

Can platelets be the early biomarkers of erectile dysfunction?

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Abstract

Objective: To assess the relationship between erectile dysfunction and platelet count and other platelet indices.

Methods: The case-control study was done at Hitit University Erol Olcok Training and Research Hospital, Turkey, and comprised patient data between January 2014 and September 2016 that was compared with age-matched controls with no history of erectile dysfunction who were randomly chosen from patients attending the urology clinic. Platelet count and other platelet indices were measured in both cases and healthy controls. Erectile status of the patients was evaluated by using International Index of Erectile Function- 5 questionnaire.

Results: There were 203 cases and 102 controls. The mean Index scores of the cases was 12.86 ± 4.55 and that of the controls was 24.65 ± 3.25 ($p < 0.001$). Platelet levels were higher in cases than controls ($p < 0.001$). But there was no statistically significant difference between the groups according to mean platelet volume values ($p = 0.309$).

Conclusion: Platelet values can be used as an early biomarker for erectile dysfunction.

Keywords: Erectile dysfunction, Platelets, Heart diseases. (JPMA 68: 515; 2018)

Introduction

The frequency of erectile dysfunction (ED), which can be simply defined as the lack of penile erection during sexual intercourse, is increasing primarily among men who are older than 40 years of age. Although ED is not a life-threatening and serious disease, it has a major negative effect on quality of life among patients with ED. Approximately 35 million in Europe and over 300 million men worldwide are suffering from ED, and the ED prevalence is increasing in healthy aging population.

The aetiology of ED can be classified as psychological, physiological or mixed. Physiological reasons include hormonal, vascular, neurogenic factors and psychological factors include conditions such as performance anxiety, and mood disorders such as depression and psychosocial stress. But the vascular reasons such as atherosclerosis of the penile arteries are one of the most common causes of this illness. Due to endothelial dysfunction and peripheral artery disease, diabetes mellitus, atherosclerosis, hypertension and coronary disease are responsible for the development of ED.¹ As a result of all these conditions, ED is considered a major health problem.

The mean platelet volume (MPV), which shows the platelet activity as platelet production and reactivity, is

commonly used. Studies showed that platelets in larger size are more active in metabolic and enzymatic conditions. Increased thromboxane synthesis, increased expression of adhesion molecules and increased platelet aggregation, which are other markers of platelet activity, are associated with elevated MPV.²

The association between vascular ED and MPV is poorly investigated. Increased levels of MPV can be seen in vascular pathologies such as diseases like diabetes mellitus, hypertension, hypercholesterolaemia, obesity and also among smokers.²⁻⁵ MPV, which is commonly used in clinical practice, is a useful biomarker of platelet activity. A study, consisting of 2809 patients and investigating the association between MPV and acute myocardial infarction, reported that elevated MPV was significantly associated with acute myocardial infarction. It suggested that MPV was a useful biomarker of cardiovascular disease.⁵

Studies showed an association between ED and ischaemic heart disease as a result of vascular lesions of the penile arteries.⁶

Due to common aetiology of vascular diseases, there might be a correlation between ED and MPV. The current study was planned to investigate if there was an association between vascular ED, platelet count and MPV.

Materials and Methods

The case-control study was done at Hitit University Erol Olcok Training and Research Hospital, Turkey, and comprised patient data between January 2014 and September 2016 that was compared with age-matched

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controls with no ED history who were randomly chosen from patients attending the urology clinic. The controls were sexually active and had a score of more than 26 according to the International Index of Erectile Function (IIEF) questionnaire.

All patients had a complete history and physical examination, including neurological examination, and also blood samples as blood glucose assay, complete blood count, testosterone, luteinizing hormones (LH), and kidney and liver function tests. Erectile functions of all patients were evaluated by using the IIEF questionnaire. The score of 26-30 represents normal function, while scores <26 indicate ED. According to IIEF-5 score, ED is classified as mild at 22-25, mild to moderate at 17-21, moderate at 11-16 and severe at 0-10.⁷

Patients with the history of neurogenic or endocrinologic ED, diabetes mellitus, hypertension, coronary artery diseases and other diseases which can affect the vascular system, haematological disorders, malignancies, acute infection and inflammatory diseases were excluded from the study. Also, patients who had undergone pelvic surgery, history of pelvic trauma and genitourinary surgeries were excluded.

All statistical analyses were performed with SPSS 22.0. Data was expressed as mean \pm standard deviation (SD), median (minimum-maximum) or frequency and percentage. Shapiro-Wilk test was used to check for normality of distribution. The significance of the difference between two independent groups were assessed by using Student's t test in case of normal data distribution, or Mann Whitney U test in case of non-normal distribution for continuous variables. Pearson's correlation coefficient or Spearman's rank correlation were used to investigate the association between two continuous variables. Receiver operating characteristics (ROC) curve analysis was performed to identify optimal cut-off value for platelet at which sensitivity and specificity would be maximal. Sensitivity and specificity values were calculated for such variables respectively. $P < 0.05$ were considered to be statistically significant.

