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Assessing the Association of Modic Changes and Clinical Outcome Before and After One-Level Lumbar Fusion

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ABSTRACT

AIM: To assess the association between Modic changes (MCs) and clinical outcomes in patients undergoing one-level lumbar fusion surgery.

MATERIAL and METHODS: A retrospective cohort study included patients (>18 years) with single-level DDD treated with one-level lumbar fusion from 2016 to 2020 at a single center. Preoperative and 2-year postoperative outcomes were collected, including the Visual Analog Scales (VAS-back and VAS-leg), Oswestry-Disability-Index (ODI), Core-Outcome-Measures-Index (COMI-back) and Short-Form-Health-Survey-36 (SF-36). The association of patient reported outcomes measurements (PROMs) with preoperative MCs on MRI were assessed. Subjects with MC2 and MC3 were pooled in the No-MC1 group and compared to MC1 group. Continuous variables were compared using independent or paired t-tests, and non-parametric data with Mann-Whitney U or Wilcoxon signed-rank tests. Categorical variables were analyzed with Chi-square or Fisher's exact test.

RESULTS: Preoperatively, the MC1 group exhibited higher ODI scores (47.05 ± 14.60 vs. 36.84 ± 13.12 ; $p=0.026$) and lower SF-36-PCs (30.80 ± 7.22 vs. 35.61 ± 5.17 ; $p=0.021$) compared to the No-MC1 group. Postoperatively, no significant intergroup differences were observed. However, the MC1 group demonstrated greater improvements in Δ ODI, Δ VAS-back, and Δ SF-36-PCs. Intra-group analysis revealed significant postoperative improvements in ODI, VAS-back, and VAS-leg in the MC1 group (e.g., Δ ODI = 29.14 ± 13.27 ; $p=0.007$), while the No-MC1 group improved in ODI and SF-36-Mental Components (Δ ODI = 21.10 ± 12.26 ; $p=0.023$; Δ SF-36-MCs = 5.98 ± 12.44 ; $p=0.003$). Notably, 7 patients did not reach the Δ ODI minimum clinically important difference, with higher prevalence in the No-MC1 group (71.4%).

CONCLUSION: One-level spinal fusion improves clinical outcomes in symptomatic degenerative disc disease. Patients with MC1 demonstrate greater functional and pain-related improvements compared to those with MC2 or MC3.

KEYWORDS: Degenerative Disc Disease, Modic Changes, Spinal Fusion, Low Back Pain, Treatment

ABBREVIATIONS: LBP: Low back pain, DDD: Degenerative disc disease, MRI: Magnetic resonance imaging, MD: Modic change, T1WI: T1-weighted imaging, T2WI: T2-weighted imaging, ASA: American Society of Anaesthesiologists score, VAS: Visual analog scale, ODI: Oswestry Disability Index, COMI-back: Core Outcome Measures Index for the back, SF-36: Short Form Health Survey 36, NPRS: Numeric pain rating scale, MCID: Minimal Clinically Important Difference

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■ INTRODUCTION

Low back pain (LBP) is a prevalent and debilitating condition among the general population (8,18). LBP arises from several causes, including traumatic injuries, degenerative changes, infections and tumors. The age-related spinal degeneration (i.e. spondylosis) affects the facet-joints, the intervertebral disc, the vertebral endplates and the ligamentum flavum, thus complicating the identification of the primary etiological factor. Degenerative disc disease (DDD) is frequently associated with LBP (22) and is one of several factors, though not the only one, contributing to the changes observed in the vertebral body marrow and vertebral endplate on magnetic resonance imaging (MRI) of the spine. These MRI signal alterations were first described by de Roos et al. (4), and later classified by Modic et al. (23).

