Published in final edited form as:

Spine J. 2012 May ; 12(5): 411–416. doi:10.1016/j.spinee.2012.03.026.

Modic Changes: Prevalence, Distribution Patterns and Association with Age in Caucasian Men

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Introduction

Modic changes (MCs) are signal variations of the vertebral endplate and the adjacent subchondral vertebral marrow seen on magnetic resonance images (MRI) [1,2]. According to the patterns of signal changes on T1- and T2-weighted images, traditionally MCs have been classified into three types [1,3]. Type 1 MCs show decreased signal intensity on T1-weighted images and increased signal intensity on T2-weighted images. While type 2 MCs demonstrate increased signal intensity on both T1- and T2-weighted images, type 3 MCs reflect decreased signal intensity on both T1- and T2-weighted images. The presence of different types of MCs together within an endplate was later regarded as mixed MCs, such as mixed type 1/2 and mixed type 2/3 [4–6].

Despite over 20 years of study, much about MCs remains either controversial or unknown. Assumed to be degenerative features of the vertebral endplate and marrow, MCs have long been suspected as a cause of low back pain [2], although this remains controversial [4,7–10]. Due to limited cases of biopsy, the pathological nature of MCs largely remains unclear [2,11]. Even the prevalence of MCs and the predominant type are uncertain. For example, the prevalence rates reported in the scientific literature widely range from 0.5% [12] to 62% [13]. Among the factors underlying the inconsistencies are variations in age and race of the subjects, back pain status [7,14] and occupation [9]. To date, there are only two reports on MCs in the general population, which come from the same cohort [8,15]. The role age may play in the pathogenesis of MCs, as well as the distribution pattern of MCs, has not yet been explored in the general population.

A systematic study of MCs in the lumbosacral region in the general population would provide fundamental epidemiological insights of MCs, as well as an important reference for

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clinical observations. The purpose of the current study was to investigate the prevalence and distribution pattern of MCs and their associations with age using a large, population-based sample. Evidence suggests that MCs are closely related to disc [16,17]. Thus, we refer to endplates containing MCs relative to the intervertebral disc and differentiate them as cranial and caudal to the adjacent disc.

Materials and Methods

Subjects

This study utilized the lumbar MRI of the Twin Spine Study cohort [18], which consists of 300 pairs of male monozygotic (MZ) and dizygotic (DZ) twin pairs (N=600). Subjects were recruited from the population-based Finnish Twin Cohort, containing virtually all Finnish sex-matched twin pairs born before 1958 and alive in 1975, which has been shown to be representative of the general Finnish population [19]. Initially, MZ twins were recruited and compared to the larger twin cohort on a variety of factors and were found to be largely representative of the Finnish Twin Cohort, which is representative of the Finnish population. Later DZ twins were recruited using identical methods [18].

Each subject underwent a structured interview and MRI examination of the lumbar spine revealing that 28 subjects had previously undergone lumbar spinal surgery. These subjects were not included in the current study. Lumbar MRIs of another 11 subjects were missing in the Twin Spine database, leaving 561 subjects for the present study (mean age 49.8 ± 7.6 years). The study was approved by the Health Research Ethics Board at the University of Alberta.

MRI Data Acquisition

The lumbar MRI were acquired with either a 1.5 Tesla Magnetom SP 4000 scanner or Magnetom Vision scanner (Siemens AG Erlangen, Germany), using a surface coil. With the Magnetom SP 4000 scanner, sagittal T1-weighted images were obtained using TR/TE times of 650/22 milliseconds and T2-weighted images using 2600/90. With the Magnetom Vision scanner, the TR/TE times were 650/12 in T1 and 2600/80 in T2W sagittal images. For both scanners, the acquisition matrix was 192×256 for T1 and 256×256 for T2, with a field of view of 260 mm (pixel size 1.02 mm). The slice thickness and inter-slice gap were 4mm and 0.4mm for sagittal images and 3 mm and 0.3 mm for axial slices. Each subject was lying supine for 30 to 45 minutes immediately prior to MRI scanning. For each imaged lumbar spine, there were 7 sagittal slices of T1-weighted images and 11 sagittal slices of T2-weighted images.