Results

There were 203 cases in group 1 and 102 controls in group 2. The mean ages of group 1 and group 2 were 50.28 ± 13.08 and 51.76 ± 11.87 years ($p = 0.07$). Platelet levels were higher in cases than controls

Table-1: Group Statistics of mean platelet volume (MPV) values and platelet counts (PLT).

	Group	Number	Mean	Standard Deviation	p
MPV	1	102	9.3911	1.56604	0.309
	2	203	9.4954	1.6612	
PLT	1	102	209.08	54.003	<0.001
	2	203	268.27	49.743	

Table-2: Area under curve (AUC) and summary statistics for Platelet in Receiver Operating Characteristic (ROC) analysis.

Platelet	
AUC* (95% CI)	0.812(0.758-0.867)
Sensitivity	97% (93-99)
Specificity	56% (46-66)
Positive predictive value	81% (76-86)
Negative predictive value	90% (80-96)
LR+	2.20 (1.77 - 2.74)
Cut-off value	201

*Area under curve 0.70 < AUC < 0.80 Moderate, 0.80 < AUC < 0.90 high 0.90 < AUC < 1 very high. LR: Likelihood ratio.

(platelet: 268.27 ± 49.74 and 209.08 ± 54.00 ; $p < 0.001$).

There was no statistically significant difference between groups according to MPV values ($p = 0.309$). Mean IIEF scores was 24.65 ± 3.25 in group 1 and 12.86 ± 4.55 in group 2 ($p < 0.001$) (Table 1, Figure 1). Mean body mass index (BMI) values of the subjects were 22.37 ± 4.53 in group 1 and 27.33 ± 3.69 in group 2 ($p < 0.001$).

Activated platelets were higher in vasculogenic ED

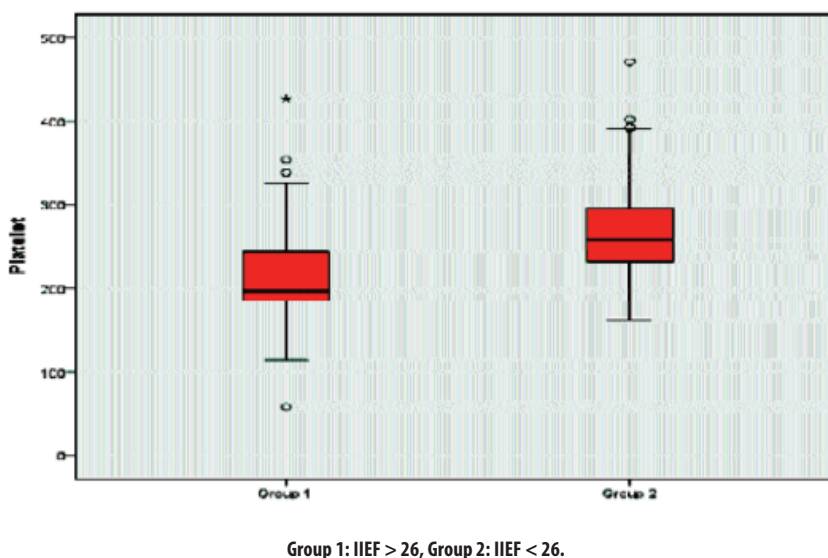


Figure-1: Boxplot of platelet count according to International Index of Erectile Function (IIEF) groups.

