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Early histologic changes in lower lumbar discs and facet joints and their correlation

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Abstract Biomechanical and histologic studies have highlighted the close functional relationship between lumbar discs and their associated facet joints, and it is conceivable that their degenerative changes are interdependent. However, separation of cause from effect remains controversial. Hitherto, no study in humans has correlated the changes histologically. The present study assessed histologic changes in lower lumbar discs and their associated facet joints in patients under the age of 40 years using classification systems developed for this investigation. A specific objective was to correlate changes in discs and facet joints. Data from 15 lower lumbar spine specimens were obtained. Three parasagittal sections per disc and one section per facet joint were graded histologically. The results were correlated with age, within the functional spinal unit (FSU), and with the adjacent level. Histologic changes were found in discs and facet joints from all FSUs. There was no correlation between the age of the subject and the degree of degeneration of the disc or facet joints at either level. The extent of disc degeneration at L4/5 correlated significantly with changes at L5/S1 ($P < 0.01$). There was no correlation between changes in discs and the associated facet joints at either level. The results of the study showed that microscopic changes are seen in the disc and facet joints from an early age and can be quite marked in some individuals before the age of 40 years. A correlation of degenerative changes within the FSU could not be established.

Key words Lumbar spine · Discs · Facet joint · Degeneration · Histology

Introduction

The precise etiology of low back pain is difficult to establish and remains unclear. It is believed, however, that degenerative changes in the spinal motion segment play an important role. These may occur in discs and associated facet joints, which are regarded as an interdependent functional spinal unit (FSU). Biomechanical studies clearly show the importance of the facet joints as a motion-restricting, as well as a stress- and load-sharing factor for the disc [1, 9, 13, 19]. Therefore, it is conceivable that degenerative changes within this "three joint complex" influence each other, but the sequence of changes and their outcome are still matters for debate [6, 15, 28]. However, a recent histologic investigation in sheep has clearly defined the possible development of facet joint arthritis as a response to disc degeneration [22].

Various classifications of lumbar disc degeneration have graded the changes macroscopically [11, 23, 30], by MRI [35], and by discography [2]. The histologic features of lumbar disc degeneration have been described in detail [8, 26, 27, 34], but no histologic grading system has been proposed.

Osteoarthritic changes of the facet joints may differ considerably from degenerative alterations in other synovial joints. Thus, osteophytes and subchondral bone sclerosis may be observed at an early stage of degeneration when the articular cartilage is frequently retained [34]. Recently, attempts have been made to classify these changes histologically [22], based on the descriptions of Lewin and Collins [7, 17].

The present study investigated the histology of degenerative changes in lower lumbar discs and facet joints using classification systems which specifically assessed early alterations that may be difficult to detect macroscopically. Accordingly, specimens from patients under the age of 40 years were examined to ascertain whether initial changes in the FSU occurred in the disc or the facet joint.

Materials and methods

The study examined L4/5 and L5/S1 motion segments from 15 patients under the age of 40 years (average 29.1, range 13–38 years). Seven patients were female and eight were male. The average weight and height was 65 kg and 165 cm respectively (data available for 11 subjects). None of the patients had a documented history of low back pain, but eight of them suffered from conditions potentially affecting musculoskeletal structures, including Marfan syndrome, Down's syndrome, amyotrophic lateral sclerosis, congenital spastic quadriplegia, osteogenesis imperfecta, diabetes mellitus, alcoholism and immunosuppression after kidney transplantation. With the exception of diabetes mellitus, where some acceleration of disc degeneration is suspected from animal studies, none of the conditions has been reported to significantly affect degenerative changes of the disc or facet joints [12].

