Erectile Dysfunction Is Positively Correlated with Mean Platelet Volume and Platelet Count, but Not with Eosinophil Count in Peripheral Blood

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Purpose: Increased eosinophil count (EC), mean platelet volume (MPV), and platelet count (PC) are important in vascular disorders which are main factors resulting in endothelial dysfunction. We aimed to investigate the association between MPV, and EC, with erectile dysfunction (ED).

Materials and Methods: Two hundred thirty participants (130 patients with ED, and 100 healthy controls) were enrolled in this study. A detailed psychosexual history obtained, and physical, and laboratory examination were performed. International Index of Erectile Function (IIEF)-5 questionnaire was used to evaluate the erectile status objectively. IIEF-5 score was applied to all patients, and IIEF-5 score under 22 was considered as ED. The MPV, PC, and EC were compared between the two groups.

Results: The mean age of the patients with ED and control group was 55.62 ± 8.90 years and 54.19 ± 4.10 years, respectively. MPV and PC levels were significantly higher in ED group (8.51 ± 1.00 fL and 8.16 ± 0.94 fL; 244.59 ± 57.3 cells/µL and 230.17 ± 48.44 cells/µL, respectively ($P < .05$). EC and white blood cell count were not significantly different between study and control groups.

Conclusions: In our study a relationship was found between elevated MPV, and PC with ED. MPV and PC may be used as a biomarker in patients with ED.

Keywords: erectile dysfunction; etiology; risk factors; blood platelets; platelet count; eosinophils; leukocyte count.

INTRODUCTION

Erectile dysfunction (ED) is defined as a difficulty in initiating or maintaining penile erection adequate for sexual inter course. Penile erection is the result of a complex interaction between psychological, neural, vascular, and endocrine factors. One of the largest current studies of ED, the Massachusetts Male Aging Study, found that ED may be present in up to half of the male population between 40 and 70 years old.[1] This condition has been estimated to affect 150 million individuals worldwide,[2] and data from The Enhancing Neuro Imaging Genetics through Meta-Analysis (ENIGMA) Consortium study in 2004 suggested that the condition is prevalent in approximately 17% of all European men are affected.[3]

Several epidemiological studies have reported that ED is a marker of cardiovascular disease (CVD).[4-6] A 2011 meta-analysis of 12 prospective cohort studies provided strong evidence that ED is indeed significantly and independently associated with an increased risk of not only CVD but also coronary heart disease, stroke, and all-cause mortality.[7] Clearly, ED is now regarded as a major health problem for the increasingly healthy aging population.

In the etiology of ED, generally, organic and psychogenic factors come together. However, if the penis is considered as a specialized vascular bed, it is well-known that vascular reasons dominate in the etiology of ED.[8] During the last 20 years, many new facts about the basic physiology and pathology of ED have been determined, especially at the molecular level. Diabetes mellitus, atherosclerosis, coronary disease, and hypertension contribute to the development of ED via endothelial dysfunction and peripheral artery disease.[9] It has also been hypothesized that ED is an early messenger of CVD.[10]

The mean platelet volume (MPV) (expressed as fem to litre, fL) is one of the leading indicator in platelet function reflecting the platelet production rate and platelet stimulation. Elevated MPVs are reported in CVDs.[11] The MPV, the most commonly used measure of platelet size, is a potential marker of platelet reactivity. Larger platelets are metabolically and enzymatically more active and have greater prothrombotic potential. Elevated MPV is associated with other markers of platelet activity, including increased platelet aggregation, thromboxane synthesis, and increased expression of adhesion molecules.[12] Furthermore, a higher MPV may take place in vascular pathologies and increase the risk of CVD, suggesting a common mechanism by which these factors may increase the risk of CVD and ED. An as-

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Table 1. Clinical characteristic of study patients.

