Differentiating Brucella Spondylitis from Tuberculous Spondylitis by the Conventional MRI and MR T2 Mapping: A Prospective Study

Hui Guo
Xinjiang Medical University Affiliated First Hospital

Siqin Lan
Xinjiang Medical University Affiliated First Hospital

Yuanlin He
Xinjiang Medical University Affiliated First Hospital

Maijudan Tiheiran
Xinjiang Medical University Affiliated First Hospital

Wenya Liu (✉ liuwenya02@163.com)
Xinjiang Medical University Affiliated First Hospital

Research

Keywords: Brucellosis, Tuberculous, Spondylitis, T2 mapping, Quantitative

DOI: https://doi.org/10.21203/rs.3.rs-388641/v1

License: © This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License
Abstract

**Background** Brucellar spondylitis (BS) and tuberculous spondylitis (TS) which cause initial bacteremia and show granulomatous lesions are the two leading types of spinal inflammatory. BS is easy to miss or maybe misdiagnosed as TS. Our purpose differentiates brucella spondylitis (BS) from tuberculous spondylitis (TS) in conventional MR imaging and MR T2 mapping.

**Methods** We performed on 26 BS and 27 TS patients in conventional MR imaging and MR T2 mapping. We analyzed the features in conventional MR imaging and also measured T2 values of the lesion vertebrae (LV) and unaffected adjacent vertebrae (UAV) in BS and TS patients, respectively.

**Results** There were no significant differences in sex, age, national between BS and TS. It was significantly lower of the severe vertebral destruction, vertebral posterior convex deformity, dead bone, and abscess scope in BS when compared to TS (p < 0.001, p = 0.005, p = 0.048, p < 0.001, p < 0.001, respectively). The vertebral hyperplasia was significantly higher in BS when compared to TS (p < 0.001). The T2 value of the LV with BS was markedly higher than that in the UAV with BS and that in the LV and UAV with TS (p < 0.001, p < 0.037, p < 0.001, respectively). The T2 value of the LV with TS was significantly higher than that of the UAV in TS and BS (p < 0.001, p < 0.001, respectively). There were no significant differences in the T2 value of the UAV between BS and TS (P = 0.568).

**Conclusions** The qualitative and quantitative evaluation may differentiate BS from TS. The conventional MR imaging helps to distinguish BS from TS by several distinctive features. MR T2 mapping has the additional potential to provide quantitative information between BS and TS.

**Key Points**

Conventional MR imaging has several distinctive features to distinguish BS from TS.

MR T2 mapping has the additional potential to provide quantitative information between BS and TS.

**MR T2 mapping might be a useful tool for a non-invasive and quantitative technique.**

**Background**

Brucella spondylitis (BS) and tuberculous spondylitis (TS) which cause initial bacteremia and show granulomatous lesions, are the two leading types of spinal infection. They have some common clinical manifestations, including back pain, fever, and increased inflammatory markers. It is challenging to precise distinguish clinically between the two groups. BS is easy to misdiagnose as TS. Conventional MRI can detect changes in the signals and morphology in the vertebrae, which are usually qualitative. However, MR T2 mapping can help visualize and quantitatively access the water content of vertebral body. T2 mapping has been used to evaluate lumbar intervertebral disc degeneration, and only
studied vertebra injury in spinal tuberculosis. The study aimed to explore whether qualitatively-quantitatively differentiate BS from TS on conventional MRI and MR T2 mapping.

**Materials And Methods**

**Study population**

This is a prospective clinical study. Patients who were clinically confirmed for BS and TS between January 2018 to December 2020 were initially considered eligible for our research (n = 68). All participants provided written informed consent. Ethical approval for the study was obtained from the ethical review committee for our hospital. Inclusion criteria were as follows:10-12 (a) diagnosis of TS was confirmed by biopsy on basing caseation granulomatosis on histopathological examination or the presence of acid-fast bacilli or the tuberculosis bacilli growth in cultures, (b) diagnosis of BS was based on the Brucella agglutination titer test (≥1:160) and isolation of Brucella species from blood, bone marrow, or tissues. (c) All patients were operated on, with sufficient histopathologic and Bacterial culture information. A total of 55 patients who met the inclusion criteria were consecutively enrolled. 2 patients were excluded as poor image quality. Finally, we included 53 patients who were performed in our study, among whom BS patients (n = 26) and TS patients (n = 27) (Fig 1).