Image Evaluation

MRI evaluations were performed on a PC workstation using either Osiris (Version 3.1, Geneva, Switzerland) or a custom-designed image analysis software, *Spine Examiner* (SpEx©, Version 2.73, Edmonton, Canada). Osiris is able to simultaneously display multiple T1- and T2-weighted images for comparison and SpEx allows further quantification of needed measurements. All the evaluations were performed by one of the authors (YW), an orthopaedic surgeon who was experienced in the measurement of MCs.

The assessments were blinded to clinical history and any previous measurements. All T1- and T2-weighted sagittal images were evaluated.

Classification of MCs

The traditional Modic classification was used in the first step of the evaluation [3]. The mixed type MCs were noted if different types of MCs were present within an endplate. In order to differentiate MCs from artefacts and signal variations resulting from other vertebral marrow abnormalities, only signal changes of vertebral bone marrow that extend from the endplate and involve two or more adjacent sagittal slices were classified as MCs. Very small regions of signal changes commonly appear in the corners of a vertebral body which are typically smaller than 5mm in diameter, were not classified as MCs in this study.

Number of endplates with MCs

The evaluation included the eleven endplates of the lumbosacral region (L1 through S1). The number of endplates with MCs, regardless of the type of MCs, was counted for each subject. The specific type and the location of MCs, such as disc level and cranial or caudal to the adjacent disc, were recorded.

Size of MCs

For each instance of MCs, the number of T2-weighted sagittal images that contained MCs was counted and used to estimate its transverse diameter. In our samples, each subject had 11 T2-weighted images, which represent approximately the full transverse diameter of the vertebral body. The width of 3 adjacent sagittal slices, which is the thickness of 3 slices plus the 2 inter-slice spaces between them, equals 27% of the width of all 11 sagittal slices. Similarly, the width of 5 and 8 sagittal slices corresponds to approximately 46% and 73% of the full transverse diameter of the vertebral body. Using the transverse diameter of MCs as an indicator, a 5-point ordinal scale was used to grade the *transverse size* of MCs. The transverse size was rated as *none* if MCs were absent; *small* if 2 to 3 slices (approximately corresponding to <25% of the transverse diameter of the vertebral body) showed MCs; *moderate* if 4 or 5 sagittal slices (corresponding to <50% of the transverse diameter) were involved; *large* if MCs presented on 6 to 8 sagittal slices (corresponding to <75% of the transverse diameter), and an evaluation of *very large* was given if MCs were present on more than 9 sagittal slices (>75%).

Further, the sagittal T2-weighted image in which the individual MCs had the largest area, was used to determine the anterior-posterior (AP) diameter of MCs and the location within the endplate. The AP diameter of the vertebral body was divided into three portions, anterior, central and posterior, and the location of the MCs was recorded correspondingly. The *AP size* of MCs was rated as *none* if there was no MCs; *small* if only one portion presented MCs; a rate of *moderate* was given if MCs involved two of the three portions and the MCs were evaluated as *large* if all the anterior, central and posterior portions of a sagittal vertebral body were involved.

Prior to obtaining the measurements for this study, we examined the reliability of MCs measurements. Intra-rater agreement was found to be excellent for Modic classification ($\kappa =$

0.88) and number of endplates with MCs ($\kappa = 0.94$) [20]. We also found good interrater agreement for Modic classification ($\kappa = 0.79$), which was similar to other studies (reported κ ranges from 0.80 to 0.91) [21,22]

Statistical Analysis

Descriptive statistics were used to depict the prevalence of MCs and the distribution of MCs in the lumbar region. χ^2 tests were used to compare the presence of MCs between the upper (L1/2, L2/3 and L3/4 discs) lower lumbar regions (L4/5 and L5/S1 discs) and between the cranial and caudal endplates. Linear and logistic regressions were used to examine the association between MCs and age. Statistical analyses were performed using STATA (Version 9.2, StataCorp LP, TX, USA).

Results

Prevalence of MCs

Of the 561 lumbar spines assessed, 55.6% (312 individuals, mean age 51.4 years) had some sort of MCs present and the remaining 44.4% (249 individuals, mean age 47.7 years) had no MCs present. Observed in 29.2% (164) of subjects, type 2 MCs were most common in our sample. While type 1 MCs were noted in only 6.4% (36) of subjects, type 1 and type 2 MCs presented together (either at the same endplate or separate endplates of a spine) in another 18.0% (101) of lumbar spines. Type 3 MCs were observed in only 2% (11) of spines and all of them were present together with type 2 MCs.