Lumbar spines were removed at autopsy and fixed in 10% neutral buffered formalin for at least 1 week. Individual motion segments of the L4/5 and L5/S1 level were prepared by bisecting the vertebrae in the mid-transversal plane with a bandsaw, taking care to preserve the posterior elements. The blocks were immersed in a solution comprising 10% nitric acid and 1% EDTA (Ethylene diamine tetraacetate) until complete decalcification was confirmed by radiography. The posterior elements were removed by separating them at the anterior limit of the pedicle. Slices, 2 mm thick, were obtained from the facet joints perpendicular to the joint line in the area of their largest thickness. The disc units were cut into multiple para-sagittal 5-mm-thick slices. All slices were processed into paraffin wax by standard methods. Tissue sections of 5 μm thickness were stained by hematoxylin and eosin.

For each level, a section from each facet joint and a section from each of the mid-sagittal, the left para-sagittal and right para-sagittal zones of the discs were analyzed histologically by one of the authors (N.C.G.). The mid-sagittal section was examined in particular to describe alterations to the nucleus, annulus, end-plate and adjacent vertebral bodies. Changes in disc morphology occur in the coronal as well as the horizontal planes [32], both of which were evident in the mid-sagittal section [30].

Table 1 Grading system of histologic changes in lower lumbar discs (*BEP* bony end-plate, *CEP* cartilaginous end-plate)

Grade	Annulus fibrosus	Nucleus pulposus	Cartilage end-plate	Margins/subchondral bone
1	Intact lamellae Narrow inter-lamellar matrix Intact annulus attachment Vessels only in outer 1/3	Homogeneity Absence of clefting	Uniform thickness Intact attachment to bone Uniform calcification < 1/5 of depth Uniform cell distribution	Even thickness of BEP Lamellar bone only Distinct junction with CEP Few vascular intrusions into CEP
2	Minor lamellar splitting and disorganization Minor widening of matrix Minor disorganization of attachment Rim lesion without reparative reaction	Minor clefting Minor cell necrosis Minor posterior displacement of annulus Minor chondrone formation	Minor cartilage thinning Small transverse fissures Irregular thickening of calcified zone Few invading vascular channels Small chondrones	Slightly uneven BEP Schmorl's nodes Minimal remodelling of BEP Small marginal osteophytes
3	Moderate lamellar disorganization Moderate widening of matrix Moderate fissuring of attachment Radiating tears, not involving outer 1/3 Minimal chondroid metaplasia Cystic degeneration Vessels in outer and middle 1/3 Rim lesion with minor reparative reaction	Moderate clefting Moderate cell necrosis Cystic degeneration Posterior displacement within annulus Centripetal extension of collagen Moderate chondrone formation	Marked cartilage thinning Marked thickening of calcified zone Many transverse fissures Many vascular channels Many chondrones	Moderately uneven BEP Vascularized Schmorl's nodes Moderate trabecular thickening Defect in bone lamellae Minimal fibrosis tissue in marrow spaces Medium-sized osteophytes
4	Extensive lamellar disorganization Radiating tears extending into outer 1/3 Extensive chondroid metaplasia Vessels in all zones Rim lesion with marked reparative reaction	Complete loss of nucleus Loose body formation Marked chondrone formation	Total loss of cartilage Calcification of residual cartilage Widespread fissuring	Marked uneven BEP Ossified Schmorl's nodes Large osteophytes Marked trabecular thickening Marked fibrosis of marrow spaces Cartilage formation

