

Complete Blood Count-Derived Inflammation Indices in Lumbar Modic Changes

Yasemin Ozkan¹, Mahmut Alpayci², Veysel Delen³

¹Adnan Menderes University, Faculty of Medicine, Department of Physical Medicine and Rehabilitation, Aydın, Türkiye

²Fizyocenter Hospital, Department of Physical Medicine and Rehabilitation, Diyarbakır, Türkiye

³Harran University, Faculty of Medicine, Department of Physical Medicine and Rehabilitation, Şanlıurfa, Türkiye

Abstract

Introduction: Complete blood count (CBC)-derived indices such as neutrophil/lymphocyte (NLR) have been proposed as indicators of systemic inflammation. Modic changes are vertebral endplate lesions associated with low back pain. Modic type 1 changes (MC1s) are inflammatory in nature and more painful than MC2s. However, there are not enough studies on the relationship between MC1s and systemic inflammation. In this study, we aimed to investigate the relationship between MC1s and systemic inflammation by considering the CBC-derived indices.

Materials and Methods: This comparative study was conducted at Harran University Hospital between March 2023 and January 2024. In the study, 24 MC1s and 24 MC2s patients were compared in terms of demographic characteristics, pain severity, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), CBC cells and CBC-derived indices.

Results: The two groups were statistically similar in terms of age ($p=0.111$), gender ($p=0.752$), BMI ($p=0.415$), pain duration ($p=0.860$), CRP ($p=0.341$), ESR ($p=0.412$), CBC cells ($p>0.05$) and CBC-derived indices ($p>0.05$). Only MC1s patients had significantly higher low back pain severity than MC2s patients [7.5 ± 1.1 (5.0-10.0) vs 6.8 ± 1.2 (5.0-9.0), $p=0.032$]. However, no significant correlation was found between pain intensity and other parameters ($p>0.05$).

Conclusions: MC1s and MC2s patients are similar in terms of inflammation markers. The greater severity of low back pain in MC1s patients may be related to the local inflammatory nature of MC1s, but not to systemic inflammation. Management of low back pain caused by Modic changes should focus on local treatment approaches.

Keywords: Low back pain; inflammation; disc degeneration; complete blood count.

Introduction

Modic changes are magnetic resonance imaging (MRI) findings. They reflect both different signal intensities and different histologic textures in the vertebral endplate. Accordingly, there are three types of Modic changes. According to MRI, Modic type I changes (MC1s) appear as low intensity on T1-weighted images and high intensity on T2-weighted images (Figure 1), while Modic type II changes (MC2s) appear as high intensity on both T1- and T2-weighted images (Figure 2). Histopathologically, MC1s reflect inflammatory bone marrow, while MC2s reflect fatty bone marrow (1, 2). Furthermore, according to histomorphometric examinations, MC1s exhibit high bone turnover, whereas MC2s show low bone formation in bone structure and activity (3). However, the etiopathogenesis of Modic changes is not clear and these lesions can potentially transform into each other over time (2). Clinically MC1s are known to be more painful (4) and associated with inflammation (2), injury (5, 6), past



Figure 1: Modic type I changes, low-intensity on the T1 and high-intensity on the T2 weighted images in the L5-S1 vertebral endplates.

infectious damage (7, 8) and autoimmune response (9), whereas MC2s are associated with mechanical loading and systemic effects (2, 5, 6).

*Corresponding Author: Mahmut Alpayci, Fizyocenter Hospital, Department of Physical Medicine and Rehabilitation, Diyarbakır, Türkiye.
E-mail: mahmutalpayci@gmail.com Orcid: Yasemin [Özkan_0000-0003-3797-483X](https://orcid.org/0000-0003-3797-483X), Mahmut Alpayci [0000-0002-4356-6763](https://orcid.org/0000-0002-4356-6763), Veysel Delen [0000-0002-8152-4628](https://orcid.org/0000-0002-8152-4628)

