Kocatepe Tıp Dergisi
Kocatepe Medical Journal
24:369-374/Temmuz 2023 Sayısı

ARAŞTIRMA YAZISI / RESEARCH ARTICLE

İDAME HEMODİYALİZ HASTALARINDA ORTALAMA TROMBOSİT HACMİ'NİN MORTALİTE ÜZERİNE ETKİSİ

EFFECT OF MEAN PLATELET VOLUME ON MORTALITY IN MAINTENANCE HEMODIALYSIS PATIENTS

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ÖZET

AMAÇ: Hemodiyaliz son dönem böbrek hastalığı olan hastalarda en sık tercih edilen renal replasman tedavisi tipidir. İdame hemodiyaliz tedavisi alan hastalarda mortaliteyi etkileyen parametrelerin bilinmesi bu hasta grubunda sağkalımı artırabilir. Ortalama trombosit hacmi (MPV) tam kan sayımı parametrelerinden biridir. MPV yüksekliğinin birçok hastalıkta mortaliteyi artırabileceği gösterilmiştir. Bu çalışmamızda idame hemodiyaliz hastalarında MPV'nin mortalite üzerine etkisini araştırmayı amaçladık.

GEREÇ VE YÖNTEM: Ocak 2010 ve Ocak 2020 tarihleri arasında hastanemizde idame diyaliz tedavisine başlanan tüm hastaların dosyaları retrospektif olarak tarandı. Hastaların demografik verileri ve laboratuar parametrelerine hasta dosyalarından ulaşıldı. MPV değeri için idame diyaliz tedavisi başlanan ilk 3 ay rutin bakılan tam kan sayımındaki MPV değerlerinin ortalaması alındı. Takip süresince ölen ve yaşayan hastalar MPV değerleri açısından karşılaştırıldı.

BULGULAR: Çalışma 129 hasta ile yapıldı. Hastaların %24.8'i (n= 32) takipler süresince ölmüştü. Ölen hastaların MPV'si yaşayan hastalara göre anlamlı şekilde daha yüksekti (11.14±1'e karşı 10.12±0.8, p<0.001). Mortaliteyi öngörmek açısından en iyi MPV değeri 10.73 olarak bulundu (%75 sensitivite ve %81.4 spesifisite ile).

SONUÇ: Yüksek MPV idame hemodiyaliz hastalarında mortalite için bağımsız bir risk faktörüdür. MPV'si yüksek olan hemodiyaliz hastalarında değiştirilebilir risk faktörlerinin daha sıkı yönetilmesi sağkalımlarını artırabilir.

ANAHTAR KELİMELER: Hemodiyaliz, Mortalite, Ortalama trombosit hacmi.

ABSTRACT

OBJECTIVE: Hemodialysis is the most preferred type of renal replacement therapy in patients with end-stage renal disease. Knowing the parameters affecting mortality in patients receiving maintenance hemodialysis treatment may increase the survival rate in this patient group. Mean platelet volume (MPV) is one of the parameters of the complete blood count. It has been shown that high MPV can increase the mortality rate in many diseases. In this study, we aimed to investigate the effect of MPV on the mortality rate in maintenance hemodialysis patients.

MATERIAL AND METHODS: The files of all patients who were started on maintenance dialysis treatment in our hospital between January 2010 and January 2020 were reviewed retrospectively. Demographic data and laboratory parameters of the patients were obtained from the patient files. For the MPV value, the mean of the MPV values in the routine complete blood count for the first 3 months after maintenance dialysis treatment was started. Patients who died and survived during the follow-up were compared in terms of MPV values.

RESULTS: The study was conducted with 129 patients. 24.8% (n= 32) of the patients died during follow-up. MPV of deceased patients was significantly higher than survived patients (11.14±1 vs. 10.12±0.8, p<0.001). The best MPV value for predicting mortality was found to be 10.73 (with 75% sensitivity and 81.4% specificity).

CONCLUSIONS: High MPV is an independent risk factor for mortality in maintenance hemodialysis patients. Tighter management of modifiable risk factors in hemodialysis patients with high MPV may improve their survival.

KEYWORDS: Hemodialysis, Mortality, Mean platelet volume.