Table 2 Grading system of histologic changes in lower lumbar facet joints

Grade	Cartilage	Osteochondral junction	Subchondral bone	Margins
1	Smooth intact surface Orderly chondrocyte distribution Orderly collagen framework	Uniform tidemark Calcification < 1/5 cartilage thickness	Uniform lamellar subchondral bone plate Uniform vascular budding into cartilage	Smooth articular margin Normal synovium Normal capsule
2	Tangential surface flaking Minimal chondrocyte death Few chondrones	Minimal irregularity of tidemark Calcification 1/5–1/4 cartilage	Minor thickening of trabeculae Small fissures at bone-cartilage junction Occasional fibrous tissue formation	Small osteophytes Minimal capsular fibrosis
3	Fissures < 1/2 total depth Loss of cartilage < 1/2 depth Moderate chondrocyte death Many chondrones	Marked irregularity of tidemark Calcification 1/4–1/2 cartilage	Moderate trabecular thickening Woven bone formation Moderate fibrous tissue formation	Moderate osteophytes Minimal-moderate appositional new bone Fibrocartilage formation Moderate capsular fibrosis Minimal-moderate synovial thickening
4	Deep fissures Areas of total cartilage loss Extensive chondrocyte death	Calcification > 1/2 cartilage	Eburnation of exposed bone Bone sclerosis Cysts Extensive fibrosis	Extensive and large osteophytes Marked appositional new bone Marked capsular thickening Marked synovial thickening

Histologic changes were assessed using the grading systems outlined in Table 1 (discs) and Table 2 (facet joints). Each facet joint was assigned four subscale scores: one each reflecting the characteristics of the cartilage, osteochondral junction, subchondral bone, and the margins. The subscale scores reflect the most severe features of the specimen on that particular scale. An overall or composite grade for each specimen was calculated by taking the mean of the four subscale scores. For the discs, overall grades were calculated for each of the three sections (mid-sagittal, left- and right-parasagittal) using a similar procedure evaluating the annulus, nucleus, cartilage end-plate and the margins/subchondral bone, and then the mean of these grades across the three sections was used for the analysis. The grading systems were validated by comparing the results of a second experienced analyst and the reproducibility of the method was assessed with repeat observations 6 months after the initial analysis. Spearman's coefficient of rank correlation was used for statistical analysis, with significance set at $P < 0.05$.

Results

There was a high correlation between the grades assigned by two independent observers to the histologic changes in the discs and the facet joints. There was also a high correlation between the grades assigned to the discs and facet joints by a single observer after an interval of 6 months (Table 3).

Table 3 Correlation coefficients for grades assigned to discs and facet joints by two independent observers *(first number)* and by one observer on two separate occasions *(second number)*

	Disc	Left facet joint	Right facet joint
L4/5	0.92*/0.91*	0.96*/0.98*	0.97*/0.97*
L5/S1	0.91*/0.91*	0.90*/0.90*	0.94*/0.91*

* $P < 0.01$

Discs

An asymmetric disposition of the nucleus with respect to the annulus was observed in three-quarters of discs. This "displacement" was observed always towards the posterior portion of the annulus (Fig. 1). The individual grades for each of the three sections per disc differed, at most, by one grade.

Fourteen discs at L4/5 and 11 at L5/S1 were analyzed, and the overall mean grade of degeneration was 2.8 at both L4/5 (SD 0.56) and L5/S1 (SD 0.43). At L4/5, changes of grade 2–2.9 were found in six discs and grade 3–4 in seven discs (Fig. 1). At L5/S1, grade 2–2.9 changes were observed in seven discs and grade 3–4 changes in four discs. In only one disc, from the youngest patient in the study, the changes at L4/5 were classified as grade 1–1.9 (Fig. 2). There was a significant correlation between the histologic grading of disc changes at L4/5 and L5/S1 ($P < 0.01$), but age did not correlate significantly with the grade at either level.

Facet joints

Thirteen paired facet joints were analyzed at L4/5, and eight paired facet joints at L5/S1. There was no significant difference between the grading of both sides at the same level, nor between the two levels in the same patient. At L4/5 the mean grade was 2.4 on each side (SD

