Postischemic Hyperperfusion on Arterial Spin Labeled Perfusion MRI is Linked to Hemorrhagic Transformation in Stroke

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Target Audience: Neurologists, Neuroradiologists and MRI scientists

Purpose: Hemorrhagic transformation (HT) is a major risk and a potentially life-threatening complication in acute ischemic stroke (AIS) patients who receive thrombolysis[1]. Past studies have linked HT with changes in blood-brain barrier (BBB) permeability and loss of cerebral blood flow (CBF) autoregulation, both of which could lead to post-treatment hyperperfusion that may occur within regions of the brain that reperfuse after initial ischemic injury. In this article, we aim to investigate risk factors associated with post-ischemic hyperperfusion detected on arterial spin labelling (ASL) along with its relationship with HT in patients with AIS in the middle cerebral artery (MCA) territory.

Methods: The study was performed on data collected from May 2010 to Sept 2013 in an ongoing prospective registry of patients evaluated with diffusion–perfusion MRI at our academic medical center. Patients who had AIS occurred within MCA distribution with baseline MRI performed within 24hr of symptom onset were included. Pseudo-continuous ASL with background suppressed 3D GRASE was performed during routine clinical MRI at various time points. Quantitative CBF maps were calculated based on a previously published model[2]. ASL CBF maps were visually inspected for presence of hyperperfusion defined as patchy areas with visually perceivable increased CBF either within or around the corresponding lesion observed on DWI images when compared with the homologous contralateral hemisphere. HT was followed during hospitalization and was graded on gradient recalled echo (GRE) scans into hemorrhagic infarction (HI) and parenchymal hematoma (PH). Finally, a free-form region of interest (ROI) was hand drawn on multi-slice CBF maps which have been normalized into the MNI template using SPM8 to delineate hyperperfusion areas by two experienced readers independently. The average CBF was acquired both in the hyperperfusion ROI and its mirror ROI and ratio between them was calculated. The weighted kappa test was used to evaluate the inter-rater agreement. The Chi-square test (and Fisher's exact test) and t-test were used to determine if there were statistically significant differences between clinical characteristics when stratified by HT or hyperperfusion. Multiple logistic regression (stepwise) analysis was used to identify predictors for HT that were significant in the univariate analysis. The Spearman's rank correlation was used to evaluate time course of hyperperfusion and grades of HT.

Results: A total of 361 ASL scans were collected from 221 consecutive patients (age=72±17 years; 45% males) with MCA stroke. The κ coefficient was 0.631, 0.803 and 0.737 for ASL imaging quality, presence of hyperperfusion and HT grades respectively between the 2 raters. Hyperperfusion was detected in 76/221 (34%) patients and can be differentiated with delayed arterial transit effects with the latter being thread-like and winding high signals within cortical vessels and corresponding high signal on ATT maps due to delayed arrival of labeled blood (Fig 2). Overall, HT affected 80/221 (36%) patients, including 23/221 (10%) HI1, 20/221 (9%) HI2, 21/221 (10%) PH1 and 16/221 (7%) PH2 (Fig 1). Hyperperfusion was more frequently detected post-treatment (OR=4.8, 95%CI 2.5-8.9, P<0.001) and with high NIHSS scores at admission (P<0.001). There was a significant association between having hyperperfusion at any time point and HT (OR=3.5, 95%CI 2.0-6.3, P<0.001), and the effect preserved in stepwise multivariate logistic regression analysis. There was a positive relationship between the grade of HT and time to hyperperfusion with the Spearman's rank correlation of 0.44 (P=0.003). There was a trend that patients with first hyperperfusion after 12 hours from stroke onset were more likely to experience PH than those with first hyperperfusion within 12 hours (Fisher's exact p-value = 0.06). Average CBF in hyperperfusion ROIs and contralateral mirror ROIs was 70.1±25.5 and 43.8±18.1ml/100g/min respectively (P<0.001) with ratio=1.7±0.5.

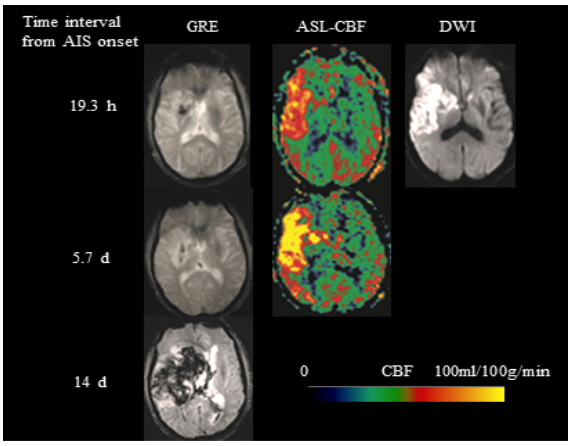

Fig. 1 Representative AIS case. HI-2 in the right basal ganglia was seen on GRE scanned 19.3 h after onset after IV tPA and clot retrieval treatment. Corresponding ASL scan showed hyperperfusion in the right MCA region. Hyperperfusion still existed on ASL 5.7 d from onset. A hematoma (PH-2) developed 14 d after onset.

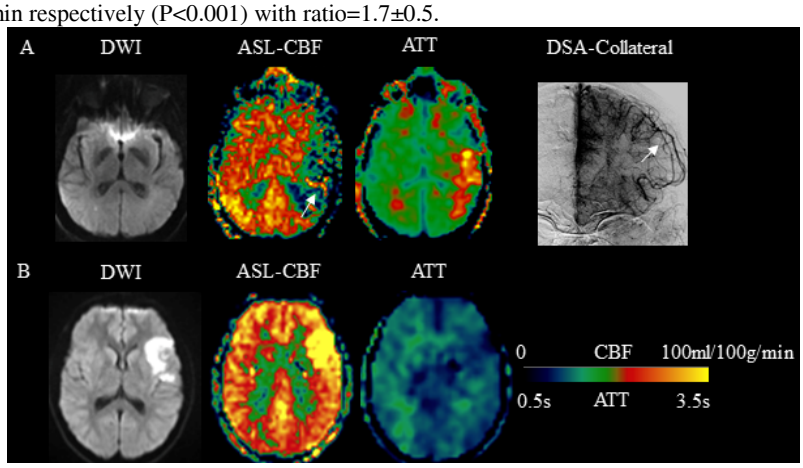

Fig. 2 Representative AIS cases with hyperperfusion or collateral circulation. A showed serpiginous collateral circulation signals on ASL-CBF maps which was demonstrated via DSA (arrows) and high signal on ATT maps. B showed patchy hyperperfusion areas detected on 4-PLD ASL-CBF maps with corresponding decreased signals on ATT maps.

Discussion and Conclusion: This study revealed that post-ischemic hyperperfusion can be reliably detected by serial ASL imaging, with a high degree of consistency between readers. While the main limitation of ASL in stroke has been the potential underestimation of tissue perfusion in the presence of prolonged arterial transit delays, hyperperfusion is easily detectable in ASL since the ATT is shortened or at least not prolonged. Hyperperfusion on ASL images acquired at any time point following stroke onset was an independent risk factor of HT. Patients presenting hyperperfusion within or around DWI lesions were approximately 3 times as likely to experience HT compared to patients without hyperperfusion. ASL hyperperfusion may provide an imaging marker of HT which may guide the management of AIS patients post tPA and/or endovascular treatments. Late hyperperfusion should be given more attention to prevent high grade HT.

References: [1] Berger C, et al. Stroke. 2001; 32(6): 1330-5. [2] Wang DJ, et al. Stroke. 2012 Apr; 43(4): 1018-24.