The prevalence of MRI-defined spinal pathoanatomies and their association with Modic changes in individuals seeking care for low back pain.

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Abstract

Introduction: Modic changes are of increasing interest, however their age and gender prevalence are not well described. To date, the associations between Modic changes and other common vertebral pathologies have only been described in small samples (n <100). Our aim was, in a large dataset of people with low back pain, to i) describe the prevalence of a range of spinal pathoanatomies, and ii) examine the association between Modic changes and stages of intervertebral disc (IVD) pathology.

Method: Common pathologies were coded from the lumbar spine MRIs from 4,233 consecutive people imaged while attending a publicly-funded secondary-care outpatient facility in Denmark. Prevalence data were calculated by pathology and by vertebral level. Prevalence was also calculated by age and gender categories for Modic changes. The association between stages of IVD pathology (degeneration, bulge, herniation) and Modic changes at L4/5 and L5/S1 was expressed using prevalence ratios (PR) and 95% confidence intervals (CI).

Results: The prevalence of Modic changes and IVD pathology were greater in L4/5 and L5/S1, compared with the upper lumbar spine. There was no significant gender difference in prevalence of Modic changes (p=0.11). The prevalence of IVD disc pathology occurring concurrently with Modic changes ranged from 11.5-17.5% (Type 1), 8.5-12.7% (Type 2) and 17.1-25.6% (Type 1 and/or 2) while the prevalence occurring in the absence of Modic changes ranged from 0.5-6.3% (Type 1), 0.3-4.9 (Type 2), 0.8-9.7% (Type 1 and/or 2). The associated PR for IVD pathology occurring concurrently with Modic changes ranged from 1.8-29.2 (p< 0.05). The highest PR (29.2) was between degeneration and Modic changes, indicating that it is rare for Modic changes to occur without disc degeneration.

Conclusions: Spinal pathoanatomy was common in this population, particularly IVD pathologies, and a consistent trend of a relatively greater prevalence in the lower lumbar spine was identified. Modic changes were more likely to be present among individuals with IVD pathology than without, which may implicate mechanical factors as being one aetiological pathway for Modic changes, although other hypotheses may equally explain this association.

Introduction

Low back pain (LBP) is a common experience across the life course, with the lifetime prevalence as high as 80% in both adults [1] and adolescents [2]. Although most people experience some form of LBP at some point in their lives, a diagnosis for the pain experience can infrequently be determined on the basis of a spinal structural disorder [3]. Consequently, most LBP episodes are diagnostically classified as 'non specific LBP' and this remains a source of frustration for patients [4] trying to understand their problem and uncertainty for clinicians developing treatment plans.

Magnetic Resonance Imaging (MRI) is the gold standard modality for imaging spinal structures *in vivo* [5]. Despite the availability of high quality images, the associations between spinal pathoanatomy visible on MR images and symptoms of LBP remain uncertain, and an ongoing topic of debate among clinicians and researchers [6-9]. There are many factors which might explain why associations between spinal pathoanatomy and LBP symptoms remain equivocal, including differences in sampling methods between studies, heterogeneity in study populations, and the multifactorial and heterogeneous nature of LBP. However, an additional limitation of earlier studies is their inadequate sample sizes for population-based generalisations of the prevalence of pathoanatomic findings among people with LBP. Large population-based studies that sample individuals with LBP symptoms and individuals with no history of LBP are required to clarify associations between spinal pathoanatomy and various LBP symptoms. However, this type of study design is difficult given the high lifetime prevalence of LBP. As a precursor however, it is important to determine the prevalence of spinal pathoanatomy among individuals with LBP, and

particularly, distributions according to age and gender, using sufficiently large datasets to allow robust generalisation of such findings.

Recently, increased attention has been directed towards vertebral endplate signal changes (Modic changes), since unlike other MRI-derived pathoanatomic findings, Modic changes have been shown to more consistently have a positive association with LBP symptoms. A recent systematic review reported significant associations between Modic changes and LBP (odds ratios from 2.0-19.9) [10], with an average odds ratio of 4.5 [11]. This preliminary evidence may suggest that individuals with LBP and Modic changes represent a specific subgroup within the heterogeneous population of individuals with LBP, where clinical signs and symptoms have an underlying pathoanatomic basis for which focused therapies may be delivered. Vertebral endplate signal changes, first described in 1987 [12], have been classified into three types by Modic et al [13]. Type 1 is seen on a T2-weighted MRI as areas of increased signal intensity and on a T1-weighted MRI as decreased signal intensity extending from vertebral endplates into the vertebral body. Type 2 is described as increased signal intensity on both T1- and T2-weight images. Type 3 is presumably bone sclerosis and is visualised as decreased signal intensity on both T1- and T2-weighted images.

