

Original Article

Meta-analysis of magnetic resonance imaging for the differential diagnosis of spinal degeneration

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Abstract: To systematically evaluate the clinical significance of magnetic resonance imaging for the identification and diagnosis of spinal degenerative changes. We searched Cochrane Library, PubMed, EMBASE, CNKI, WanFang Data, Medalink, VIP and CBM databases for clinical studies on the significance of magnetic resonance imaging for the differential diagnosis of spinal degeneration; retrieval time was from database building to October 2014. Two reviewers independently screened the literature, extracted data and evaluated methodological quality according to the inclusion and exclusion criteria. Meta-DiSc 1.4 software was used for meta-analysis. The study included six documents, 10 independent results and a total of 505 individuals. Meta-analysis showed that: In the present study, the efficacy of magnetic resonance imaging in the differential diagnosis of cervical and lumbar degeneration was firstly analyzed and discussed using the Meta-DiSc 1.4 software. SPE: $\chi^2 = 77.59$, $P = 0.000$, $I^2 = 88.4\%$; SEN: $\chi^2 = 167.25$, $P = 0.000$, $I^2 = 94.6\%$; DOR: Cochran-Q = 71.64, $P = 0.000$. Meta-analysis of random effect model showed that: SEN merge = 0.849 [95% CI (0.816, 0.878)], SPE merge = 0.745 [95% CI (0.695, 0.792)], + LR = 2.735 [95% CI (1.600, -4.676)], - LR = 0.245 [95% CI (0.122, -0.493)], DOR merge = 21.158 [95% CI (5.234, -85.529)], SROC AUC = 0.8698; the results had good stability. Then the efficacy of magnetic resonance imaging in the differential diagnosis of cervical degeneration was analyzed and the results showed that: SPE: $\chi^2 = 6.92$, $P = 0.075$, $I^2 = 56.6\%$; SEN: $\chi^2 = 81.73$, $P = 0.000$, $I^2 = 96.3\%$; DOR: Cochran-Q = 12.71, $P = 0.005$. Meta-analysis of random effect model showed that: SEN merge = 0.799 [95% CI (0.741, 0.850)], SPE merge = 0.769 [95% CI (0.683, -0.840)], + LR = 2.506 [95% CI (1.399, -4.489)], - LR = 0.363 [95% CI (0.149, -0.882)], DOR merge = 11.949 [95% CI (2.195, -65.036)], SROC AUC = 0.8210. The stability was good. Finally, analysis of six independent studies on the efficacy of magnetic resonance imaging in the differential diagnosis of lumbar degeneration was performed: SPE: $\chi^2 = 70.13$, $P = 0.000$, $I^2 = 92.9\%$; SEN: $\chi^2 = 78.35$, $P = 0.000$, $I^2 = 93.6\%$; DOR: Cochran-Q = 58.04, $P = 0.000$. Meta-analysis of random effect model showed that: SEN merge = 0.732 [95% CI (0.667, -0.791)], SPE merge = 0.883 [95% CI (0.843, -0.916)], + LR = 3.072 [95% CI (1.330, -7.091)], - LR = 0.190 [95% CI (0.063, -0.572)], DOR merge = 30.252 [95% CI (3.060, -299.13)], SROC AUC = 0.8994. Sensitivity analysis was performed by excluding each study individually and the results showed no significant changes in SEN and SPE merge, indicating good stability of the meta-analysis. Existing studies confirm that MRI had good sensitivity and specificity for the differential diagnosis of cervical and lumbar degeneration; the positive ratio in cervical and lumbar degeneration group was 3 to 10 times of that in non-degeneration control group; the efficacy for differential diagnosis was good; combined with the good maneuverability in clinical diagnosis of spinal degeneration, it can be used as effective and feasible method for clinical differential diagnosis of spinal degenerative diseases.

Keywords: MRI, cervical degeneration, lumbar degeneration, differential diagnosis, meta-analysis

Introduction

Cervical and lumbar degenerations are the most common degenerative diseases in the clinic. According to different degrees, intervertebral disc degeneration can be classified as cervical disc bulging, herniation and prolapse.

Due to loss of normal disc structure and progressive fibrosis, roughness and progressive fibrosis are produced in the annulus lamellar, finally leading to the formation of cracks and degeneration of the cervical spine, with major clinical manifestation of compression in vertebral nerves, spinal cord and blood vessels [1-6].

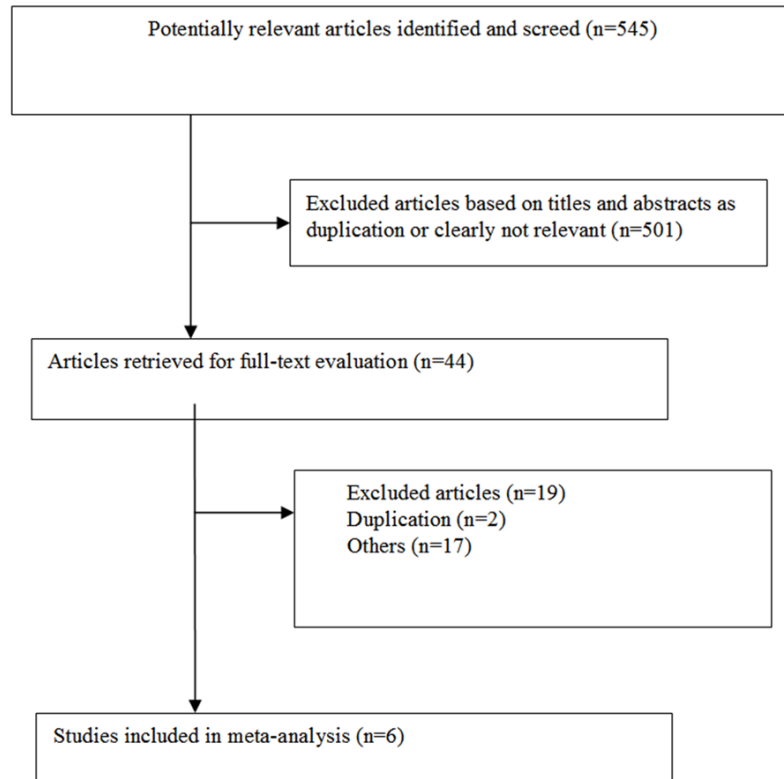


Figure 1. Screening process of articles on MRI for spinal degeneration.

