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The Relationship Between Erectile Dysfunction and Monocyte/HDL Ratio

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SUMMARY

Objective: Considering that Cardiovascular Diseases (CVD) and Erectile Dysfunction (ED) have many common risk factors and pathophysiology, we aimed to determine whether monocyte/HDL ratio is associated with ED.

Material and Method: Patients who were diagnosed with ED and examined with any other andrological complaints between November 2021 and January 2024 in our clinic were retrospectively reviewed. The erectile function of the participants was evaluated using the international index of sexual function-5 (IIEF-5) questionnaire. Hemogram, FBG, HbA1c, total cholesterol, HDL, LDL, total testosterone, Body Mass Index (BMI) and Monocyte/HDL Ratio (MHR) were calculated and recorded. Patients were categorized as having ED (Group 1) and not having ED (Group 2) according to the IIEF-5 form.

Results: The mean age of all participants included in the study was 42.49 ± 12.49 years. There were 84 (63.15%) patients in Group 1 and 49 (36.85%) patients in Group 2. Age, BMI, FBG and HbA1c levels were significantly higher in Group 1 (p=0.001; p=0.036; p=0.003; p=0.002, respectively). HDL cholesterol level was significantly lower in Group 1 (p=0.002). MHR was 0.0131 ± 0.005 in Group 1 and 0.0106 ± 0.004 in Group 2, which was significantly higher in Group 1 (p=0.009). In the ROC analysis, the cut-off value of MHR was found to be 0.0124.

Conclusion: In our study, MHR level was significantly higher in ED patients. However, prospective studies with larger participation are needed to support our findings.

Keywords: Erectile Dysfunction; IIEF; Monocyte/HDL Ratio

Abbreviations: MHR: Monocyte/HDL Ratio; CVD: Cardiovascular Diseases; ED: Erectile Dysfunction; BMI: Body Mass Index; HT: Hypertension; HDL- C: High-Density Lipoprotein Cholesterol; LDL-C: Low-Density Lipoprotein Cholesterol; IIEF-5: International Index of Sexual Function; ACS: Acute Coronary Syndrome; AIS: Acute Ischemic Stroke; EMAS: European Male Ageing Study

Introduction

Penile erection is a complex phenomenon in which neurological, endocrine, and vascular structures work in a sensitive and balanced manner [1]. During penile erection, dilation of the arteries supplying the penis, relaxation of the penile trabecular smooth muscles and activation of the corporeal veno-occlusive mechanism are required [1]. Erectile Dysfunction (ED) is defined as the inability to achieve and/or maintain a penile erection sufficient for satisfactory. sexual intercourse [2]. ED occurs in more than half of the male population aged 40-70 years [3]. Among the organic pathologies that cause ED, the most common cause is impaired arterial blood flow to the erectile tissues [4]. Vasculogenic risk factors that may cause ED include diabetes, dyslipidemia, Cardiovascular Diseases (CVD), Hypertension (HT), obesity, metabolic syndrome, sedentary lifestyle and smoking [4]. The common pathophysiological pathway underlying these risk factors is inflammation, atherosclerosis and endothelial dysfunction resulting in decreased blood flow, arterial insufficiency, or arterial stenosis [4,5]. Macrophages and monocytes have important roles in the secretion of proinflammatory and prooxidant cytokines in inflammation areas [6,7]. High-Density Lipoprotein Cholesterol (HDL- C) has been shown to protect endothelial cells against the adverse effects of Low-Density Lipoprotein Cholesterol (LDL-C) and inhibit the oxidation of LDL molecules [7,8]. The Monocyte/HDL Ratio (MHR),

recognized as a new marker of inflammation, is the ratio of inflammatory markers (monocytes) to Anti-Inflammatory Markers (HDL-C) [9]. Some studies have shown that MHR is associated with metabolic syndrome, CAD and diabetic microangiopathy [10-12]. In this study, considering that CVD and ED have many common risk factors and pathophysiology, we have aimed to determine whether MHR is associated with ED.

