



Non-contrast versus contrast-enhanced MR in the diagnosis of spondylitis: A quantitative concordance-analysis

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ARTICLE INFO

Keywords:

Concordance-analysis
Contrast-enhanced MR
Non-contrast MR
Spondylitis

ABSTRACT

Introduction: Magnetic Resonance (MR) imaging using gadolinium contrast media is an essential imaging modality in diagnosing spondylitis. However, gadolinium contrast is not widely available in Indonesia and relatively expensive. Many MR studies in Indonesia are performed without contrast administration. It is unclear how confident non-contrast MR can diagnose tuberculous spondylitis in comparison to standard contrast MR.

Purposes: This study aims to evaluate the concordance between the contrast MR and non-contrast spine MR in diagnosing tuberculous spondylitis. We also evaluate the interobserver agreement between the general radiologist and musculoskeletal radiologist in interpreting non-contrast MR of spondylitis.

Materials and Methods: A cross-sectional study using secondary data was performed to evaluate the concordance between the MR results regarding the usage of contrast media in diagnosing spondylitis. The inclusion criteria were patients over 17 years old who underwent complete sequences of contrast-enhanced MR examination of the spine, referred to radiology with the clinical diagnosis of suspected tuberculous spondylitis, spondylodiscitis, or both. All of the non-contrast and contrast-enhanced MR results were read and interpreted by two independent observers, a musculoskeletal radiologist and a general radiologist, blindly. The interobserver agreement analysis of the MR examination was conducted using *Kappa* and *McNemar* test.

Results: There was no significant difference between the contrast and non-contrast MR in diagnosing spondylitis ($P = 0.368$) and no significant difference in the interpretation of MR between the first and the second observer ($P = 0.343$). The concordance between the contrast and non-contrast spine MR in diagnosing spondylitis ($R: 0.88, P < 0.001$) and the interpretation of MR between both observers ($R: 0.65, P < 0.001$) were showed in this study.

Conclusion: There is a high concordance between the contrast and non-contrast MR in diagnosing tuberculous spondylitis. Although contrast MR is preferred as the standard imaging method of spondylitis, in case gadolinium contrast is unavailable, non-contrast MR can still provide valuable information in diagnosing spondylitis.

1. Introduction

Spondylitis, the osteomyelitis of the spine, is an infection of the vertebral body and has affected humanity for thousands of years. The incidence of spondylitis raises with aging, increasing the number of population and improvement of diagnostic modalities. Spondylitis covers about 2–7 % of cases of musculoskeletal infection worldwide. The most common manifestation found in spondylitis is back pain [1–3].

Spondylitis is developed as a secondary process of focal infection. Kotze and Erasmus (2006) showed that from a total of 69 patients with tuberculous spondylitis, also known as Pott's Disease, as many as 21 patients were having a history of pulmonary tuberculosis (TB). The level of the spine affected by spondylitis can vary, with the most common site is the lower level of thoracic vertebrae and lumbar region (Th8-L3), the upper level of thoracic vertebrae, cervical and sacrum region of vertebrae [4,5].

Abbreviations: MRI, Magnetic resonance imaging; TB, tuberculosis; WHO, World Health Organization; Gd-DTPA, gadolinium with diethylenetri-aminepentaacetic acid; SNR, signal-to-noise ratio.

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<https://doi.org/10.1016/j.ejro.2020.100306>

Received 4 October 2020; Received in revised form 3 December 2020; Accepted 4 December 2020

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Spondylitis is mostly caused by pyogenic bacteria (40–60 %) and *Mycobacterium tuberculosis* spp. (20 %). Based on the World Health Organization (WHO) data, Indonesia has become a tuberculosis endemic country which makes more cases caused by TB infection compared to pyogenic infection [6,7] the Annual Risk of Tuberculosis Infection (ARTI) in Indonesia varies from 1% to 3% [7]. The age group commonly affected by TB infection is the productive age group, while in tuberculous spondylitis, the age between 31–40 years old is commonly affected [6].