The Modic changes (MCs) are classified into 3 types: Type 1 (MC1) is characterized by a hypo-intense signal in T1-weighted imaging (T1WI) and hyperintense signal in T2-weighted imaging (T2WI) and it is indicative of vertebral body edema and hyper-vascularity caused by inflammation; Type 2 (MC2) exhibits a hyperintense signal both in T1WI and in T2WI, reflecting bone marrow ischemia and the conversion of red haemopoietic bone marrow into fatty marrow; Type 3 (MC3) displays a hypointense signal on both T1WI and in T2WI, and is considered a sign of subchondral bone sclerosis. Previous studies showed a good intra-observer and inter-observer agreement of the Modic classification (6,12,16), affirming its reliability and ease of application in the daily clinical activity (34). Various etiological factors have been identified as potential triggers for MC, including end-plate fissures and microfractures, slow-virulent discitis, autoimmunity and genetic predisposition, all of which can initiate the inflammatory cascade in bone marrow that leads to nociceptive stimulation. Bone biopsies findings show that MC1 is associated with increased bone turnover, possibly due to the inflammatory process, while MC2 show reduced bone formation/remodelling and MC3 is characterized by sclerotic changes (26).

Both symptomatic and asymptomatic subjects may present MCs. Previous studies show a significant variability regarding the association of LBP with MCs (9,10,15,34), and even less consistency observed in the correlation between MC1, MC2 and LBP. While some authors reported a positive association for both MC1 and MC2 with LBP (2,20,24,33), others found this association only with MC1 (30), and further studies found no association with either type (1,14,27). MCs have also been associated with clinical outcomes after lumbar fusion, suggesting that patients improve after fusion regardless of MCs (5,7,11,17,19,25,31). The primary aim of this study was to assess the association of MCs and Oswestry Disability Index (ODI) in patients undergoing one-level spinal fusion surgery. We investigated in particular any difference between MC1 and other types of MCs together. The secondary aim of the study was to assess the association of MCs and further clinical outcomes in the same cohort.

■ MATERIAL and METHODS

Study Design and Patients

Design: Retrospective cohort study.

Patients: A prospectively collected single-center spine surgery registry was queried to evaluate patients with diagnosis of lumbar degenerative discal disease treated with vertebral arthrodesis in our Institute from 2016 to 2020.

All patients were informed about the study and signed informed consent. This report follows STROBE guidelines.

Inclusion Criteria

- Age ≥ 18 y/o
- Diagnosis of single level degenerative disc disease treated with one-level lumbar fusion.
- Availability of preoperative lumbar MRI
- Minimum follow-up ≥ 2 years

Exclusion Criteria

The reasons for ineligibility were:

- incomplete pre-operative and post-operative clinical and radiological data
- previous spinal surgery at the same level
- early perioperative complications needing surgical treatment that could affect the outcomes.
- absence of MCs.

Modic changes (MCs) were assessed on preoperative lumbar spine MRI by two of the authors (A.N. and D.C.). In cases of non-univocal findings, a third author (F.L.) provided the final classification. Subjects with MC2 and MC3 were pooled in the No-MC1 group and compared to MC1 group.

Study Variables

Age, gender, American Society of Anaesthesiologists score (ASA) of patients were collected preoperatively. Type of surgery (type of fusion, level of fusion) was analysed. Clinical status was assessed with back and leg visual analog scale (VAS-back, VAS-leg), Oswestry Disability Index (ODI; 0%-20%= mild disability, 21%-40%= moderate, 41%-60%= severe, 61%-80%= crippled, 81%-100%= bedridden), Core Outcome Measures Index for the back (COMI-back; 0= no disability, 10= complete disability) and Short Form Health Survey 36 (SF-36; 0= greatest health limitation, 100= no health limitation) were collected preoperatively and postoperatively at 24 months.

Data Collection

Eligible patients were identified from the spine registry of the institution (SpineREG), for the period between 2016 and 2020. All patients who met the inclusion criteria and showing no exclusion criteria were enrolled.

For each case, radiographic variables were assessed in the preoperative, postoperative radiographic examination obtained within the first 12 weeks (once the patient was able to stand without any support) and clinical variables were as-

sessed before surgery and at 3-, 6-, 12- and 24-months FU. Only patients with complete baseline and 24-month follow-up PROMs were included in the present analysis (complete case analysis). Interim follow-up data (3, 6, and 12 months) were not uniformly available across all patients and were therefore not included in the main comparisons.

The measurements were made with Sectra PACS IDS7 (Sectra AB, Linköping, Sweden). Two observers independently measured all the variables.

