



Usefulness of dynamic contrast-enhanced magnetic resonance images for distinguishing between pyogenic spondylitis and tuberculous spondylitis

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Abstract

Purpose Dynamic contrast-enhanced (DCE)-MRI is used for examining the features of malignant tumours in radiology, and we can obtain more information in terms of the diffusion of the media over the course of time. The purpose of this study was to clarify the usefulness of DCE-MRI for distinguishing pyogenic spondylitis (PS) and tuberculous spondylitis (TB).

Methods Forty-five consecutive patients diagnosed with PS (68.6 ± 11.1 years old, males 30 and females 15) and 14 with TB (73.9 ± 9.1 years old, males 6 and females 8) were involved. DCE-MRI consisted of serial six sagittal images which were taken every 20 s after intravenous gadolinium administration. Degree of enhancement, presence of epidural abscess, presence of necrosis in vertebra, presence of enhancement in disc lesion, pattern of diffusion, and maximum contrast index were examined and compared between PS and TB.

Results Degree of enhancement, percentage of epidural abscess, and percentage of necrosis in vertebra were 2.1 ± 0.5 and 1.8 ± 0.8, 60.7% and 100%, 50.0% and 66.7% for PS and TB, respectively, without statistical difference. Maximum contrast index, percentage of the diffusion pattern from the disc, and percentage of enhanced disc were 108.1 ± 22.3 and 78.2 ± 35.6 s, 89.3% and 0%, and 53.6% and 0% for PS and TB, respectively, with statistical significance.

Conclusions This study indicated that longer maximum contrast index, higher likelihood of diffusion pattern from the disc, and higher likelihood of enhanced disc are more specific to PS than TB. This less invasive imaging technique is useful for more accurate diagnosis of PS and TB.

Graphic abstract

These slides can be retrieved under Electronic Supplementary Material.

The graphic abstract consists of three panels. The left panel, titled 'Key points', lists: 1. Spinal infection, 2. Pyogenic spondylitis, 3. Tuberculous spondylitis, 4. Dynamic contrast-enhanced, 5. Magnetic resonance image, 6. Diagnosis. The middle panel shows two rows of MRI images. The top row is for a 72-year-old male with pyogenic spondylitis, showing images at 0 s, 20 s, 40 s, 60 s, 80 s, 100 s, and 120 s. The bottom row is for an 80-year-old female with tuberculous spondylitis, also showing images at 0 s, 20 s, 40 s, 60 s, 80 s, 100 s, and 120 s. The right panel, titled 'Take Home Messages', lists: 1. DCE-MRI provides more specific information for distinguishing PS and TB. 2. Longer maximum contrast index, higher likelihood of diffusion pattern from the disc, and higher likelihood of enhanced disc are more specific to PS than TB. 3. This less-invasive imaging technique is useful for more accurate diagnosis of PS and TB. Each panel includes a Springer logo and a citation: Miyamoto H, Akagi M (2019) Usefulness of dynamic contrast-enhanced magnetic resonance images for distinguishing between pyogenic spondylitis and tuberculous spondylitis. Eur Spine J.

Keywords Infectious spine · Pyogenic spondylitis · Tuberculous spondylitis · Magnetic resonance image · Dynamic contrast-enhanced

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Extended author information available on the last page of the article

Introduction

The number of cases of spinal infection is increasing [1]. The patients of spinal infection are shifting to elderly and/or immunocompromised hosts, and thus, adequate diagnosis should be obtained as soon as possible because types of treatment are quite different between diseases. Moreover, they may have neurological deficit, kyphotic deformity, and deteriorating general condition if we miss the timing of the treatment. For distinguishing the diseases, interviews of the patient on the present illness and a past history of illness (e.g. previous history of TB), plain radiographs, computed tomography (CT), magnetic resonance imaging (MRI, either plain, enhanced, or both), and blood examination (including WBC, CRP, Mantoux test, and needle biopsy) can be performed to obtain a diagnosis. However, even when proceeding with such systemic examinations, it is occasionally difficult to obtain an accurate diagnosis. For example, it is reported that needle biopsy provided adequate diagnosis of the spinal infections in just 73% of cases despite the use of the invasive technique [2]. In addition, using conventional MRI and even enhanced MRI is not perfect for distinguishing between the disease types [3–7]. Chung et al. retrospectively compared 22 MRI parameters from plain and enhanced MRIs in respective 33 PS and TB patients, and they concluded that most parameters occurred in both diseases, and distinctive findings were a pattern of bone destruction with relative disc preservation and heterogeneous enhancement for TB, and a discitis pattern (disc destruction) with peridiscal bone destruction and homogeneous enhancement for PS [3].

