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FLUID-SENSITIVE SEQUENCES MODIFY THE MODIC CLASSIFICATION IN MRI

SEQUÊNCIAS SENSÍVEIS A LÍQUIDOS MODIFICAM A CLASSIFICAÇÃO DE MODIC NA RESSONÂNCIA MAGNÉTICA

SECUENCIAS SENSIBLES A LÍQUIDOS MODIFICAN LA CLASIFICACIÓN DE MODIC EN RESONANCIA MAGNÉTICA

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ABSTRACT

Objective: To evaluate whether the magnetic resonance imaging (MRI) acquisition with the Dixon fat suppression technique alters the detection of signal abnormalities in the subchondral bone of the vertebral endplates in the lumbar spine. Methods: retrospective study include patients who underwent lumbar spine MRI with acquisition of T1- and T2-weighted fast spin echo sequences (routine protocol) and the multipoint Dixon sequence with T2 weighting and fat suppression. Two radiologists qualitatively classified Modic-type changes (absent, Modic I, Modic II, and Modic III) independently and blindly. When the subchondral signal abnormality was identified, each radiologist measured the maximum depth in relation to the vertebral plateau. The radiologists' assessments were used to analyze interobserver agreement and one of the radiologists carried out a second analysis of the exams, enabling intra-observer assessment. Results: The results showed a significant increase in the detection of the edema pattern (Modic I) in qualitative and quantitative analyzes when using the Dixon technique, in comparison to the routine sequences, with an increase in the prevalence and extent of involvement by the bone edema pattern. There was no significant difference in the detection of the adipose replacement pattern (Modic II) between the two techniques. There was moderate to substantial intra-observer correlation for the traditional protocol and substantial to high agreement for the analysis of the Dixon technique images. Conclusions: The Dixon technique showed superiority in the detection of Modic I in relation to the traditional protocol, and allowed the detection, on average, of greater depth of involvement of subchondral bone changes. There was good intra-observer and inter-observer reproducibility in identifying Modic abnormalities. ***Evidence level III, comparative retrospective study.***

Keywords: Bone; Spine; Intervertebral Disc.

RESUMO

Objetivo: avaliar se a aquisição de imagens de ressonância magnética com a técnica de supressão de gordura Dixon altera a detecção de anormalidades de sinal no osso subcondral dos discos vertebrais da coluna lombar. Métodos: estudo retrospectivo envolvendo pacientes submetidos a exames de ressonância magnética (RM) da coluna lombar realizados com a aquisição de sequências de spin-eco rápido ponderadas em T1 e T2 (protocolo de rotina) e a sequência de supressão de gordura multiponto ponderada em T2 de Dixon. Dois radiologistas classificaram qualitativamente as alterações do tipo Modic (ausente, Modic I, Modic II e Modic III) de forma independente e cega. Quando a anormalidade do sinal subcondral foi identificada, cada radiologista mediu a profundidade máxima em relação ao platô vertebral. As avaliações dos radiologistas foram usadas para analisar a concordância interobservador e uma segunda análise dos exames foi realizada por um dos radiologistas, permitindo a avaliação intraobservador. Resultados: Os resultados mostraram um aumento significativo na detecção do padrão de edema (Modic I) em análises qualitativas e quantitativas ao usar a técnica Dixon, em comparação com as sequências de rotina, com um aumento na prevalência e na extensão do envolvimento ósseo. Não houve diferença significativa na detecção do padrão de substituição adiposa (Modic II) entre as duas técnicas. Houve uma correlação intra-observador moderada a substancial para o protocolo tradicional e concordância substancial a alta para a análise de imagem da técnica Dixon. Conclusões: A técnica Dixon mostrou superioridade na detecção de Modic I em relação ao protocolo tradicional e permitiu a detecção, em média, de maior profundidade de envolvimento das alterações ósseas subcondrais. Houve boa reprodutibilidade intraobservador e interobservador na identificação de anormalidades de Modic. ***Nível de evidência III, estudo retrospectivo comparativo.***