Clinical application of Magnetic Resonance Imaging (MRI) makes a breakthrough in diagnosis of cervical spinal cord disease. Around the cervical transforaminal and epidural, there is an abundance of adipose tissue, showing high luminance signal in imaging diagnosis; High signal in disc tissue, high signal in vertebral body posterior edge hyperplasia, low signal in the annulus and vertebral bone cortex and its multi-level and multi-directional scanning capability can accurately evaluate the disc degeneration, herniation and cervical stenosis. Some reports suggest that MRI diagnosis of cervical degeneration had a compliance rate of 88% with the surgery. In addition, although two-dimensional and three-dimensional MRI images could clearly determine the lesion location and scope of involvement, there are some restrictions, such as inspection fees are relatively high, a pacemaker must be fitted, the body has a paramagnetic metal and patients with claustrophobia phobia cannot accept MRI examination [7-10].

In this paper, a meta-analysis of magnetic resonance imaging for the differential diagnosis of

common spinal degeneration was conducted.

Material and methods

Inclusion and exclusion criteria

Research type: Domestic and foreign published diagnostic studies on magnetic resonance imaging for cervical and lumbar degenerations. Languages included Chinese and English.

Subjects: The study population had accepted MRI diagnosis, surgery and pathology diagnosis; literatures with available true positive value (TP), false positive value (FP), false negative values (FN), true negative value (TN) and other raw measurement data of independent diagnosis and angiography diagnosis; original studies.

Diagnostic methods: The evaluation test was MRI detection; gold standard was pathological diagnosis.

Outcome indicators: Sensitivity (SEN), specificity (SPE), positive likelihood ratio (+ LR), negative likelihood ratio (- LR), diagnostic odds ratio (DOR) and the area (AUC) under subject operating characteristic curve (SROC).

Exclusion criteria: Missing important data or unclear measurement indicators; repeated published in different journals; only topics involved in MRI diagnosis of spinal degeneration but content was independent; retrospective studies.

Search strategy

We searched Cochrane Library, PubMed, EMBase, CNKI, WanFang Data, VIP and CBM database for clinical studies on MRI diagnosis of cervical and lumbar degenerations, which were retrieved from database building to October 2014. Meanwhile manual search for MRI diagnosis-related magazines was performed. Chinese search terms included: MRI,

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Table 1. General information of included studies

Included study	Year	Age (Mean, Years)	Ethnicity	Year	TP	FP	FN	TN	Gold standard
Chao Chen	2013	44	Asian	2013	79	1	1	0	Surgical diagnosis
Jingtao Zhang-1	2013	41	Asian	2013	48	10	0	30	Surgical diagnosis
Jingtao Zhang-2	2013	45	Asian	2013	27	5	21	35	Surgical diagnosis
Jingtao Zhang-3	2013	48	Asian	2013	25	12	23	28	Surgical diagnosis
Chen X	2014	62	Asian	2014	28	0	9	13	Surgical diagnosis
Milan PS	2010	52	Asian	2010	13	22	15	10	Surgical diagnosis
Lehuui Zhang-1	2007	47	Asian	2007	47	8	9	44	Surgical diagnosis
Lehuui Zhang-2	2007	44	Asian	2007	87	12	0	9	Surgical diagnosis
Lehuui Zhang-3	2007	41	Asian	2007	87	10	0	11	Surgical diagnosis
Jianqiao X	2006	52	Asian	2006	25	4	5	66	Surgical diagnosis

Table 2. Quality assessment of included studies

Included study	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Chao Chen	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Jingtao Zhang-1	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Unclear	Y	Y	Y
Jingtao Zhang-2	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Jingtao Zhang-3	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Chen X	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Milan PS	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Lehuui Zhang-1	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Lehuui Zhang-2	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Lehuui Zhang-3	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Unclear	Y	Y
Jianqiao X	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y

Note: Specific criteria of QUADAS items were as follows: 1. whether the case spectrum contained a variety of cases and easily confusing cases? 2. Were the inclusion criteria were clear? 3. Was gold standard able to accurately distinguish the sick (malignant) and disease-free (benign) status? Was the time difference between the gold standard diagnosis and evaluation test short? Was there some changes in disease conditions? 5. Whether all the patients or randomly selected patients underwent a gold standard test? 6. Are all cases diagnosed by the same gold standard regardless of the negative or positive evaluation test results? 7. Whether the gold standard diagnosis and evaluation diagnosis were independent of each other (i.e., evaluation test was not an integral part of the gold standard diagnostic test part)? 8. Are the operation of diagnostic evaluation described in great detail and whether it can be repeated? 9. Whether the operation of gold standard test was described in great detail and the repeatability was explained? 10. Whether the results of the evaluation test were determined in the conditions that gold standard results were not informed? 11. Whether gold standard results were determined in the conditions that the results of the evaluation test were not informed? 12. When explaining the test results, were the available clinical data of the clinical data in line with that in the actual application? 13. Are the unexplained/uncertain/intermediate test results described? 14. Whether the quitted cases were described in detail? In which, the 3rd, 8th and 9th items were not necessary for evaluation; finally 11th item was determined as Cochrane diagnostic test criteria; each item was recorded as "Yes", "No" "unclear"; "Y" means the study met this standard, "No" represented the study did not meet or did not fully comply this standard; that enough information cannot be obtained from the article was "unclear".

