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Is the bone fusion affected by Modic-2 changes in single-level anterior cervical discectomy and fusion?

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Abstract

To explore the impact of Modic changes (MCs) on bone fusion after single-level anterior cervical discectomy and fusion (ACDF) with a zero-profile implant (the Zero-P implant system).

From November 2014 to November 2017, a total of 116 patients who underwent single-level ACDF with the Zero-P implant were divided into two groups according to MRI showing type 2 MCs (MC2) or no MCs (i.e., the MC2 group and the NMC group, respectively). A total of 92 (79.3%) patients were classified into the NMC group, and 24 (20.7%) patients were classified into the MC2 group. The clinical outcomes and fusion rates were retrospectively evaluated between the 2 groups preoperatively and postoperatively at 3, 6, and 12 months, and the final follow-up.

The Japanese Orthopedic Association (JOA) scores and the visual analogue scale (VAS) scores of neck pain were significantly improved compared to the preoperative scores in both the NMC and MC2 groups ($P < .05$). However, there were no differences in JOA or VAS scores between the 2 groups ($P > .05$). The fusion rates of the NMC and MC2 groups at 3, 6, and 12 months postoperatively, and the final follow-up were 33.7% and 12.5%, 77.2% and 54.2%, 89.1% and 87.5%, and 97.8% and 95.8%, respectively. The fusion rates were significantly lower at 3 and 6 months after surgery in the MC2 group than in the NMC group ($P < .05$).

The presence of MC2 did not affect the clinical outcome but delayed the fusion time following ACDF with the Zero-P implant system.

Level of Evidence is Level 3.

Abbreviations: ACDF = anterior cervical decompression and fusion, BMI = body mass index, CT = computed tomography, JOA = Japanese Orthopedic Association, MCs = Modic changes, MRI = magnetic resonance imaging, PLIF = posterior lumbar interbody fusion, VAS = visual analogue scale.

Keywords: anterior cervical discectomy and fusion, fusion rate, Modic changes, zero-profile implant

1. Introduction

Anterior cervical discectomy and fusion (ACDF) has been regarded as the gold standard for the treatment of degenerative cervical spine disease.[1,2] One of the most important indexes to assess the success of ACDF is intervertebral fusion. A solid bony fusion is the key for optimal long-term outcome.[3–5] A meta-analysis has shown that the fusion rate of single-level ACDF was 92.1%, and many factors may affect bony fusion, such as age, smoking status, comorbidities and the use of postoperative bracing.[6]

Modic changes (MCs), defined as the signal intensity changes of vertebral endplates on magnetic resonance imaging (MRI), were systematically described and classified by Modic et al in 1988.[7,8] The prevalence of MCs in cervical spine has been reported from 3% to 40.4%.[9–13] Many studies have focused on the impact of MCs in the cervical spine and demonstrated that the MCs may have a relationship with neck pain, segmental motion, axial symptoms, etc.[11,14,15] The MCs were considered as the inflammation, edema or hyperemic changes of endplates, whether they have impacts on bone fusion after ACDF was unknown. In the Li et al[16] study, the ACDF patients with Modic-2 changes at adjacent level were involved. The authors found that Modic-2 changes at adjacent level at baseline did not affect fusion rate or clinical outcome. In the lumbar spine, Kwon et al[17] have reported that the fusion rates were lower in patients with MCs compared to those without MCs after posterior lumbar interbody fusion (PLIF). However, to our knowledge, there are no studies which have focused on the fusion rates of patients with MCs at operated level after ACDF, especially at the early postoperative time points. Thus, the purpose of the current study was to

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KH and YH contributed equally to this work and should be considered co-first authors.

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evaluate the relationship between the fusion rates of patients after ACDF and MCs. As the types 2 MCs (MC2) were the most common type and represented fatty involution of the subchondral bone and marrow,[8] we compared the patients with MC2 with those without MCs firstly.

2. Methods

2.1. Patients

A retrospective study was conducted involving patients who underwent single-level ACDF with the Zero-P implant (Synthes GmbH Switzerland) for degenerative cervical spine disease between November 2014 and November 2017. The data of patients with MC2 or with no MCs (NMC) were selected. Patients with the following criteria were excluded: trauma, deformity, infection, tumour, previous cervical surgery, with osteoporosis or rheumatoid arthritis, or those with type 1 or type 3 MCs. This study was approved by the medical ethics committee of West China Hospital of Sichuan University, and all patients were informed that they were going to be in this study.

