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Selecting Patients for Treatments Based on Modic Changes: The Need for Accurate and Standardised Reporting

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ABSTRACT

Low back pain is a leading cause of disability worldwide and an economic burden on health resources. Modic changes seen on magnetic resonance images are common amongst patients with chronic low back pain. Radiofrequency ablation of the basivertebral nerve and antibiotics for low-grade disc infection are potential treatments that both rely on the presence of Modic type 1 changes. Accurate and standardised reporting of Modic changes to select patients most likely to benefit and to ensure good antimicrobial stewardship is needed but is challenging. Examples are given of varying, incomplete and/or inaccurate Modic change findings. Including the extent of Modic change and likely pathophysiological interpretation would be helpful parameters to report.

Keywords: Modic Changes; Spine Infection; MRI

Abbreviations: CLBP: Chronic Low Back Pain; BVNA: Basivertebral Nerve; MRI: Magnetic Resonance Images; MCs: Modic changes

Introduction

The World Health Organization estimates that 619 million people are living with low back pain and around 80% of people experience back pain at some point during their lifetime. It is a leading cause of disability worldwide and an economic burden on health resources that is rising with increasing life expectancy [1,2]. In the United States, overall healthcare costs associated with back pain have risen to more than 134.5 billion dollars a year [3-5]. In over 80% of cases, the cause of pain is unexplained and treatment is frequently inadequate or ineffective [6,7]. Symptoms may be influenced by psychosocial issues such as depression, catastrophizing and beliefs about pain [8,9]. After six months of conservative treatment, therapeutic options for chronic low back pain (CLBP) include intradiscal electrothermal therapy, intradiscal steroid injection, intradiscal biacuplasty or various forms of surgical fusion, all of which have variable results with no evidence of long-term benefit [10].

Radiofrequency ablation of the basivertebral nerve (BVNA) and antibiotics for low-grade disc infection are two potential treatments for CLBP that are linked to inflammation seen as active endplate changes on magnetic resonance images (MRI). Clinical trials have demonstrated improved disability scores following BVNA [11-15] and following treatment with oral antibiotics [16,17]. Intradiscal injection of local antibiotic, as opposed to oral antibiotic therapy, is currently being compared against a placebo in the Modic Trial (ClinicalTrials.gov Identifier: NCT04238676). For both BVNA and treatment with antibiotics, patients are selected on the basis of Modic changes (MCs) seen on MRI scans [18,19] which are strongly associated with low back pain [20-23]. More than 46% of patients with low back pain have MCs compared to 6% of the general population [24-26]. Pain relief following BVNA correlates with Modic type 1 (MCI) and type 2 (MCII) changes [12]. Benefit from antibiotics has been associated with MCI but not MCII alone or Modic type 3 (MCIII) [16,17,27]. Thus, correct identification and interpretation of MCs is of paramount importance to select patients most likely to benefit from treatment with either BVNA or antibiotics.

At present, in the UK, MRIs are not routinely performed (or encouraged) as part of the assessment of CLBP [28]. Furthermore, appearance of MCs varies according to the equipment and sequences used. Fields, et al. [29] have published methodological guidelines to facilitate comparable measurement of MCs. The ability to distinguish between MCI and MCII is influenced by field strength and sequence parameters; 1.5 Tesla is probably the better choice for detecting MCI which is best visualized on fluid sensitive (STIR) sequences in conjunction with T1 sequences [26]. However, both the presence and type of MCs are variably reported [30-34]. Accurate and standardised reporting of MCs is needed to optimise patient selection for either BVNA or antibiotic therapy and to ensure good antimicrobial stewardship. Here, we describe examples of variation, incomplete and/or inaccurate Modic change findings on MRI that may represent challenges to this aim.

Methods

Images from MRI scans and extracts from MRI reports have been selected from patients who expressed an interest in participating in the Modic Trial (ClinicalTrials.gov Identifier: NCT04238676) at Oxford University Hospital NHS Foundation Trust (OUH), Oxford, UK to illustrate the extent of variation in MRI reporting of MCs in patients with CLBP. This study has been approved by the OUH institutional review board as part of quality improvement in radiological reporting (application number 9320).

