
REVIEW ARTICLE**Correlation between lumbar intervertebral disc volume and corresponding apparent diffusion coefficient value in disc degeneration: A systematic review***Bilqueesa Mushtaq^{1*}, Gaurav Mishra², Anurag Luharia³, Bisma Amin¹*¹*Datta Meghe Institute of Higher Education and Research, Wardha-442001, (Maharashtra) India,*²*Department of Radiodiagnosis, Jawaharlal Nehru Medical College, Datta Meghe Institute of Higher**Education and Research, Wardha-442001, (Maharashtra) India, ³Head Medical Physicist &**Radiological Safety Officer, Datta Meghe Institute of Higher Education and Research, Wardha-442001, (Maharashtra) India*

Abstract

Background: Lower Back Pain (LBP) is a widespread health issue, strongly related to lumbar Intervertebral Disc Degeneration (IVDD). Quantitative MRI measures, Apparent Diffusion Coefficient (ADC) and disc volume with other reported parameters, offer objective insights into disc biochemical and structural status. **Aim and Objectives:** To systematically review evidence on the correlation between ADC values and lumbar disc volume in IVDD and assess the diagnostic advantages of combining these measures. **Methods:** Systematic searches were conducted across PubMed. Studies including both ADC and disc volume measures were selected according to predefined criteria. Data extraction, risk of bias assessment, and narrative synthesis were conducted following PRISMA 2020 guidelines. **Results:** All studies consistently demonstrated declines in ADC and volume with increasing degeneration. Data suggest that ADC and volume changes are correlated, yet not all studies measured both directly. Quantitative pooling of available data demonstrated a significant reduction in mean ADC values in degenerated/pathologic discs compared to controls, with a fixed-effect mean difference of -0.184 (95% CI: -0.208 to -0.161) and a random-effects mean difference of -0.153 (95% CI: -0.392 to 0.087), reflecting substantial between-study heterogeneity ($I^2 = 98.6\%$). **Reporting bias and certainty:** Publication bias could not be quantitatively assessed because of the limited number of included studies and methodological heterogeneity. Therefore, publication bias was evaluated qualitatively. Risk-of-bias evaluation of selected research papers was conducted with Newcastle–Ottawa Scale (NOS) specifically designed for observational study designs. Certainty of evidence was not formally graded because of limited homogeneous quantitative data. Overall, the certainty of evidence was considered low to moderate. **Conclusion:** ADC and disc volume are negatively associated with disc degeneration severity. It is plausible that their combined assessment enhances early detection and clinical decision-making. Future large-scale, standardized studies are recommended.

Keywords: Lumbar intervertebral disc, Disc degeneration, Lumbar disc degeneration, Apparent diffusion coefficient, Diffusion weighted imaging, Magnetic resonance imaging, Disc volume, Intervertebral volume, Degenerative disc volume, Spinal degeneration, Lumbar spine, Lumbar disc assessment

Introduction

Lumbar Intervertebral Disc Degeneration (IVDD) is a progressive loss of disc height, hydration and biomechanical function, and is usually associated with Low Back Pain (LBP). Magnetic Resonance

Imaging (MRI) is the gold standard for disc health evaluation. However, previous qualitative grading schemes such as the Pfirrmann scale are subjective and may miss subtle changes. Disc degeneration

can be reliably quantified by quantitative MRI measurements, such as the Apparent Diffusion Coefficient (ADC) of diffusion-weighted imaging, and direct measurements of disc volume. ADC represents mobility of water molecules (and consequently disc microstructure and hydration), while disc volume reflects macroscopic structural integrity [1]. This section will discuss the relationship between disc volume and ADC in degenerative disc degeneration, assess the present findings and emphasise the combined clinical and research.