Modic changes are believed to represent a sequential pathway in the same pathologic process, starting at an acute inflammatory phase (Type 1) then progressing to a granulation and marrow replacement phase (Type 2). Subsequent to this, Type 2 Modic changes may either normalise, progress to the bone sclerotic phase known as Type 3 Modic changes, or following a new herniation, revert to Type 1 [14,15]. Although this theoretic progressive pathway has been confirmed by prospective studies [15,16], there is also evidence that individuals may revert between all stages [14,15]. The aetiopathogenesis of Modic changes, specifically that of Type 1, has been

hypothesised as involving two pathways – mechanical and bacterial [17]. A progressive degenerative pathway involving the intervertebral disc (IVD), from degeneration to bulging to herniation of nuclear material, imparts maladaptive mechanical forces on the vertebral endplate [18-20], potentially leading to micro-fractures and concurrent biochemical sequelae [21-24], manifesting as an inflammatory response within and adjacent to bone tissue, defined as Modic change Type 1. Notably, histology studies provide evidence to confirm this supposition [13]. The bacterial pathway has received less attention, yet evidence for this mechanism and therapeutic applications are accumulating [17].

Similar to the sample size limitations of studies reporting the prevalence of spinal pathoanatomy, the majority of studies reporting associations between the presence of Modic changes and IVD pathology have had sample sizes of N=58-100 [25,26]. The available evidence contains some uncertainty regarding the aetiology of Modic changes. Furthermore, little information is available regarding the prevalence of Modic changes across the life course. Studies with a large dataset are required to provide robust estimates of the prevalence of Modic changes in people with LBP and the associations between Modic changes and the pathway of IVD pathology. Therefore, the aim of this study was to assemble a large case series of patients who were investigated with MRI for their LBP to i) describe the prevalence of a range of spinal pathoanatomies, and ii) examine the association between Modic changes and stages of IVD pathology.

Materials and methods

Participants

All patients who attended the Spine Centre of Southern Denmark and underwent a spinal MRI and had a narrative report generated between the years 2000-2008 were eligible for inclusion in this

study (n=5,919). This spine centre is a publicly-funded secondary-care outpatient facility specialising in the diagnosis and treatment of spinal pain. Patients were referred to the Centre by primary care clinicians (chiropractors and general practitioners). The study was approved by the Institutional Review Board and performed following the Declaration of Helsinki principles.

Imaging and reporting

A standard lumbar MRI protocol utilising a 0.2 T MRI system (Magnetom Open Viva, Siemens AG, Erlangen, Germany) had been used. All patients were imaging in a supine position. The standardised T1 and T2 imaging protocol consisted of one localizer and four imaging sequences. Axial images were performed on the three lower lumbar levels. If serious pathology was present or IVD herniations were located at higher lumbar levels, relevant supplementing sequences were performed (manuscript under review).

All images over this eight-year period were read by one of two experienced musculoskeletal radiologists. MRI narrative reports dictated by these radiologists were used as the data source for this study. Both radiologists performed descriptive radiology where they reported all abnormal findings, regardless of their clinical significance and summarized the clinically important findings in the narrative conclusion. At this institution, inter-rater reliability studies have shown convincing reliability [27,28]. From 2004, the radiologists routinely read the MRIs from a computer console. Of the 5,919 MRI narrative reports available, 1686 (28.5%) were excluded from this study on the basis of three exclusion criteria: MRI scan performed on the thoracic or cervical spine (n=1206), repeat MRI scan on the same individual (n=478), and scan date not reported (n=2). The final sample size was therefore n=4,233.