Statistical Analysis

Data were analyzed using SPSS (version 21.0, IBM, Armonk, NY, USA). Normality was assessed with the Shapiro–Wilk test. Continuous variables were expressed as mean $\pm$ SD (with 95% confidence intervals reported for main outcomes) and categorical as counts/percentages. Between-group comparisons (MC1 vs No-MC1) used independent t-test or Mann–Whitney U; within-group (pre- vs postoperative) used paired t-test or Wilcoxon signed-rank test. Categorical variables (e.g., ASA) were compared with Chi-square or Fisher's exact test. The ODI MCID (Δ ODI $\geq$ 12.7 points) defined clinically relevant improvement. Significance was set at $p < 0.05$.

RESULTS

Participants

Forty patients (Females= 25; Males= 15), with a mean age of 49.6 ± 12.8 years, scheduled for single-level lumbar fusion were included in the study (Table I). Twenty-one patients (52.5%) were included in the MC1 group, while the No-MC1 group consisted of 19 patients (47.5%). According to the ASA score, 18 patients (45.0%) were ASA I, 18 (45.0%) ASA II, and 4 (10.0%) ASA III.

Inter-group Comparison

Patients in the MC1 group had higher preoperative ODI and lower preoperative SF-36 Physical Components (SF-36-PCs) compared to patients in the No-MC1 group (Preoperative ODI was significantly higher in the MC1 group compared with the

No-MC1 group (47.1 ± 14.6 vs 36.8 ± 13.1 ; mean difference = -10.2 , 95% CI -19.1 to -1.3 , $p = 0.026$). Similarly, the preoperative SF-36 physical component score was significantly lower in the MC1 group compared with the No-MC1 group (30.8 ± 7.2 vs 35.6 ± 5.2 ; mean difference = 4.8 , 95% CI 0.8 to 8.9 , $p = 0.021$). No other outcomes demonstrate a significant difference between the two groups preoperatively (Table II). ANOVA testing for preoperative ODI across Modic groups showed no significant differences ($F(4,72) = 1.71$, $p = 0.156$, partial $\eta^2 = 0.087$, observed power = 0.50). No significant difference was found between MC1 and No-MC1 after surgery. Δ ODI, Δ VAS-back and Δ SF-36-PCs were higher in the MC1 group (Table II). Seven patients did not reach the Δ ODI MCID of 12.7 points after surgery: 2 of the MC1 group, 5 of the No-MC1 group.

Table I: Baseline Characteristics of the Study Cohort

Characteristics	n (%)
Females	25 (62.5)
Males	15 (37.5)
MC1	21 (52.5)
MC2	14 (35)
MC3	5 (12.5)
DDD L1-L2	1 (2.5)
DDD L3-L4	7 (17.5)
DDD L4-L5	9 (22.5)
DDD L5-S1	23 (57.5)
ASA I	18 (45)
ASA II	18 (45)
ASA III	4 (10)

MC: Modic change, **DDD:** Degenerative disc disease, **ASA:** American Society of Anaesthesiologists score.

Table II: Comparison of Preoperative and Postoperative Patient-Reported Outcome Measures Between the Two Groups, as Well as Difference (Δ) between Preoperative and Postoperative Status

	Preoperative			Postoperative			Δ		
	MC1	No-MC1	p-value	MC1	No-MC1	p-value	MC1	No-MC1	p-value
ODI	47.05 (14.60)	36.84 (13.12)	0.03	17.90 (13.88)	15.74 (11.70)	0.60	29.14 (13.27)	21.10 (12.26)	0.05
VAS-back	8.10 (1.26)	7.00 (2.80)	0.11	2.67 (2.59)	3.32 (2.16)	0.40	5.43 (2.29)	3.68 (3.07)	0.05
VAS-leg	6.10 (3.16)	6.11 (3.65)	0.99	2.33 (2.99)	2.32 (2.85)	0.99	3.76 (2.91)	3.79 (3.87)	0.98
COMI_back	7.95 (1.56)	7.53 (1.68)	0.41	2.38 (2.33)	3.16 (1.77)	0.25	5.57 (2.77)	4.37 (1.86)	0.12
SF36 MCs	43.49 (13.06)	44.32 (8.81)	0.83	54.56 (9.68)	50.22 (12.44)	0.24	-10.82 (14.88)	-5.98 (9.20)	0.25
SF36 PCs	30.80 (7.22)	35.61 (5.17)	0.02	45.86 (7.94)	42.82 (8.43)	0.27	-15.17 (8.97)	-6.67 (8.32)	0.01

MC: Modic change, **ODI:** Oswestry disability index, **VAS:** Visual analog scale, **COMI:** Core outcome measures index, **SF36 MCs:** Short form 36 mental components, **SF36 PCs:** Short form 36 physical components.

