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Editorial Musings

Review of Post Ischemic Stroke Imaging and Its Clinical Relevance

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ABSTRACT

In this day and age, multiple imaging modalities are available to the stroke physician in the post-treatment phase.The practical challenge for physicians who treat stroke is to evaluate the pros and cons of each technique and select the best choice for the situation. The choice of imaging modality remains contentious at best and varies among different institutions and centres. This is no simple task an there are many factors to consider, including the differential diagnosis which need to be evaluated, the availability and reliability of the imaging technique and time and expertise required to perform and interpret the scanning. Other ancillary competing interest also come into play such as the financial cost of the modality, the requirement for patient monitoring during the imaging procedure and patient comfort. In an effort to clear some of the ambiguity surrounding this topic we present some of the current techniques in use and others, which are still in the realm of research and have not yet transitioned into clinical practice.

1. Introduction

Imaging before acute ischemic stroke treatment is well established and has been the subject of multiple reviews. However, the role of post-treatment imaging in stroke is much less well defined. In patients who have undergone acute ischemic stroke treatment, bleeding, especially intracranial haemorrhage, is the most feared complication. Therefore at least a routine non-contrast computed tomography (NCCT) brain scan obtained 24 h after treatment is recommended as part of the AHA/ASA IV-tPA guidelines.

Routine post-treatment imaging helps to confirm the initial diagnosis of stroke and provides prognostic information about the stroke and its underlying aetiology. This is not a trivial issue with stroke mimic rates of up to 14% being reported [1]. Furthermore, haemorrhagic complications may not manifest themselves clinically and may therefore require the aid of routine imaging to be detected and monitored [2]. Similarly, imaging may also help in evaluating the difficult decision of when to recommence antithrombotic therapy. The volume and location of infarction and the potential presence of a haemorrhage on follow-up imaging frequently aid the responsible physician in determining when to start or recommence antithrombotic therapy, as well as providing qualitative prognostic information which may govern optimization of future patient care and the most efficient utilization of hospital and community resources.

However, the utility of performing these scans in asymptomatic stable patients remains contentious. In one single centre study over 3 years of 131 patients without clinical decline after IV-tPA, repeat imaging (either MRI or CT) only changed the management of 1 patient [3]. In the same context, a similar study showed that routine 24 h CT scans in patients without 24 h National Institute of Health Stroke Scale (NIHSS) score worsening are less likely to yield information that results in a change in care. No clinically stable patient with a pre-treatment baseline NIHSS score of $\leq$10 had parenchymal hematoma on 24 h follow-up CT [4]. These studies suggest that repeat imaging should be judiciously applied with clinical judgement.

Multiple imaging modalities are available to the stroke physician in the post-treatment phase. The choice of optimal imaging modality remains contentious and varies among different institutions and centres. The practical challenge for physicians is to understand advantages and disadvantages of each technique. There are many factors to consider, including the differential diagnosis which need to be evaluated, availability and reliability of the imaging technique, time and expertise required to perform and interpret the scanning, financial costs, patient monitoring during the imaging procedure and patient comfort. We attempt to present some of

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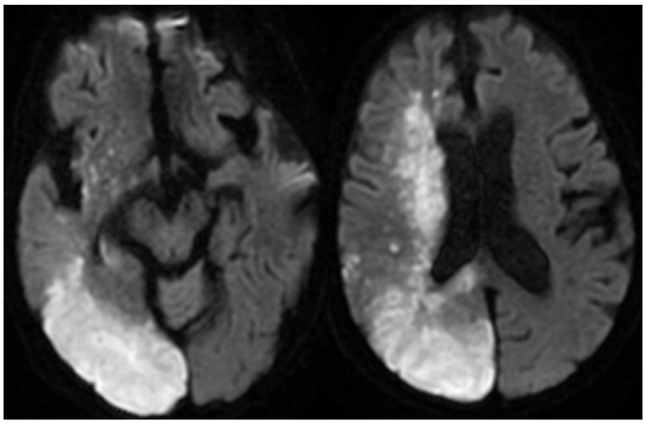

Fig 1. MRI Diffusion weighted sequence showing an acute stroke patient with a large infarct. The automated software measured the total volume as 96 mls suggesting that recanalization therapy will be at a higher risk.

the current techniques in use and others, which are still in the realm of research and have not yet transitioned into clinical practice.

2. Imaging currently used in clinical practice

2.1. Magnetic resonance imaging (MRI)

MRI is one of the most commonly performed imaging pre- and post-stroke treatment due to the wealth of information it offers. There are many different sequences available, which can tease out relevant information depending on the clinical need. The limitations are mainly costs, time and availability of scanners and physicians qualified to read and report the images.

