Evaluation of Bone Turnover in Femoroacetabular Impingement by 18F-Fluoride Positron Emission Tomography

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Introduction: Femoroacetabular impingement (FAI) is one of the recent important topic in hip disorders, however, there are still many unknown matters in its pathophysiology. In consideration of consequent osteoarthritis caused by FAI, the local bone turnover status is one of the special interests. 18F-fluoride is one of the competent bone seeker which directly reflects the osteoblast activity accompanied by bone formation. In addition, recent sophisticated positron emission tomography (PET) technology with high imaging resolution makes it possible to identify the bone remodeling abnormalities in small region. We hypothesized that local bone turnover may be accelerated in cam and pincer lesion, therefore utilized 18F-fluoride PET for FAI cases. The purpose of this study was to reveal the bone turnover status in FAI, comparing between symptomatic and asymptomatic side, and investigate the relationship with morphologic parameters.

Methods: A total of 27 patients (male:11 , female:16 , average age:53) who were diagnosed as unilateral symptomatic FAI. Informed consent was obtained for each patients before enrolling to this study. Our institutional review board approved this study. All 27 patients were diagnosed as unilateral FAI by a physical examination with anterior impingement sign and by a xylocaine test (pain relief confirmation by xylocaine injection into hip joints). Plain X-ray with anterior-posterior bilateral hip joints and cross-table lateral view was obtained for each cases. 18F-fluoride PET was performed for all cases and quantitative evaluation by standardized uptake value (SUV) was performed according to the definition of region of interest defined below description. Also the CT and MRI were performed for all cases.

Region of interest (ROI) for SUV evaluation was defined as follow. The coronal image of 18F-fluoride PET was evaluated to identify the height level of bladder in each case. In most of cases, the top level of bladder concordant with the top of femoral head and the bottom level of bladder is identified as lower level of femoral head neck junction(figure 1-A), so that we identified the acetabular level (pincer lesion) in slight proximal of bladder level (figure 1-B). Then we searched the maximum SUV in each axial image of femoral head-neck junction area (cam lesion) (figure 1-C). The symmetrical region of symptomatic side was then defined as asymptomatic side as a reference SUV (figure 1-B, C). SUVmax ratio was calculated as SUVmax of symptomatic side / SUVmax of asymptomatic region.

Figure 1. Definition of region of interest
Results: The average SUV\text{max} of cam lesion in symptomatic side was 6.06±2.28 and that of asymptomatic side was 3.67±1.24, which shows significantly higher value in symptomatic side compared with asymptomatic side. The average SUV\text{max} of pincer lesion in symptomatic side was 7.52±2.59 and that of asymptomatic side was 4.50±1.57, which shows significantly higher value in affected side compared with contralateral side. Figure 2 shows a positive correlation between $\alpha$ angle and SUV\text{max} ratio of cam lesion ($r=0.5$, $P=0.007$).

Figure 2. Correlation between $\alpha$ angle and SUV\text{max} ratio in CAM lesion

$\alpha$ angle ≥60 group showed significantly higher SUV\text{max} ratio than <60 group (figure 3).

Figure 3. Difference of SUV\text{max} ratio between $\alpha$ angle <60 and ≥60 group
There was no significant correlation between CE angle and SUVmax ratio of pincer lesion ($r=-0.32$, $P=0.10$). Bone marrow edema positive group shows significantly higher SUVmax ratio in cam lesion compared with bone marrow edema negative group ($P<0.0001$). On the other hand, there was no significant difference of SUVmax ratio in cam lesion between herniation pit positive group and negative group by CT ($P=0.26$).

**Discussion:** We confirmed the accelerated bone turn over in both of pincer and cam lesion of symptomatic side compared to asymptomatic side in FAI cases. This is the first report utilizing 18F-fluoride PET for the evaluation of bone turn over status in FAI. The implication of this study is that we successfully visualized the bone turn over status by molecular imaging modality, separating in pincer and cam lesion.

Focusing on cam lesion, $\alpha$ angle was significantly correlated with the uptake of PET. This result suggests that the severity of morphologic abnormality associates with high bone turn over in cam lesion. Because our previous study demonstrated the positive correlation between mechanical stress and 18F-fluoride PET uptake in dysplastic hip(1), we speculate that the mechanical stress has certain role for 18F-fluoride PET uptake, i.e. high bone turn over, also in pathophysiology of FAI. Although the threshold of $\alpha$ angle is still controversial, when we set the threshold at 60°, the group with $\alpha$ angle more than 60° revealed significantly higher SUVmax ratio. Thus, morphologic abnormalities possibly influence the bone metabolism abnormality.

Our previous investigation revealed the accelerated bone turn over in hip osteoarthritis, even in early stage without marked radiographic findings(2). Especially in very early stage of osteoarthritis incidence, the acceleration of bone turnover has been demonstrated in animal model(3). Although the mechanism of osteoarthritis incidence may be different between dysplastic hip and FAI, both of those mechanism has close relationship with bone turnover.

One limitation of this study is relatively small number of cases. We used asymptomatic contralateral side as a reference control, however, it should be noted that contralateral side is not considered as a normal hip joint. Nevertheless, we enrolled only unilateral symptomatic cases even with or without radiographic findings to compared the SUVmax between symptomatic and asymptomatic side.

In conclusion, we evaluated the bone turnover status in cam and pincer lesion of FAI cases by 18F-fluoride PET. Comparing with asymptomatic contralateral side, bone turnover in symptomatic affected side was significantly accelerated. In cam lesion, the acceleration of bone turnover correlated with $\alpha$.
angle. This acceleration of bone turnover probably relates with local mechanical stress exposure by repeated impingement. Further studies are needed to reveal the detailed role of this local bone turnover acceleration in pathophysiology of FAI.

**Significance:** This study clearly demonstrated that local bone turnover is accelerated in both of cam and pincer lesion. In cam lesion, morphologic parameter affected the degree of bone turnover acceleration.

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