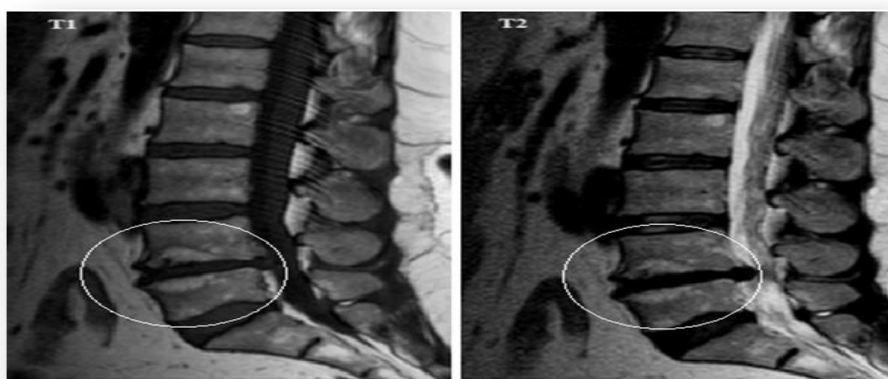


Figure 2: Modic type II changes, high-intensity on the both T1 and T2 weighted images in the L4-L5 vertebral endplates.

Table 1: Demographic and clinical characteristics of the groups.

	Modic type I changes (n=24)	Modic type II changes (n=24)	p
Age, years	43.3±9.2 (28.0-62.0)	47.7±9.2 (34.0-64.0)	0.111 ^a
F/M, n(%)	16(66.7)/8(33.3)	18(75)/6(25)	0.752 ^b
BMI, kg/m ²	27.2±4.3 (21.0-38.1)	28.1±3.3 (22.5-34.9)	0.415 ^a
Pain duration, years	8.1±6.1 (1.0-25.0)	7.9±6.9 (1.0-30.0)	0.860 ^c
Pain intensity, VAS	7.5±1.1 (5.0-10.0)	6.8±1.2 (5.0-9.0)	0.032 ^c

Values are presented as mean±SD (min.-max.), excluding gender ratio; **F/M:** Female/Male; **BMI:** Body mass index; **VAS:** Visual analog scale; ^a: The Independent t test; ^b: The Fisher’s Exact test; ^c: The Mann-Whitney U test.

There is no standardized management for Modic changes and nonoperative and individualized approaches should be preferred according to the type of changes (2, 6). Complete blood count (CBC)-derived indices (NLR, MLR, PLR, NLPR, SII, SIRI and AISI) (Table 1) have been proposed as indicators of systemic inflammation (10) and also have diagnostic (11, 12), prognostic (13, 14) and predictive (15, 16) capabilities in some diseases. CBC-derived indices of inflammation have gained popularity because they are simple, easy and inexpensive. Today, their different critical roles and inflammation-related values in various medical conditions are still of interest and intriguing (17-20). It is possible that local lesions have systemic effects, but the possible systemic features or manifestations of Modic changes have not been adequately investigated. Considering that MC1s are painful lesions (4) and have inflammatory nature (2), their relationship with systemic inflammation is a topic worthy of investigation. In this study, we hypothesized that pain and inflammation values may be increased in patients with MC1s and associated with CBC-derived inflammation indices. Therefore, we

aimed to examine MC1s patients in comparison with MC2s patients in terms of pain severity and CBC-derived indices. This may provide more information about the etiopathogenesis and effective management of MC1s.

Materials and Methods

A total of 48 patients with Modic changes (24=MC1s and 24=MC2s) were studied. Demographic characteristics of the patients were recorded and the severity of low back pain was measured using a 10 cm horizontal line called the Visual Analog Scale (no pain: 0, very severe pain: 10). Laboratory values such as C-reactive protein (CRP), erythrocyte sedimentation rate (ESR) and CBC cells including leukocyte, platelet, neutrophil and lymphocyte counts were recorded. CBC-derived inflammation indices (NLR, MLR, PLR, NLPR, SII, SIRI and AISI) were calculated as follows: NLR: neutrophil/lymphocyte, MLR: monocyte/lymphocyte, PLR: platelet/lymphocyte, NLPR: neutrophil/(lymphocyte*platelet), SII: neutrophil*platelet/lymphocyte, SIRI: neutrophil*monocyte/lymphocyte and AISI: neutrophil*platelet*monocyte/lymphocyte.

Table 2: Laboratory parameters in modic type I and type II changes.

