Can Eosinophil Count, Platelet Count, and Mean Platelet Volume Be a Positive Predictive Factor in Penile Arteriogenic Erectile Dysfunction Etiopathogenesis?

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Abstract

Blood count parameters of patients referring with erectile dysfunction (ED) were examined in this study and it was investigated whether eosinophil count (EC), platelet count (PC), and mean platelet volume values among the suspected predictive parameters which may play a role in especially penile arteriogenic ED etiopathogenesis had a contribution on pathogenesis. Patients referring with ED complaint were evaluated. Depending on the medical story, ED degree was determined by measuring International Index of Erectile Function. Penile Doppler ultrasonography was taken in patients suspected to have vasculogenic ED. According to penile Doppler ultrasonography result, patients with arterial deficiency were included in the penile arteriogenic ED group and the patients with normal results were included in the nonvasculogenic ED group. A total of 36 patients participated in the study from the penile arteriogenic ED group and 32 patients from the nonvasculogenic ED group. Compared with the nonvasculogenic ED group, the penile arteriogenic ED group's low International Index of Erectile Function score, high EC, mean platelet volume and PC values were detected to be statistically significant ($p < .001$, $p = .021$, $p = .018$, $p = .034$, respectively). No statistically significant difference was observed among the two groups when age, white blood cells, red blood cells, and hemoglobin values were considered. Pansystolic volume velocities were detected as statistically significantly low compared with the nonvasculogenic ED group in the measurements made in 5th, 10th, 15th, and 20th minutes on the right and left sides in the penile arteriogenic ED group. High MPV value and PC is a significant predictive factor for penile arteriogenic ED and vasculogenic ED and high EC is specifically predictive of arteriogenic ED.

Keywords

penile arteriogenic erectile dysfunction, eosinophil count, mean platelet volume, platelet count, penile Doppler ultrasonography

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Introduction

Erectile dysfunction (ED) is the difficulty in starting and continuing adequate erection for a satisfactory sexual performance and the stability of this condition (Hatzimouratidis, Eardley, Giuliano, Moncada, & Salonia, 2015). In 2004, the Enhancing Neuro Imaging Genetics through Meta-Analysis Consortium study claimed that nearly 17% of all European males had ED (de Boer et al., 2004). It was predicted that 322 million people will have ED around the world in 2025 (Ayta, McKinlay, & Krane, 1999).

Penile erection occurs due to the complicated interaction between psychological, neural, vascular, and endocrine factors. ED occurs due to problems occurring in all these factors and has a gradually increasing prevalence with age. Since the penis has a special vascular webbing, vascular causes play an important role in ED etiology. The vascular causes are divided into three categories as arteriogenic ED,

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venogenic ED, and mixed vasculogenic ED (Ciftci et al., 2015).

Evidences identifying that ED is an early finding for coronary artery and peripheric vascular disease have gradually increased (Hatzimouratidis et al., 2015). A meta-analysis in 2011 presented strong proofs demonstrating that ED is related to the increase in death risk caused by increased cardiovascular disease (CVD), coronary artery disease (CAD), and stroke (Dong, Zhang, & Qin, 2011).

Platelets play an important role in the atherosclerosis formation phase. Mean platelet volume (MPV) is a significant demonstrator of platelet activity and platelet function reflecting platelet production speed and platelet stimulation. MPV is a potential indicator for thrombocyte reactivity. Large thrombocytes have a more active and more prothrombotic potential in metabolic and enzymatic aspects. Increased MPV is related with indicators demonstrating thrombocyte activity such as increased thrombocyte gathering, tromboxan synthesis, and increased expression of adhesion molecules. There are studies identifying that increased MPV triggers and increases atherosclerotic processes such as acute coronary syndrome, myocardium infarction, and thrombosis (Dong et al., 2011; Kamath, Blann, & Lip, 2001; Pizzulli, Yang, Martin, & Lüderitz, 1998). It is known to be connected with the atherosclerosis process in penile arterial deficiency (Ciftci et al., 2013; Otunctemur et al., 2015). Studies claiming a positive relation between eosinophilia and vascular dysfunction are available (Otunctemur et al., 2015; Umemoto et al., 2000; Wang et al., 2006). It is known that eosinophils play an important role in endothelial dysfunction, vasoconstriction, inflammation, and thrombosis. Eosinophils stimulate thrombocyte activation and aggregation. Eosinophils also make the thrombosis formation easier by preventing thrombomodulin (Otunctemur et al., 2015; Wang et al., 2006).