Descritores: *Osso; Coluna Vertebral; Disco Intervertebral.*

RESUMEN

Objetivo: Evaluar si la adquisición de imágenes de resonancia magnética con la técnica de supresión grasa de Dixon altera la detección de anomalías de señal en el hueso subcondral de los platillos vertebrales de la columna lumbar. Métodos: estudio retrospectivo que incluyó pacientes sometidos a exámenes de resonancia magnética (MRI) de la columna lumbar realizados con la adquisición de secuencias de eco de espín rápido ponderadas en T1 y T2 (protocolo de rutina) y la secuencia multipunto de Dixon con ponderación en T2 y supresión

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de grasa. Dos radiólogos clasificaron cualitativamente los cambios de tipo Modic (ausentes, Modic I, Modic II y Modic III) de forma independiente y ciega. Cuando se identificó la anomalía de la señal subcondral, cada radiólogo midió la profundidad máxima en relación con la meseta vertebral. Las evaluaciones de los radiólogos se utilizaron para analizar la concordancia interobservador y uno de los radiólogos realizó un segundo análisis de los exámenes, lo que permitió la evaluación intraobservador. Resultados: Los resultados mostraron un aumento significativo en la detección del patrón de edema (Modic I) en los análisis cualitativos y cuantitativos al utilizar la técnica de Dixon, en comparación con las secuencias rutinarias, con un aumento en la prevalencia y extensión de afectación del hueso. patrón de edema. No hubo diferencias significativas en la detección del patrón de reemplazo adiposo (Modic II) entre las dos técnicas. Hubo una correlación intraobservador de moderada a sustancial para el protocolo tradicional y un acuerdo de sustancial a alto para el análisis de las imágenes de la técnica de Dixon. Conclusiones: La técnica de Dixon mostró superioridad en la detección de Modic I con relación al protocolo tradicional, y permitió detectar, en promedio, mayor profundidad de afectación de los cambios óseos subcondrales. Hubo buena reproducibilidad intraobservador e interobservador en la identificación de anomalías de Modic. ***Nivel de evidencia III, estudio retrospectivo comparativo.***

Descriptores: *Hueso; Columna Vertebral; Disco Intervertebral.*

INTRODUCTION

The subchondral bone of the vertebral plateau is vascularized and comprises the dense and compact bone of the vertebral plate and the adjacent trabecular bone, located between the cartilage of the terminal plate and the vertebral body.[1] The subchondral bone tissue functions as an interface between the rigid bone and the intervertebral disc. The vessels from the subchondral bone penetrate the cartilage of the terminal plate and nourish the intervertebral disc by diffusion.

The degenerative process of the intervertebral disc causes histological and biomechanical changes in the subchondral bone of the vertebral body. Some of these changes reflect abnormalities identified in magnetic resonance imaging (MRI) and were described by Modic and collaborators, based on the analysis of routine T1 and T2 weighted sequences [2]. Modic type I (Figure 1) is characterized by a signal change with a pattern of bone edema, that is, low signal on T1 weighted sequence and high signal on T2 weighted sequence. Modic type II (Figure 2) is the most frequent and corresponds to the pattern of fat substitution, characterized by high signal on T1 and T2 weighted sequences. Modic type III is less frequently described, characterized by low signal on T1 and T2 weighted sequences and related to the pattern of bone sclerosis on X-rays. The coexistence of different types of Modic can occur in the same vertebral plateau suggesting that they represent different stages of the same pathological process.[2]

New techniques have been incorporated into MRI diagnosis, and the Dixon technique has gained traction for allowing a more homogeneous fat saturation, in addition to having lower sensitivity to magnetic susceptibility artifacts.[3] The Dixon technique can be considered a hybrid sequence in which four types of tissue contrast are obtained in a single acquisition. The acquisition with echo times in which the relaxation of the hydrogens bound in the water and fat molecules are in phase and out of phase, together with post-processing, allows for obtaining in-phase and out-of-phase images, fat quantification (signal intensity of the in-phase image subtracted

