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Neutrophil to lymphocte ratio and mean platelet volume may predict the development of the pressure ulcers

Nötrofil lenfosit oranı ve ortalama trombosit hacmi bası yarası oluşumu öngörebilir

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Abstract

Aim: Inflammation may have deleterious effects on tissue healing. Pressure ulcers impair the quality of life of the patients admitted to intensive care unit (ICU) besides increasing the health costs. Neutrophil to lymphocyte ratio (NLR) and mean platelet volume (MPV) are simple and readily available markers proinflammatory state. This study aimed to investigate whether measurement of admission NLR and MPV could be useful in identification of the patients who are at elevated risk for the development of the pressure ulcers.

Methods: This retrospective cohort study evaluated 104 patients admitted to the intensive care unit of a tertiary center. Patients were divided into two groups according to the presence of pressure ulcers as follows: Patients without pressure ulcers throughout hospitalization and patients who developed pressure ulcers while hospitalized. The two groups were compared with respect to the demographic features and complete blood count parameters at admission.

Results: The NLR [8.8 (6.6) vs. 5.3 (2.6), $P<0.001$], platelet to lymphocyte ratio [322(125) vs. 234(116), $P=0.023$] and MPV [10.5 (1.5) fl vs. 9.8 (1.1) fl, $P<0.001$] were significantly higher, and length of ICU stay was significantly longer in patients with pressure ulcers than those without [16.1 (3.8) days vs. 12.5 (2.9) days, $P<0.001$]. Logistic regression analysis revealed that age ($P=0.03$), length of ICU stay ($P=0.01$), NLR ($P=0.01$) and MPV ($P=0.01$) were significantly predictive for the presence of pressure ulcers.

Conclusions: Our findings indicate that age, length of ICU stay, and NLR, and MPV, which are indicative for the preexisting inflammatory state, are independent predictors for the development of pressure ulcers in patients admitted to the ICU.

Keywords: Intensive care unit, Pressure ulcer, Neutrophil to lymphocyte ratio, Mean platelet volume, Inflammation

Öz

Amaç: İnflamasyonun doku iyileşmesi üzerinde olumsuz etkileri olabilir. Basınç ülserleri, yoğun bakım ünitesine (YBÜ) kabul edilen hastaların yaşam kalitesini bozmanın yanı sıra sağlık maliyetlerini de arttırır. Nötrofil/lenfosit oranı (NLR) ve ortalama trombosit hacmi (MPV) basit ve kolayca temin edilebilen proinflamatuar belirteçlerdir. Bu çalışma, NLR ve MPV giriş ölçümünün, basınç ülserlerinin gelişimi için yüksek risk altında olan hastaların tanımlanmasında faydalı olup olmadığını araştırmayı amaçlamıştır.

Yöntemler: Bu retrospektif kohort çalışması ile üçüncü basamak bir merkezin yoğun bakım ünitesine başvuran 104 hastanın değerlendirilmesi yapıldı. Basınç ülseri varlığına göre hastalar şu şekilde iki gruba ayrıldı: Hastanede yatış boyunca basınç ülseri olmayan hastalar ve hastanede yatış döneminde basınç ülseri gelişen hastalar. İki grup demografik özellikler ve geliş tam kan sayımı parametreleri açısından karşılaştırıldı.

Bulgular: NLR [8,8 (6,6) / 5,3 (2,6), $P<0,001$], trombosit-lenfosit oranı [322 (125) / 234 (116), $P=0,023$] ve MPV [10,5 (1,5) fl / 9,8 (1,1) fl, $P<0,001$] basınç ülseri olan hastalarda olmayanlara göre anlamlı olarak daha yüksekti. YBÜ'de kalış süresi de basınç ülseri olanlarda basınç ülseri olmayanlardan anlamlı olarak daha uzundu [16,1 (3,8) güne karşı 12.5 (2,9) gün, $P<0,001$]. Lojistik regresyon analizi yaş ($P=0,03$), YBÜ kalış süresi ($P=0,01$), NLR ($P=0,01$) ve MPV'nin ($P=0,01$) basınç ülserlerinin varlığı için anlamlı olduğunu göstermiştir.