Dynamic contrast-enhanced (DCE) MRI, in which serial image sets are obtained before, during and after the rapid intravenous administration of a gadolinium (Gd), is used for examining angiogenesis, which is the process of new vessel formation from the pre-existing host vasculature and is an essential step in tumour growth of malignant tumours such as hepatocyte cancer, prostate cancer, and Mamma carcinosis [8–10]. Angiogenesis also plays a role in pathological conditions such as infections, where it can become unregulated [11]. Using DCE-MRI, we can obtain more information in terms of the diffusion of the contrast medium along time course in contrast to conventional enhanced MRI, which displays a single snapshot of the enhancement after contrast administration.

The purpose of the present study, therefore, was to clarify the usefulness of DCE-MRI for distinguishing between two major types of spinal infection: PS and TB.

Materials and methods

Between 2007 and 2014, consecutive 59 patients who were diagnosed as having spinal infection were involved in the present study. We took plain T1- and T2-weighted MRI,

Gd-enhanced MRI, and DCE-MRI for all cases (1.5 Tesla magnet ranging, Intera; Philips, Best, the Netherlands). In DCE-MRI, seven sagittal slices at the centre of the trunk were acquired before and at 20, 40, 60, 80, 100, and 120 s after a bolus injection of Gd-diethylenetriaminepentaacetic acid (DTPA). Biopsy samples were harvested from all of them, and 45 patients were diagnosed as having PS (68.6 ± 11.1 years old, males 30 and females 15) and 14 as having TB (73.9 ± 9.1 years old, males 6 and females 8). No revision cases were included. The present study was approved by the ethical committee of the institute.

In the present study, six parameters were examined in the DCE-MRI (Fig. 1): (1) degree of enhancement, (2) presence of epidural abscess, (3) presence of necrosis in vertebra, (4) presence of enhancement in disc lesion, (5) pattern of diffusion, and (6) maximum contrast index. The degree of enhancement in (1) was graded in the image when the enhancement reached the maximum contrast during a period of 120 s after gadolinium administration. ImageJ (National Institutes of Health, USA) was used to grade the enhancement, whereby the area of the affected vertebra was framed by the line, and the mean grey value inside the frame was calculated. The value of the maximum enhancement divided by the value of pre-enhancement was analysed, and $1 < 1.5$ was graded as slight (+) enhancement, $1.5 < 2$ as moderate (++) , and $2 >$ as strong (+++). In the definition of disc lesion enhancement in (4), the enhancement of the end plate was involved. The pattern of diffusion in (5) was categorized as whether or not the enhancement arose at both cephalad and caudad end plates of the disc and spread upward and downward into the vertebral body. Maximum contrast index in (6) was categorized as the number of seconds required to reach the maximum contrast during the 120 s after gadolinium administration. These six parameters were compared between PS and TB.

Plain T1- and T2-weighted MRI and Gd-enhanced MRI were also examined, and they were classified as high intensity (brighter than the intensity of muscle), iso-intensity (equal to the intensity of muscle), and low intensity (darker than the intensity of muscle). Mixture of high and low intensity was graded as “high–low”. These gradings were also compared between the diseases (Figs. 2, 3, 4, 5, 6).

As statistical analyses, Student *t* test was used for the degree of enhancement and maximum contrast index, and Chi-square test for the presence of epidural abscess, the presence of necrosis in vertebra, the presence of enhancement in disc lesion, the pattern of diffusion, and plain T1- and T2-weighted MRI and Gd-enhanced MRI evaluations.

$P < 0.05$ was defined as statistical significance.