	Modic type I changes (n=24)	Modic type II changes (n=24)	p
Leukocyte (10 ³ /mL)	7.3±1.9 (4.3-12.3)	7.3±1.5 (5.0-10.4)	0.932 ^a
Neutrophil (10 ³ /mL)	4.0±1.4 (1.7-7.2)	4.1±1.1 (2.2-6.3)	0.763 ^a
Lymphocyte (10 ³ /mL)	2.5±0.7 (1.4-4.4)	2.4±0.6 (1.4-3.8)	0.523 ^b
Monocyte (10 ³ /mL)	0.6±0.3 (0.4-1.5)	0.6±0.1 (0.3-0.8)	0.959 ^b
Platelet (10 ³ /mL)	307.0±71.8 (177.0-418.0)	287.9±71.3 (179.0-503.0)	0.360 ^a
CRP (mg/L)	2.2±1.9 (0.2-7.4)	2.7±2.3 (0.3-9.1)	0.483 ^b
ESR (mm/h)	17.5±12.3 (1.0-51.0)	15.2±6.2 (3.0-31.0)	0.893 ^b

Values are presented as mean±SD (min.-max.); **CRP:** C-reactive protein; **ESR:** Erythrocyte sedimentation rate; ^a: The Independent t test; ^b: The Mann-Whitney U test.

Inclusion and exclusion criteria Low back pain patients with MC1s or MC2s, aged ≥18 and ≤64 years, and who gave informed consent for participation were included. On the other hand, MC3s and combination of types were excluded. We also excluded acute low back pain, spinal deformities, inflammatory diseases, cancers, heart diseases, stroke, breastfeeding, pregnancy, psychiatric disorders and extreme obesity (BMI≥40 kg/m²).

Ethical consent: This comparative study was conducted at Harran University Hospital between March 2023 and January 2024. Ethical approval was obtained retrospectively (Decision date: February 12, 2024; Decision no: HRU/24.01.27).

Statistical analyses: Descriptive statistics for continuous variables were expressed as mean±standard deviation (min.-max.); for categorical variables, they were expressed as number and percentage. The normality of the continuous variables was examined using the Shapiro-Wilk test. Independent t-test was used to determine the significance of the differences between group averages for variables that were determined to be normally distributed. Mann-Whitney U test was used for variables that did not show normal distribution. The relationships between continuous variables were analyzed using Pearson and Spearman correlation tests for normally and non-normally distributed values, respectively. Fisher's exact test was used to

compare categorical variables between groups. The significance level was accepted as 5% and calculations were made using the SPSS package program (version 27).

Results

The MC1s group consisted of 16 women (66.7%) and 8 men (33.3%), while the MC2s group consisted of 18 women (75%) and 6 men (25%). The mean age of the MC1s group was 43.3±9.2 years (range 28-62) and the mean age of the MC2s group was 47.7±9.2 years (range 34-64). There was no significant difference between the MC1s and MC2s groups in terms of age (p=0.111) and gender (p=0.752). The two groups were statistically similar in terms of BMI (p=0.415) and pain duration (p=0.860). However, the MC1s group had significantly higher low back pain severity than MC2s group (p=0.032) (Table 1). Table 2 shows statistical comparisons of some laboratory parameters between the groups. The two groups were statistically similar in terms of leukocytes (p=0.932), neutrophils (p=0.763), lymphocytes (p=0.523), monocytes (p=0.959), platelets (p=0.360), CRP (p=0.483) and ESR (p=0.893) (Table 2). Table 3 presents statistical comparisons of CBC-derived indices of inflammation between the groups. The two groups were statistically similar in NLR (p=0.431), MLR (p=0.980), PLR (p=0.421), NLPR (p=0.131), SII (p=0.885), SIRI (p=0.509) and AISI (p=0.918)

Table 3: CBC-derived inflammation indices in Modic type I and type II changes.

	Modic type I changes (n=24)	Modic type II changes (n=24)	p
NLR	1.7±0.6 (0.6-3.4)	1.8±0.5 (0.9-3.1)	0.431 ^a
MLR	0.2±0.1 (0.1-0.4)	0.3±0.7 (0.1-0.4)	0.980 ^a
PLR	131.3±48.8 (54.3-297.9)	129.7±58.0 (77.2-349.3)	0.421 ^b
NLPR	0.006±0.002 (0.0-0.01)	0.007±0.002 (0.0-0.01)	0.131 ^a
SII	521.3±243.3 (129.2-1084.6)	518.9±213.1 (204.8-1131.8)	0.885 ^b
SIRI	1.04±0.6 (0.3-2.6)	1.0±0.4 (0.3-2.3)	0.509 ^b
AISI	328.6±218.4 (66.1-995.5)	300.4±156.6 (95.7-713.0)	0.918 ^b

Values are presented as mean±SD (min.-max.); **NLR:** neutrophil/lymphocyte, **MLR:** monocyte/lymphocyte, **PLR:** platelet/lymphocyte, **NLPR:** neutrophil/(lymphocyte*platelet), **SII:** neutrophil*platelet/lymphocyte, **SIRI:** neutrophil*monocyte/lymphocyte, and **AISI:** neutrophil*platelet*monocyte/lymphocyte; ^a: The Independent t test; ^b: The Mann-Whitney U test.

