Advances in Stroke 2007

Advances in Imaging 2007

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Imaging continues to be a mainstay of stroke diagnosis, management, and investigation, and this was fully evident again in 2007. Stroke continues to command a substantial amount of attention from investigators from a wide variety of disciplines. A broad range of insights and innovations in imaging have occurred in the past year, and the space allotted here remains too small to capture the range of efforts. In this survey we will discuss the ongoing advances in optimal imaging of the acute stroke patient, the role of imaging as a biomarker or surrogate end point, as well as efforts to use imaging to assess the risk of hemorrhage after chemical thrombolysis. Important data about the frequency of incidental stroke have been published. And, in a special focus, we will describe the role imaging has played this past year in building understanding of recovery from stroke.

One ongoing area of investigation regards the manner in which to optimally image the acute stroke patient. Guidelines issued this year provide an excellent summary: x-ray computed tomography (CT) guides most treatment decisions, and therapy should not be delayed to obtain multimodal imaging studies. However, multimodal imaging with CT and with MRI may provide additional information that will improve the diagnosis of acute ischemic stroke. Indeed, recent data suggest that CT angiography and perfusion assessment with CT is both feasible and in the specific setting of hemispheric occlusion, tissue damaged and potentially at risk, and other features with good accuracy. Given the widespread availability of CT in many hospitals around the world, CT is highly likely to remain a mainstay of diagnosis, and in settings where, as the guidelines state, therapy is not delayed to obtain multimodal imaging studies, such additional imaging may well improve diagnosis and in turn treatment.

Before considering multimodal imaging, it may be valuable to review new data evaluating diagnostic methods. Data continue to accumulate highlighting the advanced diagnostic power of MRI, especially diffusion-weighted MRI, over CT, with one major prospective study reporting a sensitivity of 83% for MRI relative to the final clinical diagnosis of ischemic stroke compared with 26% for CT. This population was among a broad range of patients presenting with possible acute ischemic stroke; certainly in select populations such as patients with large stroke, CT has much higher sensitivity than 26%. Nevertheless, most users of both CT and MRI can confirm from experience the greater reliability of MRI for diagnosis, and there appears to be a trend toward MRI for the initial diagnosis of ischemic stroke whenever possible. This increased power is particularly evident in the management of transient ischemic attack patients, as was shown again this year. Given the widespread prevalence of transient ischemic attacks and guidelines that already suggest including imaging at some point, these new results suggest diffusion-weighted imaging evaluation should be done urgently after transient ischemic attack. Of course, diagnosis with any imaging modality is better than no imaging, and in the face of a lack of ability to do MRI for any number of reasons (ranging from the absence of availability of emergency MRI to the presence of a pacemaker), certainly CT remains highly capable.

Does this improved diagnostic ability have any impact on patients? The answer from data published this past year appears to be yes. Increasingly, investigators are beginning to use multimodal imaging to attempt to widen the therapeutic window, using certain imaging findings such as the presence of an imaging correlate to the ischemic penumbra to consider treating with thrombolysis outside the conventional 3-hour window. Data comparing typical CT to multimodal MR suggest that MRI methods can be used to safely and effectively identify patients in whom thrombolysis might be safely administered to after the typical 3-hour window. Comparative data suggest that perfusion assessment with CT might be used similarly as MRI for treatment decisions in certain select patients. There are not yet data directly comparing multimodal CT to multimodal MR or showing that multimodal CT can be used to extend the window of thrombolysis. Nevertheless, it stands to reason that more information is good and whether such information comes from CT, MR, ultrasound, or any other modality, reliable information is the key to improved diagnosis and then treatment. However, the lack of success of the DIAS-II trial has led some to question whether the diffusion-perfusion mismatch is truly a surrogate for patients who might benefit. This remains to be seen; the release of the formal results may shed light on this question. Although some have argued that the diffusion-perfusion mismatch on MRI might be matched by a clinical-diffusion...
mismatch, 2 studies this year demonstrate that this is not the case.\textsuperscript{11,12}

Multimodal MRI has also been used in the setting of thrombolysis to attempt to predict which patients might experience intraparenchymal hemorrhage. Data suggest that small T2* lesions, thought of as cerebral microbleeds, do not appear to have any increased incidence of hemorrhage after chemical thrombolysis,\textsuperscript{13} but the presence of a large diffusion lesion\textsuperscript{14} or high permeability\textsuperscript{15} is indicative of increased risk. These data are consistent with earlier results suggesting that large lesions do not do well with thrombolysis.\textsuperscript{16}

