Imaging evaluation of acute ischemic stroke

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Introduction

Cerebral stroke is a concern with high morbidity and mortality rates globally. Early diagnosis and assessment are important in treatment of acute ischemic stroke (AIS). In recent years, the field of neuroradiology has rapidly changed and advanced with new technology and innovations. The utility of different imaging techniques has been reported in structural and functional evaluation of the brain.[1–3] Imaging evaluation almost covers the whole evolution process of cerebral stroke, from early diagnosis to treatment strategy decisions, and from predicting the prognosis to post-stroke assessment.

Imaging of the infarction core and ischemic penumbra

The most important goal for treatment of AIS is to restore blood flow to the ischemic penumbra for the remaining salvageable tissue as soon as possible. Therefore, early and accurate identification of the infarct core and ischemic penumbra is crucial for treatment of AIS and clinical outcome. Non-enhanced computed tomographic

(CT) imaging is regularly used to exclude hemorrhage and other diseases. Certain signs on plain CT images may indicate early changes in AIS, such as obscuration of the lentiform nucleus/insular ribbon, hyperdense arterial sign, loss of the gray–white matter interface, and swollen cerebral tissue. Baseline CT showing a large area of hypoattenuation is considered as an indicator of poor outcome. However, there is insufficient evidence to identify the threshold of acute hypoattenuation that affects treatment responses as shown by CT.[4] Diffusion-weighted magnetic resonance imaging (MRI) is the most useful method for detecting hyperacute ischemia. MRI can detect abnormal cytotoxic edema in the early stage and shows clear discrimination between ischemic lesions and normal brain tissue. The abnormal extent and patterns of baseline diffusion-weighted imaging (DWI) might help to predict the clinical outcome of patients with stroke.[5,6]

Hypoperfusion abnormalities can be accurately measured using CT perfusion

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and perfusion-weighted imaging (PWI). However, validation of the perfusion threshold for the penumbra has not been established. An option is to identify the mismatch between the infarct core and hypoperfusion tissue. Variable mismatch models have been established and investigated. The most widely applicable model is DWI-PWI mismatch, but this model might not optimally define the penumbra.[7,8] Particular advances include application of arterial spin labeling (ASL) to obtain perfusion information, and this method spares patients from administration of contrast medium. ASL can delineate large perfusion deficits and perfusion-diffusion mismatches in correspondence with dynamic susceptibility contrast.[9] Susceptibility-weighted imaging-diffusion mismatch was investigated in several studies with discrepant results.[10,11] CT mismatch models that included different parameters (e.g., computed tomography angiography [CTA] source images-computed tomography perfusion [CTP] mismatch/CTP cerebral blood volume-mean transit time [CBV-MTT] mismatch/CTP cerebral blood flow-maximum of tissue residual function) were also compared with magnetic resonance (MR) models and the correlations were investigated in relation to clinical outcome.[12–14] A clinical-imaging mismatch model was also applied to estimate the amount of tissue impairment. Several studies showed that clinical National Institutes of Health Stroke Scale scores and Alberta Stroke Program Early CT Score on DWI mismatch might be associated with neurological outcome in patients treated with intravenous tissue plasminogen activator.[15,16] The clinical-CTP CBV mismatch shows lower specificity compared with the diffusion/perfusion-weighted concept.[17] Further research is required to verify whether a clinical-imaging mismatch is useful in managing acute stroke.

Patients with AIS should receive intravenous tissue-type plasminogen activator treatment within 3 or 4.5 hours of symptom onset. Imaging techniques that provide more pathophysiological information might help to extend this time window and enable selection of the most appropriate candidates for early treatment. Many large-scale, multicenter trials have investigated the use of advanced imaging techniques for evaluating thrombolytic therapy for patients with an extended time window.[18–20] The current problem for these mismatch models is a lack of validation. Some randomized, clinical trials (RCTs) that used advanced, multimodal imaging (CTP, diffusion-perfusion mismatch) for thrombolysis treatment failed to demonstrate clinical efficacy in patients.[21,22] Two recent RCTs used imaging criteria to select patients with > 6 hours from onset for mechanical thrombectomy. One trial was the DEFUSE 3 trial, which used the perfusion-core volume ratio and initial infarct size as imaging criteria.[23] The Clinical Mismatch in the Triage of Wake Up and Late Presenting Strokes Undergoing Neurointervention With Trevo (DAWN) trial used clinical-imaging mismatch (a combination of National Institutes of Health Stroke Scale scores and imaging findings on CTP or DW-MRI) as an eligibility criterion.[24] Both studies showed benefit in functional outcome at 90 days in the treatment group. Future RCTs may demonstrate additional imaging eligibility criteria to be used in selection of patients who can benefit from mechanical thrombectomy. However, more precise definitions of imaging mismatch with validation of measures for the ischemic core and exclusion of benign oligemia need to be investigated.

