Annals of Medical Research
DOI: 10.5455/annalsmedres.2019.05.266 2019;26(7):1402-5

Original Article

The role of mean corpuscular volume change in progression of osteoarthritis

Kenan Ozler

Konya Beysehir State Hospital, Clinic of Orthopaedics and Traumatology, Konya, Turkey

Abstract

Aim: The aim of our study was to evaluate the MCV, CRP, WBC changes in OA and to research whether or not any MCV, WBC changes pronto detectable by easy complete blood count (CBC), have diagnostic values for the prediction of progression of OA.

Material and Methods: Eighty-two OA and sixty-nine control patients were registered in the study. The knee OA was classified by Kellgren-Lawrence (K&L) scale. Mean corpuscular volume (MCV), white blood cell (WBC) and C-reactive protein (CRP) levels were measured.

Results: CRP and MCV levels were higher in OA than the control (p=.034 and p=.022). Multivariable regression analysis showed that increased age, BMI, and MCV levels are unassisted associated with increased risk of advance OA (OR=1.132, 95% CI:1.026- 1.249, p=.001; OR =1.148, 95% CI:1.062-1.242, p =.014 and OR = 0.492, 95% CI: 0.259-0.937, p =.031, respectively)

Conclusion: We are suggesting that instead of any complex, costly methods, easy CBC and routine biochemical parameters at the initial presentation of OA patients could also be prognostic for the likely progression of OA.

Keywords: Mean corpuscular volume; C-reactive protein; progression of knee osteoarthritis.

INTRODUCTION

Knee osteoarthritis symptoms include pain, loss of function and stiffness and it is the common cartilage degenerative disease within the world (1). Knee function scores step by step worsen in knee osteoarthritis progression (2). Many biochemical and mechanical factors are acting a role in the knee osteoarthritis progression (2).

Obesity and advancing age are important risk factors for progression of knee OA (3). Biomarkers such as interleukin-6 (IL-6) and C-reactive protein (CRP) are completely positively correlated withal cartilage degradation, pain and there for the progression of OA (4). The mean corpuscular volume (MCV) is significant for the classification of anemia. Erythrocyte size in anemia is often differently defined into normocytic, microcytic, and anemia by the marker of MCV (5).

The MPV is shown to be augmented in varied diseases and related to principally with platelet activation uncommitted the count of platelet (6). Increased MCV levels are seen in nutritional deficiencies, drug use (5), heart disease (7), dialysis patients and infectious diseases (8). In additional, MPV has been shown to be helpful in the prognosis of different non-infectious pathologies, like ischemic heart disease (9) or stroke (10), as much as other markers of unspecific inflammation. Inflammation plays a serious role in the start and also the improving of OA. Studies recommend that inflammation consist at the earliest stage of OA and conduces to the progression of OA (11,12). Inflammatory cytokines alike TNF-α, IL-1β, and IL-6 are shown to be high in patients with OA (13) and conduct the advance of OA (14). On the opposite hand, anti-inflammatory cytokines like IL-10 and IL-13 have been shown to own chondroprotective effects that decelerate the progression of OA (15).

Our purpose of this prospective study was to evaluate the MCV, CRP, WBC alteration in OA and to explore whether or not any MCV, WBC changes easily detectable by basic complete blood count (CBC), have diagnostic values for the prediction of progression of OA.

MATERIAL and METHODS

Eighty-two patients diagnosed as OA and sixty-nine control, between fifty-five and eighty-five years of age

Received: 18.05.2019 **Accepted:** 12.06.2019 **Available online:** 16.07.2019
Corresponding Author: Kenan Ozler, Konya Beysehir State Hospital, Clinic of Orthopaedics and Traumatology, Konya, Turkey
E-mail: kenozler@hotmail.com

women were recruited consecutively from the Orthopaedics Department of Beysehir State Hospital. The diagnosing of OA was made considering the Kellgren-Lawrence (K&L) scale and needed to meet all five radiological criteria for late-stage OA as follows: formation of osteophytes on the joint margins, periarticular ossicles, joint space narrowing (JSN) related to sclerosis of subchondral bone, little pseudocystic areas within the subchondral bone and altered form of the bone ends (16).

Exclusion criteria for all patients included infectious diseases, history of total knee operation or open knee surgery, septic arthritis, taking local or systemic treatments like steroids, hyaluronic acid, bone tumors, fractures, overweight, chemotherapy and/or radiotherapy, diabetes mellitus or hypertension.