Sonuçlar: Bulgularımız, önceden var olan enflamatuar durumu gösteren yaş, YBÜ kalış süresi ve NLR ve MPV'nin YBÜ'ye kabul edilen hastalarda basınç ülseri gelişimi için bağımsız belirteçler olduğunu göstermektedir.

Anahtar kelimeler: Yoğun bakım ünitesi, Bası yarası, Nötrofil lenfosit oranı, Ortalama trombosit hacmi, Enflamasyon

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Introduction

Intensive care refers to the combination of the methods used to maintain the vital functions of the patients who are critically ill. Since these patients require extensive monitorisation and catheterization, majority are prone to the development of the pressure ulcers resulting from immobilization. A pressure ulcer is defined as a new or established area of skin and/or tissue discoloration or damage which persists after the removal of pressure and which is likely due to the pressure on the tissues [1]. These ulcers usually occur over bony prominences such as the base of the spine, hips, and heels of the elderly and immobile patients, or those with acute illnesses who are admitted to the intensive care unit (ICU). The reported incidence of pressure ulcers among patients admitted to the ICU varies between 3.3% and 39.3% [2,3].

Development of pressure ulcers in a patient admitted the ICU not only increases health costs but also represent a major burden of sickness and reduced quality of life for patients. Several scales have been introduced to identify the subjects who are at high risk for the development of pressure ulcers. However, the benefits of using a pressure ulcer risk scale are of question. Some previous data indicate that clinical judgment provides similar outcomes with these scales in the identification of the high-risk patients for pressure ulcers. Therefore, there is still need for simple indicators for the detection of the patients who are potential candidates for the development of the pressure ulcers.

Complete blood count (CBC) parameters, including neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), mean platelet volume (MPV), and red blood cell distribution width (RDW) have previously shown to be useful in predicting poor wound healing in various clinical settings [4-6]. However, the roles of the aforementioned CBC parameters in prediction of the pressure ulcer development has not been studied yet.

The present study aimed to investigate whether the CBC parameters, including NLR, PLR, MPV and RDW could be useful in identification of the patients who are at elevated risk for the development of the pressure ulcers.

Materials and methods

We retrospectively evaluated 104 patients admitted to the intensive care unit of a tertiary center between September 2018 and August 2019. Written informed consent was obtained for all subjects. This study complied with the Declaration of Helsinki and was approved by the Ethics Committee and the institutional review board of Health Sciences University Sureyyapasa Chest Diseases and Chest Surgery Training and Research Hospital (116.2017.184/2020).

Those with peripheral arterial disease, recent or previous cerebrovascular event, spinal cord injury, intracranial mass, length of ICU stay > 30 days, mean arterial pressure<70 mmHg, subjects requiring vasopressors and patients with pressure ulcers at admission to ICU were excluded. Patients were divided into two groups according to the presence of pressure ulcers as follows: Patients without pressure ulcers throughout the hospitalization period and patients who developed pressure ulcers while hospitalized. Demographic and clinical data, and laboratory test values at admission were retrieved from the institutional database and the patient charts. The two groups were compared with respect to the demographic features and complete blood count parameters at admission (LH-750, Beckman Coulter, USA).

Statistical analysis

Statistical analysis was performed using SPSS for Windows, version 17 (SPSS, Chicago, IL, USA). Shapiro-Wilk test was used for normality check. Data are presented as mean (standard deviation) or median (minimum-maximum) for continuous variables regarding normality and as frequency for categorical variables. Normally distributed continuous variables were compared using the Student's t-test. Categorical variables were compared with the Pearson chi-square test. Logistic regression analysis was carried out to identify the predictors for the development of the pressure ulcers. A two-sided $P<0.05$ was considered statistically significant.

Results

A total of 104 patients, 66 males (63.5%) and 38 females (36.5%), with a mean age of 67 (14) years were included in the study. Among all, 52 had pressure ulcers and 52 did not. Demographic features and laboratory values at admission are presented in Table 1.