**MRI Protocol**

Conventional magnetic resonance imaging (MRI) and MR T2 mapping sequences were carried on all patients, and executed whole spine MRI studies. MRI scans were performed using a 1.5T MR Scanner (Siemens Healthcare, Erlangen, Germany). The parameters for conventional MRI and MR T2 mapping sequences were shown in Table 1.

**Image analysis**

MRI finding included the level of involvement, number of the affected vertebra, MRI signal (hypointense signal on T1WI, hyperintense signal on T2WI, and hyperintense signal on STIR), vertebral change (destruction, wedge, hyperplasia, bead bone, posterior convex deformity), intervertebral space, and abscess (paravertebral abscess, epidural abscess, psoas abscess, abscess scope), vertebral appendage lesion. Vertebral destruction was defined as a vertebral structure loss of worm-etched or patchy. Vertebral wedge was defined as the front edge of the vertebra is narrower than the back edge, and the vertebra was flattened. The spinal posterior convex deformity was defined as severe vertebral damage, with significant vertebral wedge changes, resulting in significant kyphosis of the spine. Vertebral appendage lesion was defined as bone edema or bone destruction of the appendage. Bead bone was defined as necrotic bone. Vertebral hyperplasia was defined as the appearance of a spur or osteophyte. MR images were analyzed
by an attending physician and an associate chief physician, and the consistency of image evaluation was evaluated.

Using the Function Tool 2 software on the post-processing workstation, we selected a region of interest (ROI) with an area of 60 mm$^2$ on the T2 mapping image and generated T2 values automatically. The ROI was placed in the middle three layers, where the lesion showed the best. Then, we obtained the T2 average value three times, which was measured repeatedly for the lesion vertebra (LV) and the unaffected adjacent vertebra (UAV) with BS and TS patients.

**Statistical Analysis**

The information of sex, national, and MRI finding were expressed as the percentage. We collected the information of age and measured T2 values of LV and UAV in the BS and TS patients. All data were expressed as mean value and standard deviation. The Chi-square analyzed the differences between the two groups, and the Student's t-test analyzed all mean value of the differences between the two groups. A P-value of less than 0.05 indicated a significant difference. The Kappa coefficient was calculated by two physicians using a consistency test.

**Results**

The demographic characteristics in the two groups were shown in Table 2. There were no significant differences in sex, age, national between the BS and the TS.

The image quality of the two physicians was consistent, and the Kappa coefficient was 0.875. MRI findings in the two groups were shown in Table 3. There were significant differences in the site of involvement, vertebral destruction, vertebral posterior convex deformity, dead bone, vertebral hyperplasia, intervertebral space change, and abscess findings between BS and TS (p < 0.05). It was significantly lower in the severe vertebral destruction, vertebral posterior convex deformity, dead bone, and abscess beyond the vertebra lesion with BS when compared to TS (p < 0.001, p = 0.005, p = 0.048, p < 0.001, p < 0.001, respectively). The vertebral hyperplasia was significantly higher in BS when compared to TS (p < 0.001). The lumbar vertebrae (69.23%) were the most common in BS. The thoracolumbar vertebrae (33.33%) and lumbar vertebrae (33.33%) were the most common in TS. It was significantly higher in the normal intervertebral space with BS (42.31%) when compared to TS (7.41%)(p < 0.05), and the narrow intervertebral space was distinctly lower with BS (57.69%) when compared to TS (81.48%)(p < 0.05). The paravertebral abscess was higher with BS (65.38%) when compared to TS (22.22%)(p < 0.05), and it was markedly lower in the psoas abscess with BS (0.00%) when compared to TS (66.67%)(p < 0.05). There were no significant differences in the number of the affected vertebra, MRI signal, vertebral wedge, vertebral appendage lesion between BS and TS (p>0.05).

The T2 values of the LV and UAV with BS and TS were shown in Fig. 2. The T2 value of the LV with BS was markedly higher than those in the LV with BS and those in the LV and UAV with TS (p < 0.001, p <
The T2 value of the LV with TS was significantly higher than those of the UAV with TS and BS (p < 0.001, p < 0.001, respectively). There were no significant differences in T2 values of the UAV between BS and TS (P = 0.568).

**Discussion**

This study demonstrated that the qualitative and the quantitative evaluation might differentiate BS from TS. Several distinctive features (site of involvement, vertebral destruction, posterior convex deformity, bead bone, vertebral hyperplasia, intervertebral space change, and location of abscess) were identified. They can distinguish BS from TS in conventional MR imaging. The T2 value of the LV with BS was markedly higher than those in the LV with TS by using the T2 mapping technique.