2.1.1. Estimation of infarcted tissue (Fig. 1)

The size of the completed infarct demonstrates the extent of irrecoverable damage and determines the level of improvement that can be expected. Final infarct volume (FIV) is therefore an independent predictor of outcome after stroke, whether measured by non-contrast CT or MRI with DWI sequences [5,6]. In a retrospective study, good outcome as defined by Modified Rankin Scale score (mRS) [7] 0–2 occurred with average lesion volumes of 16.3 mL whereas the average lesion size associated with poor outcomes was 63.4 mL demonstrating the link between lesion size and outcome [8].

Other recent studies demonstrate that FIV also has influence on clinical outcome after endovascular therapy. One such study on stroke patients treated endovascularly showed high specificity for poor outcomes with a FIV of >90 cm^3, while another determined that an infarct threshold of 50 mL demonstrates the highest accuracy for distinguishing good versus poor functional outcome [9,10].

There appears to be only small extensions in FIV between 24–48 h and 1 week on post-stroke DWI scans, which lends weight to the theory that the majority of infarcts complete their evolution between the first and second day [11]. Therefore, FIV measured by DWI MRI at 48 h appears to be a strong independent predictor of outcome [5]. Whilst DWI reversal does occur at this late timepoint, it is not usually of sufficient size to meaningfully alter the FIV as estimated on the initial follow-up imaging [12].

Nonetheless, in clinical practice, FIV determined within the first few days might be useful for early prognostication after treatment especially if reliable neurological examination is not possible due to intubation or medical complications. In addition, imaging may be useful to predict delayed neurological recovery for example as in "ischemic stunning", where there is a clinical-imaging mismatch [13].

Finally, MRI infarct volume at 6 h post IV tPA can be used to determine if patients will require ICU care. Using DWI and FLAIR sequences, the best sensitivity and specificity occurred with an infarct volume of 6.8 cc, and infarct volume was a better predictor for ICU care than NIHSS score [14]. This study indicates that MRI-based selection of patients with low probability of requiring ICU resources is feasible and such patients may be safely treated even if ICU capabilities are temporarily unavailable.

2.1.2. Diffusion weighted imaging reversal (DWI)

Unless there is early reperfusion, DWI lesions typically expand over a period of up to 24 h [15], largely attributed to involvement of part or all of the surrounding hypoperfused tissue. DWI lesion expansion occurs almost exclusively in patients who initially have a perfusion defect larger than the DWI lesion, DWI–PWI mismatch [16].

Previously it was assumed that increased signal on DWI imaging corresponded almost completely with the infarcted area. However, both animal research [17] and recent clinical studies have reported that DWI lesions can reverse, either spontaneously or after recanalization, and this phenomenon has been reported in one third of patients after recanalization therapy [18,19]. Hence, the timing of follow-up MRI is essential when evaluating DWI lesion reversal. Indeed, prominent DWI lesion reversal has been observed when the first follow-up MR was scheduled early, mostly within 12 h after treatment [19,20]. But also when the imaging is performed at 24 h after stroke onset, a today more common strategy, DWI lesion reversal has been demonstrated and shown to be sustained in subsequent imaging. From a clinical perspective, it is worth noticing that reversal at 24 h has been shown to be associated with early functional improvement in a dose-dependent relationship [21]. It might be said that DWI reversal constitutes a problem for the patient selection process whereas the 24 h DWI images accurately reflect the FVI with minimal further reversal at later time points.

2.1.3. Blood-brain barrier (BBB) permeability

The hyperintense acute reperfusion marker (HARM) is a signal seen on FLAIR sequences hours to days after stroke constituting an early marker of BBB breakdown. It is caused by accumulation of contrast in the CSF spaces, and is associated with increased rates of haemorrhagic transformation [22]. Blood brain barrier permeability increases commensurately with ischemic neuronal injury and is caused by a failure of tight junctions. This phenomenon can be measured with perfusion imaging and expressed by the "permeability surface area product" (PSAP), representing an attempt to stratify patients into those who will or will not go on to develop haemorrhagic conversion, in one study using a threshold of 0.23 mL/min/100 g [23]. Another study showed that patients with a PSAP of >0.84 mL/100 g/min was almost 30 times more likely to have a haemorrhagic transformation [22]. Whilst not used widely, this information is readily available in centres that triage stroke patients with perfusion imaging and may prove to be useful in prognostication.

2.2. CT imaging

Non-contrast CT (NCCT) remains the cheapest, quickest, most widely available and easiest method for detection of intracerebral haemorrhage after an ischemic stroke, although MRI, with appropriate sequences, may come close [24].

Hyperdense areas may frequently be detected on NCCT after acute ischemic stroke treatment. These can be due to either haemorrhage, extravasation (enhancement) of contrast medium or disruption of the blood brain barrier [25]. These lesions represent a spectrum of different degrees of microvascular permeability and loss of integrity; however, serial imaging is necessary for a

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