Table 4: Correlations of VAS with CBC-derived systemic inflammation indices.

		CRP	NLR	MLR	PLR	NLPR	SII	SIRI	AISI
MC1 (n=24)	r	-0.060	0.012	0.184	-0.027	0.030	0.062	0.059	0.118
	p	0.782 ^a	0.956 ^a	0.389 ^a	0.901 ^a	0.889 ^a	0.774 ^a	0.784 ^a	0.582 ^a
MC2 (n=24)	r	0.256	0.106	-0.129	0.009	0.048	0.158	0.076	0.039
	p	0.127 ^a	0.622 ^b	0.547 ^b	0.967 ^a	0.822 ^b	0.462 ^a	0.726 ^a	0.855 ^a
All cases (n=48)	r	0.091	0.004	0.012	0.035	-0.022	0.120	0.053	0.098
	p	0.536 ^a	0.979 ^a	0.937 ^a	0.813 ^a	0.880 ^a	0.416 ^a	0.723 ^a	0.509 ^a

CRP: C-reactive protein; **MC:** Modic changes; **NLR:** neutrophil/lymphocyte, **MLR:** monocyte/lymphocyte, **PLR:** platelet/lymphocyte, **NLPR:** neutrophil/(lymphocyte*platelet), **SII:** neutrophil*platelet/lymphocyte, **SIRI:** neutrophil*monocyte/lymphocyte, and **AISI:** neutrophil*platelet*monocyte/lymphocyte. ^a: The Spearman correlation test; ^b: The Pearson correlation test.

(Table 3). Table 4 presents the statistical correlations of low back pain severity with CBC-derived inflammation indices when MC1s (n=24), MC2s (n=24) and all cases (n=48) were evaluated separately. No statistically significant correlation was found (p>0.05 for all) (Table 4). Table 5 presents statistical correlations of CRP with CBC-derived inflammation indices when MC1s (n=24), MC2s (n=24), and all cases (n=48) were evaluated separately. No statistically significant correlation was found (p>0.05 for all) (Table 5).

Discussion

In this comparative study, MC1s patients (study group) were compared to MC2s patients

(comparison group) in terms of demographics, low back pain, CBC cells, CRP, ESR and CBC-derived indices of inflammation. Statistical analysis showed that MC1s patients had higher pain severity than MC2s patients. However, the two groups were similar in terms of demographic characteristics, CBC cells, CRP, ESR and CBC-derived inflammation indices. Furthermore, no significant correlation was found between pain severity, CRP level and CBC-derived inflammation indices. To the best of our knowledge, this is the first study to address and compare MC1s and MC2s in terms of CBC-derived inflammation indices. Previous studies have revealed that MC1s are more painful than MC2s (4) and inflammatory

Table 5: Correlations of CRP with CBC-derived systemic inflammation indices.

		VAS	NLR	MLR	PLR	NLPR	SII	SIRI	AISI
MC1 (n=24)	r	-0.060	0.321	0.133	-0.137	0.404	0.122	0.282	0.147
	p	0.782 ^a	0.127 ^a	0.537 ^a	0.523 ^a	0.050 ^a	0.571 ^a	0.182 ^a	0.494 ^a
MC2 (n=24)	r	0.256	0.073	-0.145	-0.236	0.100	0.137	0.073	0.083
	p	0.227 ^a	0.733 ^a	0.498 ^a	0.267 ^a	0.640 ^a	0.523 ^a	0.736 ^a	0.701 ^a
All cases (n=48)	r	0.091	0.198	-0.035	-0.183	0.242	0.126	0.183	0.120
	p	0.536 ^a	0.178 ^a	0.811 ^a	0.213 ^a	0.097 ^a	0.395 ^a	0.213 ^a	0.415 ^a

