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Original Article

The Impact of Modic Changes on Preoperative Symptoms and Clinical Outcomes in Anterior Cervical Discectomy and Fusion Patients

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Objective: To assess the impact of Modic changes (MC) on preoperative symptoms, and postoperative outcomes in anterior cervical discectomy and fusion (ACDF) patients.
Methods: We performed a retrospective study of prospectively collected data of ACDF patients at a single institution. Preoperative magnetic resonance imagings were used to assess the presence of MC. MC were stratified by type and location, and compared to patients without MC. Associations with symptoms, patient-reported measures, and surgical outcomes were assessed.
Results: A total of 861 patients were included, with 356 patients with MC (41.3%). MC more frequently occurred at C5–6 (15.1%), and type II was the most common type (61.2%). MC were associated with advanced age ($p < 0.001$), more levels fused ($p < 0.001$), a longer duration of symptoms, but not with specific symptoms. MC at C7–T1 resulted in higher postoperative disability ($p < 0.001$), but did not increase risk of adjacent segment degeneration or reoperation.
Conclusion: This study is the first to systematically examine the impact of cervical MC, stratified by type and location, on outcomes in ACDF patients. Patients with MC were generally older, required larger fusions, and had longer duration of preoperative symptoms. While MC may not affect specific outcomes following ACDF, they may indicate a more debilitating preoperative state for patients.

Keywords: Spine, Diskectomy, Magnetic resonance imaging, Intervertebral disc degeneration, Patient outcome assessment

INTRODUCTION

Modic changes (MC) are subchondral vertebral bone marrow lesions of the endplate and their etiology continues to be debated.[1,2] MC are noted as signal intensities visible on magnetic resonance imaging (MRI), independent of other pathologies (e.g., malignancy, rheumatic disorders).[1,3] Three types of MC (Figs. 1-3) have been identified based on T1-weighted (T1W) and T2-weighted (T2W) MRI: Type I (MC1) are characterized as hypointense on T1W but hyperintense on T2W, type II (MC2) are hyperintense on T1W and hyperintense/isointense on T2W, and type III (MC3) are hypointense on both T1W and T2W.[1] MC1 represent bony edema and inflammation, MC2 represent fatty replacement of marrow and bone, and MC3 represent

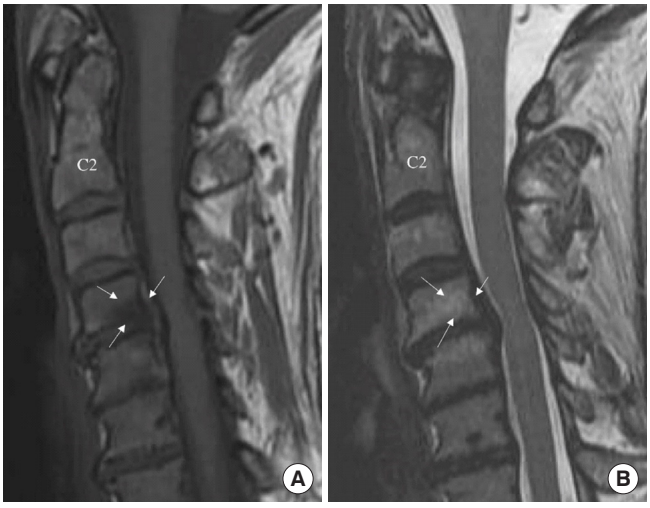

Fig. 1. (A) A T1-weighted magnetic resonance imaging (MRI) of a 59-year-old female demonstrating hypointensity at the inferior endplate of C4. (B) A T2-weighted MRI of the same patient demonstrating hyperintensity, suggesting a type I Modic change. She went on to have a 2-level anterior cervical discectomy and fusion procedure of C4–6. Arrows indicate the location of the identified Modic change lesion on T1- (A) and T2-weighted (B) imagings.

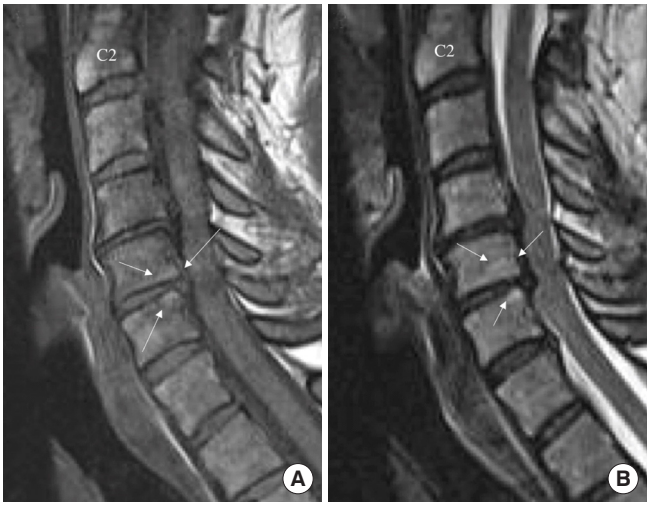

Fig. 2. (A) A T1-weighted magnetic resonance imaging (MRI) of a 41-year-old female that shows hyperintensity at the posterior-inferior endplate of C5 and the posterior-superior endplate of C6. (B) The T2-weighted MRI also demonstrates hyperintensity, suggesting a type II modic change. She went on to have a 2-level anterior cervical discectomy and fusion procedure of C4–6. Arrows indicate the location of the identified Modic change lesion on T1- (A) and T2-weighted (B) imagings.

sclerosis.[4]

MC have been extensively studied in the lumbar spine and

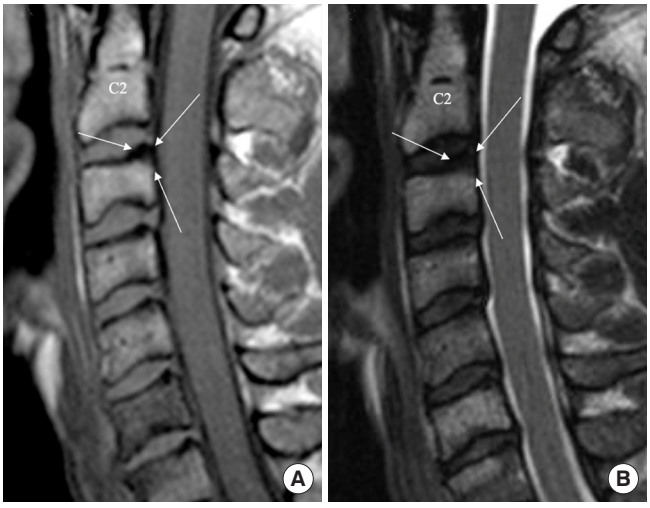

Fig. 3. (A) T1-weighted MRI of a 50-year-old female demonstrating hypointensity at the posterior-superior endplate of C3. (B) T2-weighted MRI of the same patient also demonstrating hypointensity at C3, suggesting a type III Modic change. She underwent a 2-level anterior cervical discectomy and fusion procedure of C5–7. Arrows indicate the location of the identified Modic change lesion on T1- (A) and T2-weighted (B) imagings.

been associated with the development and severity of low back pain, further underscoring the vertebrogenic impact of pain generation.[5,6] Alternatively, few studies have examined MC in the cervical spine. The prevalence of MC in the cervical spine has been shown to be around 40% in patient-based studies, with MC2 being the most frequently observed, and the C5–6 and C6–7 levels most commonly affected.[7,8] Although MC are commonly observed in the cervical spine,[7] the clinical implications of MC are not well understood, particularly as they relate to outcomes following cervical spine surgery.