2.2. Assessment of MC2 and NMC

Imaging measurements were made by two blinded researchers on MRI images obtained before surgery. MC2 was defined as a hyperintense signal on T1 sequences and a hyper- or isointense signal on T2 sequences (Fig. 1). NMC was defined as no signal changes on either T1 or T2 sequences.

2.3. Surgical technique

All anterior fusions were performed using the Smith-Robinson technique and a right-sided approach by the same surgeon. After confirmation and exposure of the appropriate vertebral levels, a Caspar distracter was used, and the disc material was removed. The endplate cartilage was scraped with a curette or high-speed electric drill to prepare for bone grafting. The posterior longitudinal ligament, osteophytes, and other compressive elements were removed to ensure adequate dural and neural decompression. After measuring the intervertebral height and width, the appropriate Zero-P implant filled with β-tricalcium phosphate (chronOS cylinder, Synthes GmbH Switzerland) was inserted with an implant holder/aiming device.

2.4. Clinical evaluation

All data were collected preoperatively and postoperatively at 3, 6, and 12 months, and the final follow-up. Japanese Orthopedic Association (JOA) scores were used to evaluate functional recovery of the nerve, and visual analogue scale (VAS) scores were used to evaluate neck pain intensity.

2.5. Assessment of bony fusion

The fusion rates were assessed on cervical spine static and dynamic X-ray images. Fusion was considered according to the following accepted criteria[18]:

(1) less than 2°of segmental movement on lateral flexion/extension views,

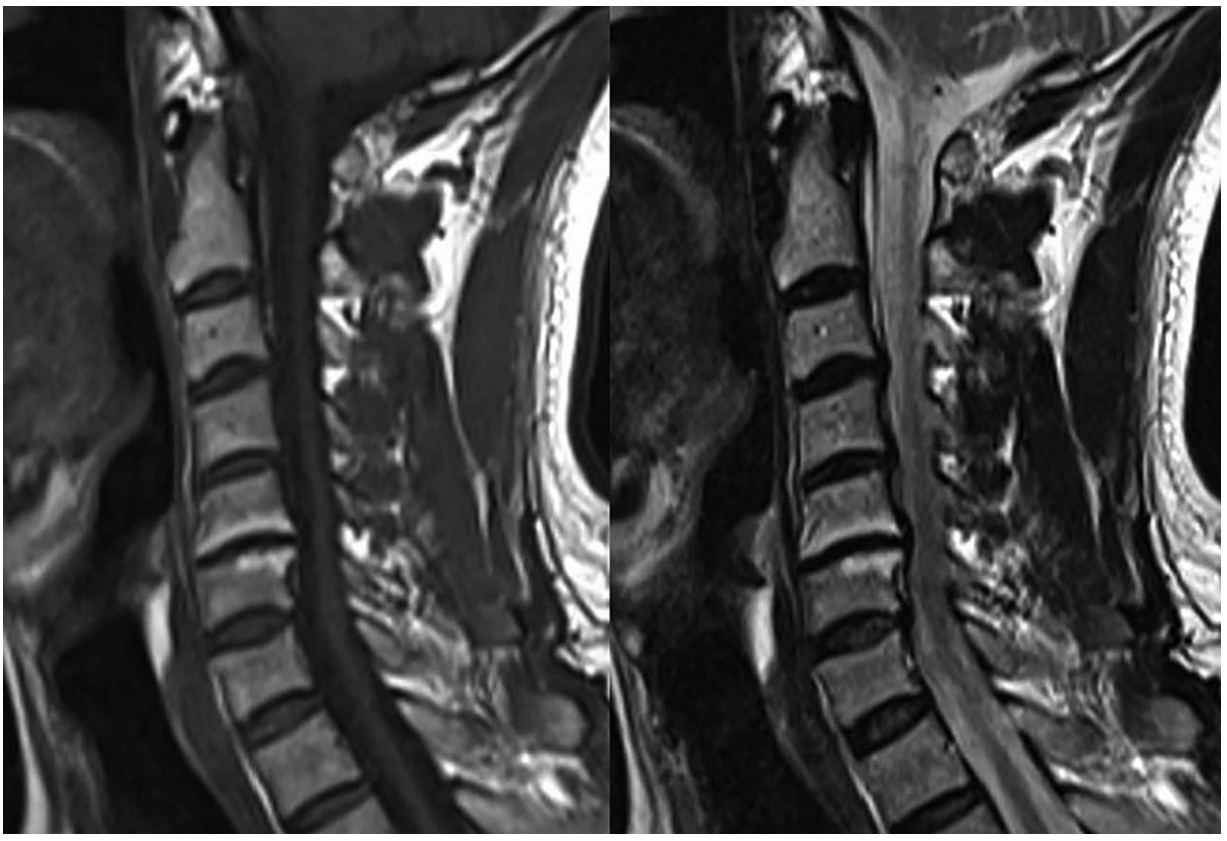

Figure 1. T1-sequence (left) and T2-sequence (right) images demonstrate C5-C6 with MC2 on MRI.

(2) absence of a radiolucent gap between the graft and endplates, and
(3) presence of continuous bridging bony trabeculae at the graft endplate interface.

When the radiographic fusion was controversial, three-dimensional computed tomography (CT) scan reconstructions were further performed to assess radiographic fusion. The assessment of bony fusion was evaluated by two blinded researchers (Dr Huang and Dr Hong), and disagreements were resolved by consensus when necessary, by a third author (Professor Liu).

The implant-related complications such as screw pull-out, screw breakage were also recorded.

2.6. Statistical analysis

The findings are presented as the mean values ± standard deviation (SD) or as counts, as indicated. Student's *t* tests were used to compare the quantitative data. Chi-square tests were used to assess the statistical significance of fusion rates between the 2 groups. Statistical significance was defined as $P < .05$. All statistical analyses were performed using SPSS (Version 19.0, Chicago, IL).

3. Results

From November 2014 to November 2017, 137 patients were undergone single-level ACDF with the Zero-P implant. According to the inclusion and exclusion criteria, 116 patients were included in the study with follow-up data collected preoperatively and postoperatively at 3, 6, and 12 months, and the final follow-up. Among them, 92 (79.3%) patients were classified into the NMC group, and 24 (20.7%) patients were classified into the MC2 group. The NMC group had a mean age of 51.38 years and a mean follow-up duration of 34 months. The MC2 group had a mean age of 46.79 years and a mean follow-up duration of 30 months. There were 45 females and 47 males in the NMC group and 13 females and 11 males in the MC2 group, with no significant difference in the numbers of males and females between the groups ($P > .05$).

The baseline demographic characteristics, including age, body mass index (BMI), operative time, blood loss and surgical levels, were evaluated, and no significant differences were observed between the characteristics in the NMC group and the MC2 group ($P > .05$) (Table 1). There was no significant difference in the incidence of postoperative dysphagia between the 2 groups ($P > .05$). Smoking may impact the fusion rate, but there was no significant difference in the number of smokers between the 2 groups ($P > .05$).

The JOA scores improved from 14.17 ± 0.78 points before surgery to 16.25 ± 0.77 points at the final follow-up in the NMC group and from 13.98 ± 0.82 points to 16.42 ± 0.83 points, respectively, in the MC2 group ($P < .05$). The VAS scores significantly decreased from 3.95 ± 1.61 points before surgery to 1.08 ± 0.89 points at the final follow-up in the NMC group ($P < .05$). Similarly, the VAS scores significantly decreased from 3.88 ± 1.45 points before surgery to 0.96 ± 0.69 points at the final follow-up in the MC2 group ($P < .05$). However, no significant differences in the JOA scores or VAS scores were observed between the NMC and MC2 groups at any observation time point ($P > .05$) (Table 2).

The fusion rates of the NMC group and the MC2 group at 3, 6, and 12 months postoperatively, and the final follow-up were 33.7% and 12.5%, 77.2% and 54.2%, 89.1% and 87.5%, and 97.8% and 95.8%, respectively. The fusion rates were significantly lower at 3 and 6 months after operation in the MC2 group than in the NMC group ($P < .05$) (Table 3, Fig. 2). One patient in the MC2 group failed to achieve bony fusion at the final follow-up (Fig. 3). He did not complain any uncomfortable, so he was still under observation.

No implant-related complications were observed during the follow-up period.

Table 1

Demographic and baseline information.