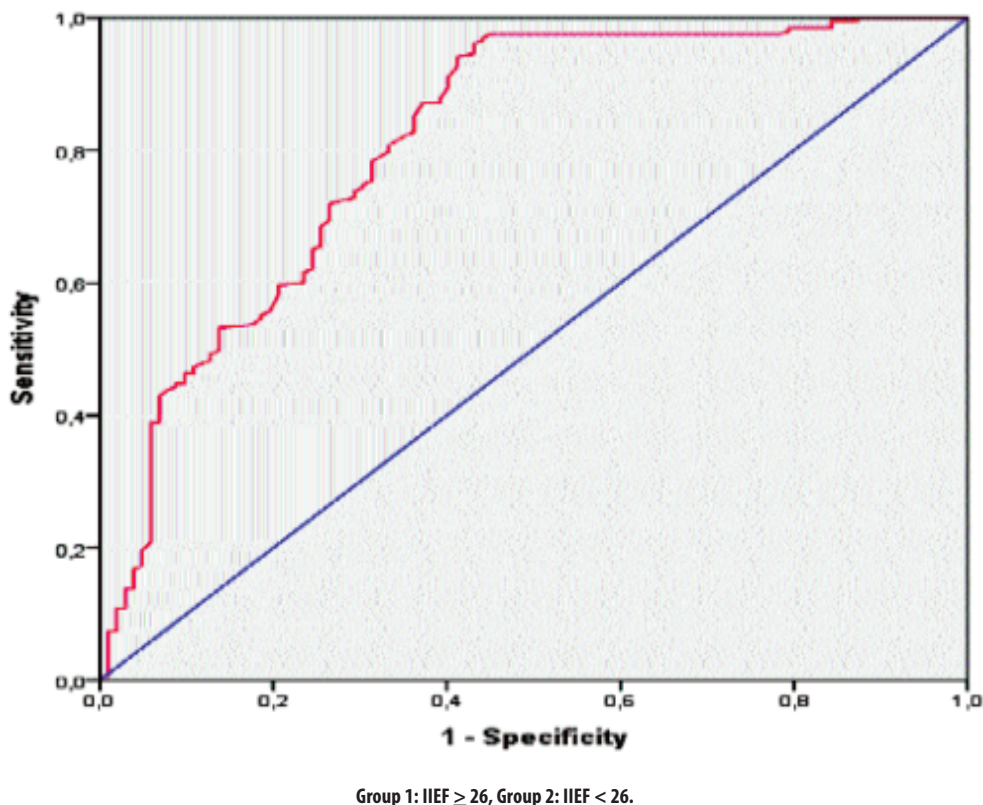


Figure-2: Receiver Operating Characteristic (ROC) curve of platelet count according to International Index of Erectile Function (IIEF) groups.

patients. A cut-off value of 201 for the platelet count was highly statistically significant ($p < 0.001$) with an optimal combination of sensitivity (97%) and specificity (56%) (Table-2, Figure-2).

Discussion

ED is a common urologic problem among sexually active male population. It results from several disorders as neurogenic and psychological pathologies but vascular disorders take a major role in these pathologies. The common risk factors between ED and coronary artery disease, such as diabetes mellitus, hypertension, obesity, hyperlipidaemia, smoking and sedentary lifestyle, indicate that these two frequently seen disorders may have a common aetiology. Studies showed that ED can be the first symptom and messenger of coronary artery diseases.⁸ One study reported that 19% of ED patients with vascular causes had angiographically documented silent coronary artery diseases and it suggested further cardiovascular evaluation for patients with ED.⁹ In another study endothelial dysfunction was seen as an important underlying pathology in both ED and coronary artery diseases.¹⁰

One study reported how this situation occurs. According to that study, this may be related to diameter of the vessels. Due to small size of penile arteries than coronary arteries, an equal-sized atherosclerotic plaque should occlude small arteries earlier, so that early occluded artery will give early symptoms as ED.¹¹

In one study on 1476 men with heart disease, myocardial infarction or vascular surgery, it was reported that the incidence of ED ranged from 39-64% in each patient group.¹²

Subclinical inflammation which affects the endothelial function plays a major role both in metabolic disorders and ED. Studies support that elevated serum inflammatory and endothelial thrombogenic compounds are associated with ED. Low-grade systemic inflammation can be the

reason of association between ED and coronary artery diseases.¹³

Due to secretion of protein from activated platelets which adheres to the vessel wall, it triggers the development of atherosclerosis and thrombus formation.¹⁴

In the light of these studies and due to common aetiology between ED and cardiovascular diseases, we investigated the relation between vascular ED and MPV and platelet count. Platelets are one of the main causes of vascular endothelial dysfunction, so that platelet activation might be associated with vasculogenic ED.

In our study, patients with erectile dysfunction had higher platelet values than the patients in control group. Similar to our study, it has been reported that the platelet count and MPV increased in patients with vasculogenic ED.¹⁵ Also, in one study on a series of 130 cases, it was found that MPV and platelet count levels were higher in ED patients than controls.¹⁶ However, in our study we could not find statistically significant difference in MPV values between the patients and the controls ($p = 0.309$).

Recent studies showed that platelet distribution which shows platelet activity can be a potential marker for predicting the severity of ED. A study on 358 ED patients mentioned that platelet distribution and MPV increased as the disease progressed.¹⁷ Also, a study reported that MPV was higher in ED group than control group and it was statistically significant.¹⁸ In the light of these studies anti-platelet therapy may play a role in the treatment of vasculogenic ED.

According to current data, platelets play a major role in the aetiology of cardiovascular diseases and vascular ED. The main reason for this pathology is endothelial dysfunction due to activated platelets. Activated platelets were higher with vasculogenic ED patients. A cut-off value of 201 for the platelet count was highly statistically significant ($p < 0.001$) with an optimal combination of sensitivity (97%) and specificity (56%).

Early diagnosis of ED may prevent cardiovascular diseases. Early prevention, such as lifestyle changes, or maybe anti-aggregant therapy may protect patients from harmful effects of cardiovascular diseases.

Conclusion

Endothelial dysfunction seems to be the key point between cardiovascular diseases and ED. Activated platelets are one of the main causes of endothelial dysfunction. Platelet values can be used as an early biomarker for ED.

Disclaimer: None.

Conflict of Interest: None.

Source of Funding: None.

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