Conventional radiography, computed tomography scanning and MR imaging have become the favored radiological modalities in making the diagnosis of spondylitis [8,9]. The infection of the intervertebral disc and its expansion are best evaluated with spinal MR. Gadolinium-based contrast usage in MR was found to improve image clarity and diagnostic accuracy in 30 % of patients undergoing MR examination. Furthermore, the usage of gadolinium with diethylenetri-aminopentaacetic acid (Gd-DTPA) enhances the diagnostic value in assessing the expansion of soft tissue mass. In diagnosing spondylitis, contrast-enhanced MR proved to have a high sensitivity and specificity with 90 % accuracy [10]. However, according to a study by Priyatmoko et al. (2014), contrast media for imaging examination in Indonesia is unevenly distributed and relatively expensive which makes many MR examinations performed without contrast [11]. There is insufficient data regarding the performance of non-contrast MR in spondylitis compared to contrast-enhanced MR. This study aims to evaluate the concordance between the contrast-enhanced MR and non-contrast MR in diagnosing spondylitis. Interobserver agreement between the general radiologist and musculoskeletal radiologist will also be analyzed.

2. Materials and methods

A cross-sectional study using secondary data was done to evaluate the concordance between the MR results regarding the usage of contrast materials in diagnosing the spondylitis. The research was held in the Department of Radiology, Dr. Cipto Mangunkusumo Hospital, Jakarta started from August 2016 to February 2017. The ethical approval to conduct the study was obtained from the Research and Ethics Committee from the Faculty of Medicine Universitas Indonesia. Permission to carry out the study on secondary data of medical records was obtained from Dr. Cipto Mangunkusumo Hospital. Patient data used in this study were kept anonymous and confidential.

The inclusion criteria were patients over 17 years old who underwent complete sequences of spine MR examination, with the clinical diagnosis of suspected tuberculous spondylitis, spondylodiscitis, or both. Exclusion criteria were incomplete secondary data, such as incomplete sequences or low *signal-to-noise ratio* (SNR). Patients with the orthopedic implant in the spine, malignancies, *Charcot spine*, *inflammatory spondyloarthropathy*, and congenital abnormalities, or under-treatment of spondylitis were also excluded from the study. Based on these criteria, a total of 33 subjects included in this study. The median age of the included subjects was 37.9 (17–71) years old. About 17 subjects (51.5 %) were female and the rest (48.5 %) were male. The spondylitis predilection of the subjects consisted of the cervical region (3.0 %), the thoracic region (36.4 %) and the lumbar region (60.6 %). MR examination of the spine was performed using Siemens Avanto 1.5 T machine with the protocol of the Department of Radiology, Dr. Cipto Mangunkusumo Hospital: The sagittal view was done with field of view 500 mm, matrix 384 × 269, slice thickness 4 mm, gap 1 mm, in T1-weighted images (TR 474 ms, TE 10 ms), T2-weighted images (TR 3000 ms, TE 92 ms), short tau inversion recovery/STIR (TR 3700 ms, TE 105 ms); The axial view was done with field of view 200 mm, matrix 320 × 256, slice thickness 4 mm, gap 1 mm, in T1-weighted images (TR 935 ms, TE 9 ms), T2-weighted images (TR 4680 ms, TE 103 ms); The contrast used in this study was 10 mL intravenous gadopentetate dimeglumine and post-contrast scan was evaluated in T1-weighted images.