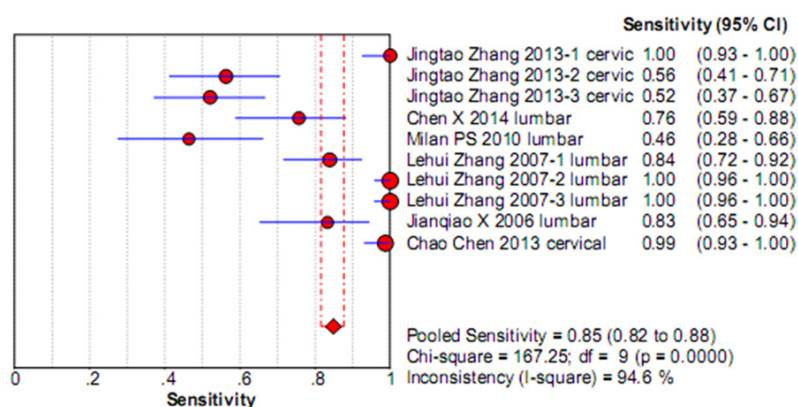


Figure 2. SEN meta-analysis of MRI for differential diagnosis of cervical and lumbar degenerations.

cervical degeneration, lumbar degeneration and differential diagnosis; English search terms included: magnetic resonance imaging; cervical degeneration; lumbar degeneration; differential diagnosis.

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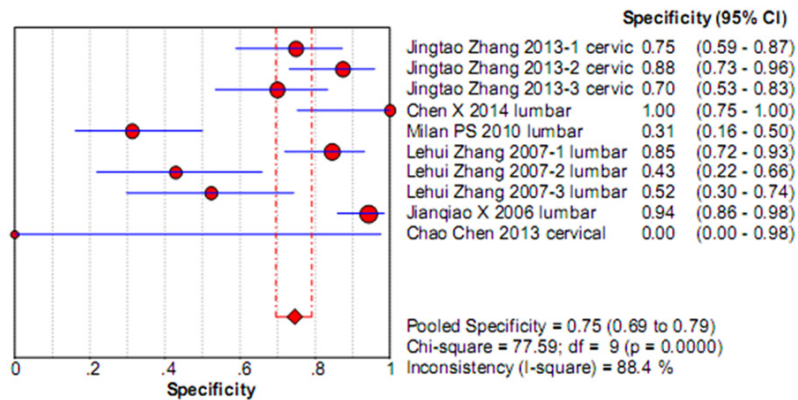


Figure 3. SPE meta-analysis of MRI for differential diagnosis of cervical and lumbar degenerations.

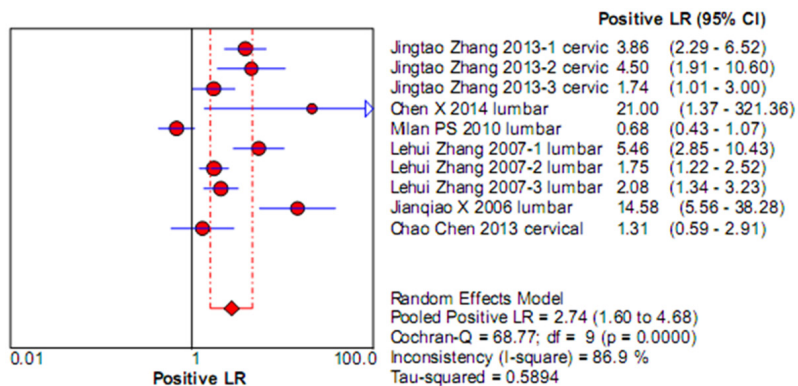


Figure 4. + LR meta-analysis of MRI for differential diagnosis of cervical and lumbar degenerations.

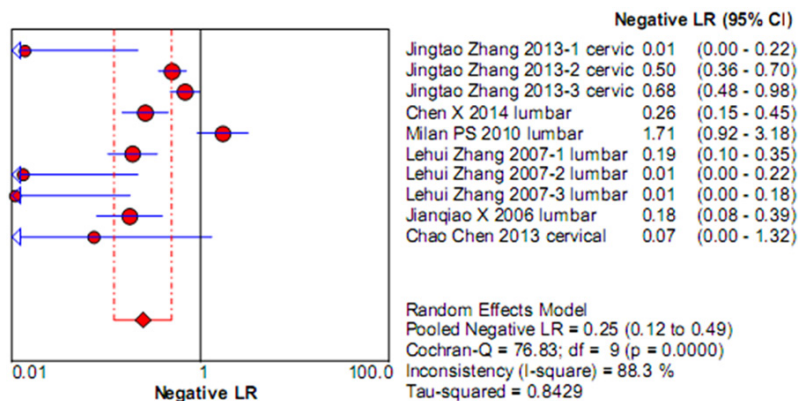


Figure 5. - LR meta-analysis of MRI for differential diagnosis of cervical and lumbar degenerations.

Literature screening, data extraction and quality assessment

Literature screening, data extraction and quality assessment were performed by two independent

reviewers according to the inclusion and exclusion criteria. In case of disagreement, it was discussed and solved by a third party. The required data mainly included: The general information of studies, including document title, year, authors, and statistical methods; the patient's basic information, including gender, age, etc., as well as literature quality evaluation.

Statistical analysis

Meta-Disc 1.4 software [11] was used for merger analysis. Random or fixed effect model was selected based on heterogeneity test results to calculate the combined effect value; estimated parameters included merging SEN, SPE, DOR and the 95% CI. SROC curve was drawn and AUC was estimated; the greater of AUC, the closer to 1.0, the better the authenticity of diagnosis [12].

Results

Characteristics of included studies

471 related Chinese documents and 74 English literatures were early selected; after the screening layer by layer, six literature and 10 independent studies were finally included [13-18], including a total of 505 individuals. Document Retrieval and screening process

was shown in **Figure 1**. The basic characteristics of included studies and quality evaluation were shown in **Table 1**; the methodological quality evaluation results were shown in **Table 2**.