Observations

Figure 1 shows classic examples of MCI, MCII and mixed MCI+MCII found in this CLBP cohort. Figure 2 shows images from MRI scans and the corresponding radiological reports that exemplify unreported MCs, incomplete reporting of MCs and inaccurate reporting of MCs. The image in Figure 2a shows clear MCI at L1/2 but the corresponding report does not mention MCs. The report corresponding to the image in Figure 2b states that 'there is Modic endplate change at L5/S1'. This patient has MCII at L5/S1 and would be unlikely to benefit from treatment with antibiotics but may be suitable for BVNA. The report corresponding to the image in Figure 2c states that the patient has MCI when the patient has MCII in the inferior endplate of L5 and a Schmorl's node in the inferior endplate of L4. The signal changes surrounding the Schmorl's node may have been interpreted as MCI. Figure 3 demonstrates variation in the interpretation of MCs depending on the level of experience and specialist knowledge of the viewer. Figure 4 illustrates two cases of MCI-associated CLBP that would be unsuitable for intradiscal injection due to inaccessible discs. Table 1 gives typical examples of inconsistency and variability of terms used in reporting MCs in patients with CLBP.

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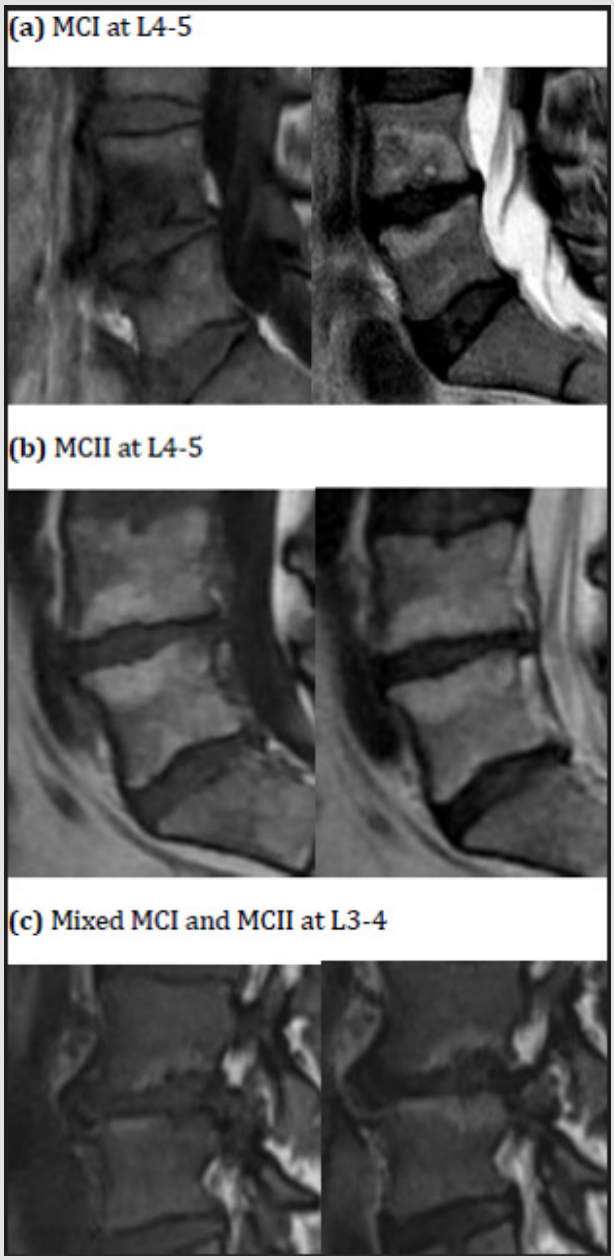

Figure 1: Examples of different types of Modic change (T1 weighted images left; T2 weighted images right).

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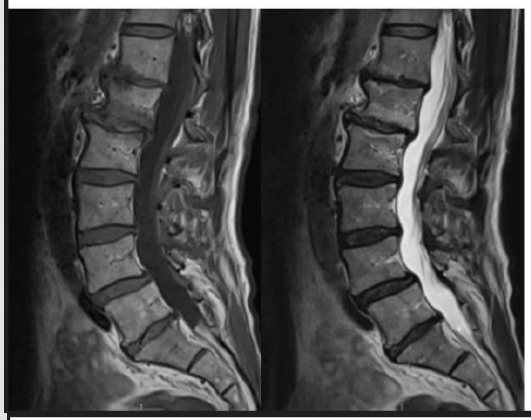
(a) Unreported MCI at L1-2



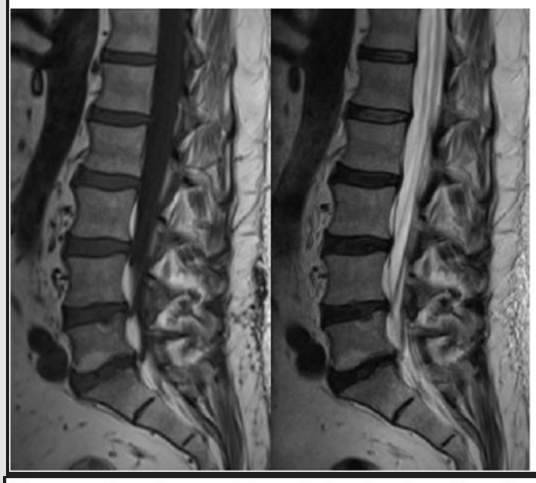
Clinical details:
Persistent low back pain with radiation to buttock and thigh.