Anterior cervical discectomy and fusion (ACDF) is a common procedure used to treat a variety of degenerative pathologies of the spine.[9,10] However, adjacent segment degeneration (ASD) has been shown to occur following ACDF,[11,12] and degenerative findings, such as MC, at the adjacent level may further increase the likelihood of ASD following fusion.[13] Moreover, while some studies have found no association between MC and postoperative neck or arm pain,[14] others have found that the presence of MC may correlate with an increased likelihood of having these symptoms following ACDF.[13,15] Therefore, further clarification of the impact of MC on clinical and surgical outcomes is warranted in order to establish more realistic expectations following cervical spine surgery, particularly as patients with evidence of MC may be more likely to undergo

surgery than those that do not have MC.[16]

Overall, little is known with respect to cervical MC and its various types, their topographical variations, and associations with pre- and postoperative symptoms/outcomes in patients undergoing an ACDF. As such, our study aimed to primarily address the preoperative presence and distribution of MC and their types in a patient cohort that underwent ACDF. Secondarily, this study aimed to determine the role of MC as it relates to patients' pre- and postoperative pain and disability profiles.

MATERIALS AND METHODS

Following approval by the Rush University Medical Center Institution Review Board (ORA#18080303), we conducted a retrospective study of prospectively collected data of consecutive patients indicated for an ACDF procedure at a single institution from 2008–2015. Further, due to the retrospective nature of the study, a waiver of informed consent was applied for and obtained. All procedures were performed by 4 spine fellowship-trained surgeons using a consistent technique. Fusion constructs ranged from 1 to 4 levels, and were supplemented with either allograft or a combination of allograft/autograft. Instrumentation consisting of anterior cervical plating was utilized. Indications for surgery included symptomatic degenerative pathology refractory to conservative management. Subjects were included if they had preoperative T1W and T2W sagittal MRIs of the cervical spine that could be assessed for the presence of MC and their types. The MRIs had a field strength of 3 Tesla with a slice thickness of 5 mm between sequential cuts. Subjects were excluded if they were under 18 years of age, or were undergoing surgery to address trauma, malignancy, and/or infection.

Demographic data collected included age (years), sex, height (m), weight (kg), whether or not the patient was a current smoker, and medical comorbidities as assessed by the validated American Society of Anesthesiologists physical status (ASA) classification grade. The ASA classification grade is a validated classification system that categorizes patients based on the severity of their comorbid conditions: ASA I refers to a normal healthy adult, ASA II refers to a patient with mild systemic disease that does not cause functional limitations, ASA III refers to a patient with a severe systemic disease that causes functional limitations, and ASA IV refers to severe systemic disease that is a constant threat to life.[17] Body mass index was calculated based on kg/m^2. Operative data included number of operative vertebral levels, duration of preoperative symptoms (months) and follow-up time (months).

Preoperative T1W and T2W MRIs were assessed for the presence of MC by sequential scanning of the cervical column, including levels C2–T1. MC were further stratified into MC1, MC2, or MC3 according to the aforementioned criteria.[1] MC were also stratified based on their level in the cervical spine, and their location relative to the fusion segment. All MRIs were independently assessed by 3 observers, and intra- and interobserver reliability was good to excellent (intraclass correlation coefficient >0.80).[18]

Preoperative symptomatology was documented, including neck pain, arm pain, sensory deficits, weakness, radiculopathy, myelopathy, and myeloradiculopathy. Patient-reported outcomes (PROs) were collected both preoperatively and at final follow-up. The PROs included the following validated outcome tools: visual analogue scale (VAS)-Neck,[19] VAS-Arm,[19] Neck Disability Index (NDI),[20] Short Form 12-Item[21] and the Veterans' Rand 12-Item.[22] Postoperative surgical outcomes collected included reoperations, pseudarthrosis, and ASD at the proximal and distal levels. ASD was diagnosed on follow-up lateral plain radiographs of the cervical spine based on the following: presence of new or enlarged adjacent level osteophytes, anterior longitudinal ligament calcification, spondylolisthesis with displacement ≥ 2 mm, disc space narrowing greater than 30% from preoperative height, and/or endplate sclerosis.[23]

Statistical analysis was performed using Stata ver. 13.1 (StataCorp LC, College Station, TX, USA). Analysis of baseline characteristics included tabulation of counts, with calculation of means and standard deviations (denoted by $\pm$). Demographic and operative data comparisons were made between the patients with MC (either any MC, MC1, MC2, or MC3) and patients without MC using Student t-test and chi-square test. Multivariate linear and logistic regression was used to assess standardized beta coefficients and odds ratios for the aforementioned MC groups with preoperative symptoms, PROs, and surgical outcomes. Selection of multivariate linear and logistic regression model variables included all collected baseline demographic and operative characteristics along with MC strata. For each dependent variable (i.e., symptoms, PROs, and surgical outcomes), we generated 28 multivariate models using each MC strata. Due to the large number of statistical models for each dependent variable, we anticipated that the likelihood of having false-positive results was high in our analysis. Therefore, we elected to perform *post hoc* corrections for multiple comparisons in order to limit our likelihood of making a type I statistical error. We chose the Šidák method, which is a statistical *post hoc* test that adjusts the p-value cutoff for significance based off

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of the number of statistical models generated per dependent variable. It is also less conservative than other multiple comparison techniques, thus minimizing the chances of overcorrection.[24] The formula for the correction was $p^* = 1-(1-0.05)^{(1/x)}$, where p* is the adjusted p-value and "*x*" is the number of regression models for each dependent variable. Given that we generated 28 regression models, we calculated an adjusted p-value cutoff of 0.0018. Rounding to 3 decimal places, we set statistical significance to $p < 0.002$ for multivariate analysis. For all other analysis (i.e., demographic and operative analysis), *post hoc* corrections were not necessary, and we set statistical significance at the usual value of $p < 0.05$. Finally, we performed a multivariate logistic regression (with the aforementioned covariates) comparing patients with MC inside versus outside the fusion segment using non-MC as a reference in order to assess the impact of include vs. excluding MC in the fusion segment. Statistical significance for this analysis was also defined as $p < 0.05$.

RESULTS

A total of 861 patients were included in this study, with 356 patients (41.3%) noted to have MC on MRI. Stratified by type, 70 (8.1%) showed MC1, 218 (25.3%) showed MC2, and 68 (7.9%) showed MC3. A summary of the continuous demographic and operative variables of each cohort is summarized in Table 1, and a summary of the categorical demographic variables of each cohort is summarized in Table 2. The mean age of patients without and with MC was 51.4 ± 11.6 years and 55.6 ± 10.5 years, respectively ($p < 0.001$). The mean ages for MC1, MC2, and MC3 were 54.8 ± 11.0, 56.3 ± 9.7, and 54.4 ± 12.5 years, respectively. Additionally, there was a significantly greater percentage of males in the MC2 group compared to the non-MC group ($p = 0.044$). There were no other significant differences in demographics observed between MC, regardless of type, and the non-MC group. Overall MC had a significantly longer preoperative duration of symptoms (months) (26.3 vs. 19.9, $p = 0.025$) and associated with more levels fused (2.0 vs. 1.8, $p < 0.001$) than the non-MC group. The mean follow-up time (months) for the MC and non-MC group was comparable (26.4 vs. 27.9). When stratified by type, MC2 (2.0, $p = 0.002$) and MC3 (2.1. $p = 0.013$) were associated with significantly more levels fused, while only MC2 was associated with a significantly longer duration of symp-

Table 1. Baseline characteristics of continuous variables in relation to patients with or without Modic changes