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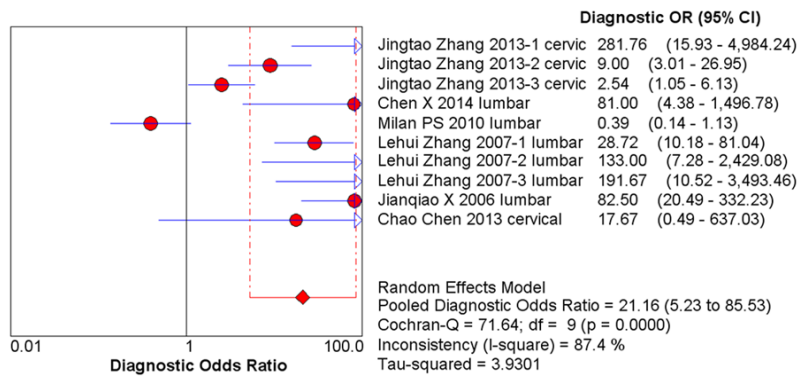


Figure 6. DOR meta-analysis of MRI for differential diagnosis of cervical and lumbar degenerations.

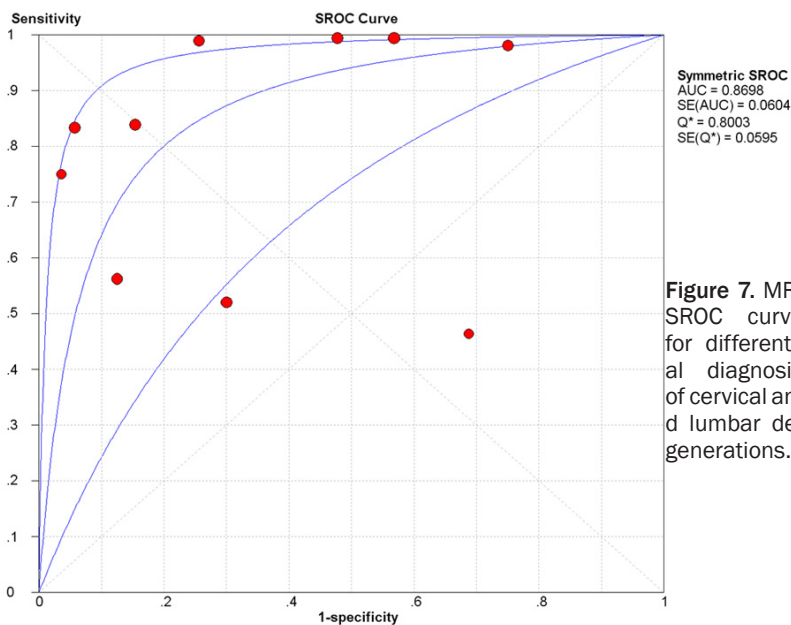


Figure 7. MRI SROC curve for differential diagnosis of cervical and lumbar degenerations.

Efficacy of MRI in the differential diagnosis of cervical and lumbar degenerations

In this study, Meta-Disc 1.4 software was used to analyze the efficacy of MRI in differential diagnosis of cervical and lumbar degenerations; 10 studies were included in the analysis, and ROC plane scatter plot showed atypical “shoulder and arm-shape”, suggesting SEN was negatively correlated with and 1-SPE, without threshold effect. Heterogeneity tests of other sources showed: SPE: $\chi^2 = 77.59$, $P = 0.000$, $I^2 = 88.4\%$; SEN: $\chi^2 = 167.25$, $P = 0.000$, $I^2 = 94.6\%$; DOR: Cochran-Q = 71.64, $P = 0.000$. Random effect model Meta-analysis showed that: SEN merge = 0.849 [95% CI (0.816, 0.878)], SPE merge = 0.745 [95% CI (0.695, 0.792)], + LR = 2.735 [95% CI (1.600, -4.676)],

- LR = 0.245 [95% CI (0.122, -0.493)], DOR merge = 21.158 [95% CI (5.234, -85.529)], SROC AUC = 0.8698. Each study will be excluded before sensitivity analysis, and the results showed that the SEN and SPE merge did not change significantly, indicating better stability of Meta-analysis (**Figures 2-8**).

Efficacy of MRI in the differential diagnosis of cervical degeneration

Meta-Disc 1.4 software was used to analyze the efficacy of MRI in differential diagnosis of cervical degeneration; 4 independent studies were included in the analysis, and ROC plane scatter plot showed atypical “shoulder and arm-shape”, suggesting SEN was negatively correlated with and 1-SPE, without threshold effect. Heterogeneity tests of other sources showed: SPE: $\chi^2 = 6.92$, $P = 0.075$, $I^2 = 56.6\%$; SEN: $\chi^2 = 81.73$, $P = 0.000$, $I^2 = 96.3\%$; DOR: Cochran-Q = 12.71, $P = 0.005$.

Random effect Meta-analysis showed that: SEN merge = 0.799 [95% CI (0.741, 0.850)], SPE merge = 0.769 [95% CI (0.683, -0.840)], + LR = 2.506 [95% CI (1.399, -4.489)], - LR = 0.363 [95% CI 0.149, -0.882)], DOR merge = 11.949 [95% CI (2.195, -65.036)], SROC AUC = 0.8210. Each study will be excluded one by one before sensitivity analysis, and the results showed that the SEN and SPE merge did not change significantly, indicating better stability of Meta-analysis (**Figures 9-15**).

Efficacy of MRI in the differential diagnosis of lumbar degeneration

Meta-Disc 1.4 software was used to analyze the efficacy of MRI in differential diagnosis of lumbar degeneration; 6 independent studies