Fig. 1 Parameters examined in the DCE-MRI. (1) Degree of enhancement (**a**: strong, **b**: moderate, **c**: mild), (2) presence of epidural abscess (white arrow in **a** and **c**), (3) presence of necrosis in vertebra (white dot arrow in **a** and **b**), (4) presence of enhancement in disc lesion (white line of **b**), (5) pattern of diffusion (white arrows in **d**, arising from the infected disc or not), and (6) maximum contrast index (seconds until maximum contrast is reached, 20–120 s)



Fig. 2 72-year-old male. He suffered back pain. Severe local kyphosis between L1 and L3 with destructive changes was exhibited in the lateral plain radiographs (black arrows). MRIs showed a mixture of iso- and low intensity in the T1-weighted image and a mixture of high, iso-, and low intensity in the T2-weighted image at T12, L1, L2, and L3. These vertebrae were moderately enhanced with gadolinium, and epidural abscess was also enhanced (white arrow)



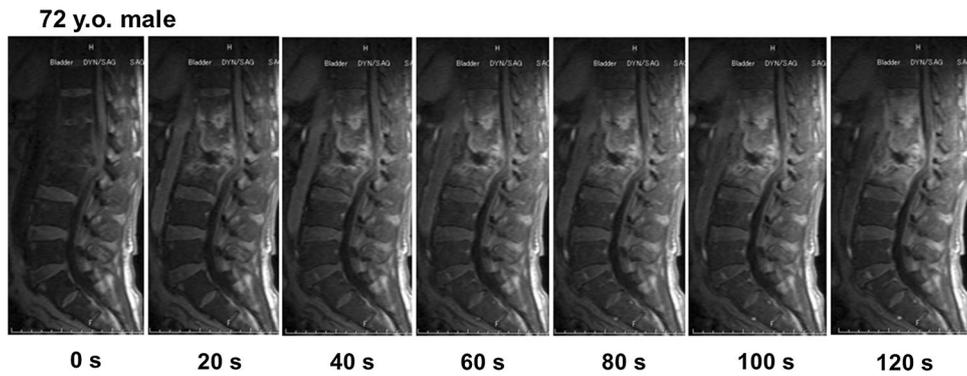


Fig. 3 DCE-MRIs from the patient of Fig. 2. The enhancement was graded as moderate. The end plates of the disc were enhanced. The diffusion spread from the end plates towards cephalad and caudad, and maximum contrast index was identified as 120 s. You will find

that T12, L1, and L3 gradually stained along the time line. Necrosis in vertebra was also seen. *E. coli* was detected from the biopsy sample, and his diagnosis was pyogenic spondylitis

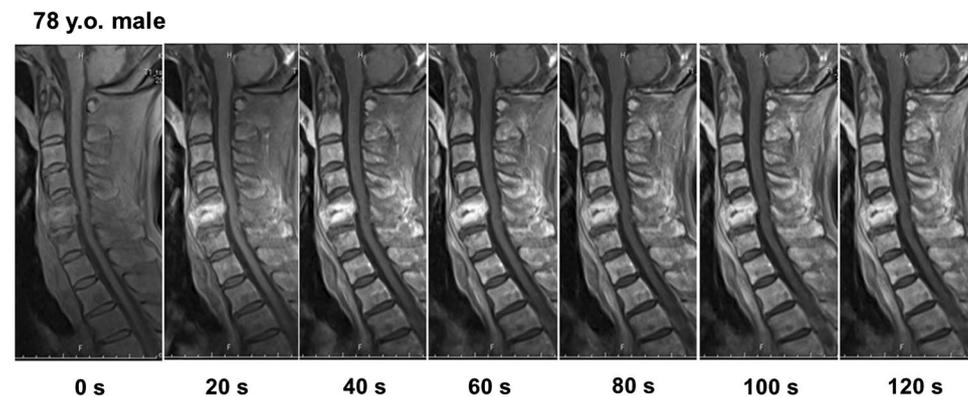


Fig. 4 78-year-old male. He suffered severe neck pain. The vertebrae of C5 and C6 were strongly stained around the disc, and the enhancement slightly spread towards cephalad and caudad. It took 60 s to

reach maximum contrast. The culture and PCR were both negative from the biopsy sample, and his histology showed the findings of pyogenic spondylitis

