



ADC Mapping and T2 Mapping of the Lumbar Spine to Assess Disc Degeneration: A Review

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Abstract

Early detection of disc degeneration and categorizing them is very important for the treatment plan and better prognosis. We aimed to assess the efficacy of apparent diffusion coefficient (ADC) mapping and T2 mapping in the early detection and grading of the severity of degenerative disc disease. In this review, the articles published until July 2022, from the PubMed database were used. All articles contained information about the application of ADC and T2 mapping in the detection of disc degeneration. A total of 40 articles were included in this review. We assessed each article for the feasibility of both techniques to categorize the degeneration. ADC values of nucleus pulposus (NP) showed a negative correlation with Pfirrmann grades and age. T2 values of NP and annulus fibrosus (AF) are significantly decreased with an increase in Pfirrmann grades. And also, as age increases, T2 values of NP and posterior AF decreased significantly. ADC and T2 mapping techniques are sensitive in the detection and categorization of disc degeneration. It is highly recommended to include quantitative magnetic resonance imaging techniques in routine spine imaging protocol in a patient with complaints of back pain.

Keywords

- ▶ diffusion
- ▶ MRI
- ▶ intervertebral disc degeneration
- ▶ spinal

Introduction

Lower back pain is known to affect 75 to 85% of people at some point of time in their lives. Degeneration of the intervertebral disc (IVD) is known to cause back pain in most individuals. The IVD is a flexible structure between vertebrae measuring ~7 to 10 mm in height and 4 cm in diameter at the lumbar level. The structure contains an outer ring of fibrous cartilage called annulus fibrosus (AF), which surrounds a gelatinous core in the center called the nucleus pulposus (NP).¹ The disc's NP loses proteoglycans (PGs) as the degenerative cascade of degenerative disc disease begins, reducing the disc's ability to imbibe and retain water. The PG drop is thought to be the first step in the vicious degenerative cycle: the IVD's biomechanical properties are harmed, hampering the disc's ability to recover from daily loading con-

ditions, resulting in a cumulative loss of IVD height and making the disc susceptible to further degradation.²

In diagnosing the lower back pain, radiological imaging plays a most important role. Magnetic resonance imaging (MRI) gives excellent soft tissue contrast without using any harmful ionizing radiation. MRI is sensitive to water within the tissue; hence, it is more sensitive toward disc degenerative disease. T2-weighted (T2W) and T1-weighted (T1W) MRIs are the most common techniques to examine the health of IVDs. Based on the T2W MRI characteristics, Pfirrmann et al³ classified degenerative disc disease. They used multiple factors to classify, such as disc structure, signal intensity, ability to differentiate between NP and AF, and the height of the disc. Thompson et al⁴ proposed a grading system to evaluate morphologic changes caused by intervertebral disc degeneration (IVDD).

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T2 mapping is an MRI technique that calculates the T2 decay time of tissue and is presented in a voxel-wise parametric map. This technique is mainly used for tissue characterization of myocardium and imaging of cartilage.⁵ The apparent diffusion coefficient (ADC) is the measure of Brownian motion of the water molecule in the tissue. This value can be obtained from diffusion-weighted imaging (DWI) sequences in MRI.⁶ Currently, the technique is widely in use for neuroimaging.

T2 mapping and ADC mapping are two advanced quantitative methods for assessing IVDD, which estimates the biochemical nature of the IVD. This review aims to provide comprehensive information about DWI and ADC mapping to better understand IVDD using a noninvasive method. This may improve the prognosis and prevent invasive intervention techniques by accurately diagnosing IVDD.

Methodology

Search Strategy

The articles from the PubMed database were used to prepare the review. Articles published between 2003 and July 2022 were selected. Phrases used in searches are “diffusion-weighted imaging in degenerative disc disease,” “ADC mapping in degenerative disc disease,” “quantitative MRI technique in degenerative disc disease,” and “T2 mapping in degenerative disc disease.” After reading the titles and abstracts of the articles, they have been shortlisted for the inclusion criteria, and then added to the final review.

Inclusion Criteria

All articles that contain information about the application of ADC and/or T2 mapping in lumbar IVDD were included in the review. The result included the comparison of quantitative MRI techniques (ADC and T2 mapping) with the grading of lumbar IVD degenerative disease (such as Pfirrmann grading system, Thompson's grading system, Modic changes, and herniation) and age.

