the disadvantages of radiation exposure are likely to be overstated unless the same patient is imaged repeatedly in a short period of time.

CT perfusion imaging may deliver more accurate information than MR perfusion imaging, but it is limited to a lesser number of slices and requires extensive postprocessing. Currently, whole brain perfusion CT imaging requires abundant doses of radiation and contrast agent, and if the lesion cannot be visualized by conventional CT imaging, placement of the perfusion CT slice to the correct region of interest relies on clinical judgment only, and furthermore, perfusion CT cannot yet be used for volumetric measurements, but
decision-making must be based on a single or few slices. On the other hand, neither hindrance is unlikely to be solved in the close future, as Mayer et al have already reported a fast image postprocessing software that prevents loss of the time for image analysis that is gained by faster imaging with CT. However, the statement by Lev and his colleagues that “the poor specificity of MR perfusion maps has taught us that quantitative CBF thresholds are necessary to identify tissue that is still salvageable but destined for infarction without early reperfusion” is very much an issue of debate. First, perfusion MRI allows for calculation of relative maps of MTT, CBV, and CBF, and attempts have been made to establish a methodology for absolute measurements of the same parameters. Second, thresholds for irreversibility have already been calculated from perfusion MRI images and can predict the final infarct size better than mere visual evaluation of perfusion maps. Third, flow heterogeneity measurements may deliver a more precise estimate of final infarct size, but constructing maps is timely, unless quick methods are available to all. Fourth, perfusion MRI can be combined with diffusion-weighted MRI that has the advantage of depicting the ischemic lesion, a clear advantage over CT imaging. DWI is used as the gold standard for determination of final infarct size in 1 study and was found to be 100% sensitive for detection of parenchymal stroke detection, whereas the same value was 83% with perfusion CT in another study, both cited by Lev et al in their letter. Many studies reporting the use of novel MRI and CT techniques, however, suffer from small numbers of examined subjects. Incorporating these methods into routine emergency evaluation and/or multicenter trials in the near future will deliver firmer data and allow for firmer conclusions.

A CT scanner within the premises of the emergency room is a very good investment, especially if it is an ultrafast helical scanner capable of performing perfusion CT and CT angiography. Still, it may be an even better investment to have an MRI scanner next to it, but it is seldom feasible. Regarding the cost-effectiveness of MRI in hyperacute stroke, it is likely to be too early to make conclusions given that only a small fraction of all costs in management of a stroke patient is imaging cost and precise evaluation of cost-effectiveness requires carefully designed prospective studies. Besides, the cost of scanners has been decreasing for years and this trend will likely continue.

In conclusion, I believe that both CT and MRI have some advantages and some disadvantages, and considering the present evidence, an “ideal” imaging method for acute stroke patients does not yet exist. As many will agree, it is of benefit for all to continue developmental research both for CT and MRI.

Turgut Tatlisumak, MD, PhD
Department of Neurology
Helsinki University Central Hospital
Helsinki, Finland

Progressive Stroke, Lacunae, and Systemic Blood Pressure
Mauro Bergui and Gianni Boris Bradac

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