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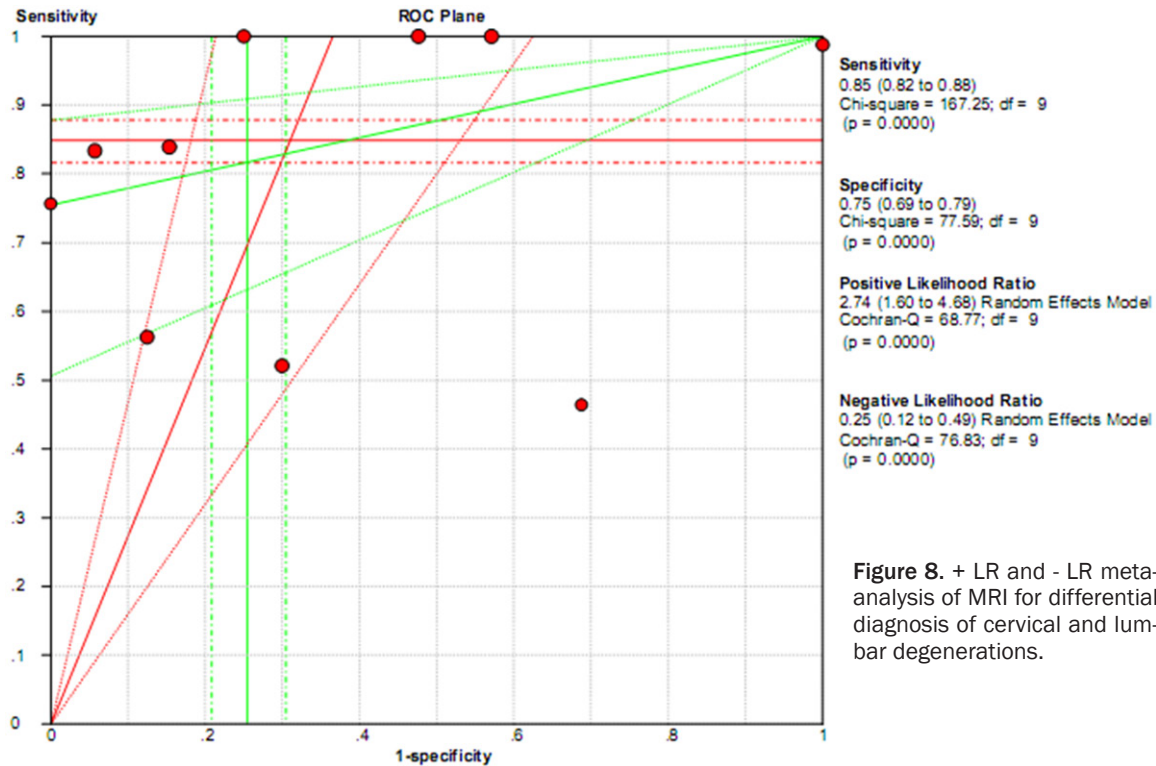


Figure 8. + LR and - LR meta-analysis of MRI for differential diagnosis of cervical and lumbar degenerations.

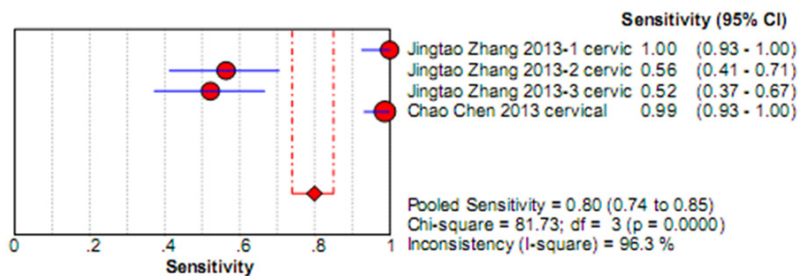


Figure 9. SEN meta-analysis of MRI for differential diagnosis of cervical degeneration.

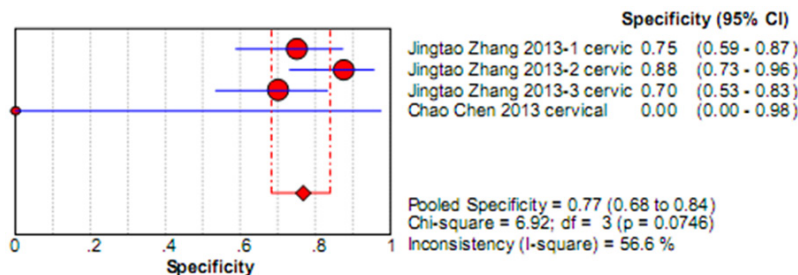


Figure 10. SPE meta-analysis of MRI for differential diagnosis of cervical degeneration.

were included in the analysis, and ROC plane scatter plot showed atypical “shoulder and arm-shape”, suggesting SEN was negatively

correlated with and 1-SPE, without threshold effect. Heterogeneity tests of other sources showed: SPE: $\chi^2 = 70.13$, $P = 0.000$, $I^2 = 92.9\%$; SEN: $\chi^2 = 78.35$, $P = 0.000$, $I^2 = 93.6\%$; DOR: Cochran-Q = 58.04, $P = 0.000$. Meta-analysis of random effect model showed that: SEN merge = 0.732 [95% CI (0.667, -0.791)], SPE merge = 0.883 [95% CI (0.843, -0.916)], + LR = 3.072 [95% CI (1.330, -7.091)], - LR = 0.190 [95% CI (0.063, -0.572)], DOR merge = 30.252 [95% CI (3.060, -299.13)], SROC AUC = 0.8994. Each study will be excluded one by one before sensitivity analysis, and the results showed that the SEN and SPE merge did not change significantly, indicating better stability of Meta-analysis (Figures 16-22).

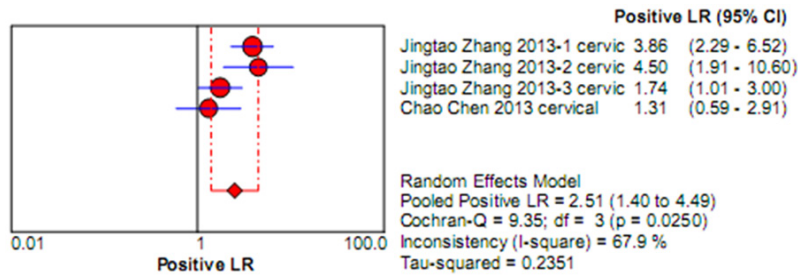


Figure 11. + LR meta-analysis of MRI for differential diagnosis of cervical degeneration.