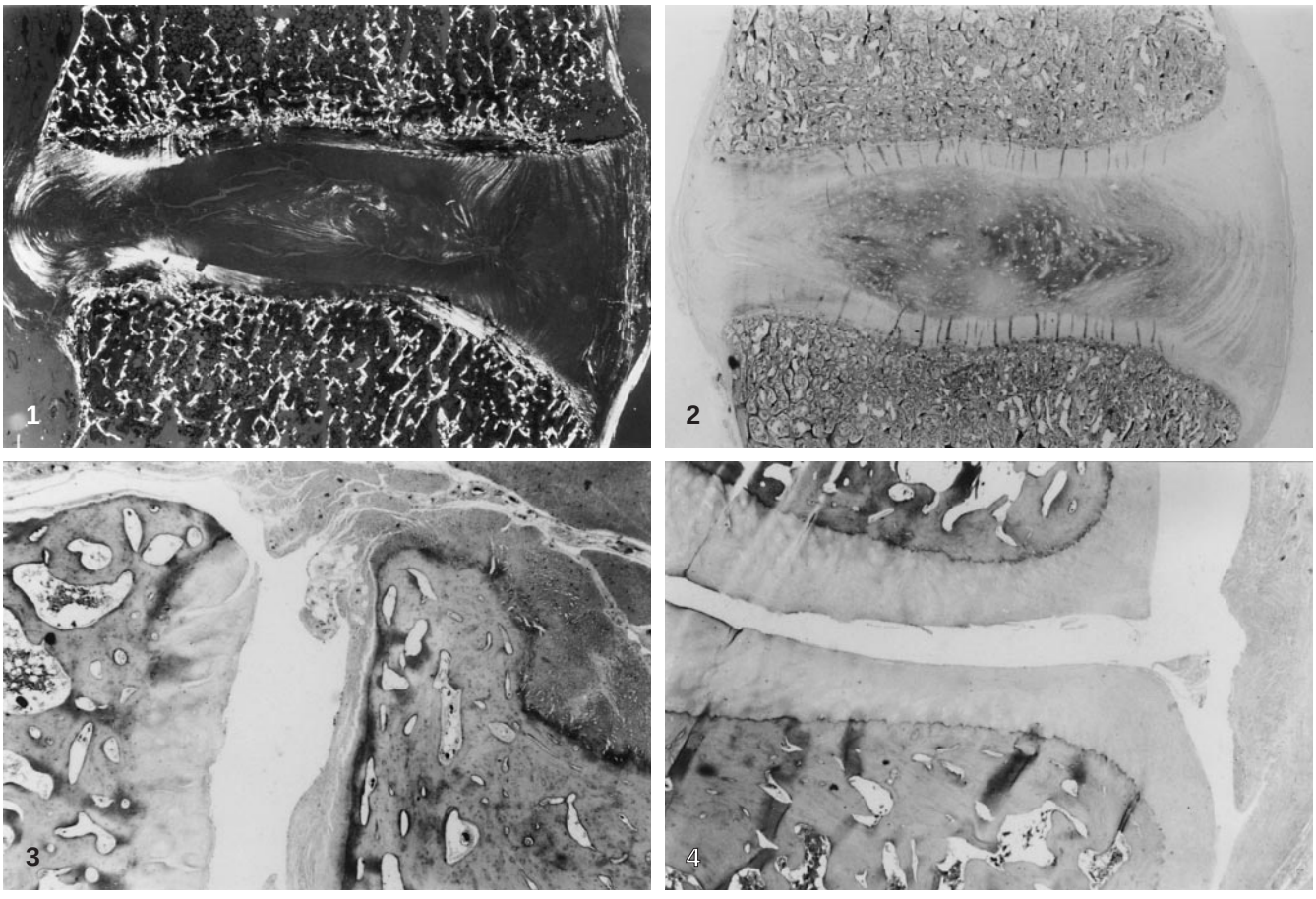

Fig. 1 Polarized light micrograph of L4/5 intervertebral disc, grade 3–4. The annulus shows extensive lamellar disorganization with increased interlamellar spacing, fiber infolding anteriorly and lamellar thinning and bulging posteriorly. The nucleus shows marked clefting and posterior displacement (× 4 original magnification)