Due to the thrombosis activity increasing effects of platelets and eosinophils, the relation between vasculogenic ED and eosinophil count (EC), platelet count (PC), and MPV is becoming popular in recent studies. There is a small number of studies on the subject in the literature (Aldemir et al., 2016; Ciftci et al., 2013; Ciftci et al., 2015; Otunctemur et al., 2015) and there is only one study examining vasculogenic ED and EC in the literature (Otunctemur et al., 2015). There are no studies specifically demonstrating the relation between arteriogenic ED and platelet functions and EC.

Blood count parameters of patients referring with ED were examined in the current study. The authors investigated whether EC, PC, and MPV values among the suspected predictive parameters which may play a role in especially penile arteriogenic ED etiopathogenesis had a contribution on pathogenesis.

Material Method

Patients referring with ED complaints between October 2014 and February 2016 were evaluated. A total of 68 patients who met inclusion criteria were included in the study. Medical histories were taken in a careful and detailed way so that psychogenic and neurological factors could be eliminated and genital and neurological examinations were made. Depending on the medical history, ED degree was determined by measuring the International Index of Erectile Function (IIEF). Hormonal, other laboratory values, follicle-stimulating hormone, luteinizing hormone, testosterone, prolactin, blood sugar, urine analysis, kidney and liver function tests, and complete blood counts were examined. Blood samples were drawn from the antecubital vein from 08:00 a.m. to 10:00 a.m. after an overnight fasting period. Blood samples were collected in tubes containing dipotassium ethylenediaminetetraacetic acid. All of the measurements were performed immediately after venipuncture to prevent in vitro platelet activation.

In patients who had morning erection problems, could not continue erection with a good quality and good response could not be received from phosphodiesterase enzyme 5 inhibitors, vasculogenic ED was suspected. Penile Doppler ultrasonography (PDU) was taken in patients suspected to have vasculogenic ED. After the operation, 60 mg papaverine HCl was applied by intracavernosal injection from the one-third zone of the penis proximally with 26 gauge 2 ml injector. Afterward, arterial and venous flows of the penis were evaluated in 5th, 10th, 15th, and 20th minutes. Measurements were made with a Siemens Acuson S2000, 9 MHz linear probe. Arterial deficiency (arteriogenic ED) was diagnosed in patients with a pansystolic blood flow velocity (PSV) under 30 cm/s, venous insufficiency (venogenic ED) in patients with end diastolic flow velocity above 5 cm/s, and mixed ED in patients with both. According to PDU results, patients with arterial deficiency were included in the penile arteriogenic ED group and patients with normal results were included in the nonvasculogenic ED group (control group). A total of 36 patients participated in the study from the penile arteriogenic ED group and 32 patients from the nonvasculogenic ED group.

Exclusion Criteria

Patients whose PDU results were reported as venous and mixed ED, patients using antiplatelet and anticoagulant drugs, patients with neurogenic or endocrinological ED, a history of pelvic surgery and pelvic trauma, or other

Table 1. Patient Findings and Complete Blood Count Values.

