

Prediction of hemorrhagic transformation in acute ischemic stroke using dynamic contrast-enhanced permeability MRI

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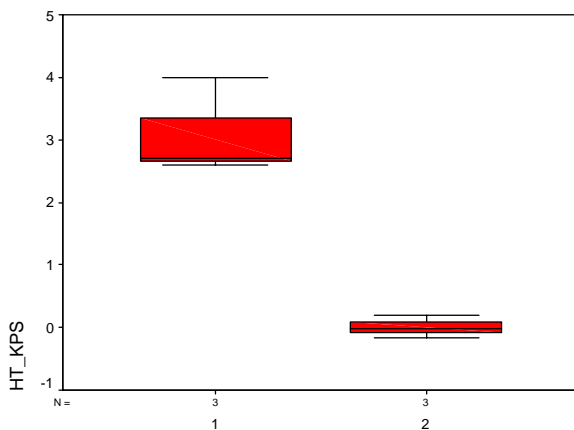
Introduction: Increased risk of intracranial hemorrhage limits the general use of tissue plasminogen activators (t-PA) in acute ischemic stroke (AIS). Although t-PA represents an important step forward in AIS management, there is a clear need to make this treatment available to a higher number of patients while reducing the risk of hemorrhagic transformation (HT). Thus, a method that identifies patients at higher risk of HT is mandated for a successful application of t-PA. The purpose of this study was to detect, quantify and categorize BBB disruptions shortly after onset of ischemic injury (within a few hours).

Materials and Methods: Ten patients (4 females, 6 males, age range 38-80years) with acute ischemic stroke not treated with t-PA were examined within 24 hours of symptom onset using a comprehensive acute stroke MRI protocol consisting of anatomical, diffusion and perfusion imaging, as well as contrast-enhanced MRA. In addition, a 3D gradient-echo (GRE) dynamic contrast-enhanced (DCE) MRI exam was performed to assess permeability/BBB integrity. All imaging was performed on a 1.5T GE Signa MR system (GE Healthcare, Milwaukee, USA) equipped with echospeed gradients and a standard neurovascular head coil. Imaging parameters for the dynamic 3D GRE acquisition were as follows: FOV 240mm, 128 x 128 matrix, FA=20 deg, slice thickness 7mm, TR=5.9ms, TE=1.5ms. Total acquisition time was 4:48 min for a collection of 31 volumes. Contrast media (Omniscan, GE Healthcare, USA; total volume of 15cc Gd-DTPA) was injected as a bolus 30 seconds following the start of the 3D acquisition. Data was transferred to an independent workstation for quantitative analysis. Parametric maps of permeability (KPS) were calculated as described previously by Roberts et al [1]. Two ROIs were selected - with one placed on the core region of diffusion or if present on the permeability abnormality (which was always within the diffusion abnormality). The second was placed on the homologous location in the contra-lateral normal hemisphere. Mean and SEM were recorded and examined for statistical significance using a 2 tailed students t-test.

Results: Three cases showed progressive enhancement associated with increased permeability in the acute phase. All 3 went on to hemorrhage at 48 hrs post symptom onset. KPS in the lesion of these cases was significantly elevated (see figure 1) compared to the contralateral normal hemisphere (3.10 ml/100g/min \pm 0.44 compared to 0.01 ml/100g/min \pm 0.10, $p < 0.01$). All other cases showed no significant increase in permeability (-0.123 ml/100g/min \pm 0.09 for the lesion compared to -0.243 ml/100g/min \pm 0.07 for the contralateral side, $p = 0.2$). Comparison of KPS in the lesion between the 2 groups (HT and non-HT) resulted in a significant difference ($p < 0.02$). ADC was reduced in all cases within the infarct zone but not significantly different between those who hemorrhaged and those who did not ($p = 0.50$). An example of a permeability map for one of the HT cases as well as a non-HT case is shown in figure 2.

Discussion: This study shows that early BBB defects in AIS can be assessed using quantitative DCE MRI. Significantly increased permeability was found in 3 cases which later on hemorrhaged. This method indicates the potential to identify patients at higher risk of HT and may allow to use physiological imaging rather than time from onset of symptoms to guide the decision to treat with t-PA. This could lead to an extension of the treatment window beyond current time constraints in those patients who have a stable BBB.

References: 1. HC Roberts et al.; AJNR 21(5):891-9, 2001



HT: 1-lesion, 2 -contralateral

Figure 1: KPS values of the lesion vs contralateral side in HT group ($p < 0.01$)

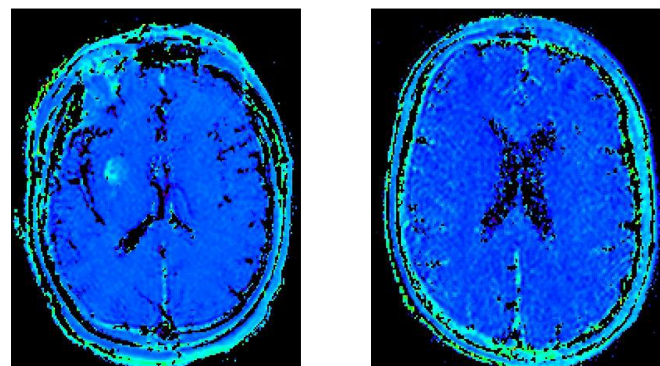


Figure 2: (a) KPS map of HT case (increased permeability indicated by arrow) and (b) non HT case