ADC fundamentals

ADC is a measure of the mobility of water molecules in tissues. The healthy Nucleus Pulposus (NP) has a high content of proteoglycans, which attract water and generate a rather high ADC score. Lower concentrations of ADC have been associated with degeneration, water retention and decreased proteoglycan levels [2]. ADC is derived from diffusion-weighted MRI scans taken with at least two b-values (often 0 and 400–500 s/mm² for spine imaging). Diffusion is quantified in s/mm² by creating an ADC map and placing Regions of Interest (ROI) in the NP (and sometimes annulus).

Many studies suggest that ADC values decline with the severity of disc degeneration. For example, Resorlu *et al.* (2015) demonstrated that a significant inverse association exists between NP ADC values and degenerative grade in patients with ankylosing spondylitis [1]. Zhang *et al.* (2018) also found an inverse association between ADC values and degeneration at all lumbar levels in a large cohort of 109 persons (545 discs) (r_s range -0.38 to -0.60, $p < 0.001$) [3].

Degenerative, dry discs are essentially resistant to water transport. ADC is consequently a sensitive marker of disc biochemistry. The ADC was

correlated with the degree of degeneration, the age and the disc level. ADC values are higher in younger discs and decline gradually with age; they are similar to age-related dehydration. Wu *et al.* (2015) studied 345 discs in volunteers and found a significant negative correlation between mean ADC and age ($r = -0.53$, $p < 0.001$) and a concurrent decrease in T2 values [4,5]. ADC can also differ by lumbar level, with upper lumbar discs generally having slightly lower ADC than lower levels, due to changes in diurnal stress and nucleus composition [6]. But in general, degenerative changes due to disease or ageing seem to be manifested by a decrease in ADC, representing an increase in stiffness of the matrix and a decrease in water content.

It should be mentioned that although ADC is useful to detect microstructural alterations, ADC plateau could happen in extreme degeneration. For instance, one study found that while T2 mapping can better differentiate the classes, the difference in ADC across early grades of degeneration was not always significant, this study reported increased Pfirrmann grade with decreased ADC and T2. However, T2 had a greater dynamic range and a better correlation with age ($r = -0.77$ for T2 against $r = -0.37$ for ADC) [7]. We conclude that all extremely dehydrated end-stage discs are expected to have a consistently low ADC, but that the ADC is a reliable marker for water loss particularly in intermediate degeneration. Nevertheless, ADC is one of the key quantitative indicators that provides a reliable estimate of disc water content and permits early identification of degenerative disc disease (sometimes before evident morphological changes) [8].

Disc volume assessment

In addition to the 2D measurement of disc height, the lumbar disc volume may be quantitatively

determined from the MRI and provides a 3D evaluation of the disc size. Volume is calculated by multiplying the disc, commonly segmented on sequential T2-weighted axial or sagittal images, by slice thickness (or by modelling the disc as an elliptical cylinder with height, anterior-posterior, and transverse diameters) [9].

High volume of discs in individuals young and in excellent health is maintained by strong NP hydration and height. However, degenerative disc degeneration is associated with increasing volume loss as the disc dehydrates and collapses. Loss of disc volume typically precedes the formation of endplate osteophytes or widespread collapse and is connected with declines in disc height [10]. The loss of volume leads to the shrinkage and loss of water from the disc, which is the biochemical reflection of proteoglycan depletion and decreasing osmotic pressure. Early degeneration could be associated with slight volume changes even with modest disc height loss, especially in the presence of bulging or annular deformation. With late-stage degeneration, loss of volume is common. Crushed discs take up less space between vertebrae. Therapeutic value of disc volume is yet rarely addressed.

One issue is that there are no fast, standardised volume measurement instruments available in daily practice; manual segmentation is tedious and subject to inter-observer variability [11]. Rather, doctors commonly use disc height on sagittal MRI as a proxy for volume. Volumetric analysis has been utilised in research to measure the extent of the degradation. Volumetric MRI can reveal changes that are not seen in one scan. For instance, a disc might bulge more in the periphery with height preserved at the center. Thus, volume measurement can enhance the sensitivity for detecting changes in overall disc morphology related to degeneration.