	Arteriogenic ED	Nonvasculogenic ED	*p*
Number	36 (52.9%)	32 (47.1%)	
Mean age	53.8 ± 11.4 (34-66)	51.2 ± 10.8 (23-57)	.511
IIEF score	8.2 ± 2.91	15.4 ± 3.49	**<.001 (s)**
MPV (fL)	9.93 ± 1.01	8.82 ± 0.92	**.018 (s)**
PC (10³/μL)	252.48 ± 56.7	235.37 ± 45.24	**.034 (s)**
EC (10³/μL)	0.36 ± 0.12	0.23 ± 0.09	**.021 (s)**
WBC (10³/μL)	7.86 ± 1.12	7.32 ±1.03	.132
RBC (10⁶/μL)	4.4 ± 0.81	4.28 ± 0.77	.185
Hgb (g/dL)	13.91 ± 1.75	13.73 ± 1.63	.627

Note. ED = erectile dysfunction; IIEF = International Index of Erectile Function; MPV = mean platelet volume; PC = platelet count; EC = eosinophil count; WBC = white blood cells; RBC = red blood cells; Hgb = hemoglobin; s = significant (in bold). Values are presented as *M ± SD*.

vascular risk factors for ED such as diabetes, smoking, or hypertension, recently diagnosed CAD or hematological disorder, active infectious disease, malignancy, immunological disease, or renal or hepatic failure were excluded.

Statistical Analysis

Statistical analysis was performed with SPSS 15.0 for Windows version 15.0 (SPSS Inc., Chicago, IL, USA). Intergroup comparisons were performed using the Mann–Whitney U test and the chi-square test was used to assess the relationship between categorical variables in the patient groups. Area under the curve was calculated by receiver operating characteristic analyses. Epidemiological diagnosis percentages were calculated by finding cutoff values. $p < .05$ was used as a threshold for statistical significance. Data were presented as $M \pm SD$.

Results

Sixty-eight patients who had PDU and met the criteria were included in the study. Penile arterial deficiency was reported in 36 patients and 32 patients were reported to be normal as the result of PDU. These patients were divided into two groups as those with penile arteriogenic ED and the control group. In penile arteriogenic ED and control group, mean age was detected as 53.8 ± 11.4 (34-66), 51.2 ± 10.8 (23-57; $p = .511$). IIEF score was evaluated as 8.2 ± 2.91, 15.4 ± 3.49 ($p < .001$). Other measurements were MPV (fL) 9.93 ± 1.01, 8.82 ± 0.92 ($p = .018$); PC (10³/μL) 252.48 ± 56.7, 235.37 ± 45.24 ($p = .034$); and EC (10³/μL) 0.36 ± 0.12, 0.23 ± 0.09 ($p = .021$).

White blood cells (WBC) were measured as (10³/μL); 7.86 ± 1.12, 7.32 ± 1.03 ($p = .132$); red blood cells (RBC) as (10⁶/μL); 4.4 ± 0.81, 4.28 ± 0.77 ($p = .185$); and hemoglobin (Hgb) level (g/dL) as 13.91 ± 1, 75, 13.73 ± 1.63 ($p = .627$). Compared with the control group, the penile arteriogenic ED group had low IIEF score, high EC, MPV, and

Table 2. Findings for Sensitivity, Specificity, and Positive Predictive Values of the Parameters Statistically Significant for Penile Arteriogenic ED.

	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	*p*
MPV	54	88	82	.018
EC	61.4	74	70	.021
PC	62	67	63.5	.034

Note. ED = erectile dysfunction; MPV = mean platelet volume; PC = platelet count; EC = eosinophil count.

PC values detected to be statistically significant ($p < .001$, $p = .021$, $p = .018$, $p = .034$, respectively).

No statistically significant difference was observed among the two groups when age, WBC, RBC, and Hgb values were considered ($p = .511$, $p = .132$, $p = .185$, $p = .627$, respectively). Patient findings and complete blood count values are reported in Table 1.

In the evaluation made with receiver operating characteristic regression analysis, statistically significant values for penile arteriogenic ED were measured as:

MPV value: sensitivity: 54%, specificity: 88%, positive predictive value 82%
EC value: sensitivity: 61.4%, specificity: 74%, positive predictive value: 70%
PC value: sensitivity: 62%, specificity: 67%, positive predictive value: 63.5%

Findings for sensitivity, specificity, and positive predictive values of the parameters statistically significant for penile arteriogenic ED are reported in Table 2.