Fig. 2 Low-power micrograph of L4/5 intervertebral disc, grade 1–1.9. The annulus shows intact lamellae with narrow interlamellar matrix anteriorly and posteriorly. The nucleus shows only minor clefting and no posterior displacement (× 4 original magnification)

Fig. 3 Low-power micrograph of the posterior one-third of a right L4/5 facet joint grade 3–4. The L5 facet *(on the right)* shows total loss of cartilage and replacement by pannus tissue. The L4 facet *(on the left)* shows deep fissures in the cartilage surface. The margin of the L5 facet shows prominent osteophyte formation and marked capsular and synovial thickening (× 20 original magnification)

Fig. 4 Low-power micrograph of the posterior one-third of a left L4/5 facet joint grade 1–1.9. Both the L5 facet *(lower)* and the L4 facet *(upper)* show smooth, intact cartilage surfaces with normal articular margins (× 20 original magnification)

right facet 0.72, SD left facet 0.75). For the mean grade of the L4/5 facet joint pair, changes of grade 2–2.9 (Fig. 3) were found in seven joint pairs, and grade 1–1.9 (Fig. 4) in four joint pairs. At L5/S1 the mean grade was 2.7 (SD 0.8) for the left joint and 2.5 (SD 0.74) for the right. For the mean grade of L5/S1 facet joint pairs, grade 2–2.9 changes were seen in five joint pairs, and grades 1–1.9 and 3–4 were observed in three cases each. Age did not correlate significantly with the histologic grading of the facet joints.

In 24 (51%) of the 47 facet joints analyzed, the concave (or superior) facet (that is, L4 facet in the L4/5 joint) was altered more severely than the convex (inferior or L5 facet in the L4/5 joint). In ten (21%) the convex facet showed more advanced changes than the concave facet. In 13 facet pairs (28%) there was no difference. The most advanced changes were located in the posterior one-third of the joint in 16 (34%), in the anterior one-third in seven (15%), and they were equally distributed between the anterior and posterior one-third in 14 (30%). In 10 (21%) no specific pattern or localization of changes was observed.

No significant correlation was found between the grades for the discs and the facet joints assessed separately at either level.

Discussion

Grading of changes

Several grading systems for lumbar disc degeneration have been proposed, the most widely used being based on macroscopic features [11, 23]. The general problem of reproducibility and comprehensiveness was addressed by Thompson et al., who introduced a five-category grading system based on gross disc morphology [30]. However, macroscopic changes alone are regarded as insufficient in assessing the relation between intervertebral discs and facet joint degeneration [28].

Grading systems based on imaging have been proposed, using discograms and MRI [2, 35]. Although histologic changes with lumbar disc degeneration have been analyzed, no grading system has yet been proposed. Based on previous descriptive studies [4, 18, 26, 34] the present study used a four-grade classification system that deliberately included early degenerative changes and allowed correlation with osteoarthritic changes in the facet joints. While there have been several previous reports describing the histologic changes in the facet joints [7, 17, 28, 29], a classification system for degenerative changes in the facet joints has been evaluated only recently [22].

Discs

Structural changes in discs have been found to increase significantly with age [5]. Early macroscopic changes may be found during the second decade, and by the third decade more than one-third of lumbar discs may show significant changes [21, 23]. Histologic abnormalities of the annulus and nucleus can be detected during the second and third decade [8, 14]. In the present study, histologic deviations from the young "normal" discs [5, 33] were observed in every disc examined between the age of 13 and 38. Whether such early changes are a normal part of aging or the result of truly pathologic processes is unknown and of questionable relevance [33]. Also, we are not aware of any larger statistical study investigating the influence of any of the underlying disorders of our patients on the histologic appearance of the spine. Therefore, a potential bias must be kept in mind interpreting the results.