Variable	Non-MC (reference)	Overall MC		MC type I		MC type II		MC type III	
	Mean ± SD	Mean ± SD	p-value	Mean ± SD	p-value	Mean ± SD	p-value	Mean ± SD	p-value
Age (yr)	51.39 ± 11.62	55.55 ± 10.51	< 0.001*	54.8 ± 11.05	0.019*	56.25 ± 9.68	< 0.001*	54.42 ± 12.49	0.047*
Body mass index (kg/m^2)	29.01 ± 6.67	29.19 ± 5.5	0.701	29.2 ± 6.89	0.836	29.42 ± 4.86	0.460	28.68 ± 5.67	0.713
Levels fused	1.8 ± 0.73	2.02 ± 0.79	< 0.001*	1.96 ± 0.79	0.151	2.03 ± 0.77	0.002*	2.06 ± 0.85	0.013*
Symptom duration (mo)	19.87 ± 26.94	26.26 ± 46.61	0.025*	26.81 ± 39.91	0.091	27.53 ± 51.02	0.021*	21.59 ± 38.25	0.670
Follow-up time (mo)	26.38 ± 24.68	27.86 ± 25.88	0.598	30.32 ± 27.86	0.467	26.87 ± 26.89	0.883	28.84 ± 22.13	0.592

MC, Modic change; SD, standard deviation.
p-values were calculated using the Student t-test and calculated relative to non-MC group.
*Statistical significance at $p < 0.05$.

Table 2. Baseline characteristics of categorical variables in relation to patients with or without Modic changes

Variable	Non-MC (reference) (n = 505)	Overall MC (n = 356)		MC type I (n = 70)		MC type II (n = 218)		MC type III (n = 68)	
	No. (%)	No. (%)	p-value	No. (%)	p-value	No. (%)	p-value	No. (%)	p-value
Female	252 (49.9)	157 (44.1)	0.127	34 (48.6)	0.823	91 (41.7)	0.044*	32 (47.1)	0.638
Current smoker	162 (32.1)	138 (38.8)	0.201	24 (34.3)	0.837	84 (38.5)	0.240	29 (42.6)	0.284
ASA PS classification ≥ III	90 (17.8)	68 (19.1)	0.976	12 (17.1)	0.607	44 (20.2)	0.641	13 (19.1)	0.862

MC, Modic change; ASA PS, American Society of Anesthesiologists physical status.
p-values were calculated using chi-square analysis and calculated relative to non-MC group.
*Statistical significance at $p < 0.05$.

toms (27.5, p = 0.021) relative to the non-MC group.

The distribution of MC by vertebral level and their prevalence in the entire patient cohort are summarized in Fig. 4. The distribution of MC by both type and location, as well as the percentage of each in relation to only MC patients, is summarized in Fig. 5. Distribution by location in relation to the planned fusion segment is summarized in Table 3. A total of 376 MC were observed, with the highest prevalence of MC occurring at C5–6 (15.1%), followed by C6–7 (13.0%). Overall MC were least likely to occur at C7–T1 (1.2%) and C2–3 (1.3%). Out of all MC, MC2 were the most common type, followed by MC1 and then MC3. Both MC1 and MC3 were most likely to occur at C5–6, followed by C4–5, while MC2 were most likely to occur at C6–7, followed by C5–6. Additionally, of the 356 patients with MC, 219 patients (61.5%) had MC within the planned fusion segment, while 137 (38.5%) had MC outside the planned fusion segment. There were 126 patients (35.4%) with MC above the planned fusion segment, and 11 patients with MC (3.1%) below the segment.

The association between the presence of specific preoperative symptoms and preoperative MC was assessed in order to determine whether MC influenced patient presentation or resulted in unique preoperative symptom profiles. The results are summarized in Table 4. Following *post hoc* analysis, no significant correlations between MC, regardless of type and location in the cervical column, and non-MC patients with respect to individual preoperative symptoms were noted. In addition, patients with MC inside the fusion segment compared to outside the fusion segment did not significantly differ in terms of specific preoperative symptoms.

Preoperative and postoperative PROs data comparing patients with MC and those without are summarized in Table 5. Simply having MC, regardless of stratification by type, did not ultimately yield any differences in pre- and postoperative PROs. Analysis by cervical level demonstrated that overall MC at C7–T1 significantly predicted higher postoperative NDI (beta = 52.17,

Table 3. Modic changes stratified by location relative to the fusion segment

Variable	Overall MC	MC type I	MC type II	MC type III
Within planned fusion segment	219 (61.5)	50 (22.8)	120 (54.8)	49 (22.4)
Outside planned fusion segment	137 (38.5)	20 (14.6)	98 (71.5)	19 (13.9)
Above planned fusion segment	126 (35.4)	19 (15.1)	90 (71.4)	17 (13.5)
Below planned fusion segment	11 (3.1)	1 (9.1)	8 (72.7)	2 (18.2)
Proximal level to planned fusion segment	89 (25)	-	-	-
Distal level to planned fusion segment	27 (7.2)	-	-	-

Values are presented as number (%).
MC, Modic change.

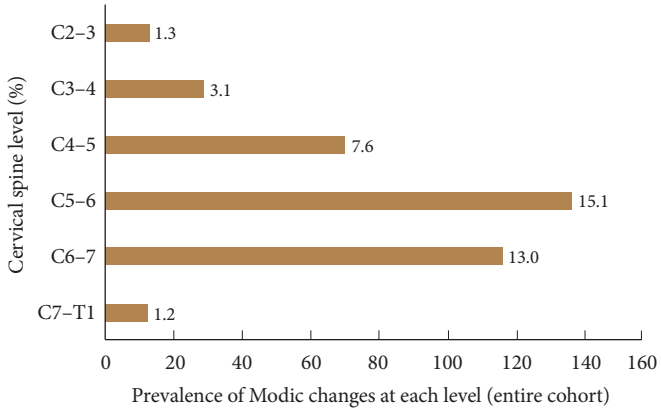

Fig. 4. Distribution of Modic changes by cervical spinal level. Data labels show the percentage of all patients with Modic changes in the context of the entire study population.

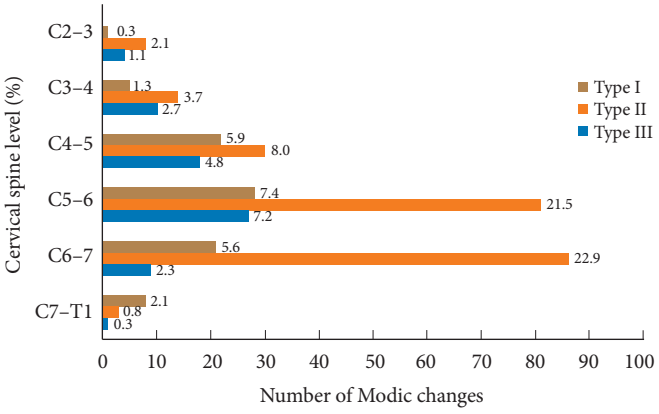

Fig. 5. Distribution of Modic changes stratified by type and level in the cervical spine. Type I Modic changes are represented in grey, type II are represented in orange, and type III are represented in blue. Data levels show the percentage of total Modic changes of that type at each level.