PSV velocities were detected as statistically significantly low compared with the control group in the measurements made in 5th, 10th, 15th, and 20th minutes on the right and left sides in the arteriogenic ED group ($p < .001$, $p < .001$, $p < .001$, $p < .001$, $p < .001$, $p < .001$,

Table 3. Pansystolic Volume (PSV) Values for Penile Doppler Ultrasonography (*n* = 36/32).

	Arteriogenic ED	Nonvasculogenic ED	*p*
5 Min right PSV (cm/s)	12.54 ± 2.8	33.6 ± 9.2	<.001
10 Min right PSV (cm/s)	14.2 ± 4.3	41.4 ± 12.1	<.001
15 Min right PSV (cm/s)	18.07 ± 4.6	42.8 ± 15.4	<.001
20 Min right PSV (cm/s)	20.4 ± 5.1	44.1 ± 17.2	<.001
5 Min left PSV (cm/s)	13.74 ± 3.6	34.08 ± 9.4	<.001
10 Min left PSV (cm/s)	17.6 ± 4.1	39.9 ± 10.9	<.001
15 Min left PSV (cm/s)	19.8 ± 4.8	41.5 ± 16.1	<.001
20 Min left PSV (cm/s)	22.2 ± 5.6	42.8 ± 16.8	<.001

Note. ED = erectile dysfunction; Min = minute. Values are presented as *M* ± *SD*.

$p < .001$, $p < .001$, respectively). PSV values for PDU results are reported in Table 3.

Discussion

ED is a common disease in studies conducted on males between 40 and 70 years of age (Akkus et al., 2002; Feldman, Goldstein, Hatzichristou, Krane, & McKinlay, 1994). It has been projected that there will be approximately 300 million men worldwide with ED by the year 2025 (Kellesarian et al., 2016).

Organic and psychological factors play a role in ED development. Organic causes play a more dominant role in ED etiology and vascular factors cause ED more among the organic causes (Mehta, Miner, & Sigman, 2013). Diseases causing vascular pathologies such as hypertension, hyperlipidemia, diabetes mellitus, and CAD are the main risk factors for vasculogenic ED and this risk increases nearly 1.5 to 4 times in the presence of these risk factors (Kefi, Demir, Seçil, & Esen, 2005; Martin-Morales et al., 2001). Vasculogenic ED forms with relaxation problems in vasculogenic ED endothelium dependent or endothelium independent straight muscle cells and atherosclerotic occlusion in cavernous arteries. Since atherosclerosis affects all vascular beds, the earliest symptom development is expected in the artery with the narrowest vein lumen. Since the lumen of the penile artery is between 1 mm and 2 mm, symptoms based on atherosclerosis in the penile artery are observed in the early period (Hatzimouratidis et al., 2015; Montorsi, Montorsi, & Schulman, 2003; Persu et al., 2009). The deficiency in penile artery flow is responsible for 55% of EDs and severe penile arterial flow inadequacy is 90% in patients in whom a response to treatment cannot be achieved with phosphodiesterase 5 inhibitors (Rogers et al., 2010).

Since MPV is a significant demonstrator of platelet function and activation and thromboembolic event incidence increases with platelet activation, the relation between vasculogenic ED and MPV and platelet number is gradually becoming more important. Arteriogenic ED plays a major role among general and vasculogenic ED causes. The current study examined the relation between penile arteriogenic ED and EC, MPV and PC specifically, unlike the studies in literature.

Eosinophils activate coagulation systems and thrombocytes. This situation may cause vasospasms in arteries. It was reported that eosinophil granule proteins may affect the cardiovascular system negatively by causing vascular injury and inflammatory cell infiltration. Studies have demonstrated that eosinophils are related with stent thrombosis, stent restenosis, and acute coronary syndromes (Otunctemur et al., 2015; Umemoto et al., 2000). Sakai et al. (2009) reported that EC is related to vasospastic angina pectoris and large thrombus formation. Strong vasoconstrictor and procoagulant effects of eosinophils make us consider the presence of a relation between EC and vasculogenic ED. Thus, EC was included as a suspicious predicative factor in the current study.