Table III: Comparison of Preoperative and Postoperative Patient-Reported Outcome Measures of Each Group

	MC1 Group			No-MC1 Group		
	Pre-op	Post-op	p-value	Pre-op	Post-op	p-value
ODI	47.05 (14.60)	17.90 (13.88)	0.01	36.84 (13.12)	15.74 (11.70)	0.02
VAS-back	8.10 (1.26)	2.67 (2.59)	0.32	7.00 (2.80)	3.32 (2.16)	0.29
VAS-leg	6.10 (3.16)	2.33 (2.99)	0.01	6.11 (3.65)	2.32 (2.85)	0.19
COMI_back	7.95 (1.56)	2.38 (2.33)	0.89	7.53 (1.68)	3.16 (1.77)	0.07
SF36 MCs	43.49 (13.06)	54.56 (9.68)	0.41	44.32 (8.81)	50.22 (12.44)	0.01
SF36 PCs	30.80 (7.22)	45.86 (7.94)	0.25	35.61 (5.17)	42.82 (8.43)	0.20

Pre-op: Preoperative, **Post-op:** Postoperative, **MC:** Modic change, **ODI:** Oswestry disability index, **VAS:** Visual analog scale, **COMI:** Core outcome measures index, **SF36 MCs:** Short form 36 mental components, **SF36 PCs:** Short form 36 physical components.

Intra-group Comparison

The intra-group analysis showed that ODI, VAS-back, and VAS-leg improved significantly in the MC1 group (Δ ODI = 29.1 ± 13.3 ; 95% CI 23.2 to 35.1; $p = 0.007$; Δ VAS-back = 5.4 ± 2.3 ; 95% CI 4.4 to 6.5; $p = 0.032$; Δ VAS-leg = 3.8 ± 2.9 ; 95% CI 2.5 to 5.0; $p = 0.009$). In the No-MC1 group, significant improvements were observed in ODI (Δ ODI = 21.1 ± 12.3 ; 95% CI 15.2 to 27.0; $p = 0.023$) and in SF-36 mental component scores (Δ SF-36-MCs = 6.0 ± 12.4 ; 95% CI -0.1 to 12.1; $p = 0.003$) (Table III).

DISCUSSION

This retrospective study assessed the association between MCs and clinical outcomes in patients with symptomatic lumbar degenerative disc disease undergoing one-level lumbar spine fusion, before and after surgery, at a minimum follow-up of 2 years. Our findings demonstrate that clinical outcomes improved in most of patients after surgery, regardless of MC type. Patients presenting MC1 exhibited higher levels of disability prior to surgery and showed a greater improvement after fusion compared to No-MC1 patients. Nevertheless, the two groups did not show any significant difference after surgery.

We found that patients with MC1 showed worse level of disability and worse physical health compared to No-MC1. However, pain intensity, mental health, and COMI were similar in both groups. The current literature is inconclusive whether MCs are associated with LBP. Saukkonen et al. (28), investigated a cohort of 1512 individuals. They highlighted a significant correlation between MC, especially MC1, and patients experiencing LBP. Additionally, a large cross-sectional study by Mera et al. (21), involving 814 individuals, showed a significant association between MC1 and LBP. Brinkjiki et al. published a meta-analysis in 2015 encompassing 14 studies including over 3000 patients (3). Their data revealed a notable association between LBP and MC1, although MC overall did not exhibit a significant correlation with LBP. More recently, Van der Graaf et al. provided a comprehensive summary of the evidence concerning the association between MRI find-