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Table 4. Association of Modic changes with preoperative symptoms

Variable	Neck pain		Radiculopathy		Arm pain		Sensory deficits		Weakness		Myeloradiculopathy		Myelopathy	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Non-MC (reference)	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-
Vertebral level														
C2–3	1.00	-	1.00	-	0.96 (0.10–9.34)	0.971	0.78 (0.12–5.04)	0.794	0.74 (0.12–4.88)	0.754	1.43 (0.19–10.62)	0.727	1.00	-
C3–4	0.38 (0.07–2.20)	0.281	1.00	-	0.71 (0.16–3.09)	0.649	0.41 (0.12–1.44)	0.163	2.14 (0.57–8.03)	0.260	0.21 (0.02–1.81)	0.156	1.00	-
C4–5	2.53 (0.30–20.84)	0.388	1.00	-	1.07 (0.37–3.01)	0.899	1.65 (0.65–4.18)	0.292	0.74 (0.32–1.66)	0.446	0.38 (0.13–1.12)	0.080	1.61 (0.28–9.39)	0.596
C5–6	1.30 (0.34–4.98)	0.698	0.13 (0.01–1.86)	0.132	0.72 (0.32–1.64)	0.435	1.71 (0.77–3.78)	0.187	0.79 (0.38–1.62)	0.518	0.56 (0.23–1.33)	0.192	0.54 (0.06–4.82)	0.579
C6–7	1.52 (0.03–8.20)	0.622	0.88 (0.03–23.38)	0.943	0.34 (0.15–0.78)	0.011	2.17 (0.89–5.34)	0.090	1.24 (0.56–2.74)	0.590	0.37 (0.13–1.09)	0.071	5.34 (1.01–28.84)	0.049
C7–T1	1.00	-	1.00	-	1.00	-	0.92 (0.08–10.81)	0.944	4.71 (0.37– 61.59)	0.229	1.33 (0.08– 23.58)	0.845	1.00	-
Overall														
Overall MC	1.43 (0.56–3.65)	0.455	0.65 (0.09–4.47)	0.657	0.69 (0.40–1.19)	0.186	1.40 (0.84– 2.33)	0.195	1.02 (0.63–1.65)	0.945	0.43 (0.23–0.786)	0.006	1.78 (0.59–5.36)	0.305
MC type I	1.00	-	1.00	-	0.54 (0.19–1.53)	0.246	2.59 (0.80–8.35)	0.112	1.32 (0.49–3.50)	0.582	0.39 (0.11–1.34)	0.136	2.98 (0.50–17.92)	0.232
MC type II	1.40 (0.47– 4.18)	0.552	0.39 (0.05–2.92)	0.357	0.74 (0.38–1.43)	0.369	1.28 (0.70–2.34)	0.425	0.99 (0.56–1.74)	0.959	0.41 (0.20–0.86)	0.018	1.48 (0.38– 5.71)	0.569
MC type III	0.75 (0.19–2.98)	0.678	1.00	-	0.58 (0.24–1.39)	0.221	1.51 (0.63–3.62)	0.352	0.68 (0.31–1.53)	0.353	0.65 (0.24– 1.73)	0.385	0.96 (0.10– 9.44)	0.972
Inside planned fusion segment														
Overall MC	1.82 (0.60–5.53)	0.288	0.48 (0.06–3.63)	0.480	0.57 (0.31–1.05)	0.070	1.67 (0.93–2.99)	0.085	0.93 (0.54–1.58)	0.779	0.47 (0.24–0.91)	0.024	1.62 (0.48–5.46)	0.436
MC type I	1.00	-	1.00	-	0.48 (0.16–1.38)	0.173	3.41 (0.91–12.70)	0.068	1.32 (0.48–3.67)	0.591	0.47 (0.13–1.68)	0.248	3.73 (0.60–23.06)	0.157
MC type II	1.21 (0.35–4.13)	0.761	0.26 (0.03–2.21)	0.217	0.63 (0.30–1.35)	0.233	1.26 (0.63–2.52)	0.518	0.78 (0.41–1.55)	0.504	0.42 (0.19–0.97)	0.042	1.39 (0.30–6.41)	0.671
MC type III	1.70 (0.19–14.99)	0.632	1.00	-	0.36 (0.13–0.96)	0.042	2.49 (0.78– 7.95)	0.122	0.79 (0.30–2.04)	0.622	0.83 (0.30–2.35)	0.734	1.35 (0.13–14.32)	0.806
Outside planned fusion segment														
Overall MC	0.84 (0.21–3.45)	0.811	1.00	-	1.32 (0.46–3.82)	0.605	0.78 (0.34–1.78)	0.559	1.36 (0.61–3.07)	0.454	0.28 (0.08–0.99)	0.048	1.94 (0.32–11.71)	0.469
MC type I	1.00	-	1.00	-	1.00	-	0.41 (0.02– 7.01)	0.535	1.19 (0.06–22.02)	0.906	1.00	-	1.00	-
MC type II	2.01 (0.24–16.90)	0.521	1.00	-	1.13 (0.35–3.64)	0.833	1.20 (0.44–3.27)	0.721	1.71 (0.66–4.42)	0.266	0.39 (0.11–1.46)	0.167	1.27 (0.13–12.32)	0.835
MC type III	0.28 (0.04–1.83)	0.185	1.00	-	2.78 (0.32–24.43)	0.356	0.56 (0.14–2.30)	0.422	0.53 (0.12–2.29)	0.395	1.00	-	1.00	-
Above planned fusion segment														
Overall MC	0.97 (0.19–5.00)	0.971	1.00	-	3.10 (0.68–14.22)	0.145	0.71 (0.30–1.68)	0.432	1.16 (0.49–2.75)	0.735	0.21 (0.04–.095)	0.043	1.00	-
MC type I	1.00	-	1.00	-	1.00	-	0.41 (0.03–7.01)	0.535	1.19 (0.06–22.03)	0.906	1.00	-	1.00	-
MC type II	1.00	-	1.00	-	4.22 (0.53–33.39)	0.172	0.95 (0.34–2.68)	0.924	1.56 (0.56–4.36)	0.393	0.30 (0.06–1.43)	0.131	1.00	-
MC type III	0.24 (0.04–1.64)	0.145	1.00	-	2.43 (0.27–21.90)	0.430	0.43 (0.10–1.93)	0.273	0.66 (0.15–2.99)	0.589	1.00	-	1.00	-
Below planned fusion segment														
Overall MC	0.57 (0.05–6.32)	0.650	1.00	-	0.15 (0.02–1.11)	0.064	1.34 (0.14–13.30)	0.801	3.43 (0.49–23.75)	0.213	0.63 (0.06–6.35)	0.696	10.10 (1.09-93.74)	0.042
MC type I	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-
MC type II	0.43 (0.04–5.15)	0.505	1.00	-	0.07 (0.01–0.84)	0.035	1.00	-	2.55 (0.31–20.76)	0.382	0.94 (0.09–10.14)	0.958	4.47 (0.31-64.31)	0.271
MC type III	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-
Proximal level														
Overall MC	0.12 (0.01–2.27)	0.156	1.00	-	0.29 (0.02–5.27)	0.402	1.00	-	1.00	-	1.00	-	1.00	-
Distal level														
Overall MC	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-	1.00	-

Calculation of p-values and coefficients was performed using multivariate linear regression with the covariates age, sex, body-mass index, smoking status, American Society of Anesthesiologists physical status classification, number of levels fused, duration of symptoms, and follow-up time.
OR, odds ratio; CI, confidence interval; MC, Modic change.