Findings:
For the purposes of the examination, the axial scan 33 is taken to pass through the L5-S1 junction.
Generalised lumbar disc dehydration with mild/moderate asymmetric loss of disc height, particularly T12 and L1 and L1-2, associated with a mild scoliosis. There are florid acute reactive endplate changes at T12-L1 anteriorly and L1-2 posteriorly on the right side.
Lumbar facet joints show moderate hypertrophy, worst at L4-5.

T12-L1: Small disc bulge. Adequate canal and foramina.
L1-2: Small/moderate broad disc/osteophyte bar. Mild canal, mild/moderate lateral recess narrowing. Mild/moderate bilateral foraminal narrowing.
L2-3: Small disc bulge. Mild canal lateral recess narrowing. Mild foraminal narrowing.
L3-4: Small broad disc bulge. Small left paracentral disc herniation, which just contacts/displaces the traversing left L4 nerve root within the lateral recess. Mild left foraminal narrowing due to osteophytes.
L4-5: Mild anterolisthesis of L4 related to facet joint degeneration. Small disc bulge. Mild canal, mild/moderate lateral recess narrowing. Mild bilateral foraminal narrowing.
L5-S1: Small broad disc/osteophyte bar. Mild indentation of the thecal sac. Otherwise adequate canal. Adequate foramina.

Otherwise normal appearances of the conus and the cauda equina.
No other abnormality.

(b) Inadequately reported MCII at L5/S1

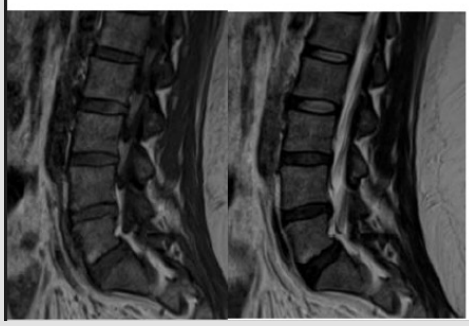


Exam Name(s): **MRI Spine Lumbar and Sacral**

Reason for Study: Longstanding lower back pain with associated bilateral sciatica. Pain effecting sleep and daily activities. No longer able to exercise. No bowel or bladder symptoms.

The conus is at T12 and is normal.
There is loss of the normal lumbar lordosis.
There is disc dehydration from L2-S1.
There is loss of intervertebral disc height from L4-S1.
At L2-3 there is some central T2 hyperintense abnormality within the central posterior disc likely to represent a small annular fissure. Axial images have not been obtained here but there is no definite neural compression.
At L3-4 there is very mild broad-based disc bulge and some bilateral facetal hypertrophy but no neural compression.
At L4-5 there is a right paracentral disc herniation with some associated intrinsic disc T2 hyperintense signal abnormality which may represent an annular fissure. There is mild bilateral facetal hypertrophy at this level and together these changes result in minor lateral recess narrowing but there is no definite evidence of neural compression.
At L5/S1 there is a broad-based disc bulge with a small focal area of disc herniation centrally. There is associated bilateral facetal hypertrophy. There is no associated neural compression.
There is modic endplate change at L5/S1.

(c) MCII in the inferior endplate of L5 and a Schmorl's node in the inferior endplate of L4 incorrectly reported as MCI



Title & Technique:MRI lumbar spine

Clinical Indication:Low back pain.

Findings:Segment L5-S1 shows a mild bulge. Bilaterally facet arthropathy noted.
Segment L4-L5 shows a right paracentral bulge without significant nerve root compromise.
Segment L3-L4 as well as L2-L3 show no significant abnormality.
There are mild degenerative changes in the vertebral endplates (Modic 1). Incidental finding of a fibroid within the uterus posteriorly measuring 25 mm.

Conclusion:Mild degenerative changes in the lumbar spine as detailed described.

Recommendation:None

Figure 2: Typical examples of MRI scans with corresponding inadequate and incorrect radiological reports (T1 weighted images left; T2 weighted images right).