To interpret the result, we collect all possible MR findings of spondylitis from literature studies, with a focus on the findings that apply to both non-contrast and contrast-enhanced MR. Any findings that apply to only contrast MR is not used in this study. Common findings are endplate erosion (defined as the irregularity of the endplate and could be accompanied with the change in shape of vertebral bodies), high signal intensity on T2WI within the disc (defined as the increase of signal intensity on T2WI), enhancement of the disc (defined as hypointense signal of the disc with enhancement on post-contrast sequences of T1WI and hyperintense on T2WI), thickening of para-vertebrae soft tissue (defined as the increase of the thickness and volume of para-vertebrae soft tissue which indicates an extension of a mass to the soft tissue), paravertebral abscess (defined as a heterogenous vertebral lesion with peripheral enhancement and hypointense of the central region on post-contrast sequences of T1WI), enhancement of the bone marrow (defined as enhancement of the bone marrow on post-contrast sequences), subligamentous extension (defined as the extension of the infection to the area of subligamentous), epidural abscess (defined as a heterogenous epidural lesion with peripheral enhancement and hypointense of the central region which caused a narrowing or compression of spinal canal), psoas abscess (defined as a heterogenous psoas muscle lesion with peripheral enhancement and hypointense of the central region), granulation tissue (defined as a heterogenous enhancement of soft tissue on the post-contrast sequences of T1WI which caused a narrowing or compression of the spinal bone marrow), compression of spinal cavity, stenosis of spinal cavity, vertebral collapse, kyphosis or scoliosis.

The results of the MR imaging were categorized into ‘not spondylitis’, ‘probable spondylitis’, and ‘definite spondylitis’. ‘Not spondylitis’ is defined as the unmet criteria of spondylitis characteristics in the MR of the spine. ‘Probable spondylitis’ is defined as the nondiagnostic condition with unclear or doubtful radiological features of the MR related to spondylitis, but clinically favorable to spondylitis condition. ‘Definite spondylitis’ is defined as the diagnostic condition which met the common features of spondylitis.

All of the non-contrast and contrast-enhanced MR results were read and interpreted by two independent observers blindly. Each of the included patient MR imaging data consisted of non-contrast and contrast examination results were read in two separate times. First, the contrast images were interpreted by the first observers and after two weeks, both observers (the first and second observer) performed a blind interpretation of the same set of MR data but without contrast sequences. The first observer was a musculoskeletal radiologist and the second observer was a general radiologist.

The quantitative data generated was entered into IBM SPSS 20 software for further analysis. The interobserver agreement analysis was conducted with *Kappa* and *McNemar* test and each variable with values of kappa 0–0.20 indicating ‘no agreement’; 0.21–0.39 as ‘minimal agreement’; 0.40–0.59 as ‘weak agreement’; 0.60–0.79 as ‘moderate agreement’; 0.80–0.90 as ‘strong agreement’; and >0.90 as ‘almost perfect agreement’. Each variable with the *P value* < 0.05 from the *McNemar* test showed a significant difference.

3. Results

Based on the interpretation of contrast MR by the first observer, 21 subjects (63.6 %) are categorized as ‘definite spondylitis’, 2 subjects (6.1 %) as ‘probable spondylitis’, and 10 subjects as ‘not spondylitis’. Interpretation of non-contrast MR resulted in 22 subjects (66.7 %) as ‘definite spondylitis’, 2 subjects (6.1 %) as ‘probable spondylitis’, and 9 subjects as ‘not spondylitis’. Interpretation of non-contrast MR by the second observer categorized 19 subjects as ‘definite spondylitis’, 3 subjects (6.1 %) as ‘probable spondylitis’, and 11 subjects as ‘not spondylitis’ (Table 1).

Nonparametric hypothetical analysis for paired samples using the *McNemar* test showed no significant difference between the contrast and non-contrast spine MR in diagnosing spondylitis ($P = 0.368$), and no

Table 1
Distribution of the spine MR reading and interpretation.

The results of the MR examination	Frequency (N)	Percentage (%)
The spine MR with contrast interpreted by the first observer	21	63.6
Definite spondylitis	2	6.1
Probable spondylitis	10	30.3
Not spondylitis		
The spine MR without contrast interpreted by the first observer	22	66.7
Definite spondylitis	2	6.1
Probable spondylitis	9	27.3
Not spondylitis		
The spine MR without contrast interpreted by the second observer	19	57.6
Definite spondylitis	3	9.1
Probable spondylitis	11	33.3
Not spondylitis		

significant difference in the reading and interpretation of MR between the first and the second observer ($P = 0.343$). The concordance between the contrast and non-contrast MR in diagnosing spondylitis (R: 0.88, $P < 0.001$) and the interpretation of MR between the first and the second observer (R: 0.65, $P < 0.001$) were showed in this study (Tables 2 and 3). There is a significant correlation of concordance between contrast and non-contrast MR with a concordance correlation coefficient of 0.94. Interpretation of two observers also shows a concordance correlation coefficient of 0.82.