There were no significant differences between the groups with respect to age, gender, BMI, presence of diabetes, hypertension, coronary artery disease and smoking habit ($P>0.05$ for all). Hemoglobin, reticulocyte distribution width, platelet count and leukocyte count were also similar in the two groups. However, NLR [8.8 (6.6) vs. 5.3 (2.6), $P<0.001$], platelet to lymphocyte ratio [322 (125) vs. 234 (116), $P=0.023$] and MPV [10.5 (1.5) fl vs. 9.8 (1.1) fl, $P<0.001$] were significantly higher, and length of ICU stay was significantly longer in patients with pressure ulcers than those without [16.1 (3.8) days vs. 12.5 (2.9) days, $P<0.001$]. As shown in Table 2, variables for which the *P*-value was <0.01 were included in the binary logistic regression. Logistic regression analysis revealed that age (OR:1.038, 95% CI: 1.002-1.075, $P=0.039$), length of ICU stay (OR:1.183, 95% CI: 1.034-1.353, $P=0.015$), NLR (OR:1.206, 95% CI: 1.032-1.411, $P=0.019$) and MPV (OR:1.456, 95% CI: 1.064-1.992, $P=0.019$) were significantly predictive for developing pressure ulcers.

Table 1: Comparison of the clinical features and laboratory measurements of the study groups

	Pressure ulcer (-) n=52	Pressure ulcer (+) n=52	*P*-value
Age, years	63.2 (15.8)	70.8 (12.2)	0.064
Gender, male	34 (65.4%)	32 (61.5%)	0.684
BMI, kg/m^2	28.6 (1.5)	28.9 (1.7)	0.441
Diabetes, n	14 (26.9%)	18 (34.6%)	0.395
Hypertension, n	25 (48.1%)	20 (38.5%)	0.322
Smoking, n	16 (30.8%)	19 (36.5%)	0.534
CAD, n	12 (23.1%)	14 (26.9%)	0.651
ICU stay, days	12.5 (2.9)	16.1 (3.8)	<0.001
Hemoglobin, g/dl	10.7 (2.0)	10.9 (1.6)	0.911
NLR	5.3 (2.6)	8.8 (6.6)	<0.001
Mean platelet volume, fl	9.8 (1.1)	10.5 (1.5)	0.012
RDW, %	14.4 (1.0)	14.1 (0.8)	0.788
Platelet count, 10^3/ul	194 (68)	221 (83)	0.080
PLR	234 (116)	322 (125)	0.023
Leukocyte count, 10^3/ul	10.1 (2.7)	10.9 (2.6)	0.098

BMI: Body mass index, CAD: Coronary artery disease, ICU: Intensive care unit, NLR: Neutrophil to lymphocyte ratio, PLR: Platelet to lymphocyte ratio, RDW: Red cell distribution width, Data are presented as mean (standard deviation (SD)) for continuous variables, and frequency (percentage) for the categorical variables.

Table 2: Predictive value of the selected variables on the development of the pressure ulcer

	Odds ratio	95% CI	*P*-value
Age	1.038	1.002 - 1.075	0.039
ICU stay	1.183	1.034 - 1.353	0.015
NLR	1.206	1.032 - 1.411	0.019
MPV	1.456	1.064 - 1.992	0.019
Platelet count	1.001	0.995 - 1.008	0.705
PLR	1.002	0.999 - 1.005	0.268
Leukocyte count	1.075	0.893 - 1.293	0.446

ICU: Intensive care unit, MPV: Mean platelet volume, NLR: Neutrophil to lymphocyte ratio, PLR: Platelet to lymphocyte ratio

Discussion

The present study investigated whether several components of CBC could prove successful in identification of subjects who are at high risk for the development of the pressure ulcers during their stay in the ICU. Our findings show that NLR, PLR, and MPV are higher and length of ICU stay is longer in patients with pressure ulcers than those without. Our results also indicate that age, NLR, MPV and length of ICU stay are independent predictors of the development of pressure ulcers in patients admitted to the ICU. Pressure ulcers, which are also known as decubitus ulcers, usually develop in subjects who are unable to change position regularly. Huge majority of the patients admitted to ICU are, therefore, at considerable risk for the development of pressure ulcers [7]. Although the development of the pressure ulcer does not likely increase the mortality rate during hospital admission, it is associated with several other complications including increased risk of infection, in-hospital malnutrition, increased length of stay, increased workload for healthcare professionals and increased healthcare costs [8,9]. Patients admitted to ICU do not perceive the increased tissue pressure and consequently cannot react to it properly due to all sedative agents they receive. Moreover, underlying diseases and deterioration of the tissue perfusion due to the altered hemodynamics or hypoxia increases the risk of pressure ulcers [10-12].