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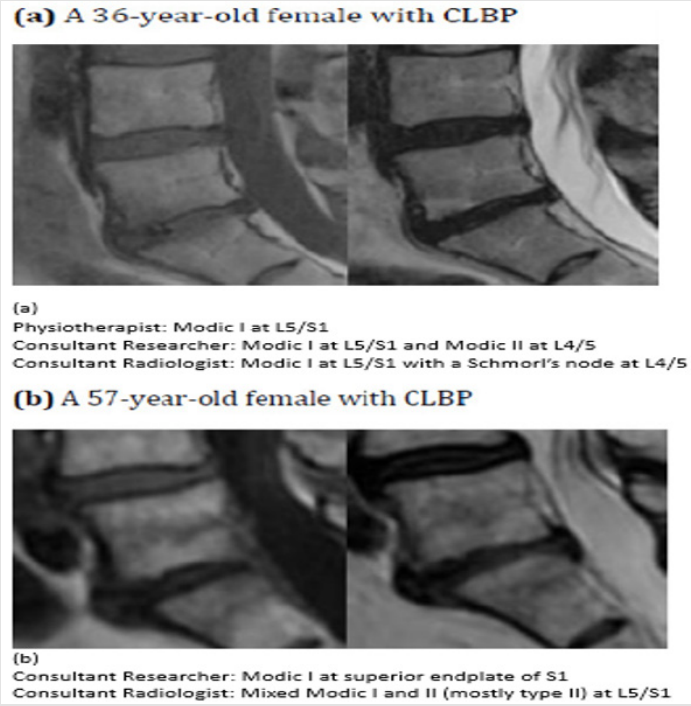

Figure 3: Examples of different interpretations of MC (T1 weighted images left; T2 weighted images right).

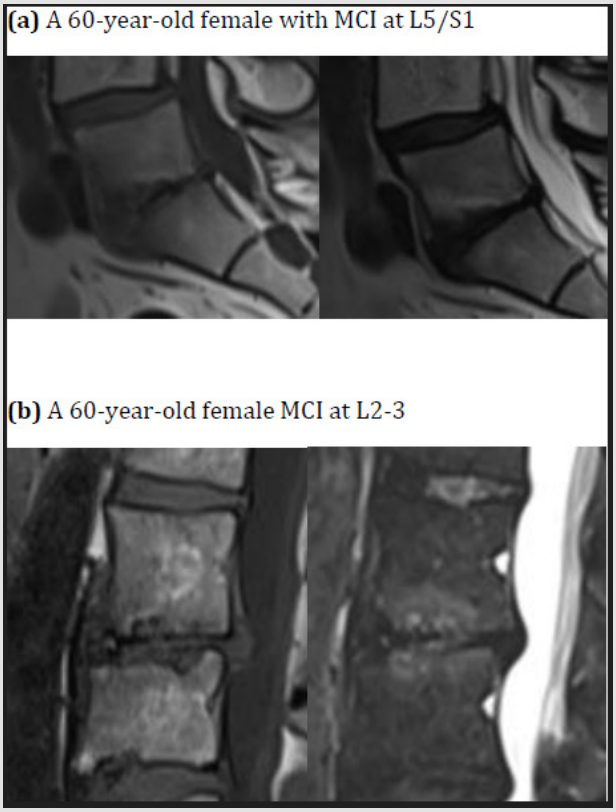

Figure 4: Two examples of MCI for which intradiscal injection may not be possible or appropriate due to lack of accessibility and disc narrowing (T1 weighted images left; T2 weighted images right).

Table 1: Examples of inconsistency and inadequacy of terms used to report MC in patients with CLBP.

Varying Terms Used to Report no MC
'no active marrow changes'
'no significant end-plate changes'
'no significant endplate marrow changes''no discrete marrow oedema'
'normal bone marrow signal'
'no active endplate modic changes'
'no significant sclerotic or fatty end plate changes' 'no evidence of discrete endplate marrow oedema'
'no significant degenerative endplate marrow oedema'
'no significant discrete juxta distal end plate or facet joint marrow oedema'
Varying Terms Used to Report MC
'small central endplate infraction'
'early modic 2 degenerative endplate change''mild endplate changes'
'minor reactive marrow change' 'small central endplate infraction''mild endplate changes'
'minor reactive marrow change
Varying Terms Used to Report MCI
'endplate oedema in the adjacent vertebral bodies''mild endplate oedema'
'severe Modic type 1 endplate change'
'moderate mixed Modic type I and 2 endplate change''minor intervertebral disc oedema also seen' 'moderate disc oedema'
'mild degenerative changes in the vertebral endplates (Modic I)'
Varying Terms Used to Report MCII
'mild modic type 2 degenerative endplate change''Modic II (fatty) marrow changes'
'mild Modic type II marrow changes''there is fatty change'
'early modic 2 degenerative endplate change'