This study showed no significant difference between the contrast and non-contrast spine MR in diagnosing spondylitis in almost the entire component observed, except for the epidural abscess (Fig. 1 and Table 4). Epidural abscess showed a concordance correlation coefficient of 0.73, a weak interobserver agreement (Kappa R-value = 0.49, $P = 0.001$), and a significant difference between contrast and non-contrast spine MR results.

This study showed no significant difference between the first and the second observer interpretation in diagnosing spondylitis in almost the entire component observed, except the thickening of para-vertebrae soft tissue and epidural abscess (Table 5). The thickening of para-vertebrae soft tissue showed a concordance correlation coefficient of 0.67, a minimal interobserver agreement (Kappa R-value = 0.38, $P = 0.005$), and a significant difference between contrast and non-contrast spine MR results. Epidural abscess showed a concordance correlation coefficient of 0.70, a no interobserver agreement (Kappa R-value = 0.12, $P = 0.151$), and a significant difference between contrast and non-contrast spine MR results.

Table 2
The concordance between the contrast and non-contrast MR in diagnosing spondylitis.

The interpretation of MR without contrast	The interpretation of MR with contrast			Total N (%)
	Definite Spondylitis N (%)	Indeterminate N (%)	Not Spondylitis N (%)	
Definite spondylitis	21 (63.63)	1 (3.03)	0	22 (66.67)
Probable spondylitis	0	1 (3.03)	1 (3.03)	2 (6.06)
Not spondylitis	0	0	9 (27.27)	9 (27.27)
Total	21 (63.63)	2 (6.06)	10 (30.30)	33 (100)

Mc Nemar test ($P = 0.368$)Kappa R = 0.88 ($P < 0.001$).
Index of concordance = $(21 + 1+9) / 33 = 0.94$.
Index of discordance = $(1 + 1+0) / 33 = 0.06$.

Table 3
The concordance of the MR interpretation between the first and the second observer.

The interpretation of MR based on the second observer	The interpretation of MR based on the first observer			Total N (%)
	Definite spondylitis N (%)	Probable Spondylitis N (%)	Not Spondylitis N (%)	
Definite spondylitis	19 (57.58)	0	0	19 (57.58)
Probable spondylitis	2 (6.06)	0	1 (3.03)	3 (9.09)
Not spondylitis	1 (3.03)	2 (6.06)	8 (24.24)	11 (33.33)
Total	22 (66.67)	2 (6.06)	9 (27.27)	33 (100)

Mc Nemar test ($P = 0.343$)Kappa R = 0.65 ($P < 0.001$).
Index of concordance = $(19 + 0+8) / 33 = 0.82$.
Index of discordance = $(2 + 2+1 + 1) / 33 = 0.18$.

4. Discussion

Magnetic Resonance (MR) imaging has become the favored radiological modalities in making the diagnosis of spondylitis due to its high sensitivity, high definition quality on evaluating the extension of the infection to the paravertebral and epidural region and its capability to evaluate the involvement of spinal canal and to differentiate the tuberculous infection from other etiologies [12,13]. In the early stage, the infection starts from the anterior region of the subchondral neighboring the vertebral endplate. The infection would spread to the lower part of the longitudinal ligament, anterior ligament and several vertebral bodies and discs. When two bodies of the vertebra are affected by the infection, the vertebral disc could lose its nutritional intake [2,7]. The observed components of MR which plays important roles in detecting those process of pathophysiology were the endplate erosion, the formation of paravertebral abscess and fluid-hyperintensity on T2WI within the intervertebral disc [14–16]. Without contrast, MR imaging could diagnose spondylitis with a concordance correlation coefficient of 0.94 and a strong interobserver agreement (Kappa R-value = 0.88, $P < 0.001$) compared to contrast imaging. The non-contrast MR imaging could show several observed features including the destruction of the vertebral body with bone marrow edema, endplate erosion, paravertebral and epidural thickening. T2WI fluid-hyperintensity within the vertebral disc which is consistent with the presence of intraosseous and intradiscal abscess formation in contrast imaging (Figs. 2 and 3). The non-contrast MR imaging showed almost perfect interobserver agreement in the observed bone marrow edema component (Kappa R-value = 0.91, $P < 0.001$) and strong interobserver agreement in several observed components including T2WI fluid-hyperintensity within the intervertebral disc, paravertebral abscess, psoas abscess and granulation tissue. The formation of paravertebral abscess showed typical features without contrast imaging. However, the determination of the border, size, and extension of the abscess was more superior in contrast-enhanced MR which makes the application of contrast inevitable to assess further complications of spondylitis, such as epidural abscess (Fig. 4).