All patients were evaluated in the outpatient clinic when they first applied. Clinical examination was performed, previous medical story was registered. Blood samples were acquired by venipuncture for complete blood count (white blood cell count [4-11/mm3], mean platelet volume (MPV) [6-12.5 femptolitre-fL], mean corpuscular volume (MCV) [80-100 femptolitre-fL], C-reactive protein (CRP) [0-6 mg/dl], Antistreptolysin-O (ASO) [0-200 IU/mL], and Rheumatoid factor (RF) [0-30 IU/mL], measurements in the biochemistry laboratory of hospital with the we use the ADVIA Centaur CP Immunoassay System (Siemens).

Statistical analysis

Data analysis was performed using SPSS for Windows, version 22 (SPSS INC., Chicago, IL, United States). The Kolmogorov- Smirnov test was used to test whether continuous variables were normally distributed or not. Homogeneity of variances was evaluated by the Levene's test. Mean variations between OA and control groups were compared with the independent sample t-test. Multivariate logistic regression analysis was used to determine a relationship between WBC, MPV, MCV, CRP, ASO, RF, and LOA. Whichever variable whose univariable test had a p-value <.05 was accepted as a candidate for the multivariable model. The Pearson's correlation test was used to examine the correlations of variables. A p-value <.05 was noted meaning.

RESULTS

Overall one hundred and fifty women were recorded in the study (82 OA and 69 BMI-matched controls). The mean age of the participants was 66.61±0.89 years for OA and 63.48±0.88 years for control (p=.051). There were no statistically significant differences in body mass index (BMI) between groups (p=.613). OA patients had significantly higher levels of CRP and MCV when compared with control (p=.034 and p=.022). There was no statistically significant difference among WBC, MPV, ASO, and RF in women between OA and control groups (Table 1).

Multiple logistic regression analyses were relevant to detect the best markers of an increased risk of LOA. Any variable whose univariable test had a p-value < .050 was putative as a candidate for the multivariable model along with all variables of known clinical importance. Multivariable logistic regression analysis revealed that increased age, BMI, and MCV levels were independently related to increased risk of LOA (OR =1.132, 95% CI:1.026-1.249, p=.001; OR=1.148, 95% CI:1.062-1.242, p=.014 and OR=0.492, 95% CI:0.259-0.937, p=.031, respectively) (Table 2).

MCV levels revealed a significant positive correlation between age and CRP in OA group (r=0.205, p=.012 and r=0.161, p=.048) (Table 3).

Table 1. Baseline characteristics, anthropometric and laboratory parameters of the OA and control groups

	OA n=82	CONTROL n=69	P- Value
Age (year)	66.61 ± 0.89	63.48 ± 0.88	.051
BMI (kg/m^2)	32.70 ± 0.68	32.15 ± 0.84	.613
WBC (/mm^3)	7.38 ± 0.25	7.48 ± 0.20	.777
MPV (fl)	11.23 ± 1.04	10.06 ± 0.12	.307
MCV (fl)	81.63 ± 0.56	79.62 ± 0.76	.034
CRP (mg/dl)	5.81 ± 0.89	3.36 ± 0.42	.022
ASO (IU/mL)	70.82 ± 5.36	91.39 ± 15.14	.172
RF (IU/mL)	10.93 ± 0.67	12.48 ± 1.20	.243

Student t-test, <.05 statistically significant. Statistically, significant p values are marked as bold text. BMI; body mass index, WBC;White Blood Cell, MPV;Mean Platelet Volume, MCV; Mean Corpuscular Volume, CRP; C-reactive protein, ASO; Antistreptolysin-O, RF; Rheumatoid Factor, fl;femptolitre

Table 2. Univariate and multivariate analysis of the relationship between variables with LOA

	LATE STAGE OA			
	Univariate		Multivariate	
	OR (95%CI)	p value	OR (95%CI)	p value
Age (year)	1.119 (1.044-1.200)	.002	1.132 (1.026- 1.249)	.001
BMI (kg/m^2)	1.094 (1.008-1.187)	.031	1.148 (1.062-1.242)	.014
WBC (/mm^3)	0.957 (0.780-1.174)	.670		
MCV (fl)	0.551 (0.316-0.961)	.036	0.492 (0.259-0.937)	.031
MPV (fl)	0.970 (0.882-1.068)	.970		
CRP(mg/dl)	1.034 (0.979-1.092)	.228		
ASO (IU/mL)	0.996 (0.986-1.007)	.492		
RF(IU/mL)	1.007 (0.934-1.086)	.851		

Logistic regression model (Binary Logistic Regression with a Single and Multi-Categorical Predictor) was used to determine the possible risk factors for WOMAC pain score in OA.<.05 statistically significant. Statistically, significant p values are marked as bold text. BMI; body mass index, WBC; White Blood Cell, MPV; Mean Platelet Volume, MCV; Mean Corpuscular Volume, CRP; C-reactive protein, ASO;Antistreptolysin-O, RF;Rheumatoid Factor,fl;femptolitre