Variables	ED Group (n=180)	Control Group (n=120)	*P* Value
Age (year)	55.62 ± 8.90	54.19 ± 4.10	.120
Diabetes mellitus, no.	41	24	.619
Hypertension, no.	50	31	.743
Triglyceride (mg/dL)	143.20 ± 68.22	146.08 ± 57.24	.243
HDL-C (mg/dL)	42.43 ± 13.19	41.24 ± 11.87	.435
BMI (kg/m^2)	26.9 ± 6.5	25.2 ± 5.3	.504
MPV (fL)	8.51 ± 1.00	8.16 ± 0.94	.015
PC (cells/μL)	244.59 ± 57.3	230.17 ± 48.44	.034
EC (cells/μL)	0.24 ± 0.18	0.21 ± 0.14	.314
WBC ($10^3/mm^3$)	7.47-1.33	7.23-1.56	.154

Abbreviations: ED, erectile dysfunction; HDL, high-density lipoprotein; BMI, body mass index; MPV, mean platelet volume; PC, platelet count; EC, eosinophil count; WBC, white blood cells.
Data are presented as mean ± SD.

sociation between ED and ischemic heart disease has been suggested as a consequence of vascular lesions of the penile arteries.[13] There is a relationship between vascular dysfunction with eosinophilia. It is known that eosinophils play an important role inendothelial dysfunction, vasoconstriction, inflammation, and thrombosis.[14] Eosinophils stimulate the activation and aggregation of platelets. Moreover, they ease the formation of thrombosis via inhibition of thrombomodulin.[15,16] Perhaps, increased eosinophil count (EC, expressed as cells/μL) could lead to ED through endothelial dysfunction.

These pathophysiological approach to the issue let us consider that ED might be associated with increased platelet count (PC, expressed as cells/μL) and volume as well as EC. In this study, we aimed to investigate the association between the MPV, PC, and EC with ED, in comparison with a control group.

MATERIALS AND METHODS

We have conducted a prospective study in participants who visited Okmeydani Training and Research Hospital. A total of 230 patients were evaluated for ED and they were divided into two groups: 130 patients suffering from ED for > 1 year were classified as a study group and 100 patients without ED who were sexually active and married were classified as a control group. Local ethics committee approval had been obtained before the beginning of the study. All patients had a complete detailed and careful history taken, with special attention to the sexual history, including details to differentiate between psychogenic and organic ED; a complete physical examination, including genital and neurological examination; blood glucose assay, urine analysis, complete blood count (CBC), and kidney and liver function. Erectile function was assessed using the five-item version of the International Index of Erectile Function questionnaire (IIEF-5), a validated, self-administered questionnaire. The score of 22–25 indicate normal erectile function, while scores < 22 indicate ED. According to the IIEF-5 score, ED was classified as severe [5–7], moderate [8–11], mild-to-moderate [12–16], or mild [17–21]. Exclusion criteria included the followings: the patients using anti-platelet or anticoagulant drugs, patients with congestive heart failure (ejection fraction < 50%), pulmonary hypertension, coroner artery disease, stroke, known peripheral atherosclerotic disease, surgical coronary intervention, percutaneous coronary angioplasty and/or stenting, stable and unstable angina pectoris, impaired renal function (creatinine > 1.4 mg/dL), unstable endocrine or metabolic diseases, patients with Peyronie's disease, acute/chronic hepatic or hepatobiliary disease, and malignancy. Patients who have undergone radical prostatectomy and/or pelvic surgery, history of pelvic trauma and taking beta-blocker, spironolactone, corticosteroids, antioxidant vitamins, and alcohol were also excluded from the study. Furthermore patients who had a recent history of an acute infection and/or high body temperature (> 38°C), an inflammatory, or an allergic disease were excluded from the study. Blood samples of all patients were taken from an antecubital vein following an overnight fasting state. Fasting blood glucose, MPV, PC, EC, white blood cell (WBC) total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglyceride (TG) levels were measured in the hospital's chemistry laboratory.

Statistical Analysis

Statistical analyses were performed by the Statistical Package for the Social Science (SPSS Inc, Chicago, Illinois, USA) version 15.0. The quantitative demographic values were evaluated by student's *t*-test or Mann Whitney *U* test whether the parameters were suitable for normal distribution or not. If the parameters are qualitative, chi-square test was used. Kruskal-Wallis test was conducted to evaluate the difference between subgroups of the patients stratified for age. Logistic regression analyses were conducted to estimate the risk ratios. Pearson correlation test was performed to determine possible correlation between MPV, and PC with IIEF-5 score. All tests were performed using a 2-tailed analysis, and a *P* value of < .05 was considered statistically significant.

RESULTS

Table 2. The study parameters stratified by age (years).

