

EMPHASISING THE IMAGISTIC AND BIOCHEMICAL ASPECTS FROM INTERVERTEBRAL DISKS

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Abstract: The aim of the present study was to emphasise the correspondence between the aspect of magnetic resonance imaging (MRI) in cases with lumbar hernia clinically manifested, stadialized according to MRI Modic classification and the histopathological aspect in patients with surgical interventions on the intervertebral disks. **Material and Method.** The study was performed on a batch of 103 cases selected from the patients admitted in the Medical Rehabilitation Clinical Hospital of the town of Baile Felix, with the diagnosis of low back pain accompanied or not by radiculopathy due to lumbar hernia, between January 2008-December 2008. All the patients were investigated by MRI. 47 intervertebral disks were taken from the operated patients for electronic microscopy studies, in order to determine mucopolysaccharides and collagen in the components of the intervertebral disk. **Results.** In 15.55% of the cases, type I MRI changes were revealed, in 22.33% type II changes, and in 62.13% type III changes. **Conclusions.** Clinical manifestations of low back pain accompanied or not by radiculopathy due to lumbar hernia had a correspondent on MRI images, expressed by Modic in 3 classes. Electronic microscopy study made on disk fragments obtained by discectomy revealed quantitative and qualitative changes of all types of collagen at the level of the 3 anatomical structures of intervertebral disk, corresponding to the MRI changes.

Keywords: magnetic resonance imaging (MRI), lumbar disk hernia, histopathological aspect

Rezumat: Scopul lucrării: demonstrarea impactului funcțional și corelația acestora în hernia de disc lombară. **Material și metodă:** Lotul este format din 103 pacienți randomizați dintre cazurile cu durere lombară joasă, examinați în Spitalul Clinic de Recuperare Băile Felix în perioada ian.-sept. 2008, investigați cu ajutorul T₁ și T₂ MRI, care a confirmat diagnosticul clinic de hernie de disc lombară. Am apelat la indici de apreciere a durerii lombare cu ajutorul chestionarului Oswestry de evaluare a calității vieții folosind chestionarul MOS SF-36 Health Survey și criteriile AMA Guides care evaluează infirmitatea, care se bazează pe mobilitatea coloanei lombare. **Rezultate:** Raportarea disabilității investigată cu chestionarul sindromului dureros lombar Oswestry, scală de evaluare funcțională, cu infirmitatea evaluată prin criteriile Ghidului Asociației Medicale Americane

(AMA), indicele de evaluare a mobilității dovedește o corelație mică ($r=0,16$), dar semnificativă ($p=0,025$). Indicatorii de calitate a vieții, înregistrați cu SF36 și infirmitatea, înregistrată cu AMA, se corelează puternic ($r=0,47$), foarte semnificativ statistic ($p<0,00001$). **Concluzii:** Afectarea mobilității găsită în hernia de disc lombară are un impact funcțional moderat asupra întregului organism dependent de tratamentul aplicat.

Cuvinte cheie: rezonanță magnetică nucleară, hernie de disc lombară, aspect histopatologic

INTRODUCTION

Disk herniation can occur in any disk in the spine, but the two most common forms are the cervical herniation and the lumbar disk herniation. The presence of pain, radiculopathy and other symptoms depend on the site and degree of herniation. Many treatments have been suggested for lumbar disk herniation, but different studies often provide conflicting results.(1).

The framework of the disk is composed of collagen fibers in the fibrous ring, which provide tensile strength, and proteoglycans in the nucleus, which provide stiffness and resistance to compression.(2,3). It is estimated that several factors, including genetic factors and changes in hydration and collagen, play a role in the development of degenerative disc disease.(4,5) Cells in herniated discs appear to have a higher degree of cellular senescence than cells in nonherniated discs and produce a greater abundance of matrix metalloproteinases. Disorders may be caused by a genetic predisposition or a tissue response to an insult or altered mechanical environment. Whatever the initial cause, a change in the morphology of the tissue is likely to alter the physiologic and mechanical functioning of the tissue.(6)

The aim of the present study was to emphasise lumbar disk hernia in subjects with clinical signs that plead for this diagnosis, the correspondence between the aspect of magnetic resonance imaging (MRI) in cases with clinically manifest lumbar hernia, stadialized according to MRI Modic classification and the biochemical aspect of intraoperative obtained biopsy material from patients with surgical interventions on the intervertebral disks.(2,8)