Table 5. Association of Modic changes with patient-reported outcomes

Variable	NDI pre		NDI post		VAS-Neck pre		VAS-Neck post		VAS-Arm pre		VAS-Arm post		SF12 pre		SF12 post		VR12 pre		VR12 post	
	Beta (95% CI)	p-value	Beta (95% CI)	p-value	Beta (95% CI)	p-value	Beta (95% CI)	p-value	Beta (95% CI)	p-value	Beta (95% CI)	p-value	Beta (95% CI)	p-value	Beta (95% CI)	p-value	Beta (95% CI)	p-value	Beta (95% CI)	p-value
Non-MC (reference)	0.00	-	0.00	-	0.00	-	0.00	-	0.00	-	0.00	-	0.00	-	0.00	-	0.00	-	0.00	-
Vertebral level																				
C2–3	26.93 (-22.11-75.97)	0.273	38.69 (1.72-75.66)	0.041	4.95 (-2.77-12.68)	0.202	2.55 (-2.85-7.95)	0.346	4.68 (-2.08-11.45)	0.169	7.85 (2.74-12.96)	0.004	0.00	-	5.08 (-9.77-19.94)	0.490	0.00	-	15.18 (-7.04-37.40)	0.171
C3–4	-5.87 (-34.65-22.92)	0.683	-15.05 (-36.71-6.61)	0.168	0.17 (-4.44-4.78)	0.941	-1.52 (-4.69-1.66)	0.341	-1.13 (-5.15-2.88)	0.572	-1.01 (-4.01-1.99)	0.500	-10.49 (-32.16-11.18)	0.323	-3.54 (-19.59-12.51)	0.655	-12.51 (-35.69-10.68)	0.271	-6.40 (-20.40-7.61)	0.355
C4–5	-8.69 (-25.08-7.70)	0.292	-5.45 (-18.79-7.89)	0.416	2.02 (-0.57-4.60)	0.123	1.16 (-0.91-3.23)	0.264	-0.11 (-2.87-2.65)	0.936	1.07 (-1.00-3.14)	0.303	1.72 (-8.09-11.53)	0.720	6.48 (-5.09-18.06)	0.263	2.86 (-7.61-13.33)	0.577	4.61 (-6.51-15.73)	0.402
C5–6	-2.10 (-15.47-11.28)	0.754	-10.44 (-20.36--0.52)	0.039	0.87 (-1.29-3.04)	0.422	-1.42 (-2.72--0.13)	0.032	-1.75 (-3.87-0.37)	0.104	-1.32 (-2.53--0.10)	0.034	7.16 (-1.51-15.85)	0.101	2.73 (-5.24-10.71)	0.492	8.72 (-0.44-17.87)	0.061	1.84 (-5.46-9.14)	0.612
C6–7	-9.84 (-26.77-7.09)	0.248	-5.53 (-18.81-7.75)	0.407	-0.79 (-3.93-2.34)	0.613	0.03 (-1.93-2.00)	0.972	-3.55 (-6.38--0.72)	0.015	-0.39 (-2.21-1.42)	0.665	0.81 (-9.47-11.08)	0.873	12.64 (-1.40-26.68)	0.076	1.51 (-9.41-12.43)	0.778	2.60 (-11.51-16.72)	0.707
C7–T1	11.20 (-23.36-45.75)	0.516	52.17 (26.28-78.05)	< 0.001*	0.59 (-4.82-6.01)	0.825	5.39 (1.58-9.19)	0.007	1.61 (-3.15-6.36)	0.498	4.60 (0.96-8.23)	0.014	0.00	-	5.41 (-19.06-29.87)	0.654	0.00	-	0.00	-
Overall																				
Overall MC	-4.87 (-13.91-4.19)	0.288	-3.74 (-12.13-4.67)	0.379	0.81 (-0.72-2.34)	0.293	-0.10 (-1.20-0.99)	0.852	-1.36 (-3.05-0.33)	0.113	-0.06 (-1.17-1.05)	0.915	2.14 (-3.81-8.09)	0.471	3.90 (-2.10-9.89)	0.198	3.14 (-3.03-9.31)	0.310	1.55 (-4.11-7.21)	0.584
MC type I	-5.37 (-22.48-11.73)	0.530	-3.69 (-15.76-8.38)	0.542	1.23 (-1.45-3.91)	0.360	-0.42 (-2.13-1.29)	0.625	-2.50 (-5.33-0.33)	0.082	-0.48 (-2.07-1.12)	0.551	0.26 (-10.74-11.27)	0.961	7.71 (-2.04-17.46)	0.118	2.00 (-9.57-13.56)	0.722	2.91 (-8.38-14.19)	0.601
MC type II	-5.23 (-17.15-6.69)	0.384	-3.64 (-14.37-7.09)	0.500	0.10 (-1.99-2.18)	0.927	-0.05 (-1.53-1.43)	0.947	-1.49 (-3.58-0.61)	0.160	0.35 (-1.15-1.85)	0.640	1.22 (-5.66-8.11)	0.720	7.19 (-1.09-15.47)	0.087	1.52 (-5.67-8.72)	0.669	5.76 (-1.94-13.46)	0.137
MC type III	0.33 (-15.52-16.19)	0.967	-6.62 (-19.75-6.51)	0.316	1.66 (-0.89-4.22)	0.197	-0.14 (-1.99-1.70)	0.877	0.40 (-1.90-2.71)	0.726	-0.32 (-2.15-1.50)	0.725	5.67 (-18.74-30.10)	0.631	-2.76 (-11.89-6.38)	0.544	9.99 (-16.04-36.02)	0.429	-3.65 (-11.90-4.60)	0.373
Inside planned fusion segment																				
Overall MC	-2.84 (-12.98-7.30)	0.578	-5.22 (-14.26-3.82)	0.254	0.80 (-0.86-2.45)	0.342	-0.34 (-1.55-0.86)	0.571	-1.55 (-3.40-0.30)	0.099	-0.37 (-1.52-0.78)	0.524	3.72 (-2.75-10.20)	0.251	6.01 (-0.35-12.37)	0.063	5.08 (-1.52-11.68)	0.127	2.66 (-3.39--8.71)	0.380
MC type I	-5.37 (-22.48-11.73)	0.530	-2.80 (-15.39-9.79)	0.657	1.23 (-1.44-3.91)	0.360	-0.75 (-2.53-1.02)	0.398	-2.50 (-5.33-0.33)	0.082	-0.87 (-2.51-0.76)	0.288	0.26 (-10.74-11.27)	0.961	7.71 (-2.05-17.46)	0.118	2.00 (-9.57-13.56)	0.722	2.91 (-8.38-14.19)	0.601
MC type II	-4.90 (-19.92-10.12)	0.516	-9.42 (-21.38-2.55)	0.120	0.09 (-2.50-2.68)	0.943	-0.81 (-2.54-0.91)	0.348	-2.59 (-4.99--0.18)	0.036	-0.84 (-2.41-0.73)	0.288	4.41 (-3.22-12.04)	0.247	7.22 (-2.12-16.56)	0.126	5.03 (-2.84-12.91)	0.202	4.37 (-3.92-12.65)	0.291
MC type III	2.59 (-14.42-19.61)	0.761	-9.94 (-23.84-3.96)	0.157	1.40 (-1.36-4.15)	0.313	-0.20 (-2.19-1.79)	0.842	0.66 (-1.82-3.14)	0.596	-0.25 (-2.21-1.73)	0.803	0.00	-	1.67 (-8.96-12.31)	0.751	0.00	-	-1.04 (-10.81-8.75)	0.830

(*Continued to the next page*)