Results

Study Selection

A total of 669 articles were found under the phrases used for searches. These were narrowed down to 40. Each article contained information about the application of both ADC and T2 mapping techniques or one among both on IVDD.

Study Characteristics

The characteristics of the study included 40 studies⁷⁻⁴⁶ conducted in 15 countries: China, the United States, Canada, Russia, Finland, Taiwan, Turkey, Almeda, Germany, Brazil, Japan, Egypt, India, Austria, and Pakistan from 2003 to May 2022.

Diffusion-Weighted Imaging

Diffusion

The human body is ~70% composed of water. Due to thermal energy, there is a random Brownian motion of the molecule

called diffusion. Diffusion depends on the structural and chemical nature of the tissues. Different tissues of the body exhibit different levels of diffusion. In addition, different pathophysiology will alter the internal cellular structure, resulting in a diffusion change. DWI is the qualitative (DWI trace) and quantitative (ADC map) representation of the diffusion of water. A total diffusion across an area of the tissue per second is called an ADC. ADC is high in free water diffusion, while ADC is low in restricted water diffusion.⁶

Theoretically, ADC can be obtained by

$$ADC = \frac{\ln(S_0/S_1)}{(b_1 - b_0)}$$

Where b_0 and b_1 are the strength gradients applied at two different times. S_0 and S_1 are signal intensities at b_0 and b_1 , respectively.⁶

Evolution of Diffusion-Weighted Imaging

The concept of DWI in the clinical application was introduced long back. This is initially used in neurological imaging, especially in stroke or white matter diseases. Later also became more efficient in oncology applications.⁶ This review article discusses the application of DWI in degenerative disc disease.

Eighteen studies discussed the significance of ADC mapping in early IVDD detection. The efficacy of the ADC map in classifying and early detection was highly significant. ADC values showed a negative correlation with the increase in degeneration.⁴²

ADC Mapping and Pfirrmann Grades

As the Pfirrmann grade increases, the ADC value of NP significantly decreased, but the ADC of AF did not show a strong correlation with Pfirrmann grades.^{7,42} Additionally, Alashwah and Eltoomy⁴² provided the ADC cutoff value for differed Pfirrmann grades by receiver operating characteristic (ROC) analysis. The cutoff value for Grades I and III was $\leq 1.77 \text{ mm}^2/\text{s}$, and for Grades III and IV $< 1.66 \text{ mm}^2/\text{s}$. Li et al⁴⁴ compared the efficacy of ADC, functional anisotropy (FA), and T2 values of lumbar disc degeneration and found ADC had the most significant diagnostic value, followed by T2 and FA values.

ADC Mapping and Age

Li et al¹⁶ conducted a quantitative MRI study on IVD of rats grouped into four, according to their age (28, 42, 56, and 70 days). A significant decrease in ADC value of the entire disc, NP, and AF was found as age increased. Also, in humans, as age increases, ADC values of the NP and entire disc decrease significantly.^{13,24}

ADC Mapping and Other Parameters

Aydin et al³⁹ found that DWI has 77% sensitivity and 100% specificity for herniation, 100% sensitivity and 50% specificity for extrusion, and 100% sensitivity and specificity for sequestration. Between nonbulging/herniated and herniated discs and between nonbulging/herniated and bulging discs, there were significant differences in mean ADC values. However,

ADC values failed to differentiate between bulging and herniated discs.^{9,41} Antoniou et al³⁷ found that ADC value and glycosaminoglycan (GAG)/water content correlate positively. A diurnal study presented a significant decrease in the ADC values of AF from morning to evening.³⁶

Comparison of ADC Mapping with Other Quantitative MRI
Li et al⁴⁴ compared the significance of ADC, FA, and T2 mapping. The study result showed that ADC has higher sensitivity, followed by the T2 value and FA value, in detecting degeneration. Aydin et al³⁹ compared the DWI and constructive interference in steady state (CISS) sequences in herniated discs, which showed that both DWI and CISS showed significantly higher sensitivity and specificity in classifying herniation.