Table 3. Correlation analysis of MCV, WBC, CRP, MPV, ASO and RF levels in OA patients

	MCV	
	r	p value
Age (year)	.205	.012
BMI (kg/m^2)	.062	.452
WBC (/mm^3)	-.061	.460
MPV (fl)	.070	.393
CRP (mg/dl)	.161	.048
ASO (IU/mL)	-.123	.132
RF(IU/mL)	-.060	.464

r; correlation coefficient, p value; statistical significance, <0.05 statistically significant, CI; Confidence interval, BMI; body mass index, WBC; White Blood Cell, MPV; Mean Platelet Volume, MCV; Mean Corpuscular Volume, CRP; C-reactive protein, ASO;Antistreptolysin-O, RF; Rheumatoid Factor, fl;femptolitre

DISCUSSION

In this prospective case-control study, CRP and MCV levels were significantly higher in the OA group than in the control group. Additionally, we also found MCV, age, and BMI to be associated with the progression of OA. Presently, it is thought that OA is related to possible mechanisms of changes in cartilage. Cytokines, like IL-6, IL-1β, and TNF –α, (17, 18) and variety of matrix metalloproteinases and numerous proteoglycans have been studied as biochemical markers in each serum and synovial fluid in knee OA (19). OA is usually related to low-grade synovitis featured by the existence of mononuclear cell infiltrates and production of inflammatory markers (20). Synovial inflammation connections with joint pain and dysfunction (21). CRP and pro-inflammatory cytokines are joined to prevailing and event OA, the progression of structural abnormalities, pain and functional deterioration among people with and without OA (22). Kozijin, et al. reported that CRP expression could also be responsible for cartilage degeneration and osteophyte formation in OA patients (23). Spector, et al. said that low CRP levels were increased in early-stage OA and that they could be involved in predicting OA progression (24). Hsieh, et al. reported that MCV is an independent risk factor for cardiovascular disease and infection-related mortality in chronic kidney diseases (25). Dujardin et al. stated that MCV may be a marker for the treatment of follow-up of the inflammatory bowel diseases (26). Khongkhatithum et al. reported that low MVC and MCHC and high RDW levels may be risk factors for arterial stroke (27). In light of the above information, MCV was found to be an independent risk factor in many diseases. There was no previous study showing that MCV may be associated with OA patients and OA progression. We found that MCV increased in OA patients and this increase could be an independent risk factor for OA progression in our study.

Mechanical factors are also important risk factors for OA progression. Studies have shown that obesity decreases the standard of life in patients, decreases in knee functions, progress in osteoarthritis progression and reduces in recovery and revision rate in patients with arthroplasty (28). Martin, et al. declared that the rate of osteoarthritis was over-filled with weighty individuals, and increased knee pain was related to obesity and age in OA (29). Additionally, severe symptoms of knee OA have been reported to extend with age (30).

CONCLUSION

In conclusion, the present case-control study shows MCV levels in the prediction of the progression of OA. Also, we recommend that rather than whichever complex, costly methods, basic CBC and common biochemical parameters at the first presentation of OA patients may be predictive for the likely advance of OA. This study needs to be validated with larger cohorts.

Financial Disclosure: There are no financial supports
Ethical approval: Ethical Committee. (approval date/number: 03.05.2018/004).

Kenan Ozler ORCID: 0000-0002-4992-5245

REFERENCES

1. Hussain SM, Neilly DW, Baliga S, et al. Knee osteoarthritis: a review of management options.Scott Med J 2016;61:7-16.
2. Johnson VL, Hunter DJ. The epidemiology of osteoarthritis. Best Pract Res Clin Rheumatol 2014;28:5-15.
3. Meneses SR, Goode AP, Nelson AE, et al. Clinical algorithms to aid osteoarthritis guideline dissemination. J Osteoarthritis Cartilage 2016;24:1487-99.
4. Perruccio AV, Chandran V, Power JD, et al. Systemic inflammation and painful joint burden in osteoarthritis: a matter of sex? Osteoarthritis Cartilage 2017;25:53-9.
5. Sarma PR. Red cell indices. In Walker HK, Hall WD, Hurst JW, editors. Clinical Methods: the history, physical, and laboratory examinations. 3rd ed. Boston: Butterworths; 1990. p. 720-3.
6. Cho SY, Lee HJ, Park TS. Mean platelet volume in patients with increased γ -glutamyl transferase. Platelets 2015;26:283-4.
7. Ueda T, Kawakami R, Horii M, et al. High mean corpuscular volume is a new indicator of prognosis in acute decompensated heart failure. Circ J 2013;77:2766-71.
8. Dratch A, Kleine CE, Streja E, et al. Mean Corpuscular Volume and Mortality in Incident Hemodialysis Patients. Nephron 2019:1-13.
9. Ki YJ, Park S, Ha SI, et al. Usefulness of mean platelet volume as a biomarker for long-term clinical outcomes after percutaneous coronary intervention in Korean cohort: a comparable and additive predictive value to high-sensitivity cardiac troponin T and N-terminal pro-B type natriuretic peptide. Platelets 2014;25:427-32.
10. D'erasmo E, Aliberti G, Celi FS, et al. Platelet count, mean platelet volume and their relation to prognosis in cerebral infarction. J Intern Med 1990;227:11-4.
11. Ayral X, Pickering EH, Woodworth TG, et al. A Potential Predictive Factor of Structural Progression of Medial Tibiofemoral Knee Osteoarthritis-Results of a 1 Year Longitudinal Arthroscopic Study in 422 Patients. Osteoarthritis Cartilage 2005;13:361-7.
12. Krasnokutsky S, Belitskaya-Lévy I, Bencardino J, et al. Quantitative MRI Evidence of Synovial Proliferation Is Associated with Radiographic Severity of Knee Osteoarthritis. Arthritis Rheum 2011;63:2983-91.