When the number of endplates with MCs was counted, 23.9% (134) of individuals had 2 endplates with MCs, 11.1% (62) had only 1 endplate involved, 8.0% (45) had 3 endplates with MCs and another 6.6% (37) of subjects had 4 endplates affected. The remaining 6.1% (34) of subjects with MCs had 5 or more endplates in the lumbar region affected. For one subject, MCs were present in all 11 endplates from the L1 through S1 vertebra.

Of the total 6171 lumbar vertebral endplates evaluated, 13.5% (830) had MCs of some type. Among the endplates with MCs, 64.2% (533) were evaluated as type 2 MCs, 16.0% (133) were type 1, 18.1% (150) were mixed type 1/2 and the remaining 1.6% (13) were noted as type 3 or mixed type 2/3.

Distribution of MCs in the lumbar region

The distribution of MCs by lumbar disc level is presented in Figure 1. Type 2 was the most common form of MCs at all lumbar disc levels. About three quarters (74.5%) of endplates with MCs were in the lower lumbar region (adjacent to L4/5 and L5/S1 discs) and were most frequent adjacent to the L5/S1 disc (Figure 1). The prevalence rates between the three intervertebral discs in the upper lumbar region (χ^2 test, $p=0.10$) were similar to one another. At the junction of the thoracic and lumbar regions, MCs were rare. In our sample, only 6 caudal endplates of T12/L1 discs were identified as having MCs.

Distribution of MCs between cranial and caudal endplates

Overall, there were 422 MCs present at the endplates cranial to a lumbar intervertebral disc and another 408 MCs in the caudal endplates. At any lumbar disc level, the presence of any type of MCs was not statistically different between the cranial and caudal endplates (χ^2 tests, $p>0.05$ for all disc levels).

Of the 824 MCs identified from L1/2 through L5/S1 disc levels (excluding the 6 MCs adjacent to T12/L1 discs), 77.9% (642) presented together at two adjacent endplates of a disc. In other words, MCs usually were present in pairs with respect to a lumbar disc. In addition, the specific types of MCs were concordant between the cranial and caudal endplates for 84.7% of the discs that had MCs at both adjacent endplates (Figure 2). The presence of MCs at one endplate was statistically significantly associated with the presence of MCs at the opposing endplate adjacent to the disc ($p<0.001$).

Distribution of MCs within the endplate

Among the 830 MCs identified, 66.0% (548) involved the majority of the AP diameter of the vertebral endplate and 17.5% (145) involved the full transverse diameter (all 11 sagittal slices). Of the 18.8% (156) of MCs that were of small AP size (1/3 of the AP diameter), 96 were primarily located in the anterior endplate, 45 were in the posterior endplate and the remaining 15 were centrally located.

The distributions of AP and transverse sizes of MCs are presented in Table 1. The size was more evenly distributed over the ordinal scale used to evaluate the transverse diameter than that used for the AP size. The shapes of MCs varied, complicating size estimates. Among the 315 MCs deemed to be of small or moderate transverse size, there were 163 (51.7%) MCs involving the entire AP diameter. On the other hand, of the 282 MCs assessed as small or moderate according to AP size, 130 (46.1%) were deemed to be large or very large based on transverse size.

Relationship between MCs and age

The presence of any type of MCs in the lumbar region was statistically associated with greater age (OR=1.07 for each additional year, $p<0.001$). When the associations between specific types of MCs and age were examined separately, similar results were obtained (OR=1.05, 1.08 and 1.06 for type 1, type 2 and mixed type 1/2 MCs, respectively, $p<0.001$).

Furthermore, an association between age and number of endplates with MCs was observed ($p<0.001$), with greater age associated with more endplates involved. An average increase of 17.4 years in age was associated with the presence of one more MCs in the lumbar region. In addition, age was statistically significantly associated with larger size of MCs (OR=1.04, $p<0.001$ for both AP and transverse size measurements).

Discussion

MCs were found to be common MRI findings in the lumbar spines of a general population sample of middle-aged Caucasian men, with type 2 MCs predominating. Mainly present in the lower lumbar region, MCs tended to affect both endplates adjacent to a disc

simultaneously, and commonly involved the entire anterior-posterior diameter of the vertebral body. The presence and size of MCs were clearly related to age, suggesting ageing or associated factors may play an essential role in the pathogenesis of MCs. These findings may provide a useful reference for clinical observations in radiology and spine care.