CRP: C-reactive protein; **VAS:** Visual analog scale; **MC:** Modic changes; **NLR:** neutrophil/lymphocyte, **MLR:** monocyte/lymphocyte, **PLR:** platelet/lymphocyte, **NLPR:** neutrophil/(lymphocyte*platelet), **SII:** neutrophil*platelet/lymphocyte, **SIRI:** neutrophil*monocyte/lymphocyte, and **AISI:** neutrophil*platelet*monocyte/lymphocyte. ^a: The Spearman correlation test.

in nature (2), whereas MC2s reflect fatty bone marrow (1, 2). However, their potential systemic presentation has not been adequately investigated. Consistent with the findings of previous studies, we found that patients with MC1s have higher low back pain severity than patients with MC2s (4). As noted in previous studies, this difference between MC1s and MC2s may be related to the inflammatory nature of MC1s (1, 4). Although previous studies have reported the inflammatory nature of MC1s and fatty bone marrow of MC2s, we found that these two groups were similar in terms of inflammation markers such as CRP and CBC-derived inflammation indices. Furthermore, no significant correlation was found between pain severity, CRP level and CBC-derived inflammation indices. On the other hand, Dudli et al (21) recently reported that intralesional CRP level correlated with serum CRP level in MC1s patients. Accordingly, CRP levels in patients with MC1s were expected to be high and correlated with CBC-derived indices of inflammation. However, the current study revealed that MC1s were not different from MC2s in terms of CRP level and CBC-derived inflammation indices. CBC-derived inflammation indices have been proposed as indicators of systemic inflammation (10) and also as diagnostic (11, 12), prognostic (13, 14) and predictive (15, 16) tools in some diseases. However, according to our results, CBC-derived inflammation indices cannot be used to differentiate between MC1s and MC2s. Furthermore, both MC1s and MC2s showed normal CRP (<5 mg/L) and NLR (1-2 range) values in this study (10). Accordingly, Modic changes cannot be considered as signs of systemic inflammation, and furthermore, MC1s and MC2 are similar in terms of systemic inflammation

indicators such as CRP and CBC-derived inflammation indices. However, the current results showing that MC1s and MC2s are unrelated to systemic inflammation seem to be inconsistent with previous findings showing a positive association of low back pain with classical inflammatory biomarkers (22, 23), considering that Modic changes are the causes of low back pain (21, 24). Similar to NLR, other CBC-derived inflammation indices investigated in the current study (MLR, PLR, NLPR, SII, SIRI and AISI) did not reveal any differences that could distinguish between MC1s and MC2s. Therefore, the hypothesis of this study that MC1s patients may have increased CBC-derived inflammation indices is not correct.

Study limitations: On the other hand, it should be noted that the current study has several limitations. Data obtained from a single center and small sample size are the main limitations. Because small sample size may reduce statistical power, especially in outcomes where there is no significant difference. Furthermore, the lack of healthy controls in the study and the paucity of relevant literature may have limited a satisfactory comparison and in-depth discussion. Nevertheless, this study is the first to address the issue and its current limitations can be addressed in future studies. Systemic inflammatory biomarkers have been found to be associated with various factors including age, race, drugs, anemia, obesity, psychiatric disorders, chronic diseases and cancers (10, 15). Thanks to the exclusion criteria applied in this study, the groups were similar in terms of these factors. Therefore, it can be said that our results were not affected by these factors and the study is reliable in this respect.

Conclusion

In conclusion, low back pain patients with MC1s are similar to patients with MC2s in terms of CRP and CBC-derived inflammation indices analyzed in this study. The greater severity of low back pain in MC1s patients may be related to the local inflammatory nature of MC1s, but not necessarily to systemic inflammation. This suggests that the management of low back pain caused by Modic changes should focus on local treatment approaches. However, the small sample size may be limiting in terms of generalizability and may have affected the strength of the study. Future findings from a larger population will provide a more robust basis.

Ethical consent: The study protocol was approved by the Harran University Hospital Ethics Committee (Date: February 12, 2024; Decision no: HRU/24.01.27).

Written consent: Written consent was obtained from all participants included in the study.

Conflict of interest: The authors report no conflicts of interest in this work.

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Originality of figures: The images used in the article are original and the necessary permissions have been obtained.

Data sharing statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Authors' contribution: Concept (Y.Ö., M.A., V.D.), Design (Y.Ö., M.A., V.D.), Materials and Data (V.D.), Analysis and Literature Review (Y.Ö.), Writing and Revision (M.A.).

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