MATERIAL AND METHOD

Selection of the cases: We have established the

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study batch through the selection of the cases with the clinical diagnosis of low back pain accompanied or not by radiculopathy through lumbar disk hernia. From the total number of 667 with this diagnosis, examined in the Medical Rehabilitation Clinical Hospital of the town of Baile Felix, between January 2008-September 2008, 103 cases have fulfilled the inclusion criteria for this study. The 667 cases were classified as follows: 341 had low back pain through disk hernia without neurological involvement and 30 of them were selected for the study; 220 had low back pain through disk hernia with radiculopathy and 26 of them corresponded for the study; 108 had surgery for lumbar disk hernia ablation and 47 of them complied with the requirements of the following protocol, necessary for the inclusion in the study.

All the patients that were included in the research were investigated by T₁ and T₂ MRI, which confirmed the clinical diagnosis of lumbar disk hernia. We used MRI Modic classification(6), which categorizes disk lesions in 3 classes, according to their severity. 47 intervertebral disks were taken from the operated patients for electronic microscopy studies, in order to determine mucopolysaccharides and collagen in the components of the intervertebral disk. Confirmed clinical cases have signed a following protocol, registration of the cases being made according to medical deontology and ethics guidelines.

After examination of lumbar radiographs that were performed in the Department of Radiology of the Medical Rehabilitation Clinical Hospital of Baile Felix, we excluded cases with lumbalgy of other etiology than disk hernia and we established the subjects that would be investigated with MRI.

Considering the specific of our clinic and addressability for patients from all over the country, MRI investigation was performed in different imagistic centres from the country.

We divided the 103 subjects in two batches: batch I with 56 cases (54.37%) with lumbar pain of disk origin and batch II composed of 47 cases (45.63%) in whom the lumbar hernia was surgically treated, but with lumbar pain +/- residual radiculopathy. After establishing the clinical diagnosis of lumbar disk hernia, confirmation of the diagnosis using magnetic resonance imaging represented the next step.

We used the classification described by Modic in three degrees of degenerescence of the intervertebral disk for stadialization using magnetic resonance imaging method.

In order to identify biochemical changes of intervertebral disks we took into study 47 pieces (n = 47) obtained after surgical intervention from the cases operated in the Neurosurgery Department of the Clinical County Hospital of the city of Oradea.

RESULTS

Using clinical and imagistic data we established the level of the lumbar disk hernia in the studied batch (table nr. 1).

Table no. 1. Distribution of cases according to the level of the lumbar disk hernia revealed by MRI

	Lumbar disk hernia level			
	L2-13	L3-14	L4-15	L5-S1
Nr. Cases	3	6	51	43

Batch I was divided in 2 subgroups, according to the presence or absence of radiculopathy (table no. 2):

- subgroup IA- included 30 cases (53.5%), from the clinical point of view with lumbar pain without radiculopathy of disk etiology.
- subgroup IB- included 26 cases (46.5%) with lumbar radiculopathy of disk etiology.

Table no. 2. Distribution of the cases in the study batches

	BATCH I		BATCH II
	Subgroup IA	Subgroup IB	
Nr. cases	30	26	47

The study included 43 women and 64 men. Mean age of the studied batch was 48.44 years +/-8.55.

IMAGISTIC STUDY. MRI examinations performed in the 103 cases (n-103), revealed the three major types of changes of the intervertebral disk and vertebral plateau, according to data published by other researchers.(7)

In 16 cases (15.55%), of whom 4 cases (25%) had surgical intervention, type I MRI changes were revealed, consisting of vertebral bodies parallel with vertebral plateau of degenerated disk that showed hyposignal on ponderate images in T1 and hyperintensity in T2. There is no radiological correspondent, are associated with incipient disk changes and allways evolves to type II changes.

It seems that Modic changes type 1 are more strongly associated with pain compared to type 2 changes. This may be due to the fact that Modic changes type 1 reflect acute stages of inflammation, whereas changes type 2 are the result of previous inflammation with progressive degeneration.

In 23 cases (22.33%) of whom 5 (21.7%) had surgery, type II MRI changes were identified, showing increasing of intensity of the signal on ponderate images in T1 and an isointense signal or slightly hyperintense in T2 images, imagistic expression of disk lesions consisting of annular protrusion and relatively recent incipient disk hernia. They do not have radiological correspondent, are associated with disk degenerescence changes (annular protrusions and incipient disk hernia) are more stable from the evolutionary point of view. It is important to mention that these cases had as clinical correspondent lumbar pain syndrome, without evident discoradicular conflict (subjective only paresthesia).