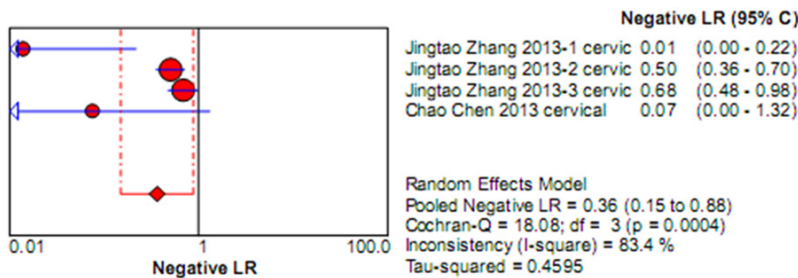


Figure 12. - LR meta-analysis of MRI for differential diagnosis of cervical degeneration

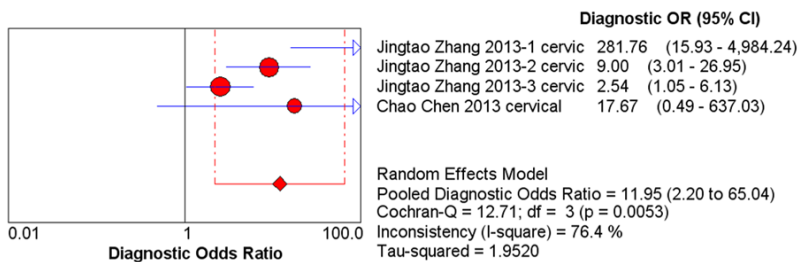


Figure 13. DOR meta-analysis of MRI for differential diagnosis of cervical degeneration.

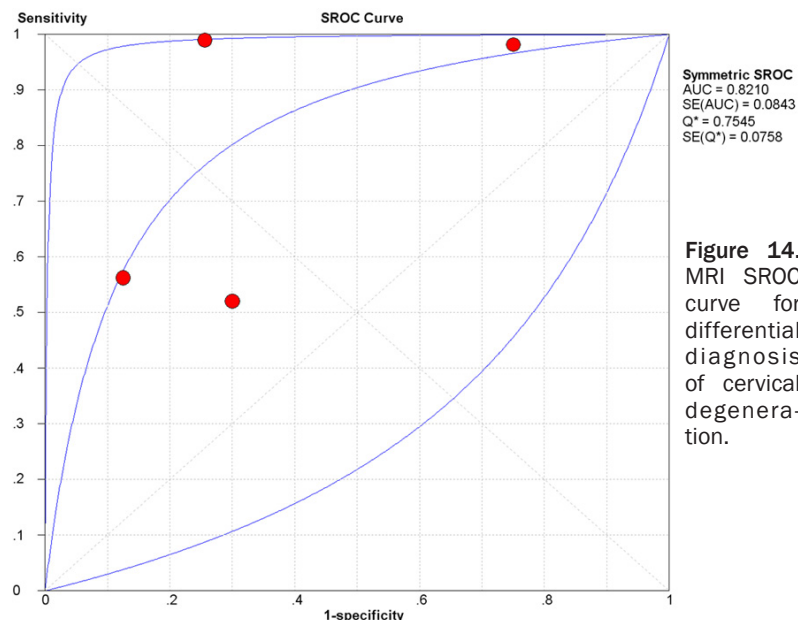


Figure 14. MRI SROC curve for differential diagnosis of cervical degeneration.

Discussion

Cervical and lumbar degenerations are the most common in spinal degeneration. In clinical, it is also one class of diseases causing serious damage to elderly population. Disc degeneration is a natural aging process. With the increasing age, intervertebral discs gradually lose flexibility, elasticity and shock absorption. The ligaments surrounding the disc (called annulus) will become fragile and can be easily torn. At the same time, the soft gelatinous central portion of the intervertebral disc (called nucleus pulposus) begins to lose moisture and shrink. The series of disc injury lead to bone spurs and thickened ligaments to support the spine, resulting in degenerative lumbar arthritis. According to different degrees, intervertebral disc degeneration can be classified as cervical disc bulging, herniation and prolapse. Lumbar degenerative disc disease mostly begins from the early multi-disc dehydration, followed by the annular tear of inner and outer annulus occurs, eventually leading to the annulus tears, which would exacerbate the process of disc degeneration and narrow the disc space narrowing; and then joints between endplate and annulus appeared osteophytes, finally endplate sclerosis Bone Bridge formed.

Normal lumbar spine plain films and scans can diagnose cervical spine degeneration; intervertebral dis-

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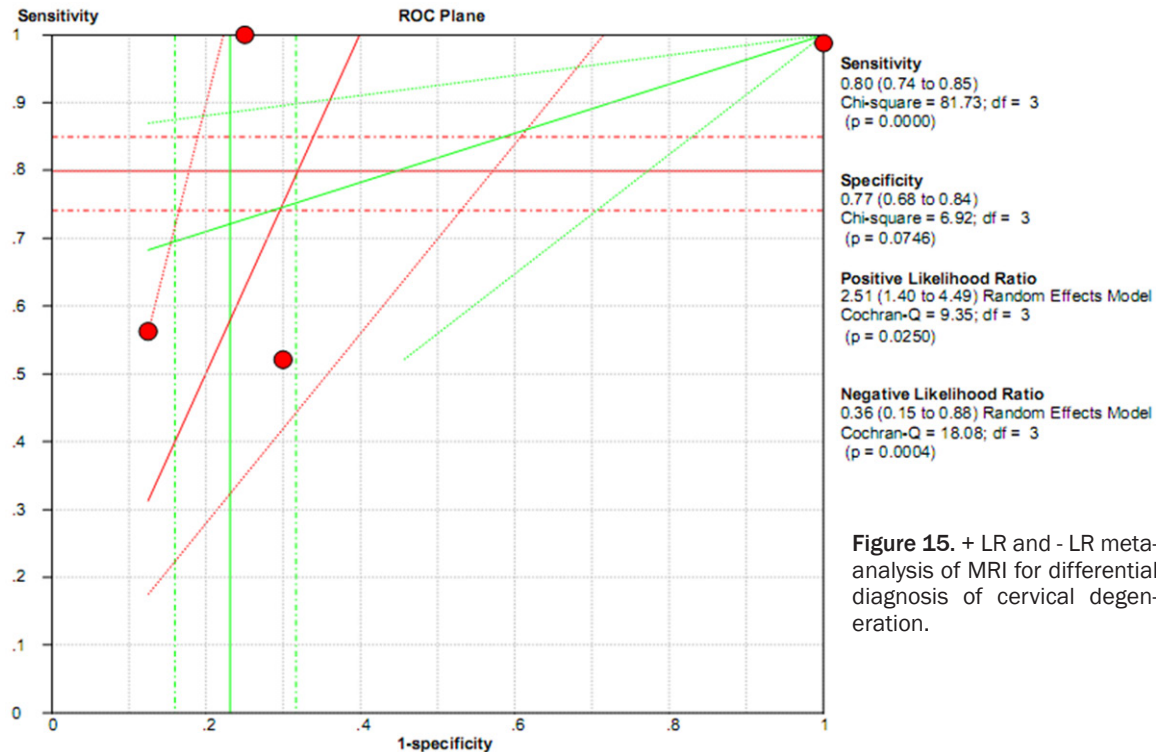