Coding of spinal MRI narrative reports

Information regarding the presence of spinal pathoanatomy was extracted from the MRI narrative reports only and was transformed into quantitative data using an electronic coding matrix developed with FileMaker Pro 9 (FileMaker Inc, CA, USA). The matrix allowed coders to nominate the presence of 14 possible pathologies including: intervertebral disc degeneration, intervertebral disc bulge, intervertebral disc herniation, nerve root compromise, Modic change Type 1, Modic change Type 2, spondylolisthesis (anterior or retro) with or without spondylosis, stenosis, scoliosis, osteophytes, facet joint arthrosis, other endplate irregularities (including Scheuermann, defects, irregularities), red flags (tumour, fracture, tuberculosis), and high intensity zones. The coders used the matrix to indicate whether pathoanatomic features were reported as present between vertebral levels T12-L5, including an option to nominate compromise of the S1 nerve root. For the purpose of coding, a vertebral segment was defined as extending from the superior vertebral endplate to the caudal aspect of the intervertebral space below, for example the T12 vertebra and T12/L1 intervertebral space. All coding was performed by three final year physiotherapy students using coding rules developed by the research team. Each student performed approximately one third of the coding of the dataset (n = 1411×3). We have previously examined the inter-rater reliability of this process using trainee clinicians and found it to be excellent (mean percentage agreement across 14 pathoanatomic categories = 99.4%, kappa range for all pathologies = 0.74-1.00, kappa range for Modic changes = 0.86 to 1.00), and in high agreement with highly trained coders (percentage agreement range = 97.8-98.1%) (manuscript under review).

Data analysis

Prevalence data were calculated by pathology and by vertebral level. In addition, prevalence was also calculated by age and gender categories for Modic changes, and the differences between categories were explored with Chi square tests. Age was grouped into 5-year bands to aid clinical

interpretations. The association between stages of IVD pathology (degeneration, bulge, herniation) and Modic changes at L4/5 and L5/S1 was expressed using prevalence ratios (PR) and 95% confidence intervals (CI). All data were analysed using SPSS Statistics 17.0 (SPSS Inc, Chicago, IL, USA) and Microsoft Excel 2008 (Microsoft Inc, Redmond, WA, USA).

Results

A total of 4,233 spinal MRI narrative reports (51.1% female) were examined. Figure 1 displays the age and gender distribution of the cohort (actual summary data are included as Appendix 1).

Table 1 lists the overall prevalence of each of the 14 pathoanatomic categories and prevalence by vertebral level (T12-S1). Stages of IVD pathology were the most common pathoanatomic finding and like most other pathoanatomic findings, IVD pathology varied across vertebral levels (50.8-85.7%). The prevalence of Modic changes and stages of IVD pathology were greater in the lower lumbar spine, particularly L4/5 and L5/S1 (11.2-61.2%), compared with the upper lumbar spine (0.4-35.2%). The prevalence of IVD pathology by age category is illustrated in Figure 2. Figure 3 displays the prevalence of Modic change types according to age while Figure 4 displays the prevalence of Modic change Type 1 and/or 2 according to gender. There was no significant gender difference in prevalence of Type 1 and/or 2 Modic changes (p=0.11). The associations between the presence of Modic changes and stages of IVD pathology at L4/5 and L5/S1 are summarised in Figure 5. The prevalence of IVD disc pathology occurring concurrently with Modic changes ranged from 11.5-17.5% (Type 1), 8.5-12.7% (Type 2) and 17.1-25.6% (Type 1 and/or 2) while the prevalence occurring in the absence of Modic changes ranged from 0.5-6.3% (Type 1), 0.3-4.9 (Type 2), 0.8-9.7% (Type 1 and/or 2). The associated PRs for IVD pathology occurring concurrently with Modic changes ranged from 1.8-29.2 (p<0.05). The highest PR (29.2) was

between degeneration and Modic changes, indicating that it is rare for Modic changes to occur without disc degeneration. The prevalence of serious pathology was 0.5% in this cohort.

Discussion

Relative to earlier studies, this study utilised a very large dataset of MRI narrative reports to describe prevalence of spinal pathoanatomy among individuals seeking care for LBP, as well as associations between stages of IVD pathology and Modic changes. Spinal pathoanatomy was common in this population, particularly IVD pathologies, and a consistent trend of a relatively greater prevalence in the lower lumbar spine was identified. Modic changes were more likely to be present among individuals with IVD pathology than without, which might support a mechanical aetiological pathway for Modic changes, although there are a number of other hypotheses that could equally explain this association [17].