Ciftci et al. (2013) compared 50 patients with vasculogenic ED with 40 healthy people and stated that MPV values and platelet numbers were statistically higher in the vasculogenic ED group. In this study, vascular endothelial cell damage occurring with thrombocyte activation was held responsible for vasculogenic ED etiopathogenesis (Ciftci et al., 2013).

Three groups including vasculogenic ED, ED after radical prostatectomy (nonvasculogenic ED), and healthy participants were compared in a current study in 2015. It was reported that MPV values and platelet numbers were statistically higher in the vasculogenic ED group compared with the other two groups.

Otunctemur et al. (2015) compared vasculogenic ED patients and a healthy control group and in addition to MPV and PC, EC was also included in the examination. Although MPV values and PC was reported as statistically higher in the vasculogenic ED group, no difference was identified in EC among the two groups.

Aldemir et al. (2016) reported that among ED and a healthy control group, MPV and platelet distribution width values were significantly higher in the ED group but the PC was not different among the two groups.

Patients having general ED and not being specified as vasculogenic ED decreases the reliability of the study (Aldemir et al., 2016).

In this study, a significant difference in MPV, PC, and EC values among the two groups was observed. MPV, PC, and EC values were detected as statistically significantly high in the penile arteriogenic ED group ($p = .018$, $p = .034$, $p = .02$, respectively). MPV and PC values were detected as high in the penile arteriogenic ED group similar to previous studies (Ciftci et al., 2013; Ciftci et al., 2015; Otunctemur et al., 2015). This situation identifies that MPV and PC values are a strong predictive factor for both specific penile arteriogenic ED and vasculogenic ED (arteriogenic + venogenic + mixed). But EC was detected as significantly higher in the penile arteriogenic ED group which is different from the study by Otunctemur et al. (2015). This situation makes us consider that EC plays a more active role in specific penile arteriogenic ED etiopathogenesis which is different from vasculogenic ED. Studies demonstrating that increasing EC has negative effects on coronary arteries have been published (Sakai et al., 2009; Umemoto et al., 2000). Depending on the negative effect of increasing EC on arteries and the results of this study, EC is a significant predictive factor in etiopathogenesis for penile arteriogenic ED. Since the studies containing MPV, PC, EC, and ED relation were conducted with patients including vasculogenic ED and general ED groups, this study will make a significant contribution to the literature.

Even though the PDU results of the patients in the control group were normal, referring with an ED complaint, the unequal number of participants in each group, not making confirmative cavernosography in patients who were reported to have arteriogenic deficiency according to PDU results and not scanning patients in the arteriogenic ED group for asymptomatic CVD can be stated are the limitations of this study. The results are significant since only patients who had normal results and arteriogenic dysfunction according to PDU test (venogenic and mixed reported patients were excluded).

Since high MPV, PC, and EC values carry vascular dysfunction risk, these patients should be examined carefully for possible asymptomatic cardiovascular system disease. System evaluation should be recommended even though a there is no known CVD in this patient group when these values are high and ED is accompanying. Treatment options should be evaluated considering that vascular dysfunction may play a more active role in the etiology in ED accompanied by high MPV, PC, and EC values.

Conclusion

High MPV value and PC is a significant predictive factor for penile arteriogenic ED and vasculogenic ED and high EC is specifically predictive of arteriogenic ED. No proof reporting that other blood count parameters such as WBC, RBC, and Hgb play an active role on penile arteriogenic ED etiopathogenesis was detected. MPV, PC, and EC values may contribute to the diagnosis on ED etiology without diagnostic invasive operations. It would be advantageous to conduct studies including a patient group including more patients and separate arteriogenic, venogenic, and mixed ED patient groups. Since possible systemic vascular dysfunction can accompany penile arteriogenic ED patients also accompanied by high MPV, PC, and EC values, cardiovascular system evaluations should be performed for these patients.

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