BS and TS are still considered public health problems worldwide, particularly in developing countries. In this study, there were no significant differences in sex, age, national between BS and TS. The difference in age was inconsistent with this reported in Liu's study. The reason may be related to the sample size.

Early diagnosis and an effective cure become critically important to minimize spinal deformity and permanent neurologic deficiencies. However, it is challenging to distinguish BS from TS. Due to similarities in the clinical signs and laboratory data, a proportion of patients may be misdiagnosed. In the current study, 69.23% of patients with BS were located in the lumbar, consistent with previous studies. However, the majority of TS cases (55.55%) were located in the lower thoracic region, findings that were consistent with those in Turunc et al. and Jung et al. By the analysis of vertebra and intervertebral space in patients, it was significantly lower of the severe vertebral destruction, vertebral posterior convex deformity, dead bone, and narrow - disappear change of intervertebral space with BS (7.41%, 3.85%, 0.00%, 57.69%, respectively) when compared to TS (70.37%, 22.22%, 48.15%, 92.59%, respectively). This widespread destruction in TS may result from the rapid involvement of the endplate (inflammatory reaction). As the progress in TS, the vertebras were destroyed increasingly severely. The wedge changes of the involved adjacent vertebras resulted in the vertebral posterior convex deformity, along with a narrow or disappeared change in the intervertebral space (Figs. 3a-c). Our study found that the vertebral destruction was significantly severer in TS when compared to BS. The findings were consistent with those in Yang et al. and Liu et al. A pathologic study pointed out that there was proteinase activity to destroy the disc and vertebra in TS. The vertebral erosion in TS was caseating granulomas and dead bone without new bone formation. As a result, the vertebra in TS presented a severe collapse on MR images. However, vertebral collapse is rare in BS. Similar findings had also been reported by Tali et al. BS is more common in the mild and focal vertebral destruction, also in agreement with previous studies. The lack of proteolytic enzymes might limit the invasion of brucella in BS. Further research demonstrated that osteoblastic activity is induced in BS, which may partly explain the less prominent bone and disc destruction than in TS. It was significantly higher of vertebral hyperplasia with BS (96.15%) than TS (29.63%). There was distinctly more vertebral hyperplasia (Figs. 4a-b) in our result when compared to previous studies. The bone erosion of the endplate in BS was accompanied
by new bone formation at the early stage. As a result, the corresponding signs in anterior osteophyte and sclerosis were observed on MR images.

The abscess of the vertebral around is a common feature, both BS and TS. Our study found that the paravertebral abscess was significantly higher with BS (65.38%) when compared to TS (22.22%), but the psoas abscess was markedly lower with BS (0.00%) when compared to TS (66.67%). There was a significant difference between BS and TS in terms of abscess spread. The abscess beyond the range of vertebral lesions was significantly higher with TS (94.44%) when compared to BS (5.88%). Small abscesses were frequent by Tali et al. Because the abscess in BS is relatively limited, it is generally difficult to spread. About 34.62% in BS showed epidural abscesses, which was following a previous study.

Previous studied showed the diagnosis and differential diagnosis in spondylitis patients on MRI was qualitative rather than quantitative. MR T2 mapping can be used to detect the early changes in physiology and morphology by water content changes in the tissues and indirectly reflect the small changes of water molecules of the tissues in the spatial information of human tissue structure and pathological and physiological conditions. Spondylitis is often caused by brucella or tubercular bacteria, early resulting in inflammatory vertebral edema, with the pathological development occurring in the destruction of the vertebra and intervertebral disc, paravertebral abscess—the result in increased random Brownian motion of water protons, which is reflected by increased T2 values. To the best of our knowledge, MR T2 mapping has been used to evaluate vertebra injury in spinal tuberculosis. However, there was no similar research on the application of T2 mapping between BS and TS. In our work, the results showed that the T2 value of the LV with BS was markedly higher than that in the LV with TS (p < 0.05) and that in the UAV with BS (p < 0.05). The T2 value of the LV was high in BS and TS (Figs. 4a-b). The reason may be a bacterium entering the vertebra through the blood to undergo a complex pathological inflammatory process (Seep, hyperplasia, and necrosis). With the inflammatory pathological lesions developing, the extracellular water content increases, and the injured locations present the congestion and edema of the different degrees. As the vertebra have occurred abnormal pathological changes, MR T2 value was increased by T2 relaxation time extended. In our work, the T2 value of the LV in BS was higher than that in TS. So, we had a preliminary result that T2 mapping may quantitatively differentiate BS from TS.