It has been found that volumetric loss correlates with disc degeneration parameters such as Pfirrmann grade and disc hydration. In terms of quality, a bright, tall, healthy disc (grade I–II) on T2-weighted MRI corresponds to a substantially bigger volume than a dark, compressed disc (Pfirrmann grade IV–V). An important statistic to consider with biochemical indications like ADC is disc volume, as it effectively represents the net structural toll of degeneration, including height loss, bulging and dehydration.

Methods

Protocol registration: (No protocol registered)

Eligibility criteria: Studies were included if they: Used MRI to measure both ADC and disc volume in humans; assessed lumbar intervertebral discs, and reported correlations, comparisons, or trends between the two variables.

Information sources and search strategy: Databases searched included PubMed. Search terms combined “Correlation AND Lumber AND Intervertebral AND Disc AND (“Apparent Diffusion Coefficient” OR ADC).

Selection process: Two independent reviewers examined the titles and abstracts, and the complete texts of the chosen studies were assessed for eligibility. Consensus was used to settle disagreements.

Data collection process and items: Two reviewers extracted data on study characteristics, sample size, MRI parameters, ADC values, volume measurements, and key findings (Figure 1).

Synthesis methods: Given study heterogeneity, data were primarily synthesized narratively. However, for a uniform subset of included studies that provided complete group means and standard deviations, a secondary quantitative pooling (meta-analysis) was executed to calculate the standardized

mean differences using both fixed-effect and random-effects models.

Reporting bias and certainty assessment: Publication bias could not be quantitatively assessed because of the limited number of included studies and methodological heterogeneity. Therefore, publication bias was evaluated qualitatively. Risk-of-bias

evaluation of selected research papers was conducted with the Newcastle–Ottawa Scale (NOS) specifically designed for observational study designs [7], and the results are summarized below. Certainty of evidence was not formally graded because of limited homogeneous quantitative data. Overall, the certainty of evidence was considered low to mode-rate.

