Functional diffusion map evaluation of perihematomal edema as an imaging biomarker for the early prediction of primary intracerebral hemorrhage outcome

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Background

Secondary neuronal injury in the perihematomal edema is one of the major factors that lead to the high morbidity and mortality in primary intracerebral hemorrhage (ICH). Diffusion magnetic resonance imaging (MRI) has been applied in studying perihematomal injury in patients with ICH but with inconstant results. Because the perihematomal injury should be complex and heterogeneous, different areas of edema with increasing and decreasing changes in diffusion would be masked in overall mean apparent diffusion coefficient (ADC). In contrast, functional diffusion maps (fDM) have been developed in which regional variations in diffusion, including both increasing and decreasing, can be quantified[1,2]. In this prospective investigation, we estimate diffusion change in perihematomal edema during acute stage (within 7 days) after ICH by using fDM. We hypothesized that early diffusion changes in perihematomal edema correlate with clinical outcome in patients with ICH and that fDM approach could be used as a predictive imaging biomarker.

Methods

29 patients of ICH were enrolled and classified into good and poor outcome groups according to their Modified Rankin Scale (mRS) and Barthel Index (BI) at 6 month after ICH. MRI scans were obtained at baseline (within 24 hours), 5 and 7 days after symptom onset. Axial T2*-weighted and fluid-attenuated inversion recovery images were acquired for volume of the hematoma and edema. Diffusion-weighted images were also acquired and the mean ADC value for the perihematomal hematoma and contralateral healthy brain are measured. The ADC maps on day 5 and day 7 were coregistered to the baseline and then computation of fDMs for the perihematomal edemas was accomplished. Individual voxels with the perihematomal edema were stratified into three categories based on the change in ADC from baseline to each time point: red voxels for which the ADC increased significantly, the blue voxels for which the ADC decreased significantly, and green voxels for which the ADC did not change significantly. The percentage of peritumoral edema within each of the three categories was than calculated as V_R (% red voxels), V_B (% blue voxels), and V_T ($V_R + V_B$).

Results

Among the clinical variables testes, age, body temperature exceed 37.5, diastolic and mean arterial pressure, and baseline white cell count were statistically different between two groups. The baseline ADC values in the contralateral healthy hemisphere were negatively correlated with patient's outcome. Two examples of fDM analysis from each group were showed in Fig.1. Fig. 2 is box plots summarizing fDM change volumes as a percentage of perihematomal volume for each patient group. We defined the thresholds for V_R, V_B and V_T as the midpoint of the lower 95th percentile of good outcome patients and the upper 95th percentile of the poor outcome for discrimination between groups, and fDM had good sensitivity and specificity. When using a V_T of day 7, threshold of 23.21, fDM had a 92.9% sensitivity (95% CI 66.1-99.8) and a specificity of 100% (CI 78.2-100) for distinguishing good outcome from poor outcome patients.

Conclusion

The pathophysiological process within the perihematomal edema is complicated and relates to both systemic and local responses[3]. Small or absence perihematomal edema on conventional MRI and CT, as well as less elevation of mean ADC value, do not always indicate lesser perihematomal injury and a favorable outcome. In patients with diverse primary brain tumors[1] as well as high-grade gliomas[2,4], fDM provided an imaging biomarker for the early prediction of treatment response and overall survival. The evidence that fDM analysis can be used as an early imaging biomarker to predict the functional outcome of acute ICH patient was clearly demonstrated in this study. Early changes in fDM, both increasing and decreasing ADC value, correlate well with patient's clinical outcome.

References

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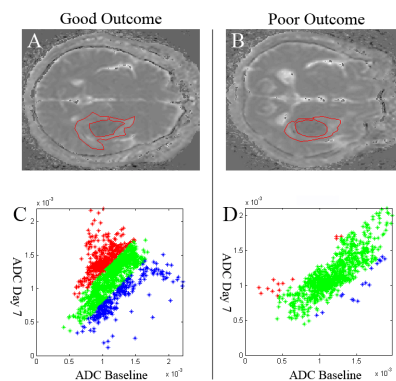
Fig. 1. Representative ADC maps and fDM scatter plots for patients of each group. (A and B) Following coregistration of the ADC maps on day 5 and day 7 to the baseline, perihematomal edemas were manually contoured on baseline ADC maps. (C and D) The scatter plots quantitatively show the distribution of ADC value changes for the entire contoured perihematomal edema. (A and C) A patient of good outcome with fDM parameters of $V_R = 28.7$, $V_B = 23.9$, $V_T = 52.6$. (B and D) A patient of poor outcome with fDM parameters of $V_R = 1.4$, $V_B = 3.0$, $V_T = 4.4$.
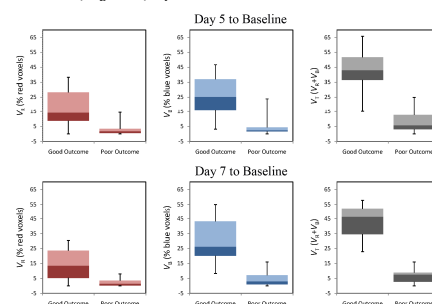

Fig. 2. Box plots summarizing fDM change volumes as a percentage of perihematomal volume for each patient group. In the upper row is the fDM change between the fifth day after stroke and base line while the lower row is of seventh day. The percentage of total volumes with the perihematomal edema is significantly different between good and poor outcome group, no matter significantly increased diffusion values (V_R), significantly decreased diffusion values (V_B) and any significantly change in ADC (V_T, $V_T = V_R + V_B$). Error bars reflect 95% confidence intervals.