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Table 5. Continued

Variable	NDI pre		NDI post		VAS-Neck pre		VAS-Neck post		VAS-Arm pre		VAS-Arm post		SF12 pre		SF12 post		VR12 pre		VR12 post	
	Beta (95% CI)	p-value	Beta (95% CI)	p-value	Beta (95% CI)	p-value	Beta (95% CI)	p-value	Beta (95% CI)	p-value	Beta (95% CI)	p-value	Beta (95% CI)	p-value	Beta (95% CI)	p-value	Beta (95% CI)	p-value	Beta (95% CI)	p-value
Outside planned fusion segment																				
Overall MC	-9.11 (-26.01-7.79)	0.283	-0.31 (-13.99-13.37)	0.964	1.00 (-1.92-3.93)	0.494	0.28 (-1.64-2.20)	0.771	-0.59 (-3.37-2.20)	0.674	1.03 (-0.96-3.03)	0.302	-6.31 (-18.98-6.37)	0.313	-2.25 (-13.35-8.85)	0.682	-5.05 (-18.86-8.77)	0.456	-0.76 (-13.25-11.73)	0.901
MC type I	0.00	-	-11.59 (-48.11-24.94)	0.526	0.00	-	2.78 (-2.52-8.09)	0.295	0.00	-	3.37 (-1.64-8.39)	0.182	0.00	-	0.00	-	0.00	-	0.00	-
MC type II	-4.15 (-21.53-13.24)	0.633	6.18 (-9.54-21.89)	0.433	0.87 (-2.17-3.90)	0.568	1.00 (-1.20-3.21)	0.363	0.19 (-2.75-3.14)	0.897	2.03 (-0.21-4.27)	0.074	-7.77 (-21.12-5.59)	0.240	5.08 (-9.77-19.94)	0.490	-6.96 (-21.51-7.59)	0.330	15.18 (-7.04-37.40)	0.171
MC type III	-15.81 (-64.59-32.97)	0.516	22.31 (-15.10-59.72)	0.235	3.40 (-4.32-11.11)	0.378	0.24 (-5.18-5.65)	0.931	-0.69 (-7.41-6.03)	0.836	-1.02 (-6.14-4.11)	0.691	5.67 (-18.75-30.09)	0.631	-14.32 (-32.01-3.36)	0.108	9.99 (-16.04-36.02)	0.429	-10.12 (-26.00-5.77)	0.201
Above planned fusion segment																				
Overall MC	-2.14 (-23.73-19.45)	0.843	2.45 (-14.92-19.82)	0.778	2.68 (-0.62-5.98)	0.109	0.18 (-2.24-2.59)	0.883	1.90 (-1.10-4.91)	0.208	1.29 (-1.19-3.78)	0.301	-6.31 (-18.98-6.37)	0.313	-2.25 (-13.35-8.85)	0.682	-5.05 (-18.86-8.77)	0.456	-0.76 (-13.25-11.73)	0.901
MC type I	0.00	-	-11.59 (-48.11-24.94)	0.526	0.00	-	2.78 (-2.52-8.09)	0.295	0.00	-	3.37 (-1.65-8.39)	0.182	0.00	-	0.00	-	0.00	-	0.00	-
MC type II	6.36 (-15.80-28.53)	0.566	14.08 (-7.19-35.34)	0.189	2.39 (-1.00-5.79)	0.162	1.10 (-1.87-4.08)	0.459	2.92 (-0.13-5.97)	0.060	2.85 (-0.13-5.83)	0.061	-7.77 (-21.12-5.59)	0.240	5.08 (-9.77-19.93)	0.490	-6.96 (-21.51-7.59)	0.330	15.18 (-7.04-37.40)	0.171
MC type III	-15.81 (-64.59-32.97)	0.516	22.31 (-15.09-59.72)	0.235	3.40 (-4.32-11.11)	0.378	0.24 (-5.18-5.65)	0.931	-0.69 (-7.41-6.03)	0.836	-1.02 (-6.15-4.11)	0.691	5.67 (-18.74-30.09)	0.631	-14.32 (-32.00-3.36)	0.108	9.99 (-16.04-36.02)	0.429	-10.12 (-26.00-5.77)	0.201
Below planned fusion segment																				
Overall MC	-21.44 (-48.32-5.45)	0.115	-5.57 (-26.22-15.08)	0.590	-2.83 (-8.23-2.57)	0.295	0.59 (-2.49-3.66)	0.702	-6.67 (-11.29--2.06)	0.006	0.56 (-2.39-3.51)	0.703	0.00	-	0.00	-	0.00	-	0.00	-
MC type I	0.00	-	0.00	-	0.00	-	0.00	-	0.00	-	0.00	-	0.00	-	0.00	-	0.00	-	0.00	-
MC type II	-21.44 (-48.32-5.45)	0.115	-5.57 (-26.22-15.09)	0.590	-2.83 (-8.24-2.57)	0.295	0.59 (-2.49-3.66)	0.702	-6.67 (-11.28--2.06)	0.006	0.56 (-2.39-3.51)	0.703	0.00	-	0.00	-	0.00	-	0.00	-
MC type III	0.00	-	0.00	-	0.00	-	0.00	-	0.00	-	0.00	-	0.00	-	0.00	-	0.00	-	0.00	-
Proximal level																				
Overall MC	0.00	-	0.00	-	0.00	-	0.00	-	0.00	-	0.00	-	0.00	-	-18.06 (-42.89-6.77)	0.519	0.00	-	-16.13 (-37.86-5.60)	0.757
Distal level																				
Overall MC	0.00	-	0.00	-	0.00	-	0.00	-	0.00	-	0.00	-	0.00	-	0.00	-	0.00	-	0.00	-

Calculation of p-values and coefficients was performed using multivariate linear regression with the covariates age, sex, body-mass index, smoking status, American Society of Anesthesiologists physical status classification, number of levels fused, duration of symptoms, and follow-up time.
NDI, Neck Disability Index; VAS, visual analogue scale; SF12, Short Form 12-item survey; VR12, Veteran's Rand 12-item survey; CI, confidence interval; MC, Modic change.
*Statistical significance at $p < 0.002$.

Table 6. Multivariate regression analyses of Modic changes with postoperative outcomes

Variable	ASD proximal		ASD distal		ASD overall		Reoperations	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Non-MC (reference)	1.00	-	1.00	-	1.00	-	1.00	-
Vertebral level								
C2–3	1.00	-	1.00	-	1.00	-	1.00	-
C3–4	2.12 (0.03–112.38)	0.711	4.14 (0.27–63.72)	0.309	1.06 (0.05–23.30)	0.969	1.00	-
C4–5	4.86 (0.72–32.67)	0.104	2.09 (0.31–14.03)	0.448	4.65 (0.80–26.94)	0.087	0.43 (0.5–3.62)	0.434
C5–6	0.16 (0.01–1.83)	0.141	1.06 (0.17–6.79)	0.949	0.24 (0.04–1.42)	0.116	0.87 (0.23–3.32)	0.834
C6–7	0.46 (0.04–4.82)	0.517	1.04 (0.14–7.58)	0.970	0.80 (0.16–4.03)	0.787	1.00	-
C7–T1	1.00	-	1.00	-	1.00	-	32.39 (1.95-536.90)	0.015
Overall								
Overall MC	0.87 (0.26–2.91)	0.816	1.36 (0.44–4.18)	0.589	0.88 (0.34–2.30)	0.798	0.65 (0.23–1.83)	0.413
MC type I	4.62 (0.36–59.64)	0.241	1.24 (0.14–10.68)	0.847	5.46 (0.60–49.89)	0.133	0.57 (0.07–4.84)	0.606
MC type II	0.42 (0.08–2.14)	0.296	0.88 (0.22–3.47)	0.852	0.45 (0.13–1.52)	0.200	0.57 (0.15–2.19)	0.416
MC type III	0.62 (0.06–6.99)	0.724	4.34 (0.61–30.70)	0.142	0.94 (0.14–6.50)	0.952	1.51 (0.37–6.07)	0.565
Inside planned fusion segment								
Overall MC	0.74 (0.19–2.89)	0.662	1.27 (0.36–4.54)	0.710	0.78 (0.27–2.31)	0.660	0.91 (0.31–2.67)	0.859
MC type I	1.29 (0.07–23.15)	0.863	1.84 (0.18–18.39)	0.604	3.28 (0.30–35.33)	0.327	0.61 (0.07–5.18)	0.647
MC type II	0.52 (0.09–3.06)	0.473	0.97 (0.20–4.78)	0.972	0.37 (0.09–1.58)	0.180	0.57 (0.11–2.84)	0.493
MC type III	0.23 (0.01–4.91)	0.345	2.17 (0.22–21.46)	0.508	0.63 (0.07–5.77)	0.683	1.13 (0.21–6.00)	0.882
Outside planned fusion segment								
Overall MC	1.32 (0.13–13.24)	0.813	1.90 (0.30–11.96)	0.497	1.54 (0.27–8.93)	0.628	1.00	-
MC type I	1.00	-	1.00	-	1.00	-	1.00	-
MC type II	0.08 (0.01–3.11)	0.175	0.85 (0.8–9.31)	0.892	0.74 (0.08–6.88)	0.792	0.57 (0.06–5.04)	0.614
MC type III	4.38 (0.3–606.69)	0.557	38.16 (1.09–1336.83)	0.045	3.40 (0.05–223.71)	0.566	2.83 (0.27–29.55)	0.385
Above planned fusion segment								
Overall MC	1.34 (0.13–13.54)	0.804	1.01 (0.10–10.26)	0.995	0.76 (0.10–6.03)	0.793	1.00	-
MC type I	1.00	-	1.00	-	1.00	-	1.00	-
MC type II	0.08 (0.01–3.12)	0.176	1.00	-	0.10 (0.00–2.35)	0.155	0.74 (0.08–6.57)	0.790
MC type III	4.38 (0.03–606.69)	0.557	38.16 (1.09–1336.83)	0.045	3.40 (0.05–223.71)	0.566	1.00	-
Below planned fusion segment								
Overall MC	1.00	-	1.00	-	1.00	-	1.00	-
MC type I	1.00	-	1.00	-	1.00	-	1.00	-
MC type II	1.00	-	1.00	-	1.00	-	1.00	-
MC type III	1.00	-	1.00	-	1.00	-	1.00	-
Proximal level								
Overall MC	1.00	-	7.55 (0.35–161.86)	0.196	1.00	-	1.00	-
Distal level								
Overall MC	1.00	-	1.00	-	1.00	-	1.00	-