This study focussed on reporting the prevalence of IVD pathology and Modic changes and the likelihood of their co-existence in a population with LBP. Nonetheless, considering sample size limitations in earlier studies, we chose to also report the prevalence for a range of other spinal pathoanatomies in an attempt to provide clinicians and researchers with robust prevalence estimates for spinal pathoanatomy. The prevalence of IVD pathology we observed was somewhat higher than that reported in the literature. For example, in a study of 474 symptomatic patients referred for MRI, Modic et al reported a prevalence of 68% for IVD degeneration [13] compared with 44.1 % by Baithwaite [25] and 78% by Caragee [26]. The higher prevalence in the current study may be due to the majority of patients referred to the Spine Centre being people with chronic spinal pain or due to differences in inclusion criteria. We identified that the prevalence of IVD pathology

increased with age, and this finding is consistent with other reports in symptomatic [29] and asymptomatic populations [30], highlighting progressive spinal degeneration across the life course. Although the prevalence appeared to decrease after 80 years of age, these estimates should be interpreted with caution owing to the considerably smaller sample size in these upper age categories (n=46). Intervertebral disc degeneration was common in late adolescence and had a higher prevalence than IVD bulge and herniation, albeit the sample size in this age category was low (n=65). Nonetheless, these data mirror the degenerative stages of IVD pathology, such that degeneration precedes more serious pathology like bulge, herniation and Modic changes. The higher prevalence of IVD pathology in the lower lumbar spine compared with more cranial levels is consistent with observations in the literature [13,31,32] and is likely to be attributable to greater loading at these levels [33].

Like other pathoanatomies, the prevalence of Modic changes was also most common in the lower lumbar spine and may be due to the relatively greater compression and shear forces imposed at these vertebral levels compared with more cranial levels [33]. The overall prevalence of Modic changes was similar to median prevalence reported in a systematic review examining this issue among cohorts with and without LBP (Type 1: 15 %, Type 2: 24 %) [10]. The prevalence profile of Modic changes mirrored that of IVD degeneration and herniation where there was an increasing prevalence with age up to 45 years, after which it plateaued. This finding is also consistent with earlier studies which report a peak prevalence in middle-age [10]. Notably, the prevalence of Type 2 Modic changes was lower than Type 1, particularly during early adulthood and the difference became less pronounced later in the life course. This finding may relate to the evolutionary pathologic pathway of Modic changes, where Type 1 changes generally precede Type 2 [14,15]. There was no gender difference in the prevalence of Modic changes, consistent with data from the

general population [34]. Although females appear to have a higher prevalence of Modic changes between the ages of 66-75, these data should be interpreted in the context of a relatively low sample size in this age category.

The data suggest that Modic Type 1 precedes the onset of Modic Type 2 (Figure 3) but this needs to be cautiously observed due to the limitations on inference from cross-sectional data.

The hypothetical aetiology of Modic changes occurring through a mechanical pathway might be supported by our results, though it is also possible that such changes are a by-product of other aspects of disc degeneration. Modic changes were 1.8-29.2 times more likely to be present with IVD pathology than in the absence of IVD pathology. However, these PRs should be interpreted in the context of the prevalence data reported (Figure 5). Although some prevalence estimates were very high, this may be an artefact of low prevalence of Modic changes co-existing with IVD pathology (8.5-25.6%). At L4/5, the prevalence of Modic changes occurring with IVD pathology was similar between IVD degeneration and bulging, but higher for IVD herniation. A similar pattern was not observed at L5/S1, where the PRs were relatively equal. A strong longitudinal association between a previous IVD herniation followed by Modic changes has been reported [35] and this observation is consistent with the theory of mechanical factors leading to the development of Modic changes [17].

A significant strength of this study is that prevalence data, and associations between spinal pathoanatomy and Modic changes, were based on a very large sample size. To our knowledge, the sample size we used is the largest reported in the literature to date. The electronic coding matrix we developed provided an efficient and secure mechanism to transform a broad range of pathoanatomic information from MRI narrative reports to a quantitative format using a process for which reliability

has previously been established (manuscript under review). The population described in this study was attending a secondary-care facility for LBP. Although debate exists regarding the clinical relevance of pathoanatomic findings from MRI, we cannot generalise the prevalence data beyond people seeking care for LBP.