13. Mabey T, Honsawek S.Cytokines as Biochemical Markers for Knee Osteoarthritis. World J Orthop 2015;6:95-105.
14. Sokolove J, Lepus CM. Role of Inflammation in the Pathogenesis of Osteoarthritis: Latest Findings and Interpretations. Ther Adv Musculoskelet Dis. 2013;5:77-94.
15. Jansen NW, Roosendaal G, Hooiveld MJ, et al. Interleukin-10 Protects against Blood-Induced Joint Damage. Br J Haematol 2008;142:953-61.
16. Kellgren JH, Lawrence JS. Radiological assessment of osteoarthrosis. Ann Rheum Dis 1957;16:494-502.
17. Attur M, Krasnokutsky-Samuels S, et al. Prognostic biomarkers in osteoarthritis. Curr Opin Rheumatol 2013;25:136-44.
18. Kapoor M, Martel-Pelletier J, Lajeunesse D, et al. Role of proinflammatory cytokines in the pathophysiology of osteoarthritis. Nat Rev Rheumatol 2011;7:33-42.
19. Kumm J, Tamm A, Lintrop M, et al. Diagnostic and prognostic value of bone biomarkers in progressive knee osteoarthritis: a 6-year follow-up study in middle-aged subjects. Osteoarthritis Cartilage 2013;21:815-822.
20. Robinson WH, Lepus CM, Wang Q, et al. Low-grade inflammation as a key mediator of the pathogenesis of osteoarthritis. Nat Rev Rheumatol 2016;12:580-92.
21. Scanzello CR, Goldring SR. The role of synovitis in osteoarthritis pathogenesis. Bone 2012;5:249-57.
22. Quartana PJ, Finan PH, Page GG, et al. Effects of insomnia disorder and knee osteoarthritis on resting and pain-evoked inflammatory markers.Brain Behav Immun 2015;47:228-37.
23. Kozijn AE, Tartjiono MT, Ravipati S, et al. Human C-reactive protein aggravates osteoarthritis development in mice on a high-fat diet. Osteoarthritis Cartilage 2019;27:118-28.
24. Spector TD, Hart DJ, Nandra D, et al. Low-level increases in serum C-reactive protein are present in early osteoarthritis of the knee and predict progressive disease. Arthrit Rheum 1997;40:723-7.
25. Hsieh YP, Chang CC, Kor CT, et al.Mean Corpuscular Volume and Mortality in Patients with CKD.Clin J Am Soc Nephrol 2017;12:237-44.
26. Dujardin RW, Meijer B, de Boer NK, et al. Usefulness of mean corpuscular volume as a surrogate marker for monitoring thiopurine treatment in inflammatory bowel disease.Eur J Gastroenterol Hepatol 2016;28:991-6.
27. Khongkhatithum C, Kadegasem P, Sasanakul W, et al. Abnormal red blood cell indices increase the risk of arterial ischemic stroke in children. J Clin Neurosci 2019;62:17-20.
28. Xu S, Lim WJ, Chen JY, et al. The influence of obesity on clinical outcomes of fixed-bearing unicompartmental knee arthroplasty. Bone Joint J 2019;101:213-20.
29. Martins GC, Martins Filho LF, Raposo AH, et al. Radiographic evaluation and pain symptomatology of the knee in severely obese individuals - controlled transversal study. Rev Bras Ortop 2018;53:740-6.
30. Wanaratna K, Muangpaisan W, Kuptniratsaikul V, et al. Prevalence and Factors Associated with Frailty and Cognitive Frailty Among Community-Dwelling Elderly with Knee Osteoarthritis.J Community Health 2019;44-587-95.