T2 Mapping

T2 mapping is another quantitative MRI technique that measures the T2 relaxation time of the tissue. T2 mapping measures the pixel-wise T2 relaxation time of the tissue. This requires acquiring multiple T2W images in series, coregistration of multiple images, pixel-wise evaluation of T2 relaxation timings, and quantitative parametric map reconstruction. The formula for pixel-wise calculation of relaxation time is

$$S(x, y) = Mo(x, y)e^{\frac{-TE_{T2p}}{T2(x, y)}} + C$$

Where $S(x, y)$ is the signal intensity at a pixel location (x, y) , $Mo(x, y)$ is the steady state signal, TE_{T2p} is T2 preparation time, and $T2(x, y)$ is the T2 relaxation time at a location (x, y) , and C is a constant offset depends on the fitting model.⁴⁷

Currently, T2 mapping is mostly used in the CartiGram of the knee joint and assessment of the myocardium. This review discusses the application of T2 mapping in lumbar disc degeneration.

Thirty studies discussed the significance of T2 mapping in early disc degeneration disease detection. T2 values are compared with many parameters such as degeneration grades, herniation, age, and diurnal. T2 values showed a significant negative correlation with the degree of degeneration.¹⁷

T2 Value and Pfirrmann Grades

With the increase in Pfirrmann grades of the IVD, the T2 relaxation value of NP and AF decreased significantly.^{7,26,35,43} Noebauer-Huhmann et al³³ compared the T2 relaxation values with modified Pfirrmann grades, which showed a moderate negative correlation. Additionally, Alashwah and Eltoomy⁴² provided T2 cutoff value for different Pfirrmann grades by ROC analysis. The cutoff value for Grades I and II was 110 milliseconds, II and III was <93 milliseconds, III and IV was 87 milliseconds, and IV and V were 79 milliseconds.

T2 Value and Age

As age increases, there was a significant decrease in T2 values.⁷ Further stratification of T2 value into NP, anterior

AF, and posterior AF shows a negative correlation, except at posterior AF at L5S1 level.²²

T2 Value and Other Parameters

A study by Ogon et al⁸ showed T2 value of posterior AF showed a significant negative correlation with visual analog scale score and a significant positive correlation with Japanese orthopaedic back pain evaluation questionnaire score. Another study by Ogon et al⁴⁶ showed T2 value of posterior AF was significantly lower in group neuropathic pain) than nociceptive pain. Ogon et al¹⁰ analyzed the correlation between T2 values and segmental mobility. Moreover, the study shows that the T2 value was significantly correlated with segmental mobility. T2 was also found to be significant with water content and GAG content of the IVD.^{14,17} Diurnal studies presented a significant decrease in the T2 value of the NP and a significant increase in the T2 values of AF from morning to evening.^{32,36} Another study by Sun et al³⁰ proved a negative correlation between Thompson's degenerative disc grading and a positive correlation between collagen type II and aggrecan content.

Comparison of T2 Mapping with Other Quantitative MRI

Menezes-Reis et al³⁴ compared the T2 and T1 mapping with age and concluded that only T2 mapping was negatively correlated with age. Welsch et al²⁵ compared T2 and T2* mapping with Pfirrmann grades. Both showed a negative correlation with Pfirrmann grades.

ADC and T2 Mapping in IVDD

Ludescher et al³⁶ studied diurnal T2 and ADC changes in NP and AF and found a significant decrease in the T2 value in NP and an increase in AF. However, ADC significantly decreased in AF. With this, they concluded that a combination of T2 and ADC mapping would be more sensitive in detecting IVDD. ADC and T2 values were equally and significantly correlated with Pfirrmann grades.^{7,13,24,26} Shen et al¹⁵ reported on the correlation of ADC and T2 values with different lumbar disc levels and locations of the same discs. Both values decreased with disc level from cranial to caudal. Also, in the same disc from the periphery to the central region, values increased in either direction from anterior to middle and posterior to the middle.

Discussion

The present review included 40 studies to examine the efficacy of ADC and T2 mapping in the early detection of lumbar disc degeneration by comparing them with multiple parameters, such as disc degenerative grades, biochemistry, age, etc., and extracted the significance of each method from all articles selected.

IVD is divided into the central NP and the peripheral part called AF. Abundant sulfated GAGs are found throughout the NP, which is covered in a loose web of type II collagen. About 25% (dry weight) collagen, 20 to 25% (dry weight) noncollagenous proteins, and the remaining dry weight (~50%) is composed of PG in the NP. The nucleus may support spinal

compressive pressures because of the “swelling pressure” that its PGs osmotically exert. Comparatively, the AF is composed primarily of coarse type I collagen fibers, contains 70% (dry weight) collagen, and has a low PG content.² Loss of PGs and collagen type II is seen during the early stages of disc degeneration. PG loss causes a decrease in the ability to bind water, which causes dehydration. Later, type I collagen fibers replace type II collagen fibers in the annulus, changing the tissue’s ability to withstand tension.⁴⁸