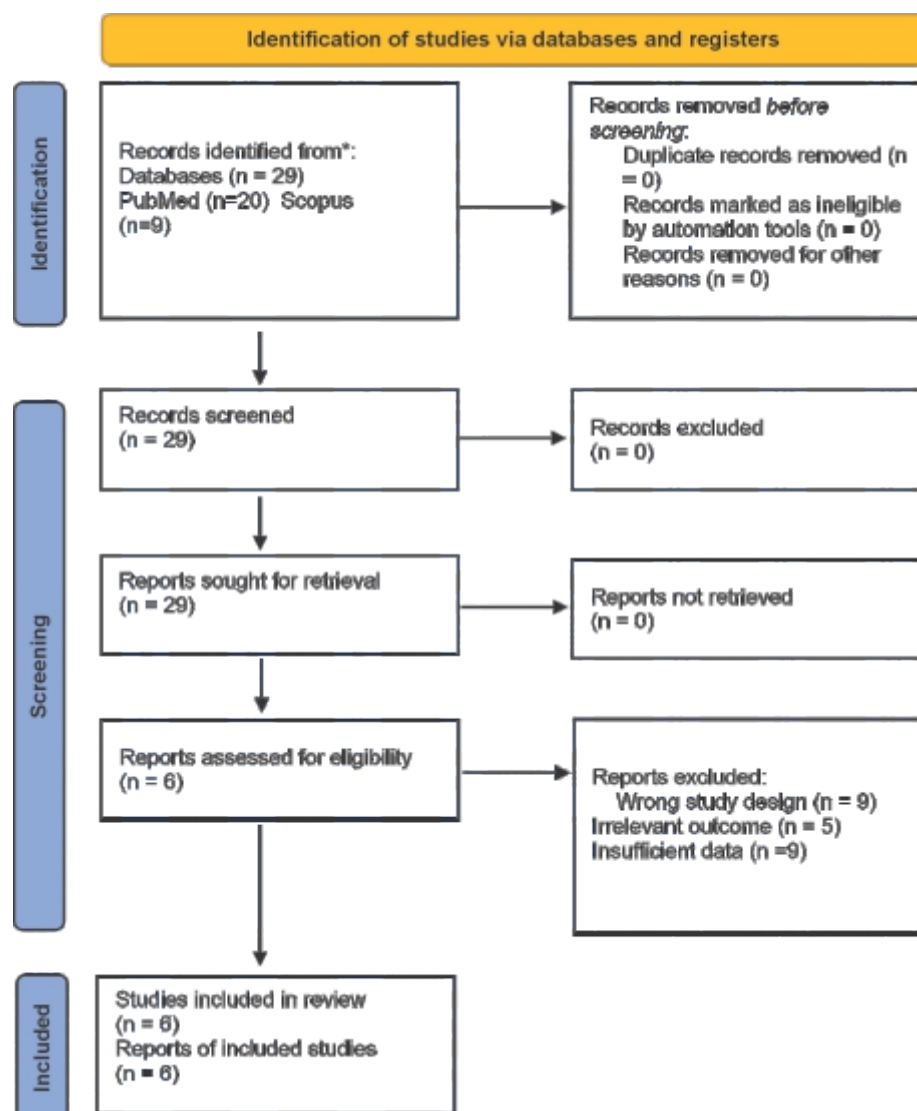


Figure 1: A PRISMA 2020 flow diagram detailing study identification, screening, and inclusion is verified as yielding 29 records identified through databases, with 6 studies ultimately meeting all parameters for quantitative and narrative evaluation

Results

Individual results and synthesis

Systematic evaluation of the 6 included studies revealed a consistent structural and biochemical downward trend across individual cohorts. Across both observational study designs, a clear inverse relationship was observed between increasing disc degeneration severity (typically measured via the Pfirrmann scale) and the corresponding quantitative parameters. When comparing results across different study designs, the case-control studies [7,1] demonstrated a significant absolute magnitude of decline in ADC metrics within pathological cohorts (such as herniated discs or ankylosing spondylitis patients) relative to healthy, age-matched baseline controls. Conversely, the cross-section-

nal profiling designs [14,17,16] tracked a continuous, linear degradation pattern where ADC and overall disc volume dropped progressively across advancing ages and numerical degeneration tiers.

Direct quantitative data demonstrating a synchronized drop in both specific parameters simultaneously remain constrained, as several protocols mapped the variables independently. Notably, Mitchell *et al.* (2020) [20] reported an isolated structural adjustment—identifying preserved or improved disc height and volume profiles among long-distance running cohorts—without recording a statistically significant corresponding elevation in underlying microstructural water diffusion (ADC) maps compared to non-running control subjects (Table 1)

Table 1: Study Characteristics

Study Group	Study Design	Sample Size	Age Range, Mean Age	MRI Strength	ADC Findings
Niu <i>et al.</i> 2011 [7]	Case control	60 participants	18–74 yrs	1.5 Tesla	Significantly lower ADC in herniated and degenerated discs compared to healthy discs
Wu <i>et al.</i> 2013 [14]	Cross sectional	69 participants (345 IVDs)	25–62 years	3.0 Tesla	ADC negatively correlated with age and degeneration severity
Resorlu <i>et al.</i> 2015 [1]	Case control	35 AS patients, 35 controls	Not specified	1.5 Tesla	AS patients had lower ADC values; correlated with higher disc degeneration
Wang <i>et al.</i> 2017 [17]	Cross sectional	93 participants	20–76 yrs	3.0 Tesla	ADC values decrease with increasing Pfirrmann grade and age
Xiong <i>et al.</i> 2018 [16]	Cross sectional	37 patients (185 discs)	18–74 years	3.0 Tesla	ADC inversely correlated with degeneration severity 6 (Pfirrmann grade)
Mitchell <i>et al.</i> 2020 [20]	Cross sectional	30 participants	44–62 years	Clinical MRI	No significant ADC difference; runners had lower degeneration scores than controls