An asymmetric positioning of the nucleus towards the posterior annulus was observed in three-quarters of discs. The number of lamellar bundles in the anterior annulus is greater compared to the number in the posterior portion, a finding which was confirmed in this study [20, 31]. However, the functional anterior annulus is not wider than the functional posterior annulus, and the highest intradiscal stresses occur in the inner and middle posterior annulus [3]. Furthermore, values for tensile moduli and failure stresses have been found to be larger in the anterior annulus compared to the posterior portion [10]. Thus, a shift of the nucleus towards the posterior annular portion is conceivable, especially as the middle posterior annulus has been found to contain a relatively high percentage of discontinuous lamellar bundles [20, 31]. In more severe cases ruptures will occur in the inner layers of the annulus (six cases in this study), eventually resulting in complete radial annular tears, which are indeed almost exclusively found in the posterior annulus [25]. Peripheral or rim lesions are, in contrast, more frequently observed in the anterior annulus, which was also confirmed in this study. The progressive failure of the inner annulus induced by this lesion [24] was observed in one case.

Facet joints

Early onset of cartilage fibrillation, as found in this study, has also been reported by others [28, 29]. The concave facet tended to show more advanced changes than the convex facets, with more advanced changes in the peripheral one-third of the joint surface compared with the center of the joint. Swanepoel et al. have also found, in a macroscopic analysis of cartilage fibrillation, that more pronounced changes occurred in the peripheral and mainly posterior portions of both surfaces [28]. These findings may be due to the coronal orientation of the anterior facet joint at the lower lumbar levels, which results in this portion being mainly loaded in flexion [1, 29]. The posterior portion has a more sagittal orientation and is subjected to shearing forces from insertion of the fibrous capsule and fibers of multifidus [29].

Taylor and Twomey also analyzed histologic changes with respect to the joint location, and found pronounced cell hypertrophy and vertical fibrillation of cartilage in the anterior third of the concave facet [29]. The posterior two-thirds were characterized by splitting of cartilage occurring parallel to the bony interface. While, in the present study, advanced changes were also more often posterior, there was no definite pattern in distribution of histologic changes, and cell hypertrophy was observed both anteriorly and posteriorly. Despite the young age group studied, we found instances of partial or total loss of cartilage, and cartilage replacement by pannus tissue in some cases.

Correlation

The pattern of load sharing between an intervertebral disc and its corresponding facet joints is complex and depends on the type of force, position of the FSU, preload applied, and other factors [1, 16]. In addition, degeneration of a component of the FSU may considerably alter loading paths. With disc space narrowing, loading of the facet joints increases significantly in compression and extension where peak pressures can reach values otherwise

only reported in the hip joint [1, 9]. Alternatively, facet joint destruction results in increased loading of the adjacent disc through alternate paths and may accelerate its degeneration [13]. Therefore, it is not surprising that marked degenerative changes in the disc are always accompanied by marked osteoarthritic alterations of the facet joints, and when the disc appears normal the corresponding facets are also normal [34]. Moore et al. have shown in sheep spines that facet joints undergo osteoarthritic changes in response to disc degeneration [22]. Our study does not confirm a clear time-sequence of changes, probably because it reflects a static assessment of a dynamic process. Butler et al. also concluded that discs degenerate before facets, by assessment of disc degeneration by MRI and facet joint arthritis by CT [6]. However, some other studies have not confirmed this relationship, as facet joints with marked cartilage damage and no detectable associated disc degeneration have been reported [28].

Conclusion

This study has confirmed that microscopic changes occur in discs and facet joints at L4/5 and L5/S1 from an early age, with advanced changes often encountered. Nevertheless, it was not possible to demonstrate a correlation with age, for either the discs or the facet joints at the same level. Moreover, grades of disc degeneration did not correlate with those for facet joints. The grade of change at L4/5 correlated significantly with L5/S1.

Since the histologic assessments are being made of different anatomical structures, the grades for the discs and facets may be correlated, but it may be that results cannot be validly compared on a quantitative basis. Moreover, it is not possible to conclude that pathologic changes progress more rapidly in one element relative to the other in the young adult lumbar spine.

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