An important limitation of this study is that individuals with no history of LBP were not sampled and therefore we cannot address the issue of the clinical relevance of pathoanatomy to LBP symptoms. Further large-scale studies are required to clarify this issue given the reports of spinal pathoanatomic findings among asymptomatic individuals [30,8,9], including Modic changes [36]. These data in this study show a trend towards an increased reporting of Modic changes over time, despite the routine reporting of Modic changes since 1999 based on a suspicion that they were associated with pain. We believe this time trend reflects a shift in the referral patterns to the Spine Centre, as over time, referrals had an increased proportion of herniation and post-herniation patients. Finally, this study was cross-sectional in design and therefore we neither infer causation between IVD pathology and Modic changes nor comment with certainty regarding the natural history of spinal pathoanatomy across the life course or the pathologic sequence of Modic changes.

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Figure Captions

- Figure 1 Age and gender distribution of the cohort (n=4233).
- Figure 2 Prevalence (%) of intervertebral disc (IVD) degeneration, bulge and herniation according to age category.
- Figure 3 Prevalence of Modic changes according to age category and type of Modic change (Type 1, Type 2, Type 1 and/or 2). Individuals with Type 1 and/or 2 changes are only counted once.
- Figure 4 Prevalence of Modic change Type 1 and/or 2 by age and gender.
- Figure 5 Prevalence of individuals with different stages of intervertebral disc (IVD) pathology (degeneration, bulge, herniation) occurring both with and without Modic changes at L4/5 (A-C) and L5/S1 (D-F). Prevalence ratios (95% confidence intervals) for the presence of each type of Modic change occurring with disc pathology are presented.

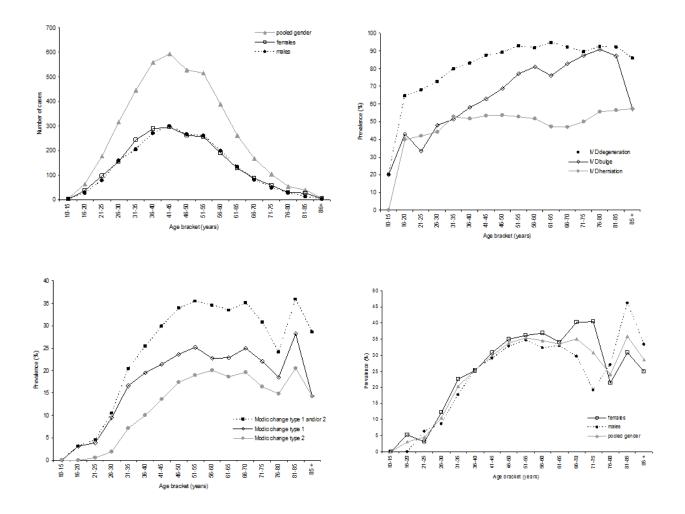


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Figure 4 Prevalence of Modic change Type 1 and/or 2 by age and gender.