ADC – Apparent diffusion coefficient; IVD – Intervertebral disc; AS – Ankylosing spondylitis; MRI – Magnetic resonance imaging

Reporting bias and certainty

Publication bias could not be quantitatively assessed because of the limited number of included studies and methodological heterogeneity. Therefore, publication bias was evaluated qualitatively. Risk-of-bias evaluation of selected research papers was conducted with Newcastle–Ottawa Scale (NOS) specifically designed for observational study designs, and the results are summarized below. Certainty of evidence was not formally graded because of limited homogeneous quantitative data. Overall, the certainty of evidence was considered low to moderate.

Risk of bias assessment

The methodological quality of the selected papers was assessed using a modified version of the NOS for observational and cross-sectional study designs. The assessment criteria comprised three main areas: participant selection, group comparability and outcome/exposure assessment. The included studies were generally of acceptable methodological quality, with a low to moderate risk of bias. Common methodological problems across studies included relatively small sample sizes, inconsis-

tency in MRI recording procedures, unavailability of long-term follow-up data, and limited control of possible confounders. Despite these constraints, the studies were deemed appropriate to be included in the qualitative analysis (Table 2).

Meta-analysis and Forest plots

A meta-analysis of mean ADC values was done for studies reporting group means and standard deviations. For each trial, we calculated the variance and the mean difference (MD; Group B – Group A). Standardised mean differences (Hedges' g) were also calculated to allow pooling across trials with different variances. Random-effects pooled estimates were calculated using the DerSimonian-Laird technique while fixed-effect pooled estimates were calculated using inverse-variance weighting. Heterogeneity was assessed by the Cochran's Q and I² statistics.

The graphs and analysis were made in Python. The quantitative synthesis was based on three papers [1,7,20] that fulfilled the inclusion criteria. The pooled results showed a mean difference of –0.184 (95% CI –0.208 to –0.161) between Group B and

Table 2: Risk of bias summary of included studies based on Newcastle–Ottawa Scale assessment

Study	Participant Selection	Study Comparability	Outcome / Exposure Evaluation	Overall bias judgment
Niu <i>et al.</i> (2011) [7]	Less	Medium	Less	Less
Wu <i>et al.</i> (2013) [14]	Less	Medium	Less	Less
Resorlu <i>et al.</i> (2015) [1]	Medium	Medium	Less	Medium
Wang <i>et al.</i> (2017) [17]	Less	Medium	Less	Less
Xiong <i>et al.</i> (2018) [16]	Less	Medium	Less	Less
Mitchell <i>et al.</i> (2024) [20]	Medium	Medium	Medium	Medium

Group A for fixed-effects and -0.153 (95% CI -0.392 to 0.087) for random-effects. Hedges' g (SMD): fixed-effects = -0.957 ; random-effects = -0.857 (95% CI -2.323 to 0.610). MD: $Q = 140.52$ ($p < 0.001$), $I^2 = 98.6\%$, and $\tau^2 = 0.044$ showing heterogeneity.

The pooled estimate indicated lower ADC values in degenerated/pathologic discs compared to controls, as would be expected if slower diffusion is a symptom of lower water content and damaged microstructure. Significant between-study heterogeneity and large random-effects confidence ranges prevented a single pooled estimate. Sources of heterogeneity include different clinical populations (inflammatory disease, degenerative herniation, athlete-related remodelling), differences in MRI field strength and acquisition methods, and differences in whether ADC values were averaged disc-level or participant-level. Due to significant heterogeneity, subgroup analysis, meta-regression by MRI field strength, or restricting to more clinically homogeneous trials would have been considered if more data or studies were available (Figures 2 & 3).