Geliş Tarihi / Received: 05.08.2022
Kabul Tarihi / Accepted: 01.10.2022
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INTRODUCTION

Chronic kidney disease (CKD) is defined as the persistence of kidney dysfunction for more than three months. End-stage renal disease is present when the estimated glomerular filtration rate is less than 15 ml/min/1.73 m^2, and such a patient has renal replacement therapy options such as kidney transplantation, peritoneal dialysis, and hemodialysis (1). According to the Turkish Society of Nephrology Registry data, as of 2020, hemodialysis has been the most frequently used treatment modality among patients receiving renal replacement therapy, with 72.6% (2). There are many factors affecting mortality in patients under the maintenance dialysis treatment. While some factors related to dialysis may be risk factors for mortality, some demographic and laboratory characteristics related to the patient may also be risk factors for mortality (3, 4). In the study of Erdoğmuş et al., diabetes mellitus, cerebrovascular disease and high CRP were found to be independent risk factors for mortality (5).

Mean platelet volume (MPV) is defined as the mean volume of platelets as femtoliters (fL) in the circulating blood. In recent years, it has been shown that MPV not only shows the mean platelet volume, but also can be a risk factor for many clinical conditions (6 - 9). Henning et al. showed that hemodialysis patients having higher MPV had more frequent coronary heart disease than patients having lower MPV (10). Considering that cardiovascular causes are the leading cause of mortality in hemodialysis patients, we designed our study considering that MPV may also play a role in this mortality.

In this study we aimed to investigate the effect of MPV on mortality in patients on maintenance hemodialysis.

MATERIAL AND METHODS

Patients and MPV

The files of all patients (n= 154) who started to receive maintenance hemodialysis therapy in our hospital between January 2010 and January 2020 were reviewed retrospectively. Patients older than 18 years of age, receiving hemodialysis treatment for more than 3 months, without autoimmune disease, without hematological or oncological disease were included in the study. Patients younger than 18 years of age, those with autoimmune disease, those receiving hemodialysis treatment for less than 3 months, and those with oncological or hematological malignancies were excluded from the study. Twenty five patients (thirteen because of the diagnosis of hematologic or oncologic malignancy, four due to hemodialysis treatment for less than 3 months, two because of autoimmune disease and six because of insufficient file data) were excluded from the study.

Ethical Committee

Ethics Committee approval was received at the Ethics Committee of Afyonkarahisar Health Sciences University; meeting dated 01.07.2022 (code of ethics committee: 2011-KAEK-2, meeting number: 2022/8, decision number: 359).

Statistical Analysis

Categorical variables were presented as frequencies and percentages. Categorical variables were compared with chi-square test between groups. Continuous variables were checked for the normal distribution with Shapiro Wilk test. Normally distributed continuous variables were presented as mean±standart deviation. Non-normally distributed continuous variables were presented as median and interquartile range (IQR25-75). Independent samples t test was used to compare the means of normally distributed continuous variables between groups. Mann Whitney U test was used to compare the median of non-normally distributed continuous variables between groups. Univariate and multivariate logistic regression analysis carried out to determine risk factors associated with mortality. The ROC curve was used to determine the threshold values that could be used to predict mortality. Youden index was used to select the best predictive value of MPV. Then patients were divided into two groups according to MPV threshold value. Kaplan Meier method was used for survival analysis. MPV groups were compared for survival with logrank test. Statistical analyzes were done using SPSS 26.0 (IBM Corp. 2019 IBM SPSS Statistics for Windows, version 26.0. Armonk, NY: IBM Corp) package program. All the p values presented were bidirectional and the values with $p<0.05$ were expressed as statistically significant.

RESULTS

The study was conducted with 129 patients on maintenance hemodialysis. While 75.2% (n= 97) of the patients were alive during the follow-up, 24.8% (n= 32) died. Of these 32 patients 43.8% (n= 14) died due to cardiovascular causes, 18.8% (n= 6) died due to cerebrovascular causes, 15.6% (n= 5) died due to sepsis, 12.5% (n= 4) died due to gastrointestinal bleeding and 9.4% (n= 3) died due to unknown causes. **Table 1** shows the comparison of the groups in terms of demographical parameters and comorbidities.