	NMC	MC2	*P* value
N	92	24	
Age (yr)	51.38 ± 11.66	46.79 ± 11.14	.086
Sex (n)			.647
Female	45	13	
Male	47	11	
BMI (kg/m^2)	23.60 ± 2.44	24.33 ± 2.75	.202
Operative time (min)	132.6 ± 24.6	132.6 ± 25.2	.985
Blood loss (ml)	35.54 ± 22.88	37.08 ± 18.29	.086
Level (n)			.979
C3-C4	7	2	
C4-C5	15	3	
C5-C6	60	16	
C6-C7	10	3	
Postoperative dysphagia (n)	16	4	1.000
Smoker (n)	27	5	.406

BMI = body mass index, MC2 = Modic-2 changes, NMC = with no Modic changes.

4. Discussion

It is generally accepted that solid arthrodesis is necessary for optimal outcome in ACDF.[4,19] According to the study of Wright et al,[20] the absence of bony fusion was correlated with higher VAS scores of neck pain. Schroder et al[21] also reported less satisfactory clinical outcomes in patients with nonunion than in patients who achieved bony fusion. Additionally, nonunion may lead to the occurrence of pseudarthrosis, which is a likely cause of neck symptoms.[22,23] Thus, many studies have concentrated on improving the fusion rate of ACDF using a plate, getting patients

Table 2

Evaluate of JOA score and VAS score of neck.

	NMC	MC2	*P* value
JOA score			
Pre-op	14.17 ± 0.78	13.98 ± 0.82	.261
3 months	15.39 ± 0.86*	15.04 ± 1.00*	.090
6 months	15.82 ± 0.86*	15.42 ± 1.10*	.060
12 months	16.14 ± 0.87*	16.25 ± 1.07*	.606
Final follow-up	16.25 ± 0.77*	16.42 ± 083*	.352
VAS score of neck			
Pre-op	3.95 ± 1.61	3.88 ± 1.45	.846
3 months	2.55 ± 1.12*	2.54 ± 1.10*	.961
6 months	1.77 ± 1.06*	1.79 ± 0.93*	.933
12 months	1.24 ± 1.05*	1.17 ± 0.96*	.761
Final follow-up	1.08 ± 0.89*	0.96 ± 0.69*	.549

JOA = japanese orthopaedic association, MC2 = Modic-2 changes, NMC = with no Modic changes, VAS = visual analogue scale; Pre-op, preoperative.
* Significant difference compared with preoperative value ($P < .05$).

Table 3

The fusion rates of the groups at each follow-up period.

	NMC	MC2	*P* value
3 months	33.7% (31/92)	12.5% (3/24)	.042*
6 months	77.2% (71/92)	54.2% (13/24)	.025*
12 months	89.1% (82/92)	87.5% (21/24)	.823
Final follow-up	97.8% (90/92)	95.8% (23/24)	.584

MC2 = Modic-2 changes, NMC = with no Modic changes.
* Significant difference between two groups ($P < .05$).

to quit smoking, etc.[24,25] However, the reported fusion rates of single-level ACDF still have not reached 100%.

Pertzen et al[26] reported that the speed of fusion was combined with implant complications. Patients with delayed fusion may suffer more implant complications, such as screw cut-outs, screw fractures and pseudarthroses. Some case reports have also shown that implant-related failures occurred early after ACDF because of the absence of bony fusion.[27,28] Therefore, the earlier bony fusion is important in ACDF.

MCs were considered a type of inflammatory change in vertebral endplates and subchondral bone marrow. The pathophysiology of MCs is complex. According to Modic et al,[8] type 1 changes demonstrated an inflammatory phase of the degenerative process; type 2 changes represent fatty involution of the subchondral bone and marrow; and type 3 changes demonstrated cicatrization phase of disc degeneration. In previous studies, inflammatory mediators such as interleukins, prostaglandin E2, PGP 9.5, and TNF were shown to be relevant to MCs.[29–31] Adams et al[32] showed that minor damage to a vertebral body endplate leads to progressive structural changes in the adjacent intervertebral discs. Albert et al[33] reported that the discs infected with anaerobic bacteria were more likely to develop MCs in the adjacent vertebrae than those in which no bacteria were found or those in which aerobic bacteria were found.