ings and LBP in a review including 31 studies (32). Among these studies, 67% reported a positive correlation between all types of MC and LBP, while 100% of the studies identified a significant association between MC1 and LBP. Kovaks et al. conducted a case-control study involving the examination of lumbar MRIs from 304 patients, comprising 240 individuals with LBP and 64 pain-free controls (15). In contrast to our findings and the aforementioned results, the study failed to establish a significant correlation between LBP and MCs. They even found a lower prevalence of MCs in subjects with LBP compared to controls without LBP (80.4% vs 87.5%). Similarly, Kleinstück et al. reported analogous outcomes in a prospective study investigating the relationship between MRI-detected degenerative changes and the outcomes of conservative treatment in a cohort of 48 patients (13). Notably, they found no correlation between pain levels and MCs. According to a 2018 systematic review and meta-analysis conducted by Herlin et al. (9), the association between MCs and LBP appears to be inconsistent. They found only 6 out of 13 studies reporting a significant positive association between MC1 and LBP. MC2 was positively associated with LBP in 4 out of 10 studies. The authors concluded that there is no significant difference between MC1 and MC2 and their association with LBP. It is plausible to infer that the divergent outcomes may be attributed to the heterogeneity of sample characteristics, gender distribution, clinical endpoints, study quality and the prevalence rates of both MCs and LBP. Although current literature and our data struggle to find a clear consensus, it seems that MC1 are closely associated with LBP, reflecting the active inflammatory process within the vertebral bone marrow that triggers pain signals. MC2 and MC3, which involve fatty replacement and subchondral bone sclerosis respectively, are considered more stable and chronic stages of the degenerative process. These later stages may not generate the same inflammatory response or active nociceptive stimulation, potentially leading to a weaker association with the experience of pain.

At 2-years follow-up after single-level lumbar fusion, none of the assessed outcomes showed a significant difference between the two groups anymore. This is because MC1 patients reported a greater improvement in ODI, VAS-back and SF-36-

PCs compared to No-MC1 patients. Looking at the intra-group variation before and after surgery, ODI improved significantly in both MC1 and No-MC1 groups. However, pain improved significantly only in MC1 and SF-36-MCs only in No-MC1. It is worth noting that, although not statistically significant, No-MC1 subjects had a decrease of both LBP and leg pain (VAS_ back from 7.00, SD= 2.81 to 3.32, SD= 2.16; VAS_leg from 6.11, SD= 3.65 to 2.32, SD= 2.85) and MC1 patients had an increase of SF-36-MCs. Jiao et al. observed improvements in pain and ODI among patients with MC1, MC2 and those without MC (11). The MC1 group exhibited greater improvements in ODI and VAS; however, the authors did not conduct a statistical analysis comparing the MC1 group with the other groups in order to determine the significance of this finding. Conversely, Ulrich et al. (31), in a prospective study including 205 subjects with degenerative lumbar spinal stenosis undergoing surgery (decompression alone or decompression and fusion), found no influence of MCs on clinical outcomes. Interestingly, baseline assessments showed no difference in pain and quality of life between patients with and without MCs, probably due to a higher prevalence of MC2 in the MCs group. Regardless of MCs, all groups demonstrated similar improvement of EQ-5D-3L and numeric pain rating scale (NPRS) after surgery. Similarly, Djurasovic et al. reported improvements in pain, SF-36-PCS and ODI at 2 years after lumbar fusion (5). In contrast to the current study, differences from baseline values were comparable between MC1 and MC2 groups. Only the MC3 group showed little or no change from baseline (albeit based on a small sample size). Notably, patients without MCs experienced outcomes comparable to MC1 and MC2 groups. Additional studies by Ohtori et al., MacLean et al., and Shahmohammadi et al. found no preoperative differences in pain and disability between patients with MC1 and those with MC2 before undergoing posterolateral (Ohtori and Shahmohammadi) or transforaminal (MacLean) lumbar fusion (19,25,29). These authors also reported postoperative improvements in all MC groups, however no significant difference was observed across the groups. The existing literature suggests that MCs are unreliable predictors of surgical outcomes. Nonetheless, our results raise the question of whether subjects with more active bone changes, i.e. MC1, might anticipate a greater improvement in pain and disability after lumbar fusion. Moreover, there is a paucity of literature on outcomes in patients with MC3, emphasizing the need for further research in this specific group of patients. As opposed to MC1, which represents an active inflammatory process, MC3 represents a sclerotic stage of degeneration with reduced vascularity of bone marrow and reduced segmental motion. This chronic but stable condition is less likely to be an active pain generator. The number of patients who presented with MC3 in our series was too small to be analyzed separately, and therefore MC3 was pooled with MC2. Nonetheless, it is possible that MC3 is a 'burnt-out' phase of the degenerative cascade in which the motion segment becomes less involved in pain. Hence, the choice to proceed with fusion surgery in MC3 patients should not be made from MC3 alone but also from the overall clinical context, such as symptom correlation, mechanical instability, and adjacent degeneration.