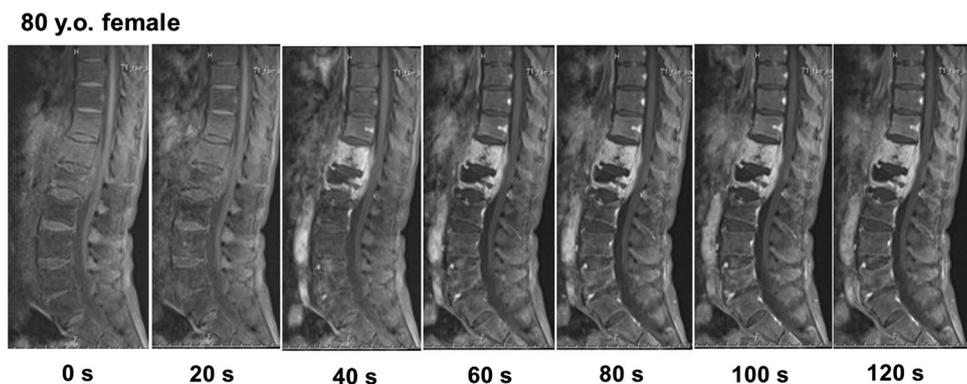


Fig. 5 80-year-old female. She suffered low back pain and sciatic pain in her bilateral lower extremities. The vertebrae of T12 and L1 were strongly enhanced. No enhancement of the disc was seen. We did not find the diffusion pattern in which the enhancement spread towards cephalad and caudad from the disc. It took 60 s to reach max-

imum enhancement. Necrosis of the vertebra and epidural abscess were seen. She was diagnosed as having tuberculous spondylitis because of PCR, positive Mantoux test, and the histological findings from the biopsy sample

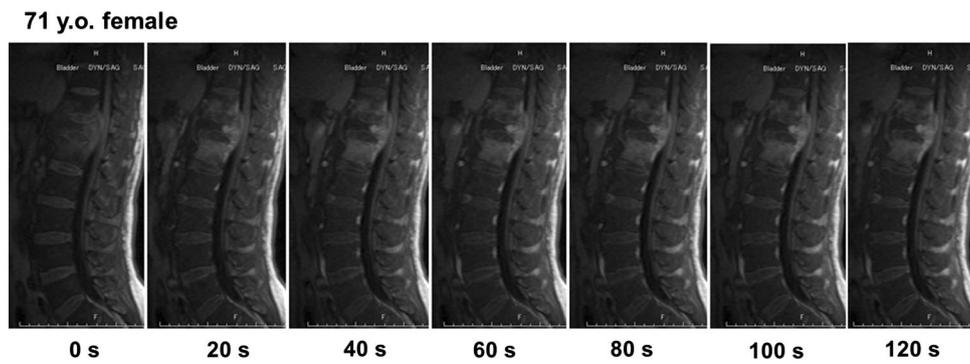


Fig. 6 71-year-old female. She suffered back pain and motor weakness of the lower extremities. The vertebrae of T11, 12 and L1 were mildly enhanced. It took 40 s to reach maximum contrast. Neither the enhancement of the end plate nor the diffusion pattern was found.

Epidural abscess was seen. She was diagnosed as having tuberculous spondylitis because of PCR and the histological findings from the biopsy sample

Table 1 Data of PS and TB in dynamic contrast-enhanced MRI

	PS	TB	P value
Degree of enhancement	2.1 ± 0.5	1.8 ± 0.8	N.S.
Presence of epidural abscess	60.7%	100%	N.S.
Presence of necrosis in vertebra	50.0%	66.7%	N.S.
Maximum contrast index (seconds)	108.1 ± 22.3	78.2 ± 35.6	P < 0.05
Pattern of diffusion (arising from the infected disc or not)	89.3%	0%	P < 0.05
Presence of enhancement in disc lesion	53.6%	0%	P < 0.05

PS pyogenic spondylitis, TB tuberculous spondylitis, MRI magnetic resonance image

Results

The degree of enhancement, the percentage of epidural abscess, and the percentage of necrosis in vertebra were 2.1 ± 0.5 and 1.8 ± 0.8, 60.7% and 100%, and 50.0% and 66.7% for PS and TB, respectively, but no statistical difference was found (Table 1). On the other hand, maximum contrast index, the percentage of the diffusion pattern from the disc, and the percentage of enhanced disc were 108.1 ± 22.3 and 78.2 ± 35.6 s, 89.3% and 0%, and 53.6% and 0% for PS and TB, respectively, with statistical significance (Table 1).