Our study found that all of the subjects with endplate erosion and paravertebral abscess showed fluid-hyperintensity on T2WI within the intervertebral disc indicating a chronic progression of spondylitis which started at the endplate of vertebrae and spread to subligamentous forming an abscess and expanded to the disc [14,17]. The subligamentous expansion could be interpreted without contrast with the concordance correlation coefficient of 0.88.

The granulation tissue could be observed as a heterogeneous enhancement of soft tissue on the post-contrast sequences of T1WI [17]. Nevertheless, our findings showed that the granulation tissue could be interpreted clearly in non-contrast imaging. The epidural abscess

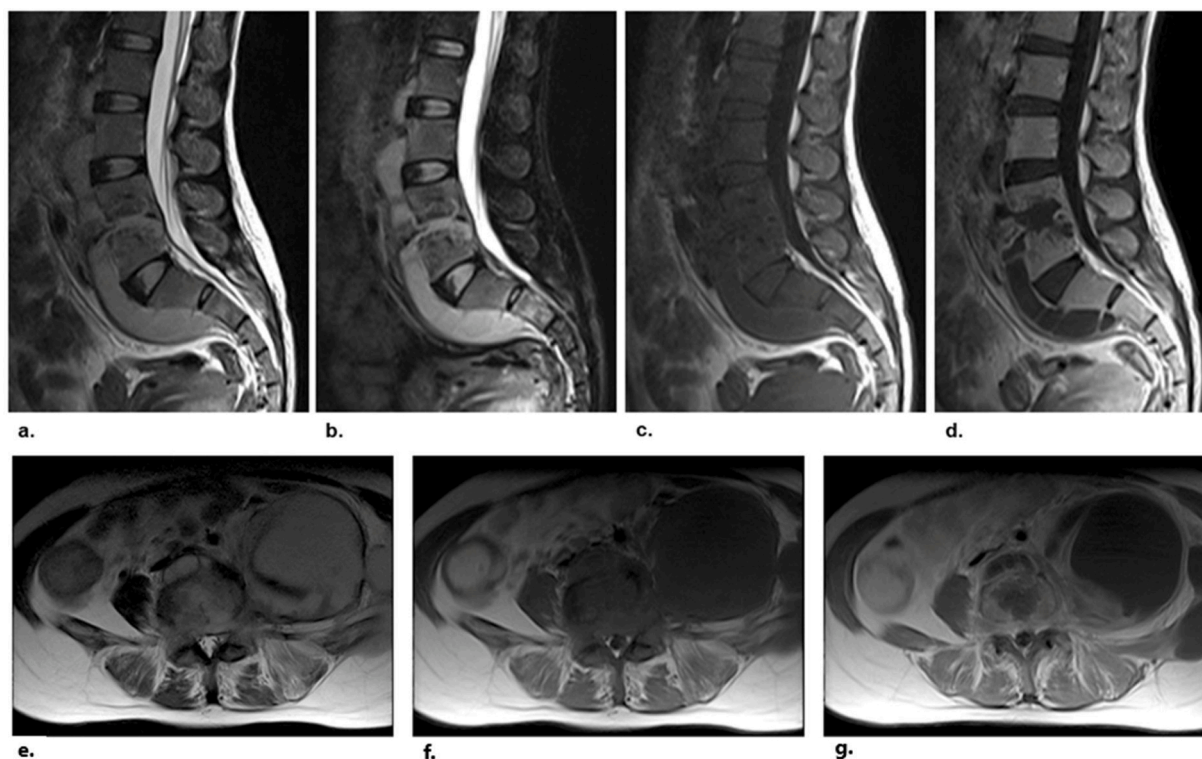


Fig. 1. The MR examination showed no significant difference between the contrast and non-contrast. Bone destruction of L4-L5 vertebral body with endplate erosion and complex fluid collection in the L4-5 intervertebral disc and prevertebral region from L3 until S3, as shown in the sagittal view of T2WI (a), STIR (b) and T1WI (c) sequences, identified as abscess formation. Post-contrast T1WI sequence confirms multifocal rim-enhancement of the intradiscal and prevertebral abscess, as suspected in non-contrast MR (d). The axial view at the level of L4-5 intervertebral disc in T2-weighted (e) and T1-weighted (f) images shows "dirty" T2WI fluid-hyperintensity within the disc, prevertebral, and at the left psoas muscle. Post-contrast T1WI (g) confirms the presence of bone destruction and abscess formation as identified in non-contrast images.

Table 4

Comparison of observed components between contrast and non-contrast spine MR interpretation by the first observer.

Observed Components	McNemar <i>P-value</i>	Kappa R	Kappa <i>P-value</i>	Concordance correlation coefficient (<i>pc</i>)
Endplate erosion	0.125	0.73	0.000	0.88
T2WI fluid-hyperintensity within intervertebral disc	1.000	0.88	0.000	0.94
Paravertebral soft tissue thickening	0.219	0.61	0.000	0.82
Paravertebral abscess	0.500	0.87	0.000	0.94
Bone marrow edema	1.000	0.91	0.000	0.97
Subligamentous extension	0.125	0.75	0.000	0.88