In 64 cases (62.13%) of which 38 had surgical intervention (59.3%) MRI investigation revealed type III changes, showing decreasing of intensity of the signal on ponderate images both in T1 and T2, being correlated on usual planar radiographic images with extensive bone sclerosis. They are associated with disk hernia, disk

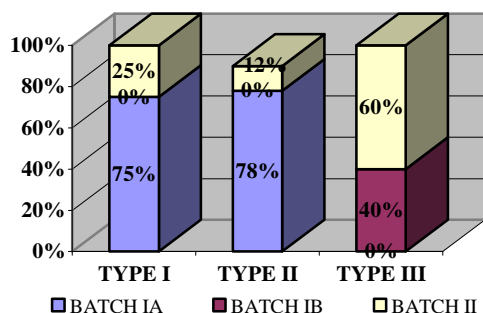
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extrusion, free disk fragment, lesions of the posterior vertebral ligament. From the clinical point of view, the symptoms of old, neglected discovertebral lesions are present (table No. 3, picture no. 1).

Table no. 3. Distribution of the cases according to the types of MRI changes

MRI IMAGES		Total nr of cases-percent	BATCH IA	BATCH IB	BATCH II
TYPE I CHANGES	hyposignal in T1 hypersignal in T2	16 (15.53%)	12 (75%)	-	4 (25%)
TYPE II CHANGES I	hypersignal in T1 and an isointense signal or slightly hyperintense in T2	23 (22.33%)	18 (78.26%)	-	5 (10.63%)
TYPE III CHANGES	hyposignal both in T 1 and T2	64 (62.13%)	-	26 (40.62%)	38 (59.37%)

Picture no. 1. Distribution of the cases according to MRI changes



BIOCHEMICAL STUDY

Biochemical studies aimed:

- to determine mucopolysaccharides and collagen in the components of intervertebral disk;
- to determine chondroitin-sulphate and kerato-sulphate as degradation products of mucopolysaccharides (MPZ);
- evidentiation of the modified ratio between kerato-sulphate/chondroitin-sulphate;
- tracking the reduction of the metachromasy of nucleus pulposus.

Studies have been performed on intervertebral disk fragments, which were obtained through discectomy. Column and paper adsorption chromatography were used. In order to determine kerato-sulphate and chondroitin-sulphate cationic colorant i.e. toluidine blue (Hirsch colorant) was used. The same dye was used in order to evidentiate metachromasy of nucleus pulposus. The colorant dye modified its colour from blue to red. The matrix is intensively metachromatic when using toluidine blue, but less colorable with PAS, thus revealing the richness in glycosaminoglycans (acid mucopolysaccharides) and poorness in neutral polysaccharides.(2,3,5)

Analysis of the biochemical composition of intervertebral disk revealed (table no. 4, picture no. 2):

- in 9 cases (19.14%) the presence of kerato-sulphate

and chondroitin-sulphate in almost equal rates.

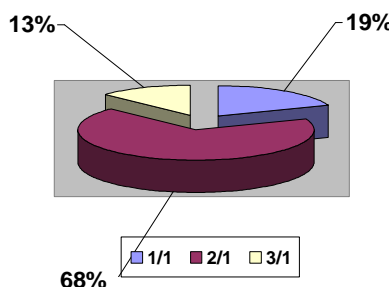
- in 32 cases (68.08%) an increase of almost 2/1 of kerato-sulphate was evidentiated.
- in 6 cases (12.76%) an increase of 3/1 of kerato-sulphate against chondroitin-sulphate was found.

Reduced metachromasy of intervertebral disk was noticed for cases from the second and third categories.

Table no. 4. Distribution of the cases according to kerato-sulphate/chondroitin-sulphate ratio

	Biochemical changes Kerato-sulphate/chondroitin-sulphate ratio		
	1/1	2/1	3/1
No. of cases	9	32	6
Percentage	19,14%	68,08%	12.76%

Picture no. 2. Distribution of the cases according to biochemical changes



Researchers pointed out that aging causes inevitable and progressive changes in disc matrix composition. "Simple" aging of degenerated intervertebral disk is accompanied by a slight decrease of mucopolysaccharides, from 6.5 % dry weight at 20 years, to 5.5 % at 60 years, after having a maximum of 9 % at 40 years, and by increasing of the collagen content with one third until stadium III of degenerescence. Our results revealing that kerato-sulphate/chondroitin-sulphate ratio increases with nucleus aging are concordant with data from other reports. (3)

DISCUSSIONS

In this study, we managed to determine degradation products of MPZ (chondroitin-sulphate and kerato-sulphate), change of kerato-sulphate/chondroitin-sulphate ratio, increasing of metachromasy of both the nucleus pulposus, and different types of collagen.