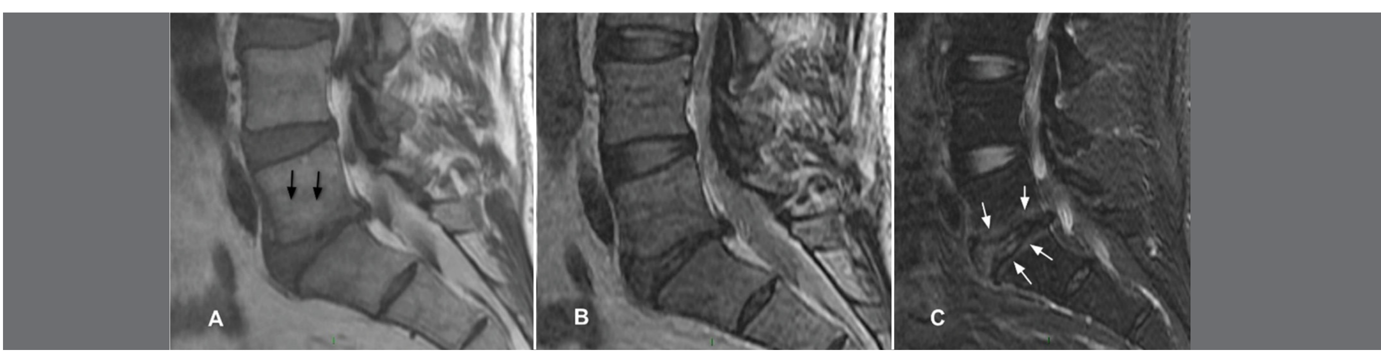

Figure 1. Figures A and B show magnetic resonance images of the lumbosacral spine with the sequences *fast spin echo* (FSE) weighted in T1 and T2. The black arrows in figure A indicate the presence of adipose replacement of the bone marrow adjacent to the lower vertebral plateau of L5, with increased signal intensity suggesting Modic type II. In Figure C, the image from the Dixon FSE T2 sequence with fat suppression clearly shows the concomitant presence of a pattern of bone edema, indicative of Modic I.

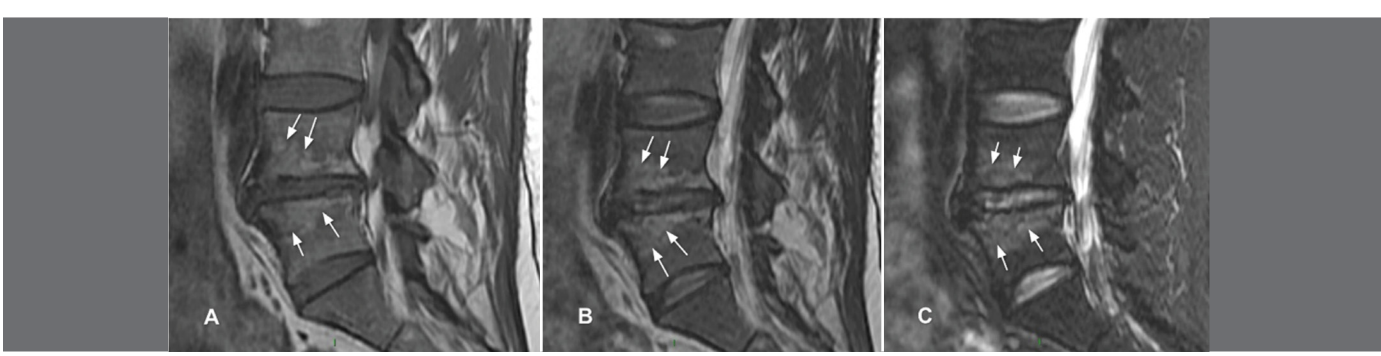

Figure 2. Figures A and B show magnetic resonance images of the lumbosacral spine respectively with the FSE sequences weighted in T1 and T2. The white arrows point to areas of adipose replacement of the bone marrow (Modic II) adjacent to the vertebral endplates in the L4-L5 disc space. Figure C shows a pattern of bone edema (Modic I) in the Dixon FSE T2 sequence with fat suppression also indicated by the white arrows, illustrating that the use of fat suppression can complement the interpretation of the present abnormalities and substantially modify the Modic classification.

from the signal intensity of the out-of-phase image), and images sensitive to water/liquid (summing the signal intensity of the in-phase and out-of-phase sequences).[3]

Maeder and colleagues suggested that the Dixon technique can be used to replace traditional MRI protocols.[4] These authors showed similar results in detecting metastases in the spine using this technique compared to established protocols, but with the advantage of a shorter examination acquisition time.[4]

The original Modic classification was based on traditional T1 and T2 weighted MRI sequences; however, it is reasonable to assume that the use of liquid-sensitive sequences with fat suppression may increase the detection of the pattern of bone edema compared to routine sequences, as these sequences have greater sensitivity to the presence of intra- or extracellular water.