Epidural abscess	0.004	0.49	0.001	0.73
Psoas abscess	0.250	0.82	0.000	0.91
Granulation tissue	1.000	0.81	0.000	0.91
Spinal stenosis	1.000	0.57	0.001	0.82
Collapse of vertebral body	0.500	0.87	0.000	0.94
Kyphosis or scoliosis	1.000	0.82	0.000	0.91

component showed a lower concordance index compared to the others (73 %). This condition happened as a result of the extension of the abscess could be better seen if there was a clear enhancement, especially within contrast imaging. In several subjects, the epidural abscess could be identified from its size, which is relatively small compare to paravertebral and psoas abscess and can be easily missed in non-contrast MR.

We found that from all subjects who clinically were diagnosed with spondylitis, spondylodiscitis, or suspect for both diseases, about 63.6 %

Table 5

Comparison of observed components in diagnosing spondylitis with non-contrast MR between the first and the second observer.

Observed Components	McNemar <i>P-value</i>	Kappa R	Kappa <i>P-value</i>	Concordance correlation coefficient (<i>pc</i>)
Endplate erosion	1.000	0.94	0.000	0.97
T2WI fluid-hyperintensity within intervertebral disc	0.500	0.88	0.000	0.94
Paravertebral soft tissue thickening	0.001	0.38	0.005	0.67
Paravertebral abscess	0.125	0.76	0.000	0.88
Bone marrow edema	1.000	0.92	0.000	0.97
Subligamentous extension	1.000	0.94	0.000	0.97
Epidural abscess	0.002	0.12	0.151	0.70
Psoas abscess	1.000	0.87	0.000	0.94
Granulation tissue	0.500	0.85	0.000	0.94
Spinal stenosis	1.000	1.00	0.001	1.00
Collapse of vertebral body	1.000	1.00	0.000	1.00
Kyphosis or scoliosis	1.000	1.00	0.000	1.00

were diagnosed as spondylitis by contrast imaging and 66.7 % by non-contrast imaging. The analytical study showed no significant difference between the contrast and non-contrast spine MR in diagnosing spondylitis ($P= 0.368$), and no significant difference in the reading and interpretation of MR between the first and the second observer ($P= 0.343$). The discrepancy between the first and second observer is found in detecting paravertebral soft tissue thickening and epidural abscess. These differences could happen due to the size of the lesion, the inability