Identifying IVDD at the earliest may be essential when applying therapeutic interventions that might stop or perhaps reverse IVDD. The routine protocol for lumbar disc degeneration includes T1 and T2 sagittal, T2 axial, and T2 sagittal fat-saturated sequences. A morphological grading system using the T2 signal pattern from the IVD is currently in use to classify the disease. The limitation of such a system was different interobserver agreements. This limitation could be overcome by using quantitative MRI techniques.¹³ The quantitative MRI techniques used are DWI, T1rho, T2 mapping, and diffusion tensor imaging. DWI measures the magnitude of water molecule diffusion within the tissue, and T2 mapping calculates the T2 decay time of the tissue.^{6,47} Both these techniques are more sensitive than other techniques in the quantification of IVD.^{14,44}

T2 values of the IVD were influenced by the translational and rotational motion of the water molecules, whereas the ADC value was only sensitive to water content but not affected by any motions.³⁵ All studies presented a significant negative correlation between Pfirrmann grade and the ADC/T2 values.^{7,26,35,43} Yu et al²¹ evaluated the ADC value with a 10-point Pfirrmann classification-based score rather than five grades. Nevertheless, there was large overlapping of ADC values in Pfirrmann grades. Sun et al³⁰ also found a significant negative correlation between the T2 value and Thompson’s grades for disc degeneration. As degeneration was a continual and slow process, with the morphological assessment, using quantitative MRI techniques to classify the disease would be helpful, especially in the early stages of the disease.

The prevalence of disc degeneration is increased with age, that is, 37 to 96% from 20 to 80 years of age of asymptomatic individuals.⁴⁹ Similarly, multiple studies showed a significant negative correlation between T2/ADC mappings and age.^{22,35,43} Menezes-Reis et al²² compared the efficacy of T1 and T2 relaxometry, concluding that T2 mapping is superior to T1. Li et al¹⁶ conducted a study on rats with four groups, with an increase in age. The study concluded that ADC value in NP and AF decreased as age increased. All results support the significance of T2 mapping and ADC mapping in the early detection of IVDD.

The ability to alter the height of IVD is mainly governed by the fluid flow, which is regulated by the PGs’ capacity to retain fluid inside. There was a 10% variation in the disc height between morning and evening, that is, disc height decreased by 0.1 to 0.6 mm after daily activity.⁵⁰ Inconsistent with these results, several articles showed a decrease in the T2 value in NP and an increase in the T2 value in AF. This might be due to the pressing of water out of NP into peripheral AF.^{32,36} Also, a decreased ADC value of AF was

found, but no changes in NP. ADC was mainly sensitive to the diffusion of structure, which contains more parallel fibers.³⁶

Many studies discussed the T2/ADC values at different parts of the IVD, such as whole disc, NP, anterior AF, and posterior AF. Menezes-Reis et al²² studied subjects between the ages of 20 and 40 years. The study found a negative correlation between the T2 value of NP, posterior AF, and entire disc with aging and no correlation with T2 values. However, interestingly, the T2 value of the anterior-most part of posterior AF showed a significant increase in T2 values in two groups, normal and subjects with herniation.¹⁹ This could be because of the influence of NP. Therefore, the increased water content in the anterior part of the posterior AF could increase the T2 signal.⁴⁵

Few studies suggest that ADC was more sensitive in detecting IVDD than T2 mapping.^{13,44} However, Niu et al²³ suggested that the T2 value would be more sensitive toward detecting early disc degeneration. And several studies suggest the sensitivity to detect degeneration was equal.^{7,26,36}

The limitation of the studies includes the lack of a gold standard to confirm or classify the degeneration.^{9,15,18,24,25,35} Multiple articles used a small population.^{12,17,21,29,31–33,36} Morphological grading might change from MRI at different field strengths due to variations in image quality.²⁵ Artifacts caused by the flow of cerebrospinal fluid might interfere in the clear distinguishing NP and AF.⁹ There was no evidence justifying nonspecified lower back pain correlated with degeneration.⁴⁶

Conclusion

In conclusion, ADC and T2 mapping techniques are sensitive in quantifying early IVDD, while such changes are not visible in conventional MRI sequences. Adding T2 mapping or ADC mapping to conventional MRI protocol is highly recommended to rule out IVDD.

Conflict of Interest

None declared.

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