Previous studies of MCs have focused on the lumbar spine, which suggested a relationship with bony fusion. Kwon et al[17] compared the fusion rates between different types of MCs after PLIF. In the 351 patients (no degeneration: 259, type 1: 26, type 2: 55, type 3: 11), the fusion rates of MCs were significantly lower than the fusion rates in those without MCs, especially in those with type 3 MCs at 3 years or later after surgery. MCs were not rare in cervical spine. According to Mann et al[12] study, MCs were observed in 40.4% of patients over the age of 50 years. Gao et al[34] reviewed 278 patients with single-level MCs and nerve compression symptoms and reported that MCs were seen in 76 patients (27.34%). Few studies have focus on the impact of MCs on bone fusion. Li et al[13] observed 106 patients who underwent single-level ACDF from C4 to C7 and found that the fusion rates were similar between the patients with and those without MCs at 2 years after surgery. However, the fusion rates were only reported at the last follow up. Whether the bone fusion would be affected by MCs at the early time after ACDF have not been reported yet.

In our study, the prevalence of MC2 in single-level ACDF patients was 17.5%. We retrospectively analyzed the medical records of 116 patients with single-level ACDF who were followed at least 12 months postoperatively according to the presence or absence of MC2. We found that the most common level of MC2 was C5-C6, which was consistent with the findings reported by others.[9,10] The relationship between MCs and neck pain is controversial. In our study, the VAS scores of neck pain were slightly higher in patients with MC2 before surgery, but there was no statistically significant difference. The fusion rates of MC2 were not significantly difference at 12 months postoperatively and the final follow-up, but the difference was observed at 3 months and 6 months postoperatively, which meant that the fusion time was delayed in patients with MC2. For these non-fusion patients, a longer time of wearing cervical collar was requested to avoid the implant-related complications. Although no implant-related complications had been observed during the follow-up period, they complained a more inconvenience life after surgery.

The exact reason for the impact of MC2 on bone fusion remains unclear. We speculate that this effect may be due to changes in the endplate microenvironment. Although the endplate cartilage was scraped during the operation, but the bony endplates were retained, which means the changes caused by MC2 still exist and may impact bone fusion.[35] Another reason may be due to the implant. The Zero-P implant system consists of a PEEK interbody spacer, a titanium alloy plate and

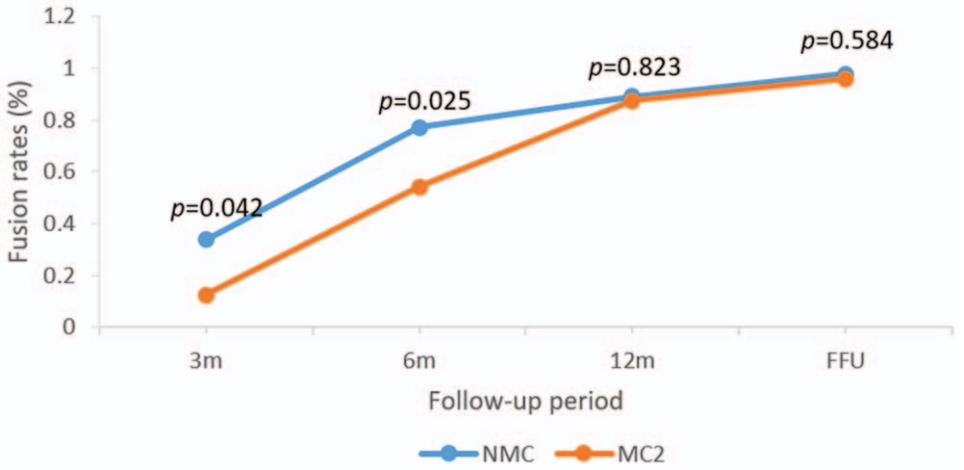

Figure 2. The fusion rates of 2 groups at follow-up period.