Figure 15. + LR and - LR meta-analysis of MRI for differential diagnosis of cervical degeneration.

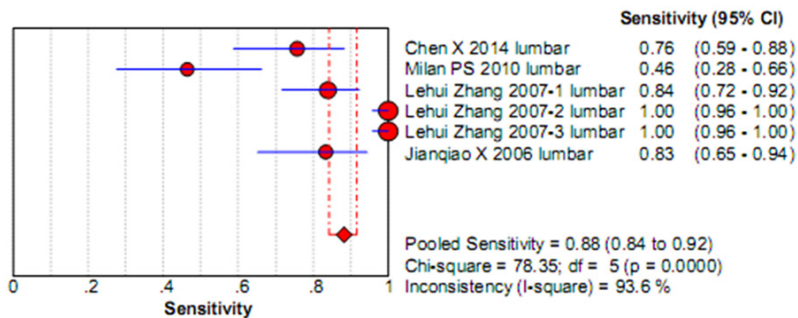


Figure 16. SEN meta-analysis of MRI for differential diagnosis of cervical and lumbar degeneration.

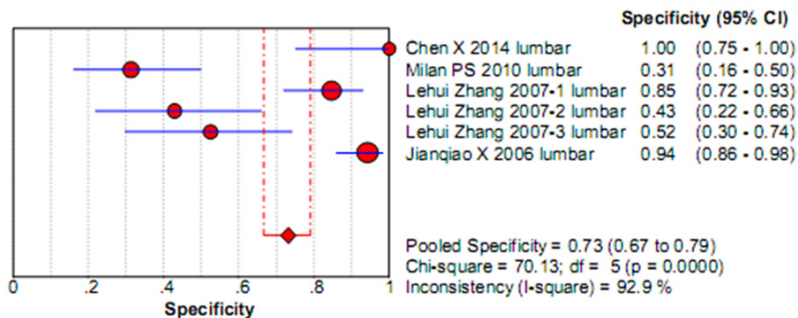


Figure 17. SPE meta-analysis of MRI for differential diagnosis of lumbar degeneration.

displays greater superiority [1-5, 19-22]. The clinical application of MRI techniques provides a great space for the diagnosis of spinal cord disorders. In most cases, we will use MRI or CT to help diagnose lumbar disc degeneration. MRI can clearly show the location of disc herniation and nerve root compression. MRI multi-level and multi-directional scanning allows it to accurately evaluate the cervical and lumbar disc degeneration, herniation, cervical stenosis, cervical vertebral segmental instability and spinal cord compression [5-9, 22, 23].

In this study, a systematic review of six domestic and foreign literature, 10 independent studies and a total of 505 patients was performed. In this study, Meta-

cography plays a decisive role in evaluating the degeneration of adjacent intervertebral disc

segments; for the patients with two or more sections of lumbar degeneration, discography

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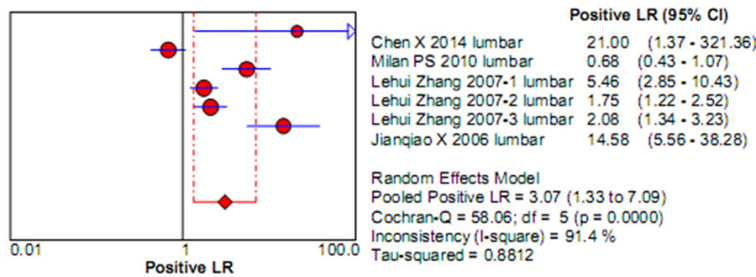


Figure 18. + LR meta-analysis of MRI for differential diagnosis of lumbar degeneration.

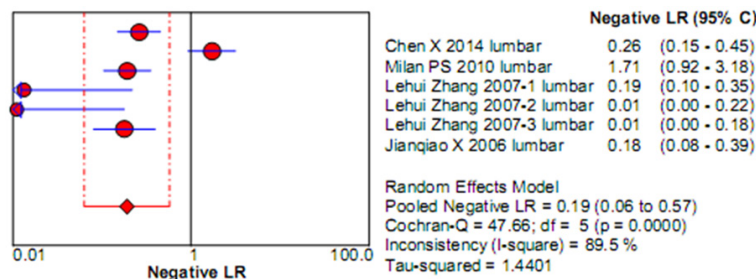


Figure 19. - LR meta-analysis of MRI for differential diagnosis of lumbar degeneration.

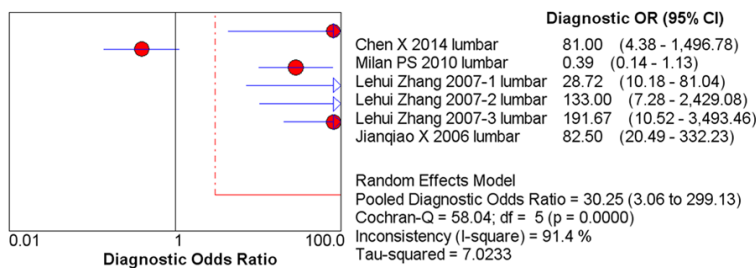


Figure 20. DOC meta-analysis of MRI for differential diagnosis of lumbar degeneration.