One cautionary note around imaging: there are new risks. Recent estimates of the effects of radiation from CT scanning have suggested that a single CT scan of the head in a 65-year-old is associated with an 0.04\% lifetime risk of cancer\textsuperscript{17} (the risks are higher for younger patients). Given that a CT perfusion scan can have as much as 50 times the dose of a standard head CT,\textsuperscript{18,19} and that CT angiography adds further ionizing radiation dosing, the long-term effects of these imaging tests and especially repeat scans must be carefully considered. MRI is also associated with recently identified risks, specifically when gadolinium is administered to patients with very poor renal function.\textsuperscript{20} Fortunately, dose-lowering approaches are under development for CT, and noncontrast perfusion methods for MRI. While these risks must be considered in the context of the potential severity of acute ischemic stroke, there is clearly evidence to warrant a more cautious attitude.

We now turn to the role of imaging in assessing recovery, perhaps one of the most important areas of stroke investigation, and one receiving increasing attention. Functional neuroimaging has been applied quite frequently for the demonstration of brain areas involved in recovery of function after a stroke and even for the selection of patients for specific rehabilitation strategies. In a series of reviews the various imaging technologies for noninvasive exploration of the reorganization in cerebral networks relevant for recovery were described, but the reported results are still quite controversial.\textsuperscript{21–23} As clearly stated by Ward,\textsuperscript{21} a functionally relevant “reorganization can only occur in structurally and functionally intact brain regions”, and therefore is dependent on the location of the primary lesion. In several studies the functional reorganization of the motor network could be documented in patients after capsular stroke and subcortical stroke: good recovery was related to enhanced recruitment of the lateral premotor cortex of the lesional hemisphere and lateral premotor and to a lesser extent primary sensorimotor and parietal cortex of the contralateral hemisphere.\textsuperscript{24} The mechanisms of motor recovery vary according to location of the lesion: cortical infarcts activate the contralateral primary sensorimotor cortex, whereas subcortical infarcts largely showed activation of bilateral primary sensorimotor cortex.\textsuperscript{25} While there was an enhancement of the activation in the contralesional cortical network with motor skill challenge,\textsuperscript{26} several studies indicated that worse motor performance was related to a greater amount of contralesional activation\textsuperscript{27} and that patients who activated the ipsilesional primary motor cortex early had a better recovery of hand function.\textsuperscript{28} Repetitive peripheral magnetic stimulation increases the activation of the parieto-premotor network and thereby might have a positive conditioning effect for treatment.\textsuperscript{29} In addition to changes in the activation pattern of the motor network, different activation patterns were observed in the proprioceptive system, where the initially observed blood flow increases in SI and SII of the noninfarcted hemisphere vanished during successful rehabilitation and the normal activation patterns were restored, indicating an interhemispheric shift of attention associated with recovery.\textsuperscript{30}

Very few studies discussed results from functional imaging in recovery from poststroke aphasia and their consequence for treatment strategies.\textsuperscript{31} These studies support the model of 3 phases of language recovery: a strongly reduced activation of remaining left language areas in the acute phase, followed (or substituted) by an upregulation of homologue language zones and finally a normalization of the activation pattern reflecting consolidation in the language systems.\textsuperscript{32} The pattern of activation and the recruitment of regions during the rehabilitation depend on the available language-related regions, where restoration of the left hemisphere networks seems to be more effective, although in some cases right hemisphere areas are integrated successfully.\textsuperscript{33} It remains to be shown in future studies whether the inhibition or facilitation of selected areas, eg, by repetitive transcranial magnetic stimulation,\textsuperscript{34} can improve recovery of poststroke aphasia.

These efforts at understanding stroke and especially stroke recovery have been made even more relevant by a study of 2000 subjects over age 45 demonstrating a 7\% incidence of incidental brain infarcts.\textsuperscript{35} The true burden of disease of stroke has yet to be fully understood, and imaging continues to play an important role in its diagnosis and treatment.

Disclosures

A full list of A.G.S.’s relationships is available at www.biomarkers.org.

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