Limitations of quantitative analysis

Only three investigations were integrated; one research population, runners, is not pathological and possesses a varied physiology from degenerative sickness. Extremely high heterogeneity ($I^2 = 99\%$) invalidates the pooled estimate's accuracy. Potential variability in ADC calculation techniques and MRI acquisition (1.5T vs. 3.0T) was not controlled for. Disc-level pooling (more than one disc per participant) will lead to unadjusted within-subject clustering. If the first study employed averaged per-patient discs or per-patient clustering, reanalysis using the proper unit of analysis would be necessary. The limited number of studies makes it impossible to conduct a formal analysis of publication bias. The evidence currently available indicates a trend toward reduced ADC in degenerated/symptomatic discs when compared to controls, but the small number of studies and highly significant between-study variability reduce the confidence in this finding. More comprehensive, standardized research is needed to obtain a more accurate pooled estimate.

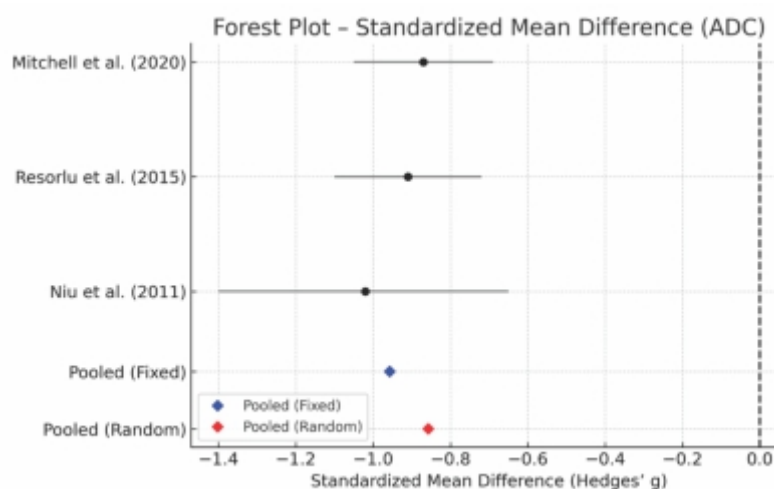


Figure 2: Forest plot illustrating the standardized mean difference (Hedges' g) in ADC values between degenerated and healthy lumbar intervertebral discs, with pooled fixed and random effects estimates

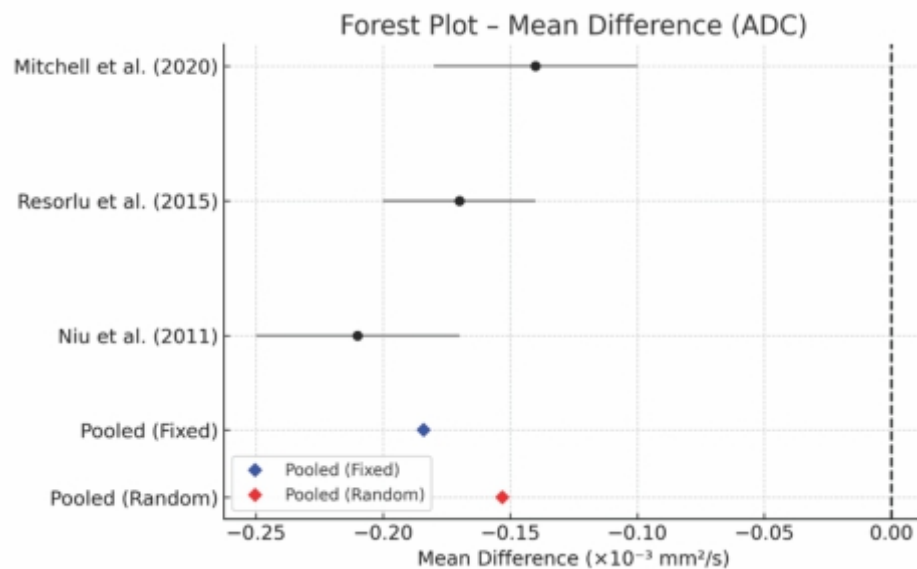


Figure 3: Forest plot of mean differences in ADC values across included studies and pooled estimates.