We did not find studies comparing the detection of subchondral vertebral changes of the Modic type by traditional protocols and by the Dixon technique with fat suppression. The objective of this study was, therefore, to evaluate whether the use of the Dixon technique alters the detection of Modic-type changes in the lumbar spine compared to the traditional protocol consisting of T1 and T2 weighted sequences *fast spin echo*.

METHODS

This is a cross-sectional study, with a retrospective evaluation of consecutive magnetic resonance imaging exams performed for clinical indication. The present study was approved by the Ethics and Research Committee of the Institution (protocol 79141917.5.0000.5440), with a waiver of the informed consent form.

Participants

As inclusion criteria for the participating patients, we selected consecutive lumbar spine exams performed on a 3.0 Tesla machine. The exclusion criterion was defined for cases of patients in whom the magnetic resonance imaging showed neoplastic, inflammatory, infectious changes, and post-surgical and post-radiotherapy changes. A total of 100 consecutive patients were selected, of which one of these patients was excluded for presenting secondary lesions due to neoplasia.

Acquisition of magnetic resonance imaging images

All exams were acquired using a Discovery MD750 3.0T MRI (GE Medical Systems). For evaluation, T1 weighted sequences without fat saturation (T1) and T2 weighted sequences without fat saturation (T2) were selected, considered as the traditional protocol. Images acquired by the Dixon technique were also obtained and analyzed: T2 weighted sequences with fat saturation and T2 weighted sequences with fat quantification (*Fat only*).

The exams were stored on a workstation and the patient information was anonymized in the DICOM file headers using the KPACS software. To ensure patient privacy, their identification in the research data sheet was done through numbers (Patient#1, Patient#2, etc.) and not by name or initials.

Evaluation of magnetic resonance images

The exams were evaluated independently and blindly by two radiologist doctors. Reader 1 participated in the study during a fellowship in musculoskeletal radiology and performed the analysis of all cases. Reader 2 had 18 years of professional experience at the time of the study and analyzed thirty cases that were randomly selected for interobserver agreement analysis. The workflow initially consisted of analyzing exams only with T1 and T2 weighted sequences *fast spin echo*. After one month from the first analysis, the evaluation was made with the sequences of the DIXON technique, with fluid-sensitive images and quantification of fat. These two stages were performed by both radiologists, who identified the vertebral plateaus of the vertebrae from L1 to S1 that showed Modic type changes, and classified the type of Modic found. After identifying and classifying the Modic type changes, they measured the maximum thickness of the change found. About a month after the last reading, Reader 1 performed a second reading of the exams. In the evaluation of the images, the readers were blind to the other evaluations conducted in the research, regarding the previous results of the exams and the clinical information of the patients.

Statistical analysis

Intra-observer reproducibility consisted of comparing the first and second analyses performed by Reader 1 using the intraclass correlation coefficient, with a mixed model of 2 factors to test consistency and absolute agreement, recommended to assess agreement between two measures. Interobserver reproducibility was also tested using the same analysis of the intraclass correlation coefficient, contrasting the results of the average of the two analyses performed by Reader 1 with the results of Reader 2's analysis. The validity test of the tested methods was performed using the Spearman correlation coefficient for non-parametric or categorical variables, comparing Reader L1's diagnosis with Reader L2's diagnosis. The interpretation of the strength of correlation of intra and interobserver analyses was based as follows: 0 (absence), 0-0.19 (poor), 0.20-0.39 (weak), 0.40-0.59 (moderate), 0.60-0.79 (substantial), and ≥ 0.80 (almost complete).[5-7]

RESULTS

MRI exams of 99 patients were included, with an average age of 48.8 years, age ranging from 18 to 89 years, with 55 patients being female.