Fig. 2. An example of the MR examination of clinically suspected for tuberculous spondylitis of the lumbar spine (sagittal view). Non-contrast sagittal view MR images performed in STIR (a), T2WI (b) and T1WI (c) shows extensive destruction of L2-L3 vertebral body with bone marrow edema, endplate erosion, paravertebral and epidural thickening. T2WI fluid-hyperintensity within the L2-3 disc and L2 vertebral body is consistent with abscess formation. Post-contrast T1WI image (d) confirms the presence of intraosseous and intradiscal abscess formation.

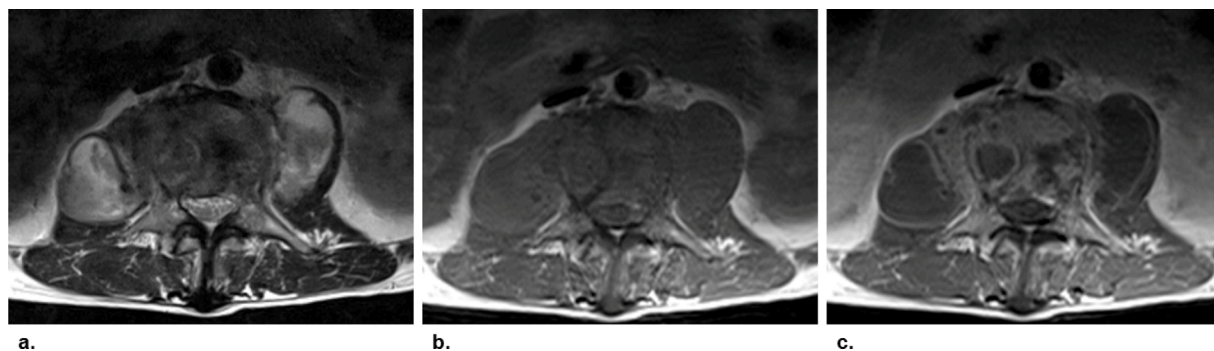


Fig. 3. An example of the MR examination of clinically suspected for tuberculous spondylitis of the lumbar spine (axial view). The examination was done at the level of L2-3 in T2-weighted (a) and T1-weighted images (b). There is bone destruction of the vertebral body with "dirty" T2WI fluid-hyperintensity within the bone and both psoas muscles, consistent with abscess formation. Post-contrast T1-weighted image (c) confirms the abscess formation as a multifocal rim-enhanced structure.