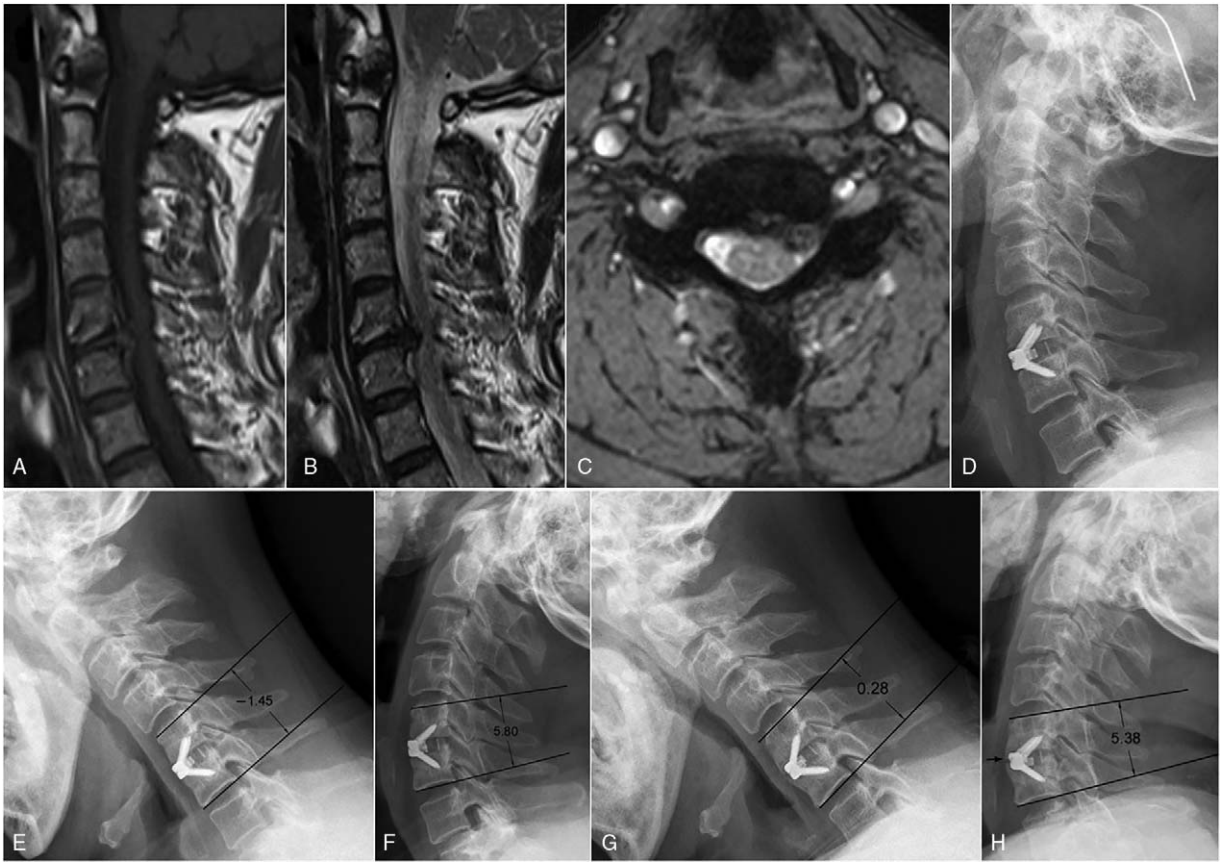

Figure 3. A, B and C: a 57-year-old man had a disc herniation at C5-C6 with MC2. D: He accepted a single-level ACDF with Zero-P implant at C5-C6. E and F: at 12 months postoperatively, there were 7.25° of segmental movement on lateral flexion/extension views. G and H: at the final follow-up, 36 months postoperatively, the segmental movement was still 5.1 degrees. The hyperplasia osteophyte could be observed at anterior of the vertebral bodies (black arrow).

four locking screws. In our study, the fusion material was the β-tricalcium phosphate which may be more sensitive on the changes of endplates.[36] The exact mechanism needs to be explored in the future.

We suggest that some measures should be taken for patients with MC2 upon receiving ACDF. First, many studies have reported that the use of an autograft is a more efficacious strategy for bony fusion,[6,37] an autograft may be considered at the time of ACDF in patients with MC2. Second, the plate and cage system have been reported to have a more stabilization than the Zero-P implant system.[38,39] It prefers to use the plate and cage for fusion in the patients with MC2 to reduce the risks of implant-related implications. But the efficiency of plate and cage need to be verified in the future.

Our study has some limitations. First, only patients with MC2 were involved in the study. In the future, the fusion rates of all three types of MCs should be studied. Second, only one implant system was contained in the study. Finally, this was a single center retrospective study and the number of patients was relatively small. In the future, prospective, multicenter, large-scale studies should be performed to confirm the results.

5. Conclusion

The presence of MC2 did not affect the clinical outcome but delayed the fusion time following ACDF with the Zero-P implant.

Acknowledgments

The authors declare that they have no conflict of interest concerning the materials or methods used in this study or the findings specified in this study.

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