Calculation of p-values and odds ratios was performed using multivariate logistic regression with the covariates age, sex, body mass index, smoking status, American Society of Anesthesiologists physical status classification, number of levels fused, duration of symptoms, and follow-up time.
ASD, adjacent segment degeneration; OR, odds ratio; CI, confidence interval; MC, Modic change.

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Table 7. Multivariate regression analyses comparing surgical outcomes in patients with Modic changes inside the fusion segment, outside the fusion segment, and patients without Modic changes

Variable	ASD			Reoperations			Pseudarthrosis		
	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value
Non-MC (reference)	1.00	-	-	1.00	-	-	1.00	-	-
MC Inside	0.77	0.27–2.21	0.629	0.91	0.31–2.67	0.859	1.29	0.79–8.5	0.794
MC Outside	1.39	0.26–7.56	0.703	1.00	-	-	1.00	-	-

Calculation of p-values and odds ratios was performed using multivariate logistic regression with the covariates age, sex, body-mass index, smoking status, American Society of Anesthesiologists physical status classification, number of levels fused, duration of symptoms, and follow-up time. Statistical significance was set at $p < 0.05$.
ASD, adjacent segment degeneration; OR, odds ratio; CI, confidence interval; MC, Modic change.

95% confidence interval, 26.28–78.05; $p < 0.001$). Presence of MC versus non-MC, regardless of the type, did not significantly alter preoperative or postoperative PROs when MC was included in the fusion segment. Similarly, MC versus non-MC, regardless of type, outside the fusion segment or at the adjacent levels also did not significantly alter PROs. When comparing patients with MC inside the fusion segment and those with MC outside the fusion segment, no significant differences in PROs were appreciated.

Analysis of surgical outcomes was performed using multivariate logistic regression, and the results are summarized in Table 6. Overall, MC did not significantly correlate with postoperative ASD or reoperations within the follow-up period included in this study. Stratification by type and location, even when at the adjacent level, also did not yield any significant correlations when comparing patients with MC to those without. Comparison of surgical outcomes in patients with MC inside the fusion segment versus outside the fusion segment is summarized in Table 7. When comparing patients with MC inside versus patients with MC outside the fusion segment, no differences in postoperative outcomes of ASD, pseudarthrosis, or reoperation were noted.

DISCUSSION

To our knowledge, this is the first study to address systematic mapping of MC in the cervical spine, their association with preoperative symptoms, pain, and disability as well as postoperative outcomes in ACDF patients. In addition, our study also compared MC patients to non-MC patients in order to assess whether the presence of MC had any impact on preoperative symptomatology, PROs, and postoperative surgical outcomes. In our analysis, we found that the presence of MC was associated with advanced age and more fused levels during surgery. The most common type observed was MC2, followed by MC1 and then MC3. Only MC2 was associated with male sex. The most common levels affected were C5–6, followed by C6–7. While we did not find any associations between MC and specific preoperative symptoms, we did find that MC was associated with a significantly longer duration of symptoms. We also found a significantly higher level of postoperative patient-reported disability associated with MC at C7–T1. However, MC, regardless of type or location, did not increase postoperative rates of reoperation or ASD within our follow-up period of 2 years. Patients with MC inside versus those outside the fusion segment also did not differ in terms of preoperative symptoms or postoperative outcomes. These results suggest that while MC may not be associated with specific symptom profiles or surgical complications of ACDF, such as ASD or revision surgery, MC may indicate a generally chronic and more debilitating state for the patient. Such information provides vital clinical reference for the surgeon in managing patient expectations, predicting outcomes and personalizing management protocols even further.

Patients with MC were found to be significantly older than patients who did not have MC. A similar relationship was observed across all 3 types of MC. Previous studies in both the lumbar and cervical spine have also found an association between MC and advanced age.[8,25] A 10-year prospective study by Matsumoto et al.[26] found that the development of new MC was associated with increasing age, as well as the development of degenerative changes in the cervical spine. This suggests that the development of MC may be linked to structural damage to the spine that accumulates over time. In addition, we observed that patients with both overall MC and MC2 had significantly longer durations of symptoms compared to patients without MC. Qiao et al.[27] analyzed MC in the context of cervical spondylosis myelopathy, and found that MC tend to occur in pa-

tients with symptoms longer than 18 months. This could suggest that MC, particularly MC2, are the result of long-standing pathology and accumulation of degenerative changes. We also observed a statistically greater percentage of males in the MC2 group relative to the non-MC group. Male sex has previously been found to be a risk factor for MC.[25] However, other studies have found that sex and lifestyle factors (i.e., physical loading) may not play as large a role to the status and dynamics of the intervertebral disk.[28]

In terms of distribution, overall MC, specifically MC2, were most prevalent at C5–6. Both MC1 and MC3 were most commonly observed at C5–6, while MC2 was mostly seen at C6–7. These results are consistent with previous studies that have also found MC2 to be the most common type in the cervical spine, and C5–6/C6–7 to be the levels most commonly affected.[7,8] MC, particularly MC1 and MC2, have been shown to be interconnected, with a subset of MC2 progressing to MC3.[29] A prospective study by Mann et al.[30] of cervical spine patients with neck pain with MC found that 12/19 motion segments (63%) eventually converted from MC1 to MC2, but non-MC2 to MC1 conversion occurred. This transient nature observed in MC1, along with relative stability observed in MC2, could explain the higher prevalence of MC2 observed in our study. Conversely, the conversion of MC2 to MC3 may be rarer than the interconversion of MC1 and MC2. This could potentially explain the relative sparsity of MC3 observed in the cervical spine. However, the issue of MC interconversion was not in the scope of this study, and warrant future investigation to further delineate the origins and nature of cervical MC. In terms of location, lower cervical levels, particularly C5–6, have the most mobility, as well as the greatest load bearing in the cervical column.[31] Forces transmitted down the column to the lower levels could induce greater mechanical stress and instability to these levels, thus resulting in the development of MC. In addition, given the dynamic nature of MC, there is the possibility that fusion may alter properties of MC in the cervical spine. If this were the case, assessment of MC after surgery could provide valuable information regarding cervical spine adaption to the fusion construct, and may indicate whether degenerative findings, such as MC, are improved or worsening after surgery. In the present study, we did not assess long-term postoperative MRIs following fusion, and the question of how MC change after fusion could be another interesting topic for future studies.