Limitations

Due to the small sample size included in this study, MR T2 mapping sequence scanning needs to be further studied by expanding the sample size in the diagnosis and differential diagnosis with BS and TS. Another limitation was that we didn’t determine the stage of disease between BS and TS in this series. Therefore, the T2 value may be potentially inaccurate.

Conclusion
The qualitative and quantitative evaluation may differentiate BS from TS. The conventional MR imaging helps to distinguish BS from TS by several distinctive features. MR T2 mapping has the additional potential to provide quantitative information between BS and TS.

**Abbreviations**

BS Brucella spondylitis

TS Tuberculous spondylitis

MRI Magnetic resonance imaging

LV Lesion vertebrae

UAV Unaffected adjacent vertebra

STIR Short-tau inversion recovery

ROI Region of interest

**Declarations**

**Acknowledgments**

The authors thank Peipei Yang, Yuanyuan Wang, and Haiyan Huang for scanning data.

**Fund**

The authors gratefully acknowledge the financial support provided by the Xinjiang Uygur Autonomous Region Natural Science Foundation of China (Grant no. 2017D01C300).

**Author Contributions**

H.G. and W.L. conceived the idea. H.G. and W.L. wrote the main manuscript text, and H.G. prepared figures 1-3. Y.H. and M.T. collected the data. S.L. and Y.H. and M.T. performed the literature search. All authors reviewed the manuscript. All authors approved the final version for submission.

**Ethical approval and consent to participate**

All participants provided written informed consent. Ethical approval for the study was obtained from the ethical review committee for our hospital [Grant No.20170214-111].
Conflict of Interests

The authors declare that there is no conflict of interest regarding the publication of this paper.

Consent for publication

All authors agree to publish.

References

1. Cordero M, Sanchez I. Brucellar and tuberculous spondylitis. A comparative study of their clinical features. J Bone Joint Surg Br 1991; 73:100-103

2. Turunc T, Demiroglu YZ, Uncu H, et al. A comparative analysis of tuberculous, brucellar and pyogenic spontaneous spondylodiscitis patients. J Infect 2007; 55:158-163

3. Lagerstrand K, Hebelka H, Brisby H. Low back pain patients and controls display functional differences in endplates and vertebrae measured with T2-mapping. Eur Spine J 2019; 28: 234-240

4. Raudner M, Schreiner MM, Hilbert T, et al. Clinical implementation of accelerated T2 mapping: Quantitative magnetic resonance imaging as a biomarker for annular tear and lumbar disc herniation. Eur Radiol 2020VN (Online ahead of print)

5. Zhang C, Lin Y, Han Z, et al. Feasibility of T2 Mapping and Magnetic Transfer Ratio for Diagnosis of Intervertebral Disc Degeneration at the Cervicothoracic Junction: A Pilot Study. Biomed Res Int. 2019; 2019: 6396073

6. Ishikawa T, Watanabe A, Kamoda H, et al. Evaluation of Lumbar Intervertebral Disc Degeneration Using $T_1$ρ and T2 Magnetic Resonance Imaging in a Rabbit Disc Injury Model. Asian Spine J 2018; 12: 317-324

7. Hebelka H, Miron A, Kasperska I, et al. Axial loading during MRI induces significant T2 value changes in vertebral endplates-a feasibility study on patients with low back pain. J Orthop Surg Res 2018; 13: 18

8. Toren L, Hebelka H, Kasperska I, et al. With axial loading during MRI diurnal T2-value changes in lumbar discs are neglectable: a cross sectional study. BMC Musculoskelet Disord 2018; 19:25

9. Yang PP, Guo H, Yao J, et al. The application of T2 relaxation time mapping in spinal tuberculosis. Chin J Osteoporos 2016; 22: 72-76

10. Oztekin O, Calli C, Adibelli Z, et al. Brucellar spondylodiscitis: magnetic resonance imaging features with conventional sequences and diffusion-weighted imaging. Radiol Med 2010; 115: 794-803