Note: MC: Modic Changes; CLBP: Chronic Low Back Pain; MCI: Modic Type 1 Changes; MCII: Modic Type 2 Changes

Discussion

MCs are observed in about 6% of the general population but 46% of patients with low back pain [25]. For those individuals with MCs, pain is commonly continuous and it disrupts sleep [33,35]. The causal role represented by MCs in CLBP, however, remains controversial due to their multi-factorial aetiology. Their pathogenesis may be degenerative, familial, infective, traumatic, or due to autoimmunity or instability [30] and the absence of standardised radiological nomenclature contributes to difficulties in understanding their significance [32]. In order for MCs to usefully inform treatment choice, particularly for emerging therapies, it is imperative that accurate and precise reporting of Modic changes should form part of any standard report using the appropriate Modic type nomenclature. In addition, disc level(s) and endplate(s) affected should be clearly specified and distinguished from other entities such as Schmorl's nodes [36]. Quantifying the extent of MCs is likely to be more useful than subjective descriptions such as 'early', 'mild', 'small', 'minor', 'moderate' or 'severe'. We suggest that radiological reporting of MCs should include type, site, extent and likely pathophysiological interpretation. Examples are provided in Table 2.

MCI are active changes characterised anatomically by disruption and fissuring of the endplate, the presence of extracellular water, micro-fractures of the trabeculae and vascularized tissue in the adjacent bone marrow [18,19]. They are seen as hypo-intense signal intensities on T1-weighted spin-echo sequences and hyper-intense signal intensities on T2-weighted sequences [37].

Table 2: Suggested terminology to use for reporting MCI, MCII and no MC for patients with CLBP.

Suggested Phrases to Report MCI
There are Modic I changes (high signal on T2 and low signal on T1 weighted images) [e.g. at the superiorendplate of L4/5]. The total volume of Modic I change is [e.g. 1.4 cm^3]. This may represent bone oedema due to low grade infection within the adjacent intervertebral disc.
Suggested phrases to Report MCII
There are Modic II changes (high signal both on T1 and T2 weighted images) [e.g. at the superior endplateof L4/5]. The total volume of Modic II change is [e.g. 1.4 cm^3]. This may represent fatty infiltration of the bone marrow due to degenerative change at the site.
Suggested Phrase to Report no MC
There are no clearly defined Modic changes to suggest active inflammatory changes, fatty infiltration or sclerosis at the vertebral endplates.

Note: MC: Modic Changes; CLBP: Chronic Low Back Pain; MCI: Modic Type 1 Changes; MCII, Modic Type 2 Changes

Histologically, MCI represents inflammation and bone marrow oedema thought to be due to low-grade disc infection [38]. Treatment with antibiotics, therefore, is likely to be appropriate for patients with MCI changes. MCII are inactive changes characterised by marrow ischemia and fatty marrow replacement [18,19]. They are seen as hyper-intense signal on both T1- and T2-weighted sequences [37] and are more frequently found amongst individuals with degenerative disc disease [39-41]. Disc degeneration is associated most commonly with MCII but may also be associated with MCI. Mounting evidence that vertebral endplates play a significant role in CLBP [42,43] has led to a general consensus that BVNA is likely to provide clinical benefit to patients with either MCI or MCII [44,45]. It is becoming an increasingly established intervention for CLBP [14,46,47] despite the fact that

ablation destroys tissue and long-term follow-up is awaited [48]. MCI has been associated with greater pain intensity than MCII [49-53], with the pain directly correlating to the extent of MC [54]. There is, however, inconsistency in reports of a potential association between resolution of oedema (i.e. MCI) and symptom relief [17,35,55-57]. The most recent study suggests that any reduction in MCI may not be not clinically relevant but the volume of MCI was not quantified [57]. Further studies are needed to inform CLBP treatment pathways associated with mechanical degeneration and low- grade infection.

Conclusion

MCs are common MRI findings amongst those with CLBP but reporting of MCs often remains variable and unstandardised. We suggest that encouraging increased standardisation of Modic reporting is essential for research into CLBP and selection of patients most likely to benefit from emergent therapies. Inclusion of type, site and extent of MCs, as well as the likely pathophysiological interpretation, are useful parameters that could help and influence research opportunities.

Acknowledgements and Conflict of Interest

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