Could Functional Perfusion MRI Predict Later Occurrence of Steroid-Associated Osteonecrosis? An Experiment Study in Rabbits

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Background: Early diagnosis or detection of osteonecrosis is very important as its prognosis is stage-dependent. Up to date, the most sensitive and commonly used modality for early ON detection relies on the abnormal signal of conventional MRI (T1-weighted and T2-weighted MR imaging), which matches the necrotic and repairing reaction in bone and marrow. As ischemia is the defined pathway leading to steroid-associated osteonecrosis (ON). Early detection of ischemic condition may help predict later ON occurrence. Bone marrow perfusion function evaluation by perfusion magnetic resonance imaging (MRI) may be a unique modality for this application.

Materials and Methods: Twenty-five adult male New Zealand white rabbits were used in this study. Lipopolysaccharide (LPS) and methylprednisolone (MPS) were administrated for ON induction based on a published protocol. T1-weighted and fat suppression T2-weighted MR imaging (conventional MRI) were performed for ON lesions detection based on the abnormal signal in the proximal femora at week 0 as the baseline (before LPS injection), week 1 and week 2 after MPS injection. At the same time, the blood perfusion function in the proximal femora was measured by perfusion MRI. Maximum Enhancement (ME) – an index of MRI perfusion function was analyzed. After MRI scanning, the proximal femora were prepared histopathologically for ON lesion analysis. The rabbit with bilateral histopathological ON lesions was defined as ON+ rabbit and included into ON+ group evaluated at week 1 and week 2 respectively, and that without ON lesions in bilateral femora was classified into ON- group. For the underlying mechanism of perfusion change, the extravascular marrow fat cells were measured and the intravascular endothelium inflammation injury indicator of tissue factor (TF) expression and thrombus formation were detected.

Results: In ON+ group, ME in perfusion MRI showed a significant decrease at week 1 and week 2 as compared with the baseline (P<0.01). There was a more than 50% decrease in ME at week 1 in ON+ group; while there were no detectable ON lesions by conventional MRI at week 1, though 93% (14/15) rabbits could be detected at week 2 in ON+ group. In ON- group, ME showed a slight decrease at week 1 (less than 30%), and nearly recovered to normal at week 2 as compared with the baseline. Histological results showed a much larger average marrow fat area and more severe marrow blood sinusoids compression from surrounding crowded fat cells, and stronger positive TF expression in marrow endothelium and more thrombus formation in ON+ rabbits than ON- rabbits.

Conclusions: This study demonstrated that functional perfusion MRI could predict development of steroid-associated ON. Our experimental data suggested that perfusion MRI might be a sensitive non-invasive modality for monitoring steroid-associated ON in patients.

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Fig 1 Comparison of sensitivity of perfusion MRI and conventional MRI: T1W (TR/TE=425/20 msec, echo train length=3), fat suppressed T2W (TR/TE= 2500/70 msec, echo train length=10) in prediction of ON development in proximal femora. Aa-Ca: Representative signal-intensity curve for ON+ femur at week 0 (Aa), week 1(Ba) and week 2 (Ca), showing a great decrease at week 1 and a slight recover at week 2 in ME; Ab-Cb: Corresponding conventional MR imaging in the same ON+ femur showed no detectable abnormal signal in week 0 (Ab) and week 1 (Bb) with homogeneous intermediate or high signal intensity on T1W images; while at week 2 it showed clear abnormal signal in the proximal femora with low signal-intensity area surrounded by high signal intensity area in the proximal femora on fat suppressed T2W images (Cb, white arrow).