In terms of T1-weighted plain MRI, 41 cases (91%) were graded as low intensity, 3 cases as iso-intensity, and 1 case as high–low intensity in PS, and 13 cases (93%) were graded as low intensity and 1 case as iso-intensity in TB. There was no statistical difference between the diseases (Table 2). In terms of T2-weighted plain MRI, 34 cases (75.6%) were graded as high intensity, 7 cases as iso-intensity, 3 cases as low intensity, and 1 cases as high–low intensity in PS, and 8 cases (57.1%) were graded as high intensity, 4 cases as iso-intensity, and 2 cases as low intensity in TB. There was no statistical difference between the

Table 2 Data of PS and TB in T1- and T2-weighted MRI and dynamic contrast-enhanced MRI

	PS	TB	P value
T1-weighted			
High	3	0	N.S.
Low	41	13	
Iso	1	1	
T2-weighted			
High	34	8	N.S.
Low	3	2	
Iso	7	4	
Gd-enhanced			
High	34	12	N.S.
Low	0	0	
Iso	11	2	

PS pyogenic spondylitis, TB tuberculous spondylitis, MRI magnetic resonance image

diseases (Table 2). In terms of Gd-enhanced MRI, 34 cases (75.6%) were graded as high intensity and 11 cases as iso-intensity in PS, and 12 cases (85.7%) were graded as high intensity and 2 cases as iso-intensity in TB. There was no statistical difference between the diseases (Table 2).

Discussion

The present study has indicated that DCE-MRI, which can capture a depiction of physiologic alterations as well as morphologic changes of angiogenesis, provides more specific information for distinguishing PS and TB. Lang et al. compared heuristic and pharmacokinetic parameters measured by DCE-MRI amongst myeloma, metastatic cancer, lymphoma, and TB, and concluded that washout slope had the best diagnostic performance; however, they did not evaluate PS [12]. Therefore, the present study is the first report to indicate the usefulness of DCE-MRI for distinguishing between PS and TB. Although the parameters (1), (2), (3) and (4) may also be evaluated using conventional enhanced MRI, reading more numbers of the images along the time course makes the evaluation to be performed more easily in this method. That is, longer maximum contrast index, higher likelihood of the diffusion pattern from the disc, and higher likelihood of the enhanced disc are more specific to PS rather than TB. On the other hand, we did not find any significantly different findings between the diseases in plain and Gd-enhanced MRIs.

Recently, the role of angiogenesis in infectious diseases has been elucidated; for example, Zielonka et al. reported that sera from TB patients constituted a source of mediators that participate in angiogenesis and prime monocytes for the production of proangiogenic factors [13]. Seyedmajidi et al. also reported immunohistochemical expression of angiogenesis-related markers such as CD34 in pyogenic granuloma of gingiva [14]. However, the precise mechanism related to angiogenesis in the diseases is still being researched. To explain the results in that it took more time to reach the maximum staining in PS than TB, we speculated that the pattern of angiogenesis may be different between the diseases. In fact, recent research reported that the inhibitor for angiogenesis can be a treatment option for TB [15]. Future studies will be needed to understand the pathogenesis of the diseases.

Whereas it is well known that a higher rate of disc preservation, which may be due to a lack of proteolytic enzymes in mycobacteria, has been reported to be more frequently seen in TB compared to PS [3–5], the tendency to have more destruction around the disc may reflect on the results of the present study in which there are a higher likelihood of the diffusion pattern arising from the disc and a higher likelihood of the enhanced disc lesion in PS compared to TB.

The limitations of the present study should be noted. The numbers of TB patients were relatively small because of the rarity of the disease. The artefact from the major vessels is also one of the potential cons of DCE-MRI; therefore, it may disturb doctors to read the findings [16].

Size of the vertebra depending on the regions may also affect the reading quality, i.e. the cervical region may be more difficult to read than the lumbar spine. Although the present study has indicated that DCE-MRI is a useful adjuvant method when diagnosing infectious spine, systemic reviews including microbiologic and histological examinations are still important for definite diagnosis.

Compliance with ethical standards

Conflict of interest In this study, the authors have no potential conflict of interest.

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