In our analysis, no significant associations between MC and specific preoperative symptoms were noted. Interestingly, we did not observe a relationship between MC and neck pain. In the lumbar spine, MC has been linked to symptoms of low back pain.[32] Other studies have found that MC in the cervical spine may also relate to neck pain, although the results are mixed.[26,33,34] The lack of association with MC and preoperative neck pain observed in our study may reflect that both the non-MC and MC groups were being treated for debilitating spinal conditions, and thus they may have had similar levels of neck pain. The pathological reasons that underlie MC are still unclear, and future work is necessary to determine the mechanisms for their development, as well as their association with pain.

In terms of PROs, we did not observe differences in outcomes when looking at overall presence of MC, but did observe differences when analyzing by location. The presence of MC at C7–T1 was significantly related to higher levels of patient-reported postoperative disability, as measured by the NDI. While this finding may indicate a marginal clinical relationship between MC and outcomes after ACDF, a general lack of similar findings at more cephalad segments suggests this result may be due to an element of confounding. For example, the prevalence of MC at C7–T1 in our entire cohort was only 1.2%. Potentially, the observed increase in postoperative NDI in the MC cohort could be explained by a small sample size bias, especially given that the 95% confidence interval was large. Alternatively, in the present study, MC at C7–T1 were relatively rare, and patients with such phenotypes may have had diffuse degenerative pathology across multiple cervical segments. As such, it is unclear whether MC at C7–T1 is a true biomarker for worse postoperative symptomatology, or rather a proxy for patients with worse baseline cervical spine disease. Conversely, this finding could suggest that the present study was underpowered to determine the true postoperative effect size of MC at other cervical segments. In a previous study, Zehra et al.[35] noted that the relationship between lumbar spine endplate defects (such as MC) and patient-reported pain and disability is highly correlated. However, what effect preoperative MC may have on subjective postoperative outcomes remains a topic of debate. In a systematic review on the course of MC after posterior lumbar fusion, Portella and Acioly[36] noted that it is difficult to prove what effect surgical treatment may have on MC in the lumbar spine. Specifically, as most patients generally experience an improvement in symptoms after fusion, it is unclear whether MC are being addressed in a clinically meaningful way through surgery. Irrespective, MC may often regress and/or progress following lumbar fusion, suggesting that such findings are dynamic phenomena and are likely sensitive to the biomechanical changes introduced through an operative procedure.[36] Future study is war-

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ranted to determine how and why the vertebral endplate responds to such interventions, and to determine if such changes are clinically significant.

Given the close relationship between MC and degenerative changes, we hypothesized that MC, particularly at the adjacent level to the fusion segment, could have an effect on the development of ASD and rates of reoperation following ACDF. However, our multivariate analysis of surgical outcomes yielded no significant associations with MC, even when the MC was at the adjacent level. Few studies have assessed the role of cervical MC on the development of ASD. Li et al.[13] examined the effect of MC2 on outcomes following ACDF, and concluded that there may be an association between MC2 and development of ASD. In cases where degenerative findings such as MC are at adjacent levels, one consideration in preoperative planning of a fusion is whether to extend the fusion segment to include those levels in the construct. A study by Hilibrand et al.[37] examined the incidence of new onset adjacent segment disease in patients who underwent single-level versus multilevel cervical arthrodesis, and found that single-level fusion and pre-existing degenerative findings at the adjacent level were major risk factors for developing new onset adjacent level disease. The authors recommended that in patients with pre-existing symptomatic degenerative findings at the adjacent level, the cervical fusion construct should be extended to include these levels. However, other studies have found that multilevel fusions are associated with more perioperative complications and higher rates of reoperation compared to single-level ACDF.[38] Therefore, determining whether adjacent level pathology requires stabilization is critical to promote a good clinical outcome. Recent work looking at adjacent level spondylolisthesis, another degenerative finding potentially linked to ASD, has demonstrated no differences in PROs or the development of ASD compared to patients without the pathology.[39,40] Our results similarly suggest that when generating a preoperative plan for ACDF, the planned segment may not necessarily need to be extended to include degenerative findings at adjacent level if it is not related to the index pathology.

This study has several limitations. First, we chose to perform *post hoc* corrections for multiple comparisons in order to limit the likelihood of making a type I statistical error. We chose to do this given that we ran a large number of statistical models for each outcome measure. Due to this correction, several potentially significant results were excluded in our analysis. These results should cautiously be interpreted, as we were particularly conservative in our analysis. In addition, our study only includes data from a single institution. Thus, our patient population may not be representative of a wider demographic, and interpretation of these results should be cautiously applied to a broader context. In addition, the non-MC and MC cohorts differed in several baseline characteristics, such as age. Differences in these baseline characteristics may introduce confounding into our univariate analysis. We recognized this and attempted to address the potential for confounding by including all baseline characteristics as covariates when creating our multivariate models. Outcome data for our study population was also limited, which may have limited the power of our analysis. Nonetheless, the outcome parameters assessed in our study were extensive, consisting of multiple PROs, and the imaging data analyses were performed in a systematic, prospective manner to minimize bias in measurement with enhanced reliability. Future studies could aim to assess the differences in patient-reported and clinical outcomes between MC types in larger cohorts, with further replication in other ethnic populations. Finally, our study did not assess the interaction between MC and other degenerative pathologies, such as endplate abnormalities or spondylolisthesis. Future studies could also focus on examining the relationship between MC and other degenerative phenotypes, and whether the combination of multiple phenotypes could impact clinical outcomes following cervical fusion.

CONCLUSION

To our knowledge, this is the first study to systematically and comprehensively analyze the impact of MC on preoperative and postoperative outcomes in ACDF patients. The most common type of MC observed was MC2, and the most common level involved was C5–6. MC, including MC1, MC2, and MC3, were associated with advanced age. Only MC2 was significantly higher in males. Overall MC, MC2, and MC3 were associated with more levels fused. Overall MC, as well as MC2, were associated with longer duration of symptoms. However, regardless of stratification by type and location, MC was not associated with specific preoperative symptoms profiles or postoperative incidence of ASD or reoperations within the follow-up period of approximately 2 years. Patients with MC at C7–T1 reported greater levels of disability following surgery. However, the prevalence in the entire cohort of MC at C7–T1 was low (1.2%), and this finding may be explained by a small sample size bias. The presence of MC, even though they are associated with degenerative changes, does not seem to alter specific preoperative symptoms or surgical outcomes following ACDF. Moreover, the surgical outcomes did not differ when MC was inside or outside

the fusion segment. However, given that MC was associated with advanced age, a longer duration of symptoms, and more levels fused, the presence of MC may indicate a more debilitating and degenerative preoperative state for patients with MC relative to those without MC who suffer from degenerative pathology in the cervical spine. Findings from our study are important to help manage patient expectations, shed light upon predictive modeling of ACDF patients, and improve management algorithms. Future studies are needed to further assess the more detailed nature of MC involvement and extent at the subchondral vertebral region with other MRI phenotypes and outcomes.

CONFLICT OF INTEREST

The authors have nothing to disclose.

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