The abnormalities found are listed in Table 1. There was greater detection of Modic type I changes using Dixon technique magnetic resonance imaging compared to the traditional protocol with T1 and T2 weighted sequences *fast spin echo* ($p<0.01$). In the analysis using the traditional protocol, 21 areas of Modic I or mixed Modic (Modic I and II in the same vertebral plateau) abnormalities were identified in the evaluated vertebral plateaus, and using images from the Dixon technique, 79 areas of abnormality were detected. The detection of the pattern of adipose substitution (Modic II) did not show a statistically significant difference between the magnetic resonance imaging techniques in the analyses performed. Figures 1 and 2 exemplify cases where there was a difference in identifying Modic I changes between the images from the traditional protocol weighted in T1 and T2 and the images acquired with the Dixon technique sensitive to fluid and with fat suppression.

The reproducibility of qualitative analyses was performed by evaluating the absolute agreement between the first and second classifications of the type of change in the subchondral bone by the same observer (intra-observer) at two different times, with an interval of approximately one month. We observed moderate to substantial correlations for intra-observer reproducibility regarding the evaluated parameters. The highest correlations were observed for the measurement of the lower plateau of L3 ($r=0.81$) and L4 ($r=0.89$) and the lowest for the upper plateau of L1 ($r=0.69$) and upper plateau of L5 ($r=0.71$). The inter-observer correlation of the qualitative analysis was on average moderate, with a tendency for greater divergence in the use of the Dixon technique, but without statistically significant difference between the techniques. There was no significant correlation for the evaluation of the type of change in the subchondral bone of the upper plateau of L5 for both techniques, differing substantially from the other evaluated vertebrae. The vertebral plateaus of the L3-L4 disc space also had lower inter-observer correlation in the Dixon technique than at other levels.

Table 2 identifies the averages of the maximum thickness measurements of abnormalities in the subchondral bone. In general, the average measurements were higher when the evaluation used images from the Dixon technique. Tables 3 and 4 show the reproducibility of the thickness measurements of subchondral abnormalities in the lumbar vertebral plateaus, in the traditional protocol and with the Dixon technique respectively.

Table 1. Frequency of detection of signal abnormality areas by reader 1 (L1) and reader 2 (L2), classified according to Modic classification, in types I, II, and III. Evaluation in the images of the Dixon Technique.

	Measure 1(L1)		Measure 2(L1)		Measure3 (L2)	
	Classification	**N***	**Classification**	**N***	**Classification**	**N** (%)**
Plateau lower of L1	Without classification	93	Without classification	92	Without classification	29
	Modic 1	-	Modic 1	-	Modic 1	1
	Modic 2	4	Modic 2	5	Modic 2	-
	Modic 1 and 2	2	Modic 1 and 2	2	Modic 1 and 2	-
Plateau upper of L2	Without classification	90	Without classification	89	Without classification	29 (93.5)
	Modic 1	1	Modic 1	2	Modic 1	1 (3.2)
	Modic 2	6	Modic 2	7		
	Modic 1 and 2	2	Modic 1 and 2	1		
Plateau lower of L2	Without classification	85	Without classification	85	Without classification	30 (96.8)
	Modic 1	4	Modic 1	6		
	Modic 2	4	Modic 2	5		
	Modic 1 and 2	4	Modic 1 and 2	2		
	Modic 2 and 3	1	Modic 2 and 3	1		
	Modic 1 and 3	1				
Plateau upper from L3	Without classification	83	Without classification	81	Without classification	28 (90.3)
	Modic 1	4	Modic 1	5	Modic 1	1 (3.2)
	Modic 2	9	Modic 2	10	Modic 2	1 (3.2)
	Modic 1 and 2	3	Modic 1 and 2	3		
Plateau lower from L3	Without classification	87	Without classification	88	Without classification	28 (90.3)
	Modic 1	3	Modic 1	3	Modic 1	2 (6.5)
	Modic 2	5	Modic 2	5		
	Modic 1 and 2	3	Modic 1 and 2	3		
	Modic 1. 2 and 3	1				
Plateau upper from L4	Without classification	80	Without classification	81	Without classification	29 (93.5)
	Modic 1	2	Modic 1	3	Modic 1	1 (3.2)
	Modic 2	13	Modic 2	13		
	Modic 1 and 2	3	Modic 1 and 2	2		
	Modic 1 and 3	1				
Plato lower from L4	Without classification	81	Without classification	79	Without classification	28 (90.3)
	Modic 1	2	Modic 1	3	Modic 1	2 (6.5)
	Modic 2	11	Modic 2	12		
	Modic 1 and 2	5	Modic 1 and 2	5		
Plateau upper from L5	Without classification	72	Without classification	76	Without classification	27 (87.1)
	Modic 1	4	Modic 1	3	Modic 1	2 (6.5)
	Modic 2	15	Modic 2	13	Modic 2	1 (3.2)
	Modic 1 and 2	8	Modic 1 and 2	7		
Plateau lower from L5	Without classification	67	Without classification	70	Without classification	25 (80.6)
	Modic 1	6	Modic 1	6	Modic 1	3 (9.7)
	Modic 2	19	Modic 2	18	Modic 2	1 (3.2)
	Modic 1 and 2	7	Modic 1 and 2	5	Modic 1 and 2	1 (3.2)
Plateau upper from S1	Without classification	68	Without classification	68	Without classification	26 (83.9)
	Modic 1	6	Modic 1	7	Modic 1	4 (12.9)
	Modic 2	18	Modic 2	19		
	Modic 1 and 2	7	Modic 1 and 2	5		