This study has several limitations. First, its retrospective design and relatively small sample size restricted the methodological options. Moreover, the limited sample size also resulted in reduced statistical power (observed power = 0.50, β = 0.50), which increases the likelihood of Type II error. Thus, non-significant results, particularly in the inter-group comparisons, should be interpreted with caution. In particular, we were not able to perform multivariable adjustment for potential confounders (e.g., age, sex, ASA class, fusion level/technique, baseline scores), nor to apply longitudinal mixed-effects modeling, as interim follow-up data (3–6–12 months) were incomplete in several patients. Second, although MCs classification was performed independently by two authors with adjudication by a third in cases of disagreement — an approach we considered sufficient to ensure consistency — we did not calculate inter- or intraobserver reliability metrics (kappa/ICC). Third, due to the very limited number of patients with MC3, we pooled MC2 and MC3 cases. While this approach was necessary to allow for meaningful comparisons, it may have obscured potential biological differences. Furthermore, patients without MCs were excluded to focus on the effect of MCs subtypes, which reduces the generalizability of the findings to the entire degenerative disc disease population. Given the exploratory nature of the study and the limited sample size, we did not adjust for multiple comparisons and the results should therefore be interpreted with caution. However, our findings align with more recent research, contributing valuable information to the existing knowledge. Due to the limited number of patients with MC3, we opted to combine them with patients with MC2, considering both type of bone changes as senescent. Additionally, a control group comprising subjects without MCs was not included.

Most of our findings are consistent with previous studies reinforcing the notion that MCs constitute only one aspect of the comprehensive clinical assessment of individuals with spinal disorders. Despite MC1, reflecting vertebral body edema and suggesting a more active and painful bone condition, several other factors affect the clinical manifestation of lumbar pathologies, along with the outcomes following fusion surgery. In this context, MCs can provide additional information to refine level selection and support patient counseling. However, they should be interpreted as complementary to, rather than substitutive of, a careful clinical and radiological assessment in order to provide the best possible surgical indication.

■ CONCLUSION

MCs may assist in discerning the most painful spinal levels and could aid surgeons in foreseeing which patients are likely to benefit the most from lumbar fusion. Surgical intervention, when appropriately indicated, improves clinical outcomes in patients suffering from symptomatic degenerative disc disease undergoing a single-level fusion. Furthermore, patients with MC1 experience greater improvements in clinical outcomes following a one-level fusion surgery in comparison to those with MC2 and MC3.

Declarations

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Availability of data and materials: The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Disclosure: AR is consultant for Nuvasive; RC and MD are consultant for Nuvasive – Medacta; DV is consultant for Stryker; PB is consultant for Nuvasive – Medacta – Alphatec – K2M and has received research support from K2M – DePuy – J&J – Nuvasive and royalties from Nuvasive. The funding bodies and the competing interest did not influence the outcome or interpretation of findings.

Ethics Statement: This study was performed in line with the principles of the Declaration of Helsinki. The institutional ethics committee granted ethical permission (second amendment to the SPINEREG protocol issued on 13/04/2016), and all the patients had provided written informed consent for the potential use of the results of their examination for scientific purposes.

AUTHORSHIP CONTRIBUTION

Study conception and design: FM, VS

Data collection: AN, AR

Analysis and interpretation of results: DV, MD

Draft manuscript preparation: FL, DC

Critical revision of the article: FM, VS, FL, DC, AN, AR, DV, MD, RC, PB

Other (study supervision, fundings, materials, etc...): PB, RC

All authors (FM, VS, FL, DC, AN, AR, DV, MD, RC, PB) reviewed the results and approved the final version of the manuscript.

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