Variables	40-50 (n = 31)	50-60 (n = 66)	60-70 (n = 75)	*P* Value
Platelet count (cells/μL)	237.99 ± 37.5	240.05 ± 61.04	247.82 ± 56.32	.530
Mean platelet volume (fL)	8.24 ± 0.68	8.54 ± 1.08	8.60 ± 1.09	.553
IIEF-5 score	15.12 (7-22)	16.19 (7-22)	13.16(6-21)	.001

Abbreviation: IIEF, international index of erectile function.
Data are presented as mean ± SD.

A total of 230 patients between the ages of 40 and 65 years were analyzed and divided into two groups: 130 patients with ED and 100 patients without ED (control group). The baseline characteristics of the patients are demonstrated in **Table 1**. The mean age was 55.62 ± 8.90 years in patients with ED and 54.19 ± 4. 10 years in control group. There was no significant differences between two groups with respect to age, body mass index (BMI), frequencies of diabetes mellitus, hypertension, smoking and levels of fasting blood glucose, Total-C, LDL-C, HDL-C, TG, and WBC ($P > .05$ for all). We compared the MPV, PC, EC values between groups. It seems that the patients with ED have higher MPV and PC levels than control group. MPV level was 8.51 ± 1.00 fL in patients with ED and 8.16 ± 0.94 fL in control group. PC level was 244.59 ± 57.3 μL in patients with ED and 230.17 ± 48.44 μLin control group. There was statistically significant difference for MPV and PC levels between the patients with ED and control group ($P < .05$) (**Table 1**). In logistic regression analyses the parameters assumed to be related to ED were examined. The patients were stratified into three groups as 40-50 years, 50-60 years, and 60-70 years. Patients with > 70 years old and < 40 years old were not evaluated as separate group, since the frequencies of them were not suitable for a robust statistical analysis. Although MPV and PC were not statistically different between each group, IIEF-5 score was statistically different. The details are demonstrated in **Table 2**.

We also evaluated the groups in terms of ED severity which was classified as mild, mild to moderate, moderate and severe. When examining the distribution of the patient frequencies into the subgroups stratified by ED severity, there was statistically significant difference between three groups ($P = .02$). The details are shown in **Table 3**.

In logistic regression analyses the parameters assumed to be related to ED were evaluated. The parameters were adjusted for age, diabetes mellitus, hypertension, dyslipidemia, and alcohol consumption. **Table 4** represents the 95% confidence interval (CI) and adjusted odds ratios (ORs) for the associations between certain relevant associated risk factors and ED. Patients with higher PC (OR = 1.005; 95% CI: 1.003-1.010) and MPV (OR = 1.256; 95% CI: 1.088-1.4) had increased risk for development of ED. The EC was not correlated-with ED in logistic regression model.

DISCUSSION

ED is one of the most prevalent urological disorders resulting from variable organic and psychologic derangements. Vascular pathologies take great part in organic causes via the impairment of endothelial function which is crucial in erection physiology. The presence of a number of common risk factors, the presence of several known pathophysiologic links, and a number of retrospective association studies have reinforced the idea that the link between ED and CAD is important and real. This idea is defined that ED and coronary artery disease (CAD) are different manifestations of a common underlying vascular pathology. ED may be the early clinical manifestation of a generalized vascular disease and carries an independent risk for cardiovascular events.[17,18] Many patients present with underlying systemic CVD and their first symptom can be ED.[19] One study of 132 men correlated angiographic results with ED symptoms and scores on the IIEF-5; 58% reported experiencing ED before the diagnosis of CVD.[20] Prospective angiographic study showed that almost one in five men presented with erectile function abnormalities of vascular origin had angiographically documented silent CAD.[21] In the light of this information, young men with ED may be ideal candidates for cardiovascular risk factor screening and medical intervention.

ED precedes other manifestations of systemic atherosclerosis, such as CAD and cerebrovascular disease, may be partially explained by blood vessel size.[22] The penile arteries are typically 1 to 2 mm in diameter, whereas the coronary arteries are 3 to 4 mm in diameter and the carotid arteries, 5 to 7 mm in diameter. Therefore, an atherosclerotic plaque of a given size should occlude and hemodynamically affect a penile artery earlier than a coronary or carotid artery. Ultimately, small arteries such as the pudendal and penile arteries begin to degenerate, and end-organ ischemia results.