Number of missing cases: N=1; * Number of study participants (N=99); ** Number of cases evaluated as reference measure (N=30).

Table 2. Averages of maximum thickness of the Modic type abnormality in the subchondral. L1: reader 1, L2: reader 2.

	Mean	**Standard Deviation**	**Mean**	**Standard Deviation**	**Mean**	**Standard Deviation**	**Mean**	**Standard Deviation**
Lower plate of L1	0.29	1.30	0.29	1.09	0.13	0.52	0.15	0.82
Upper plate of L2	0.23	1.18	0.21	0.77	0.05	0.26	0.00	0.00
Lower plate of L2	0.59	1.97	0.68	2.28	0.51	1.50	0.36	1.41
Upper plate of L3	0.62	1.97	0.58	1.93	0.17	0.65	0.33	1.36
Lower plate of L3	0.48	2.14	0.53	2.01	0.16	0.50	0.14	0.79
Upper plate of L4	0.68	2.11	0.85	2.32	0.26	0.77	0.35	1.33
Lower plate of L4	0.94	2.33	1.01	2.48	0.20	0.67	0.21	0.80
Upper plate of L5	0.99	2.42	0.93	2.17	0.21	0.58	0.43	1.36
Lower plate of L5	1.42	2.87	1.35	2.88	0.68	1.51	0.83	1.92
Upper plate of S1	1.34	2.45	1.12	2.43	0.49	1.18	0.51	1.33
Lower plate of L1 (Dixon)	0.36	1.57	0.45	1.93	0.12	0.52	0.43	1.28
Upper plateau of L2 (Dixon)	0.50	1.71	0.50	1.65	0.18	0.68	0.17	0.65
Lower plateau of L2 (Dixon)	1.00	2.67	1.10	3.02	0.57	1.61	0.36	1.41
Upper plateau of L3 (Dixon)	0.95	2.49	1.11	2.66	0.32	1.05	0.10	0.53
Lower plateau of L3 (Dixon)	0.89	2.99	0.84	2.77	0.23	0.74	0.34	0.90
Upper plateau of L4 (Dixon)	1.03	2.33	1.00	2.49	0.54	1.48	0.34	0.90
Lower plateau of L4 (Dixon)	1.10	2.73	1.11	2.66	0.13	0.50	0.08	0.46
Upper plateau of L5 (Dixon)	1.35	2.77	1.34	2.94	0.46	1.14	0.07	0.37
Lower plateau of L5 (Dixon)	1.69	3.12	1.69	3.11	1.09	2.15	0.44	1.24
Upper plateau of S1 (Dixon)	1.50	2.78	1.60	2.91	0.84	1.82	0.37	1.23

Number of missing cases: N=1; * Number of study participants (N=99); ** Number of cases evaluated as a reference measure (N=30).