Proteins- polysaccharides complexes from intervertebral disks are characteristic in at least three aspects:

As mentioned before, they seem to contain both kerato-sulphates and chondroitin-sulphates joined by covalent bonds with the same proteic support. Results of some studies performed on human intervertebral disk demonstrated the existence of a larger content of sulphurated aminoacids than expected. The quantity of mucopolysaccharides, especially chondroitin-sulphate decreases with age, in parallel with dehydration.(2,5)

Hallen reported that as the nucleus becomes older, quantities of hexozamin and sulphates, components

of proteins-polysaccharides complexes, decrease. Polysaccharides bind the vast majority of water, thus, a decrease in the quantity of water must be accompanied by a reduction of the sugar. On the other hand, in the fibrous ring hexosamin may determine an increase during the first 20 years of life, after this age its value stabilizes.(1) Thinks become also complicated because kerato-sulphate/condroitin-sulphate ratio increases with aging of the nucleus. As kerato-sulphate and condroitin-sulphate are joined to the same proteic molecules, this change of percentages seems to reflect an alteration of metabolism speed for the molecules of proteins-polysaccharides complex. Many studies revealed that the content in polysaccharides of the disks decreases slowly with age and very quickly in disk hernia.(2,4)

Herniated disks are characterized by global decrease of mucopolysaccharides and increase of collagen in parallel with the duration of the clinical evolution. Authors draw the conclusion that degenerescence represents a perturbation of the chemical composition, which at a certain moment becomes irreversible, and they say that simple senescence is accompanied by progressive rupture of the bonds between polysaccharides and non-fibrillar proteins, whereas degenerescence is marked by numerous ruptures, which also concern other chemical bonds.(1,4)

The degree of degeneration has widely been documented by the grading systems based on its morphologic change in the evaluation of intervertebral disc degeneration.(6,10)

A comprehensive knowledge of the changes in the biologic behaviour of the cells and in the matrix component of the disc is a new challenging area in the research of pathophysiological mechanism of the disc degeneration.

Therefore, a histochemical grading system of disc degeneration that could explain and pair with the degree of changes in the disc morphology, whether by its gross look or its appearance in the magnetic resonance imaging(MRI), is required. However, a microscopic or histochemical grading system of disc degeneration that is suitable to match these morphologic changes has not been established yet. As an alternative, the degree of apoptosis has previously been proposed as a scale of disc degeneration by many investigators. In the sequence of these proposals, some authors have reported correlation between the degree of apoptosis and the age. However, they found no direct correlation between the degree of apoptosis and the degree of disc degeneration.(10) Collagens and proteoglycans are the primary structural components of the intervertebral disc macromolecular framework.

The study of images captured by resonance may be of much help for clinical practice and for investigative procedures of disc degenerative disease.(10)

As MRI investigation was regulately performed in our cases, establishing of an association between the obtained results and a trusty analysis of anatomic implication was possible in this study.(8) It is obvious that factors such as pain intensity and the pattern and extension of lumbar disk hernia as well, may differ from a group to another, thus explaining the differences that occur in the reported results regarding conservative treatments, from the speciality literature.(7,9)

CONCLUSIONS

1. The research demonstrated the importance of identifying changes and localization of hernia with a predicting role on the evolution and treatment, consequently with a benefic effect for medical practice.
2. Clinical manifestations of low back pain accompanied or not by radiculopathy due to lumbar hernia have a correspondent on MRI images, expressed by Modic in 3 classes.
3. The study underlines the importance of existence of some markers for the diagnosis and evolution of disk hernia, useful for appreciation of therapeutic decision.
4. From results analysis it was noticed that 4/5 from the cases in whom disk hernia was treated by surgery had typical advanced changes at the level of the lesion on MRI images.
5. From the biochemical point of view degeneration of intervertebral disk is expressed by depolymerization of proteoglycans.
6. Correlations that were obtained, with concordances between these investigated parameters, give us hope for an early diagnosis of disk hernias, by associating intervertebral disk cell biochemistry data with MRI images.
7. Due to this clinical, biochemical and imagistic study we have elaborated a biological fundamentation of the Modic imagistic stadialization.

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