Table 1: Comparisons of groups in terms of demographical and comorbidities

Parameters	All patients (n=129)	Alive (n= 97)	Death (n= 32)	p
Age (years)	59.39±5.7	58.69±4.7	61.5±7.6	**0.015**
Female gender (%-n)	38.8-50	37.1-36	43.8-14	0.535
CKD etiology (%-n)				
DN	30.2-39	29.9-29	31.3-10	
HN	21.7-28	22.7-22	18.8-6	
CGN	17.1-22	16.5-16	18.8-6	0.814
PKD	4.7-6	5.2-5	3.1-1	
Obstructive	10.1-13	10.3-10	9.4-3	
Unknown	16.3-21	19.6-19	6.3-2	
Vascular access (%-n)				
Catheter	32.6-42	18.6-18	75-24	**<0.001**
AVF	67.4-87	81.4-79	25-8	
Diabetes mellitus (%-n)	30.2-39	29.9-29	31.3-10	0.876
Hypertension (%-n)	35.7-46	22.7-22	75-24	**<0.001**
Hyperlipidemia (%-n)	27.1-35	18.6-18	18.8-6	0.489
Smoking (%-n)	27.9-36	19.6-19	53.1-17	**0.001**
CAD (%-n)	21.7-28	16.5-16	18.8-6	0.674
CVD (%-n)	13.2-17	11.3-11	18.8-6	0.365
CHF (%-n)	13.2-17	8.2-8	9.4-3	0.759

CKD= chronic kidney disease, DN= diabetic nephropathy, HN= hypertensive nephropathy, CGN= chronic glomerulonephritis, PKD= polycystic kidney disease, AVF= arteriovenous fistula, CAD= coronary artery disease, CVD= cerebrovascular disease, CHF= congestive heart failure

Table 2 shows the comparison of the groups in terms of laboratory and clinical parameters. Multivariate regression analysis showed that vascular access as catheter, hypertension, smoking and higher MPV are independent risk factors for mortality in patients on maintenance hemodialysis (p= 0.001, p= 0.002, p= 0.014 and p=0.006, respectively). **Table 3** shows univariate and multivariate regression analysis for mortality. An MPV value of 10.73 fL was found to have the best predictive value with 75% sensitivity and 81.4% specificity in predicting mortality (AUC= 0.791, 95% CI= 0.693-0.889, p<0.001) **(Figure 1)**. Patients with an MPV≥10.73 fL had an overall survival of 42.9% [median survival was 56 months (95 %CI= 36.2-75.8 months)], while this rate was 90.8% [median survival was 73 months (95% CI= 48.9-97.1 months)] for patients with an MPV<10.73 fL. Patients with an MPV<10.73 fL had a statistically significantly higher survival (p= 0.008) **(Figure 2)**.

Table 2: Comparison of the groups in terms of laboratory and clinical parameters

Parameters	All patients (n=129)	Alive (n= 97)	Death (n= 32)	p
Age (years)	59.39±5.7	58.69±4.7	61.5±7.6	**0.015**
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Table 3: Univariate and multivariate regression analysis for mortality

	Univariate		Multivariare	
Parameters	OR (95% CI)	p	OR (95% CI)	p
Age	1.086(1.014-1.165)	**0.018**	1.086(0.983-1.201)	0.104
Dialysis with catheter	13.167(5.093-34.041)	**<0.001**	15.256(4.125-24.511)	**0.001**
Hypertension	10.227(4.033-25.937)	**<0.001**	7.491(2.086-26.893)	**0.002**
Smoking	4.653(1.976-10.956)	**<0.001**	4.245(1.338-13.469)	**0.014**
MPV	3.731(2.118-6.578)	**<0.001**	4.173(2.673-7.749)	**0.006**

MPV= mean platelet volume

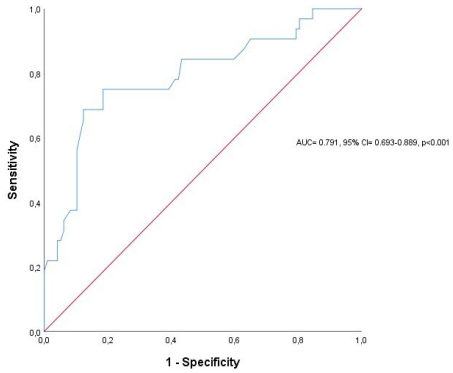

Figure 1: ROC curve as a mortality predictor for MPV

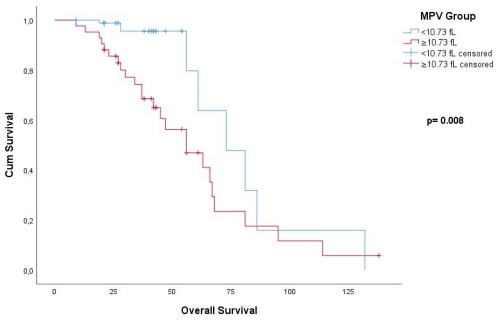

Figure 2: Comparison of survival between MPV groups

DISCUSSION

The present study revealed that higher MPV is closely associated with higher mortality rates