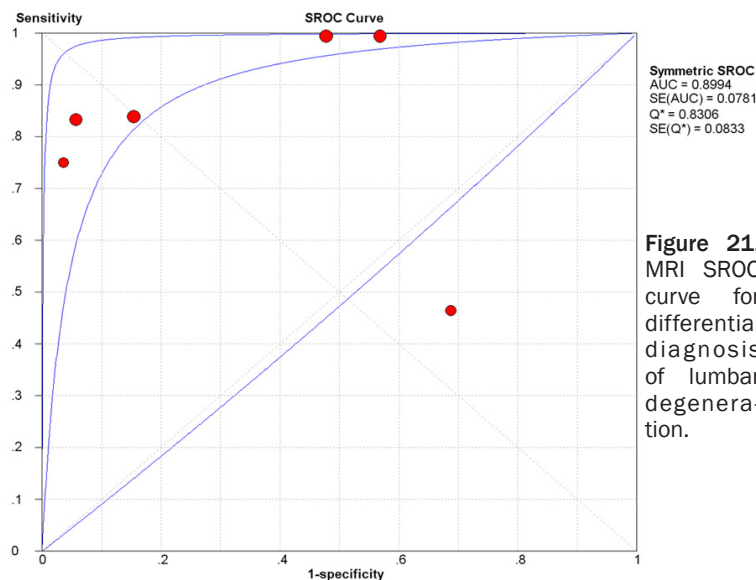


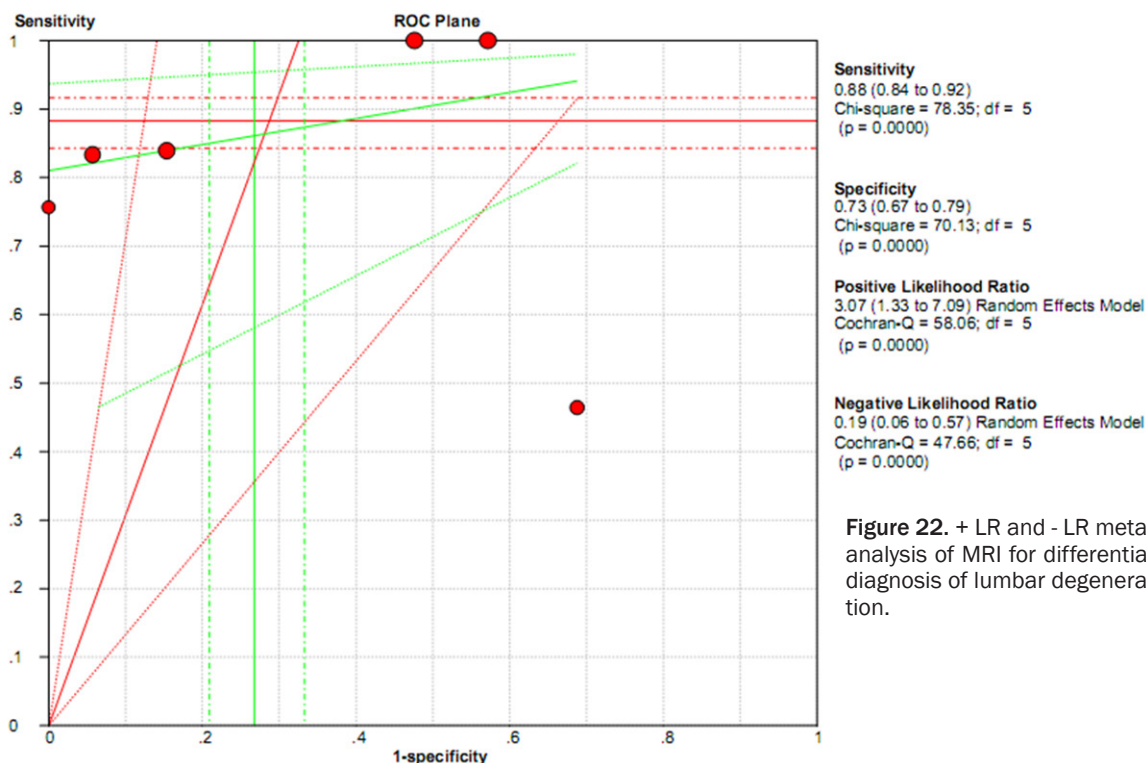
Figure 21. MRI SROC curve for differential diagnosis of lumbar degeneration.

Disc 1.4 software was used for analysis; firstly, efficacy of MRI in the differential diagnosis of cervical and lumbar degenerations were analyzed and discussed; the combined sensitivity was about 85% and the specificity was about 75%; The positive rate of combined diagnosis in the case group was 21 times of that of the control group; the AUC was 0.8698, and the analysis results had a good stability. Then the efficacy of MRI in the differential diagnosis of cervical degeneration and lumbar degeneration were analyzed and discussed respectively; the results suggested that: for the diagnosis of cervical degeneration, the combined sensitivity was 80% and specificity was about 77%; the positive rate of combined diagnosis in the case group was about 12 times of that in control group; the area under the curve was 0.8210; the stability of the analysis was good. Finally the six independent studies of MRI and lumbar degenerative differential diagnosis were analyzed; the combined sensitivity was about 73% and specificity was around 88%; the positive rate of combined diagnosis in case group was 30 times of that in control group; AUC was 0.8994, and the results had good stability. Although the number of included studies was not large in the separate analysis of cervical and lumbar degenerations, in general, our findings suggested that MRI had good sensitivity and specificity for the differential diagnosis of spinal degeneration, which could be used as effective and feasible method for clinical differential diagnosis.

Disclosure of conflict of interest

None.

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