11. Ozaksoy D, Yücesoy K, Yücesoy M, et al. Brucellar spondylitis: MRI findings. Eur Spine J 2001; 10:529-533

12. Gao M, Sun JM, Jiang ZS, et al. Comparison of Tuberculous and brucellar Spondylitis on MRI images. Spine 2016; 42:113-121
13. Liu XX, Li H, Jin C, et al. Differentiation Between Brucellar and Tuberculous Spondylodiscitis in the Acute and Subacute Stages by MRI: A Retrospective Observational Study. Acad Radiol 2018; 25:1183-1189

14. Dasari S, Naha K, Prabhu M. Brucellosis and tuberculosis: Clinical overlap and pitfalls. Asian Pac J Trop Med 2013; 6: 823-825

15. Mete B, Kurt C, Yilmaz MH, et al. Vertebral osteomyelitis: Eight years' experience of 100 cases. Rheumatol Int 2012; 32: 3591-3597

16. Colmenero JD, Ruiz-Mesa JD, Plata A, et al. Clinical findings, therapeutic approach, and outcome of brucellar vertebral osteomyelitis. Clin Infect Dis 2008; 46: 426-433

17. Li T, Liu T, Jiang ZS, et al. Diagnosing pyogenic, brucella and tuberculous spondylitis using histopathology and MRI: A retrospective study. Exp Ther Med 2016; 12:2069-2077

18. Jung NY, Jee WH, Ha KY, et al. Discrimination of tuberculous spondylitis from pyogenic spondylitis on MRI. Am J Roentgenol 2004; 182: 1405-1410

19. Yang X, Zhang Q, Guo X. Value of magnetic resonance imaging in brucellar spondylodiscitis. Radiol Med 2014; 119:928-933

20. Sapico FL, Montgomerie JZ. Pyogenic vertebral osteomyelitis: report of nine cases and review of the literature. Rev Infect Dis 1979; 1:754-776

21. Tali ET, Koc AM, Oner AY. Spinal brucellosis. Neuroimag Clin N Am 2015; 25:233-245

22. Li T, Li W, Du Y, et al. Discrimination of pyogenic spondylitis from brucellar spondylitis on MRI. Medicine 2018; 97: e11195

23. Sharif HS, Clark DC, Aabed MY, et al. Granulomatous spinal infections: MR imaging. Radiology 1990; 177:101-107

24. Galhotra RD, Jain T, Sandhu P, et al. Utility of magnetic resonance imaging in the differential diagnosis of tubercular and pyogenic spondylodiscitis. J Nat Sci Biol Med 2015; 6:388-393

25. Yilmaz MH, Mete B, Kantarci F, et al. Tuberculous, brucellar and pyogenic spondylitis: comparison of magnetic resonance imaging findings and assessment of its value. South Med J 2007; 100:613-614

26. Sharif HS, Aideyan OA, Clark DC, et al. Brucellar and tuberculous spondylitis: comparative imaging features. Radiology 1989; 171:419-425

27. Yang HJ, Behzad S, Pang JN, et al. Free-breathing, motion-corrected, highly efficient whole heart T2mapping at 3T with hybrid radial-cartesian trajectory. Magnetic Resonance in Medicine 2016; 75:126-136

Tables

Due to technical limitations, tables are only available as a download in the Supplemental Files section.

Figures
Figure 1

Flowchart of the study population with brucella spondylitis and tuberculous spondylitis.

68 consecutive patients clinically confirmed for BS and TS at our institution, from between January 2016 to December 2018

6 Excluded
Of the 68 patients, 6 who were not operated on were excluded.

A total of 62 patients who were performed surgical treatment were consecutively enrolled.

7 Excluded
2 patients with pyogenic spondylitis, and 1 who was metastatic tumor were excluded; 4 patients were excluded without sufficient histopathologic and Bacterial culture information

A total of 55 patients who met the inclusion criteria were consecutively enrolled.

26 brucellar spondylitis
27 tuberculous spondylitis

2 Excluded
2 cases were excluded as poor image quality
Figure 2

This group T-test results of T2 values for the lesion vertebra and the unaffected adjacent vertebra between brucella spondylitis and tuberculous spondylitis.
Figure 3

The sagittal MR T1WI, the sagittal MR STIR, the coronal MR T2WI.
Figure 4

The sagittal MR T1WI, the sagittal MR STIR.
Figure 5

Sagittal MR T2WI showed a high signal of the fifth lumbar vertebra, and sagittal MR T2mapping showed the measurement of the fifth lumbar vertebral lesion.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Table1.doc
- Table2.doc
• Table3.doc