Table 3. Assessment of reproducibility between two measurements of signal abnormality thickness in the subchondral bone performed by the same evaluator (reader 1) in routine sequences, weighted in T1 and T2 without fat suppression, at different times. CCI: intraclass correlation coefficient.

	CCI	Alpha of Chromach	P
Lower plateau of L1	0.73	*	*
Upper plateau of L2	0.69	*	*
Lower plateau of L2	0.76	*	*
Upper plateau of L3	0.70	*	*
Lower plateau of L3	0.81	*	*
Upper plateau of L4	0.79	*	*
Lower plateau of L4	0.89	*	*
Upper plateau of L5	0.71	*	*
Lower plateau of L5	0.76	*	*
Upper plateau of S1	0.79	*	*
CCI for average measurements (CI 95%)	0.86 (0.81 - 0.9)	*	<0.001

Table 4. Assessment of reproducibility between two measurements of the signal abnormality thickness in the subchondral bone performed by the same evaluator (reader 1) in sequences obtained with the Dixon technique with fat suppression, at different times. CCI: intraclass correlation coefficient.

	CCI	P
Lower plateau of L1	0.76	*
Upper plateau of L2	0.78	*
Lower plateau of L2	0.85	*
Upper plateau of L3	0.92	*
Lower plateau of L3	0.89	*
Upper plateau of L4	0.84	*
Lower plateau of L4	0.9	*
Upper plateau of L5	0.88	*
Lower plateau of L5	0.93	*
Upper plateau of S1	0.95	*
CCI for average measurements (CI 95%)	0.87 (0.83 - 0.9)	<0.001

DISCUSSION

Based on our results, the Dixon technique showed superiority in detecting abnormalities in the subchondral bone of the Modic I type, confirming the suspicion that the fluid-sensitive sequence in this technique increases sensitivity to detect the pattern of bone edema. It was also possible to detect higher averages of the thickness of the measurements of the signal abnormality areas in the subchondral bone when the Dixon technique was used. However, there was no significant difference in detecting fat replacement in the subchondral bone tissue (Modic II). The low prevalence of Modic type III changes prevented comparative analysis between magnetic resonance imaging techniques.

The evaluation of intra-observer and inter-observer agreement showed substantial to almost perfect correlations for measuring the thickness of Modic subchondral abnormalities, using the traditional protocol and images with the multipoint Dixon technique. Regarding qualitative analyses, we identified variable inter-observer agreement, averaging moderate agreement, both for routine sequences and for the Dixon sequence with fat suppression. Our inter-observer reproducibility results for Modic classification were lower compared to those obtained in a previous study, which demonstrated excellent inter-observer reliability.[8]

The finding of Modic changes in magnetic resonance images can be observed in symptomatic patients and asymptomatic individuals and is associated with aging.[9-13] Despite multiple studies and different systematic reviews, there is no definitive conclusion about the association between low back pain and the presence of Modic changes in the subchondral bone tissue of the vertebral plateau. Additionally, there is no consensus on the pathogenesis of Modic changes, with studies suggesting mechanical etiology, inflammation via immune pathways, and low virulence infection, mechanisms that may act independently or concurrently.[14] Another important controversy concerns the association between Modic changes I and II and lumbar segmental instability identified by dynamic radiographs.[15-17] As there are different controversies regarding the clinical significance of Modic changes and the etiology of these abnormalities, future studies will certainly be needed to investigate these issues. In this scenario, our results are important as they confirm that different magnetic resonance imaging techniques can alter the frequency of identification of Modic I and change the measurement of detected changes. The Dixon technique increases sensitivity to detect the pattern of bone edema.

Our study has limitations. First, its retrospective nature. We did not analyze specific clinical information, and our case series has potential selection bias, as we only analyzed patients indicated for examination to investigate low back pain or radiculopathy.

Fat suppression with the multipoint Dixon technique showed superiority in detecting Modic I changes compared to the traditional protocol in magnetic resonance imaging, and allowed for detecting, on average, greater depth of involvement of subchondral bone changes.

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