Several preventative measures have been introduced to reduce the magnitude and/or duration of pressure between a patient and the supporting surface and to treat the wound which results from the pressure [13, 14]. However, non-selective application of these measures for all patients admitted to the ICU is not only time consuming but also costly.

Thus, various scales have been developed to identify the patients who are at high risk for development of pressure ulcers [15]. However, the evidence indicating the accuracy of risk assessment scales for pressure sores is vague, and it is not clear that these scales are better than clinical judgement or that they improve outcomes [16].

A recent prospective cohort study of 335 patients who were hospitalized in ICU revealed that presence of diabetes, treatment with vasopressors, endotracheal intubation, length of stay on ICU, and level of consciousness were associated with the development of pressure ulcers [17].

However, a recent meta-analysis of 17 studies and 19,363 patients have reported that there was no single factor which could explain the occurrence of pressure ulcers among the risk factors including age, length of ICU stay, diabetes, time of MAP <60-70 mmHg, mechanical ventilation, length of mechanical ventilation, intermittent hemodialysis or continuous veno-venous hemofiltration therapy, vasopressor support, sedation and turning [16,18].

Nevertheless, the need for a simple, readily available, and costless biomarker for the identification of the risk for the development of pressure ulcer is continuing. We, therefore, investigated whether CBC parameters could facilitate the identification of those at elevated risk for pressure ulcers and found out that age, NLR, MPV and length of ICU stay were predictive for the development of pressure ulcers. Older age and longer ICU stay as predictors of pressure ulcers is somewhat consistent the evidence derived from the previous studies [19-21]. However, high NLR and MPV have been established as predictors for pressure ulcer development for the first time. Platelets are enucleated cells which are traditionally considered to be solely involved in primary hemostasis and coagulation as a response to various kinds of physiologic triggers. However, emerging evidence indicates that platelets have additional roles in other physiopathological processes including inflammation, tissue regeneration and wound healing [22-24]. Recent findings from in-depth platelet signaling studies show that platelets actively participate in immunity and may exhibit deleterious effects in certain conditions such as in systemic inflammatory response syndrome and acute vascular diseases. Mean platelet volume is a measurement of the average size of platelets found in the blood stream which is universally available with routine blood counts by automated hemograms. An elevation in MPV level has been shown in several clinical conditions with chronic inflammation including ankylosing spondylitis, rheumatoid arthritis, chronic cardiovascular diseases, hypertension, and dyslipidemia [25-27].

Moreover, higher MPV was associated with poor wound healing in patients undergoing total abdominal hysterectomy [28]. In addition to MPV, NLR is another marker for pro-inflammatory state and has been associated with several diseases presenting with subclinical inflammation including peripheral vascular disease and coronary artery disease [29-31].

With this in mind, we speculate that the preexisting inflammatory state, as indicated by the presence of high MPV and NLR in our subjects with pressure ulcers, complicates tissue healing and gives rise to the development of decubitus ulcers. We suggest that clinicians should pay attention to the admission levels of NLR and MPV, which are widely available, easily derived, and reproducible markers of inflammation, to identify the subjects at elevated risk for the development of pressure ulcers.

Limitations

This study also has some limitations. First, our results represent the analysis of retrospective data. Therefore, we cannot reach accurate conclusions to recommend NLR and MPV as a routine part of the evaluation of patients admitted to the ICU. However, we concur that our findings are encouraging for future prospective and randomized trials investigating the predictive role of inflammatory markers in the development of pressure ulcers.

Conclusions

Results of the present study show that NLR, PLR, and MPV are higher and length of ICU stay is longer in patients with pressure ulcers than those without. Our findings also indicate that age, NLR, MPV and length of ICU stay are independent predictors for the development of pressure ulcers in patients

admitted to the ICU. The preexisting inflammatory state indicated by the high NLR and MPV might have contributed to the development of the pressure ulcers. We suggest that clinicians should pay attention to the admission levels of NLR and MPV, which are widely available, easily derived, and reproducible markers of inflammation, to identify the subjects at elevated risk for the development of pressure ulcers.

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