Table 3. Erectile dysfunction severity stratified by age (years).

ED severity, no.	40-50 (n = 31)	50-60 (n = 66)	60-70 (n = 75)	*P* Value
Mild	6	35	17	
Mild to moderate	16	15	33	.02
Moderate	7	10	14	
Severe	2	6	11	

Abbreviation: ED, erectile dysfunction.

Table 4. Multivariate logistic regression analysis for the risk factors for erectile dysfunction adjusted for age, diabetes mellitus, hypertension, alcohol consumption, and dyslipidemia.

Variables	OR	CI (95%)	*P* Value	Wald
Mean platelet volume	1.256	1.088-1.484	.014	7.083
Platelet count	1.005	1.003-1.010	.026	4.236
Eosinophil count	0.937	0.821-0.993	.165	0.031

Abbreviations: OR, odds ratio; CI, confidence interval.

[23] Pathophysiologic link between ED and CAD is endothelial dysfunction. Many patients with ED exhibit evidence of inflammation and endothelial dysfunction independent of their CAD status.[24,25]

Endothelial dysfunction is the key event in the pathophysiology of ED and, importantly, men with penile vascular.[24] Endothelial dysfunction can carry a heightened risk of future CAD events because it results in dysregulated intimal proliferation, inappropriate vasoconstriction, and a pro-inflammatory environment that causes plaque destabilization.[26] The fact that ED and atherosclerotic vascular diseases share such a large number of common risk factors has led to the clinical consensus that most cases of organic ED are probably part of the spectrum of atherosclerotic vascular disease.[10]

There are many studies about the relationship between MPV and some thrombotic and cardiac disorders.[27,28] It has been demonstrated that MPV is correlated with platelet function and activation.[29,30] Small platelets have lower functional capabilities than larger ones.[30] There are many evidences suggesting the important role of MPV as a marker of inflammation, disease activity and efficacy of anti- inflammatory treatment in several chronic inflammatory disorders. Therefore, MPV has been used as an indicator of platelet function for inflammatory diseases.[29-31] Due to vascular causes, we investigated the relationship between ED and MPV, and PC. In a study by Ciftci and colleagues[32] on 90 cases, PC and MPV values were increased in patients with vasculogenic ED. In our study, we found that the MPV and PC values were significantly higher in patients with ED than in the controls.

Eosinophils activate coagulation system and platelets, and they also cause vasospasm such as coronary artery spasm. Also eosinophil granule proteins are involved in vascular injury, and eosinophils may also affect cardiovascular system through inflammatory cell infiltration.[33] Recent studies showed that eosinophils were associated with stent thrombosis, stent restenosis, and acute coronary syndromes. Umemoto and colleagues reported that peripheral ECs were significantly higher in patients with severe coronary spasm than that in patients with no spasm. They also speculated that EC could predict vasospastic angina pectoris.[33] Eosinophils are equipped with several granule-associated molecules that play a role in the occurrence of thrombosis and vascular injury. Eosinophils generate an increased tendency to thrombosis through leukocyte, platelet stimulation, and release of tissue factor.[34-36] All these effects contribute to procoagulation through preventing the activation of thrombin and formation of endorsing fibrin. Sakai and colleagues demonstrated that large thrombus has greater EC both in thrombi and in peripheral blood.[37] They also speculated that thrombus growth might be facilitated in patients with higher EC in the peripheral blood.[37] The powerful vasoconstrictor and procoagulant effects of eosinophils, made us hypothesize that there might be a correlation between EC and ED. Increased EC in patients with ED might be due to vasoconstriction and thrombosis.

Study addressing the relationship between EC and ED has not been conducted yet. Thrombotic and vascular effects of EC and CAD with common etiology of ED are known. In light of this, we might hypothesize that ED could be associated with higher MPV and PC. However, there was no significant relationship between ED and EC in our study. Further studies with larger population are needed to yield more reliable results in this issue.

CONCLUSIONS

There is a relationship between elevated MPV, and PC with ED, through endothelial dysfunction. Whereas there is no statistically significant relationship between ED and EC. In the light of this data, MPV and PC values may be used as a biomarker in patients with ED.

CONFLICT OF INTEREST

None declared.

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