Arterial stenosis, occlusion, and thrombus imaging

Severe stenosis and occlusion of large cerebral arteries are related to patients' treatment and prognosis. MR angiography

or CTA is important in multimodal imaging protocols to assess arterial stenosis or occlusion. A thrombus or clot usually blocks the proximal part of the cerebral artery and is a major concern in treating acute stroke thrombolysis or mechanical thrombectomy. Indirect confirmation of thrombi can be performed through observing obstruction of arterial blood flow, while directly visualizing the thrombus may be more useful. Imaging manifestations and the pathological component of obstructive thrombosis are closely related to the therapeutic response and clinical prognosis.

Plain CT "dense artery" sign may indicate a thrombus, but its sensitivity is poor. Susceptibility-weighted MRI along with standard MRI may be more useful for detecting thrombus. Susceptibility-weighted imaging is superior to fluid-attenuation inversion-recovery MRI and CT in detecting cerebral thromboemboli.[25] Molecular MRI and positron emission tomography-based thrombus imaging in animals have shown optimal results that may require further investigation in human studies.[26,27]

Imaging assessment of the collateral circulation

The collateral circulation plays a crucial role in the pathophysiology of ischemic stroke, and is closely related to the treatment response and the patient's prognosis.[28] The presence of good collateral circulation may help sustain the penumbral area and enhance the rates of successful reperfusion.[29] The first grade of collateral circulation (circle of Willis) can be visualized using CTA, MR angiography, and digital subtraction angiography. The secondary collateral circulation (leptomeningeal arterial supply) could only be visualized and assessed by conventional angiography in previous years. However, with development of neuroimaging techniques, understanding of the collateral circulation has been greatly enhanced in recent years.[30] Multiphase or dynamic CTA is an independent predictor of radiological and clinical outcomes of patients with AIS. CTA provides information of arterial, capillary, and venous phases of cerebral arteries, and it has a higher accuracy compared with single-phase CTA for assessment of collaterals.[31] CTP source images can also be analyzed at different points of time around the ischemic region to assess the collateral circulation status. In recent years, the presence of arteries via artifacts (arterial transit artifact) on ASL cerebral blood flow images and territory ASL has been applied to evaluate the collateral circulation.[32,33] Despite the invasive nature of digital subtraction angiography, it is the gold standard and the best method for assessing different grades of the collateral circulation. Noninvasive methods, including CTA, MR angiography, and ASL imaging, can also provide direct or indirect evaluation of first and second grade collaterals. Acute stroke imaging protocols should include one of these noninvasive methods for assessing the collateral circulation, either based on CT or MR techniques.

Post-stroke imaging assessment

After vascular recanalization, imaging needs to be performed to observe progression of the lesion, including the condition of recanalization, reperfusion status, and hemorrhagic transformation. Although hyperperfusion after vascular recanalization is rare, it requires a lot of attention. Major hyperperfusion in an ischemic region often leads to hemorrhagic transformation or worsening of the disease, known as reperfusion injury. Perfusion imaging can provide related information for hyperperfusion after treatment. The Modified Thrombolysis in Cerebral Infarction score is a current assessment tool

with proven value in reflecting the reperfusion status and predicting clinical outcomes.[34]

Although imaging-guided treatment for AIS still requires more clinical evidence, multimodal imaging plays a major role in diagnosis and treatment of stroke. Advanced imaging modalities may help perform a paradigm shift in stroke imaging from simply providing diagnosis to providing comprehensive assessment for patients, with the final goal of establishing individualized medical treatment. This scope is expected to be the future direction in this field and be fulfilled with application of advanced imaging techniques.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

Funding

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