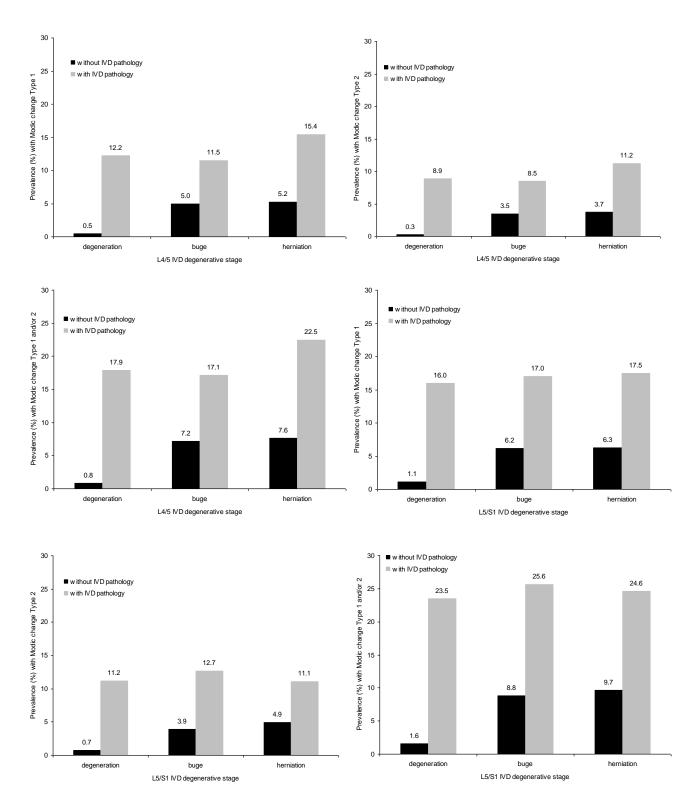


Figure 5 Prevalence of individuals with different stages of intervertebral disc (IVD) pathology (degeneration, bulge, herniation) occurring both with and without Modic changes at L4/5 (A-C) and L5/S1 (D-F). Prevalence ratios (95% confidence intervals) for the presence of each type of Modic change occurring with disc pathology are presented.

Modic prevalence

Table 1 Prevalence of 14 possible pathoanatomies, expressed as a percentage, overall and by vertebral level and segment.

Pathoanatomic category	Vertebral level and segment							
	Any	T12,	L1,	L2,	L3,	L4,	L5,	S1 nerve
	level*	T12/L1	L1/L2	L2/L3	L3/L4	L4/L5	L5/S1	root
Modic change Type 1	19.8	0.3	1.0	2.3	3.4	7.6	9.7	
Modic change Type 2	13.2	0.2	0.8	1.7	1.6	5.5	6.8	
Modic change Type 1 and/or 2 #	27.4	0.4	1.7	3.5	4.3	11.2	14.3	
Intervertebral disc bulge	65.2	3.1	9.1	15.8	23	40.7	32.9	
Intervertebral disc degeneration	85.7	13.8	20.3	26.8	35.2	61.2	58.1	
Intervertebral disc herniation	50.8	0.7	1.3	2.9	6.6	24.3	30.7	
Facet joint arthrosis	11.7	0.1	0.4	1.1	3.6	8.7	6.9	
High intensity zone (HIZ)	13.6	0	0.3	1.2	3	7.3	5.4	
Osteophytes	22.5	3.2	6.7	8.5	6.9	7.7	6.7	
Nerve root compromise	28.7	0	0.2	0.5	1.4	3.5	13.5	13.6
Scoliosis	8.8	1.8	1	2.1	2.4	2.8	0.8	
Spondylolisthesis (antero, retro)	14.9	0	0.3	1.4	2.7	6.6	6.1	
Stenosis	15.4	0	0.4	2.1	4.8	9.9	5.6	
Red flags (cancer, fracture, tuberculosis)	0.5	0.1	0.3	0.1	0.2	0.1	0.1	
Other endplate irregularities (Scheuermann, defects, irregularities)	19.0	6.8	4.2	4.5	3.5	5.5	4.4	

Modic prevalence

* Prevalence of a pathoanatomic finding at one or more vertebral levels/segments, # refers to the presence of either type of Modic change where individuals are counted only once.

Appendix

Appendix 1 Age and gender distribution of the participants included in the cohort, expressed as the number of cases (percentage).

Age category (years)	Females	Males			
10-15	3 (60.0)	2 (40.0)			
16-20	38 (58.5)	27 (41.5)			
21-25	98 (55.4)	79 (44.6)			
26-30	155 (49.2)	160 (50.8)			
31-35	243 (54.4)	204 (45.6)			
36-40	290 (51.8)	270 (48.2)			
41-45	295 (49.6)	300 (50.4)			
46-50	263 (49.7)	266 (50.3)			
51-55	257 (49.7)	260 (50.3)			
56-60	190 (49.0)	198 (51.0)			
61-65	129 (49.0)	134 (51.0)			
66-70	87 (51.8)	81 (48.2)			
71-75	57 (54.8)	47 (45.2)			
76-80	28 (51.9)	26 (41.8)			
81-85	26 (66.7)	13 (33.3)			
≥ 86	4 (57.1)	3 (42.9)			
Total	2163 (51.1)	2070 (48.9)			