Using a strict criterion in MCs evaluation, the current study revealed that 55.6% of the subjects studied had one or more endplates with MCs in the lumbosacral region. This prevalence rate was relatively high, but is consistent with results of previous studies of MCs in 55% of Finnish male train engineers (age range 36–56 years) [9] and 49% of 44-year-old Danes [8]. According to systematic reviews MCs are more prevalent in back pain patients than in asymptomatic volunteers, in adults than in adolescents and younger children, and more common in Europeans than in Asians [23,24].

Type 2 was the predominant form of MCs in our sample. As type 1 MCs was assumed to reflect ongoing inflammation and type 2 to represent fatty degeneration [2], the predominant type of MCs may influence the association between MCs and back pain symptoms. Moreover, the conversion from one type of MCs to another under certain circumstances [2,5,25] may alter the distribution of types of MCs. In the present study, we also found that the coexistence of type 1 and type 2 MCs within an endplate was common. This mixed type is believed by some to be an intermediate stage in the pathological evolution between type 1 and type 2 MCs [4–6]. In concordance with most previous studies [2,8–10,16,25], type 3 MCs were rare in the current study and most were present together with type 2.

MCs were found to usually affect both the cranial and caudal endplates of a disc with the same type of MCs affecting both adjacent endplates. This distribution pattern of MCs occurring in pairs with respect to the disc was noted when MCs were first observed, but had not been subsequently documented [1,2]. Based on this phenomenon, MCs were regarded as a manifestation of disc degeneration, particular in severely degenerated discs [16,17]. Furthermore, recent longitudinal findings suggest that local disc conditions, such as disc degeneration, bulging and herniation, determine the occurrence of new MCs [15]. The close relationship between disc degeneration and MCs indicates that disc degeneration may be a key step in the development of MCs.

The size of MCs, such as from height, area or volume measurements, has been suggested as an indicator of severity of individual MCs [5,10,20,21]. Yet, the acquisition of a sound size measurement is challenging. The distribution of MCs within the vertebral endplate and marrow is complex, as evident in our study finding that MCs judged as small or moderate in size in one plane may be of large size in another. An ideal size measure would be a 3D volume measurement, which may not be realistic in most settings. The transverse size of MCs defined in this study was more evenly distributed across the ordinal scale, as compared to AP measurements of which about 2/3 MCs were rated as large, suggesting it may be a preferable index to use when considering MCs size. Estimating the transverse size of MCs by counting the number of sagittal slices containing MCs is also a simple, practical method. Yet, the method does pose a study limitation. While the real transverse diameters of vertebral bodies vary from subject to subject, the T2-weighted sagittal scans were fixed at 11 slices for all spines in this study. This could have introduced measurement error, particularly

in subjects who had very small or very large vertebral bodies. Another study limitation is that all subjects were men. However, in the vast majority of previous studies no significant differences were found in prevalence rates of MCs between men and women [23].

To our knowledge, the association between MCs and age has not been explored in a general population sample. In accordance with earlier observations that MCs are rare in children [12] and young adults [26], but common in middle-aged adults [9], the current study confirmed an association between age and the presence of MCs. Moreover, older age was associated with a greater number of endplates affected and MCs of larger size. The finding that MCs strongly relate to age suggests a degenerative nature of MCs, and an essential role for aging or associated factors in the pathogenesis of MCs. The similarities between disc degeneration and MCs, such as both being more common in the lower lumbar region and associated with age, as well as the close relationship between them, indicate that disc degeneration and MCs may share a common causal pathway.

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Figure 1.

The distribution of specific type of MCs by disc level. Percentages refer to a total of 561 discs examined at each level.

Figure 2.

The distribution pattern of single vs. paired MCs. MCs usually affect both opposing endplates of a lumbar intervertebral disc. Percentages refer to a total of 561 discs examined at each level.

Table 1

The distribution of anterior-posterior (AP) and transverse size of MCs.*

Size	Small	Moderate	Large	Very Large
AP	18.8% (156)	15.2%(126)	66.0%(548)	—
Transverse	13.4%(111)	24.6%(204)	33.1%(275)	28.9%(240)

* : The percentages referred to a total of 830 MCs endplates identified in this study. In the parentheses are the numbers of endplates with MCs.