

Association between spinal disc degeneration and deficits in endplate perfusion

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Introduction:

Musculoskeletal disorders of the spine are a major health problem associated with debilitating back pain, which leads to significant psychosocial and economic consequences. The majority of chronic back pain is associated with degeneration of the intervertebral disc (IVD), which can manifest itself in many different clinical conditions. However, the factors that lead to disc degeneration and its pathophysiology are still not completely understood. As a result, diagnosis and treatment may involve redundant procedures, which require inordinate amount of expenses and patient suffering.

Intervertebral disc (IVD) is avascular; nutrition is supplied (and waste is removed) via diffusion mechanism from the capillary beds of the cartilaginous vertebral body (VB) endplates. Disruption in subchondral bone/endplate perfusion of VB has long been suspected as a major factor in pathogenesis of IVD degeneration [N Boos, *et al.* Spine 27:2631–2644, (2002)]. In the presented study we used dynamic contrast-enhanced MRI (DCEMRI) to investigate the endplate (EP) perfusion and its association with disc degeneration.

Methods:

The study was approved by the UCI IRB and written consents were obtained from the subjects. 15-sagittal slices (3mm) were acquired from nine subjects (age: 27–62y; mean 45y) with 3D GE sequence (TR/TE=3.4ms/1.2ms, flip-angle=30°, 0.81×0.81mm² in-plane resolution and 36.4s frame rate). The contrast (Gd-DTPA-BMA, 0.1 mmol/kg) was administered manually as a bolus via an antecubital vein at the start of the 3rd dynamic frame. T2 weighted MRI were acquired for conventional Pfirrmann grading of disc degeneration as well as diffusion weighted MRI (DWI) data to quantify disc degeneration (TR/TE=4000ms/66ms, NEX=7, 2.4×2.4mm² in-plane, b=0 and 600 sec/mm²). ROIs were drawn manually on pre-contrast images of the DCEMRI set to segment out the subchondral EP. 10 separate subchondral EP ROIs (L1-inferior EP down to S1-superior EP) were drawn for the 5 IVDs. In each EP, volume-averaged signal enhancement time course were calculated and percent enhancement curve were generated with respect to the baseline intensity before injection. The degree of disc degeneration was graded using mean Apparent Diffusion Coefficient (ADC) inside the disc (Table 1) (grade 1: no discernible degeneration; 4: significant degeneration). Our group and several others have shown that ADC is highly correlated with the widely accepted Pfirrmann grades.

| | ADC |
|---------|-----------|
| grade 1 | 1.76-1.93 |
| grade 2 | 1.42-1.69 |
| grade 3 | 1.08-1.42 |
| grade 4 | 0.38-0.86 |

Table 1. grading disc degeneration based on mean ADC values.

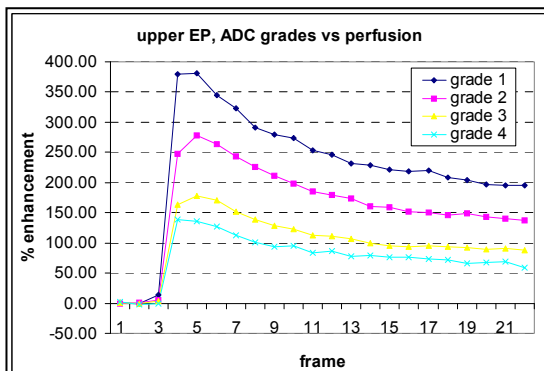


Fig.1. Time-intensity curves from DCEMRI experiment. e.g., grade 1 curve is the average percent signal enhancement within the endplates of all grade-1 IVDs. Enhancement decreases with increased IVD degeneration.

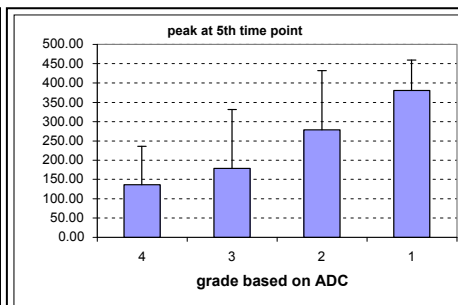


Fig.2. Mean and standard deviation at the 5th time point of each curve in Fig.1. Decrease in peak enhancement was seen with increased degeneration.

Results:

The results showed that increased degree of disc degeneration was associated with significantly lower enhancement (blood perfusion) in the corresponding EPs (Fig.1). Fig.2 shows the mean and standard deviation at the 5th time point of contrast enhancement for each disc grade. It illustrates reduced perfusion with increasing disc degeneration. We also discovered that age contributes to the reduction in perfusion. Fig.3 shows perfusion in endplates of

only grade-3 discs for three age groups (young, middle age and old). So, we explored if higher grades were mostly from older and lower grades were mostly from younger subjects; this would mean that both reduction in perfusion and ADC could be mainly age related, and possibly not associated. Fig.3 already demonstrated that patients with grade 3 discs were not dominantly from the old age group. To explore this further, we plotted age versus ADC (not shown) and observed that for ADC values between 0.68 and 1.84, which spanned basically the whole range of disc grades, there was no correlation with age (Pearson's $r(0.05)$). Only a few highest ADC values (>1.84) were exclusively from the young subjects (age: 27-28) and a few lowest (<0.68) were from old subjects (age: 55-62).

Discussion and Conclusion:

Our results provide evidence that reduced blood perfusion in IVD EPs is associated with the degree of degeneration of the discs in human volunteers. This is in accord with the literature that suggested that poor nutrient and oxygen delivery could be a major factor in IVD degeneration. We also demonstrated that blood perfusion decreases with age. However, we did not find significant correlation between age and ADC (degree of disc degeneration), except for the two extreme ends of the ADC spectrum. Those possibly biased grade 1 and 4 discs slightly but it did not appear to be the main factor. Therefore, we concluded that the level of disc degeneration and decrease in perfusion were associated and it was not mainly driven by age related changes in our subject population. Even though we did not see age as the major factor in disc degeneration in

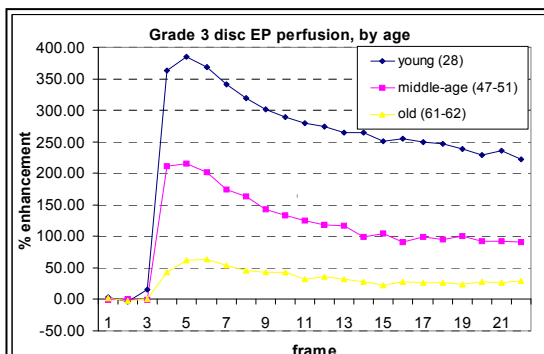


Fig.3. Time-intensity curves for only EPs of grade 3 discs for different age groups.

our small cohort, it is known that age is a factor. Therefore, in a large population study the relationship between perfusion and disc degeneration should be studied within confined age groups so that age factor can be eliminated. These findings could aid us differentiate disc degeneration associated with normal aging versus other pathological conditions that lead to this disease. This technique could be an invaluable tool for clinicians who would like to assess the efficacy of drugs or other nonsurgical treatments of IVD degeneration. Early improvements in perfusion, in the absence of major endplate calcification, may prognosticate potential recovery of degenerating IVDs. Since endplate calcification is also implicated as another factor in poor nutrient delivery to the disks, it is possible that the patient might have normal blood perfusion but degenerated disc due to calcified endplates. This possibility should also be taken into account and the study has to be expanded with a larger subject population to explore these findings in more detail.

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