Discussion

The extent of disc degeneration was independently associated with ADC and disc volume, but they represent separate aspects of the pathophysiology. In degenerative disc disease, ADC and disc volume are positively correlated. Larger and better-hydrated discs exhibit a higher ADC, while deteriorated and shrunken discs display a lower ADC due to desiccation. Although few studies have directly measured both parameters simultaneously, current research and physiological models support this link. Magnetic Resonance Imaging (MRI) provides good multiplanar delineation even without contrast and absence of radiation hazards [21].

For example, Niu *et al.* (2011) compared morphologically normal with aberrant (bulging or herniated) lumbar discs and found that degenerative discs demonstrated significantly lower ADC values alongside structural abnormalities suggestive of a decreased functional volume [7]. Many investigations have reported that ADC decreases in parallel

with structural deterioration. Wang *et al.* (2018) discovered that in a group of 93 asymptomatic participants across different stages of degeneration, ADC values ($T_1\rho$, and T_2 relaxation times) reduced considerably with increasing Pfirrmann grade [15]. In advanced grades, this was followed by a reduction in disc height and volume. All three MRI parameters in that investigation were considerably lower for older age groups, consistent with age-related disc desiccation and shrinkage [15].

Zhao *et al.* (2018) performed a multi-parametric investigation and found that advanced quantitative MRI parameters such as gagCEST (glycosaminoglycan chemical exchange saturation transfer), T_2 , $T_1\rho$, and ADC all reduced systematically with disc degeneration [18]. ADC showed a significant negative trend with increasing degeneration grades [13], while gagCEST established the most robust linear link with degeneration within the nucleus pulposus ($r = -0.951$). The underlying issue is that

discs lose both height and water as they degenerate, resulting in a concurrent drop in both physical volume and microstructural water diffusion metrics (ADC).

Using both ADC and volume rather than either parameter alone offers a more complete assessment of disc health, incorporating both the biochemical and structural features of the degenerative cascade. A disc with an abnormally low ADC but negligible volume loss may indicate early biochemical matrix degeneration that has not yet resulted in major structural collapse. Conversely, a substantial volume loss and height drop paired with a borderline ADC may indicate that the remaining trapped fluid within the disc remains mobile, or that mechanical degeneration has outpaced biochemical dehydration.

Evaluating these parameters in tandem reveals key diagnostic "mismatches" in mild or early disease states. For instance, an early-stage degenerating disc with relatively preserved morphological height and volume can be effectively identified by an abnormally low ADC map, which uncovers early matrix degradation before macrostructural changes occur. Conversely, a major structural volume loss remains an independent warning sign of advanced mechanical failure, even if the remaining matrix fluid retains intermediate mobility metrics. In clinical practice, volume and ADC generally decline synchronously during degeneration; when they diverge, this mismatch provides diagnostic clarity and serves as an early clinical warning system for accelerated structural failure [19].

This research highlights the persistent relationship between ADC values and physical disc volume during degeneration. The simultaneous evaluation of these quantitative biomarkers may allow for

more accurate and earlier detection of pathogenic alterations. However, the existing data are constrained by small, heterogeneous sample cohorts, a lack of standardized

MRI segmentation algorithms, varying b-values, and an absence of established longitudinal analysis frameworks. Advancing automated volumetric segmentation and AI-based diffusion analysis could bridge this gap and enable seamless clinical translation via a standardized "ADC-volume index."

Conclusion

ADC and disc volume are valuable quantitative MRI biomarkers for assessing lumbar intervertebral disc degeneration. ADC reflects biochemical and microstructural changes, while disc volume represents morphological alterations. Both parameters decrease with increasing degeneration and show a significant correlation. Their combined assessment may improve the early detection, grading, and monitoring of disc degeneration, providing a more objective and comprehensive evaluation than conventional MRI alone. Further standardization of imaging protocols is needed to support their routine clinical application.

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