in patients on maintenance hemodialysis. In our literature search we did not find any study investigating MPV and mortality in patients on hemodialysis. Previous studies have found that higher MPV is associated with higher mortality in various clinical conditions. In a systematic review and meta-analysis Chu et al found that elevated MPV is associated with acute myocardial infarction, mortality after myocardial infarction and restenosis after coronary angioplasty (11). In a review published by Pafili et al., they emphasized that measuring MPV may prove useful in cardiovascular disease assessment in patients with established coronary artery disease (12). MPV has been associated with mortality not only in cardiovascular but also in many different diseases. Zampieri et al. investigated MPV changes and mortality in critically ill patients in a prospective study and they found that an increase in MPV was associated with higher mortality (13). Chen et al. found that higher MPV is an independent risk factor for mortality in patients with severe pneumonia (14). There have also been some publications on MPV in hemodialysis patients. Henning et al. investigated whether MPV was associated with coronary heart disease in hemodialysis patients. In this study they included 518 patients on maintenance hemodialysis and found that MPV may be associated with coronary heart disease in hemodialysis patients (10). In a 5-year cohort study of 149,118 incident hemodialysis patients, hemodialysis patients with a higher MPV were found to be at higher mortality risk (15). In our study, we found that patients with a higher MPV at the start of maintenance hemodialysis had higher mortality rates. We also found that MPV is an independent risk factor for all-cause mortality in patients on maintenance hemodialysis.

The best type of vascular access for maintenance hemodialysis is an arteriovenous fistula. Astor et al. showed that patients with catheter had higher complication and mortality rates than patients with arteriovenous fistula (16). In a study conducted using the DOPPS (Dialysis Outcomes and Practive Patterns Study) data system, 28,196 hemodialysis patients were examined between 1996 and 2004 (13). After correcting for demographics, comorbid conditions, and laboratory values, mortality was found to be 32% higher in patients with catheters compared to arteriovenous fistula (17). Our study revealed that having hemodialysis via a catheter is an independent risk factor for mortality in patients on maintenance hemodialysis. This finding is similar to the data in the literature.

Hypertension is a well-known cardiovascular risk factor for the general population (18). However, this close relationship has not been seen in patients on maintenance hemodialysis. Foley et al. showed that each 10 mmHg lower predialysis mean arterial blood pressure was associated with a 36% higher risk of death (19). Our study groups were similar in terms of both systolic and diastolic blood pressure values. We think that the patient's diagnosis of hypertension may be a risk factor for mortality as a result of complications that may have developed due to hypertension. We found that the history of hypertension is an independent risk factor for mortality in patients on maintenance hemodialysis.

Smoking is associated with an increased risk of mortality for patients of all age groups (20-22). Li et al. investigated the effects of smoking on mortality in 22,230 hemodialysis patients in the study they conducted (23). In this study, increased mortality risk was found in all smokers, although it was highest in hemodialysis patients who were heavy smokers compared to non-smoker hemodialysis patients. In another study, Causland et al. investigated the association of smoking status and all-cause, cardiovascular, and infection-related morbidity and mortality in patients on maintenance hemodialysis. They included 1842 patients and found that smoking was associated with higher all-cause mortality, higher cardiovascular mortality and higher infection-related mortality (24). In our study, we found that smoking negatively affects survival and is an independent risk factor for all-cause mortality in patients on maintenance hemodialysis.

In their cross-sectional study of 82 hemodialysis patients, Yayar et al. found that MPV was associated with carotid intima-media thickness (25). Based on this result, they emphasized that MPV may play a role in atherosclerotic processes. Our study also shows that high MPV is associated with an increased risk of mortality in hemo-

dialysis patients. We think that atherosclerotic processes associated with MPV play a role in this increase in mortality.

Our study has some limitations. First, it is a single-center study and second, it has a small number of patients. Our study is important because it is the first study investigating the effect of MPV on mortality in patients on maintenance hemodialysis.

In conclusion, in our study, MPV, smoking, the presence of hypertension, and catheter were found to be independent risk factors for all-cause mortality in maintenance hemodialysis patients. In order to reduce the risk of mortality in patients with high MPV, it would be logical to quit smoking and prefer more arteriovenous fistulas as vascular access. Prospective, larger studies may reveal more clearly the effects of MPV on mortality in hemodialysis patients.

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