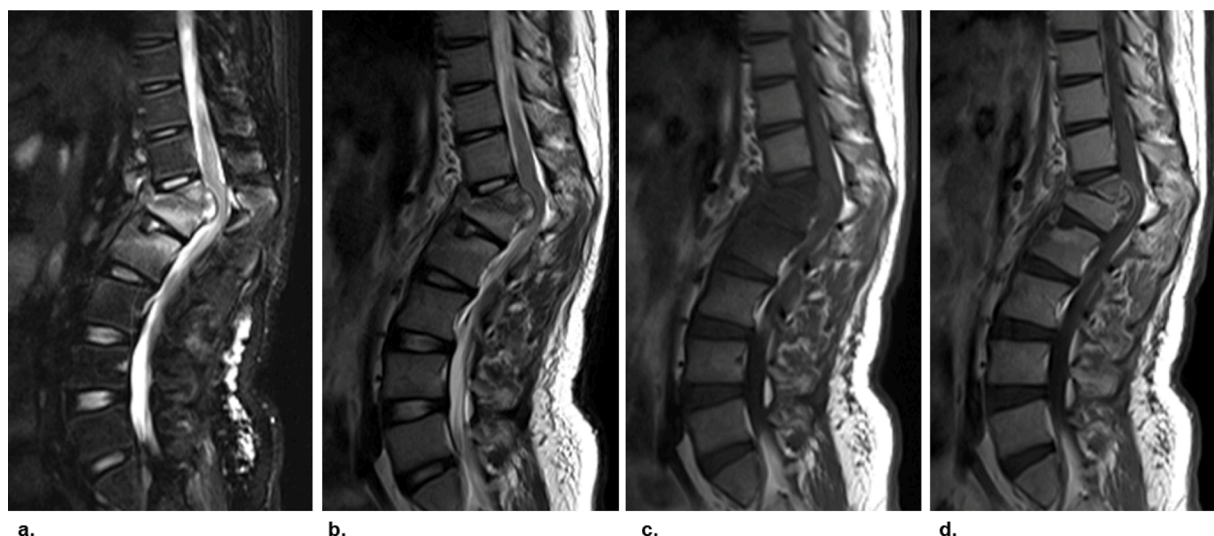


Fig. 4. An example of non-contrast MR limitation in evaluating epidural abscess. Non-contrast MR in sagittal view of STIR (a), T2WI (b), and T1WI (c) shows bone marrow edema of the T12-L3 vertebral body, vertebral collapse and kyphosis of T12-L1, endplate erosion of L2, and T2WI fluid-hyperintensity of the L1-2 intervertebral disc. Both T1WI and STIR also show focal fluid collection posterior to the T12-L1 vertebral body, suggestive of epidural abscess contributing to spinal canal stenosis. Epidural abscess is confirmed at the post-contrast T1-weighted image (d).

of non-contrast MR in showing enhancement, and probably due to different experiences of both observers.

There are some limitations to this study. All the subjects with spondylitis in this study were late-stage tuberculous spondylitis, which is commonly found in Indonesia. MR usually shows severe bony destruction with prominent abscess formation, which is relatively easy-to-evaluate compare to early-stage spondylitis. Identification of each component may also influence one another, for example, the interpretation of T2WI fluid-hyperintensity as abscess formation is probably influenced by the presence of bone marrow edema, bone destruction, and paravertebral soft tissue thickening, as one entity of spondylitis. Furthermore, the non-contrast MR imaging is limited in ruling out the differentials, therefore, the category of 'not spondylitis' could not be specified.

5. Conclusion

There is a high concordance between the contrast and non-contrast MR in diagnosing tuberculous spondylitis in this study. This may provide valuable information for the patient's workup, in case gadolinium contrast is unavailable. This study shows how far non-contrast MR can diagnose spondylitis, in comparison with a standard contrast MR examination. However, contrast-enhanced MR should always be regarded as the standard in imaging method, either to establish the definitive diagnosis and its complications or detecting other differential diagnoses.

Funding Statement

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Ethical statements

The ethical approval to conduct the study was obtained from the Research and Ethics Committee from the Faculty of Medicine Universitas Indonesia. Permission to carry out the study on secondary data of medical records was obtained from Dr. Cipto Mangunkusumo Hospital. Patient data used in this study were kept anonymously and confidential.

The author(s) declare that this manuscript has not been published previously and not under consideration for publication elsewhere.

Disclosure

The author(s) received no financial support for the research, authorship, and/or publication of this article. The authors declare that there is no conflict of interest regarding the publication of this paper.

CRediT authorship contribution statement

Marcel Prasetyo: Conceptualization, Methodology, Writing - review

& editing, Visualization, Supervision, Project administration, Software. **Aldi Semanta Sirath:** Conceptualization, Software, Data curation, Investigation, Writing - original draft. **Krishna Pandu Wicaksono:** Conceptualization, Software, Data curation, Investigation, Writing - original draft. **Joedo Prihartono:** Formal analysis, Software, Supervision. **Stefanus Imanuel Setiawan:** Data curation, Writing - review & editing, Project administration.

Declaration of Competing Interest

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

Acknowledgement

The authors wish to thank Daniel Ira Rosenthal, MD (The Massachusetts General Hospital, Boston) for inspiring this study.

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