Material and Methods

Participants were included in the study after obtaining the approval of the clinical research ethics committee and in accordance with the principles of the Declaration of Helsinki. Patients who applied to the urology outpatient clinic of our hospital between November 2021 and January 2024 due to andrological complaints were retrospectively reviewed. The erectile function of the patients was evaluated using the 5-question form of the International Index of Sexual Function (IIEF-5). Patients with an IIEF-5 score of 22 and above were considered healthy/normal in terms of erection, while those with a score below 22 were considered ED. Exclusion criteria; patients with any endocrinological disease other than type 2 DM such as hyperprolactinemia, hypogonadism and hypo/hyperthyroidism, neurological disease, hematological disorders, accompanying malignancies, psychiatric disease, ED-related drug and addictive substance use, collagen tissue disease, history of previous penile or pelvic surgery/trauma/radiotherapy, history of spinal cord trauma, presence of penile curvature/Peyronie's disease, chronic liver failure, chronic renal failure. In addition, patients with missing data were excluded from the study. IIEF-5 score, anamnesis and physical examination findings of the patients were obtained from archive records. Hemogram, FBG, HbA1c, total cholesterol, HDL, LDL and total testosterone results were recorded from peripheral blood samples. MHR value was calculated by dividing serum monocyte level by HDL cholesterol level.

As a control group, patients who were examined for an andrological reason other than ED (Peyronie's disease, ejaculation disorders, infertility, etc.) and whose IIEF-5 score was 22 and above were included in the study. The patients were divided into two groups as Group 1 (ED) and Group 2 (control), and comparisons were made. Statistical analysis was performed using SPSS 21.0 (IBM SPSS for Windows). Data were expressed as number, percentage, mean and standard deviation. Comparison between two independent groups was performed by Student's t-test. ROC analysis was performed for the cut-off value of MHR in predicting ED. Statistical significance was accepted as $p<0.05$.

Results

A total of 133 patients with a mean age of 42.49 ±12.49 years were included in the study. There were 84 (63.15%) patients in Group 1 and 49 (36.85%) patients in Group 2. The mean age of Group 1 was 47.14 ±11.70 years and the mean age of Group 2 was 34.51 ±9.45 years, which was significantly higher in Group 1 (p=0.001). The mean BMI was 27.88 ± 3.49 kg/m2 in Group 1 and 26.85±2.09 kg/m2 in Group 2 and was significantly higher in Group 1 (p=0.036). The mean FBG was 116.21±64.79 mg/dL in Group 1 and 87.59±20 mg/dL in Group 2 and the difference was significant and higher in Group 1 (p=0.003). The mean HbA1c was 6.15±1.68 % in Group 1 and 5.39±0.43 % in Group 2, which was significantly higher in Group 1 (p=0.002). The mean HDL cholesterol level of Group 1 was 41.56±9.63 mg/dL, while the mean HDL cholesterol level of Group 2 was 46.99±9.90 mg/dL, which was significantly higher in Group 1 (p=0.002). The mean monocyte/HDL ratio was 0.0131±0.005 in Group 1 and 0.0106 ± 0.004 in Group 2, which was significantly higher in Group 1 (p=0.009). The data of all participants are presented in Table 1 and the comparison between Group 1 and Group 2 is presented in (Table 2). MHR was found to be associated with ED in ROC analysis, with 0.66 of AUC, 0.536-0.730 of 95% CI and p=0.011. According to ROC analysis, MHR cut-off value above 0.0124 seems to be associated with ED with 47% sensitivity and 76% specificity (Figure 1).

Table 1: Data of all participants.

Data	Mean ± SD	Minimum	Maximum
Age (years)	42.49 ± 12.49	24	70
BMI (kg/m^2)	27.50 ± 3.08	19.03	40.39
Fasting Blood Glucose (FBG) (mg/dL)	105.67 ± 54.56	54	412
Glycolyzed Hemoglobin (HbA1c) (%)	5.87 ± 1.40	3.79	13.89
Triglyceride (mg/dL)	154.88 ± 106.42	40	765
Total Cholesterol (mg/dL)	187.89 ± 39.26	43	283
HDL Cholesterol (mg/dL)	43.56 ± 10.04	15.6	73.7
LDL Cholesterol (mg/dL)	115.85 ± 36.08	11.4	210
Total Testosterone (ng/dL)	468.84 ± 151.33	300	1009
Hemoglobin (g/dL)	15.16 ± 1.06	11.4	17.7
Leukocyte (mcL)	7.54 ± 1.96	3.52	13.60
Neutrophil (mcL)	4.39 ± 1.43	1.11	8.33
Lymphocyte (mcL)	2.35 ± 0.64	1.01	4.59
Monocyte (mcL)	0.49 ± 0.14	0.20	1.03
Monocyte/HDL ratio	0.012 ± 0.005	0.003	0.036

Table 2: Comparison of data between the two groups.

Data	Group 1 (n:84) (mean ±SD)	Group 2 (n:49) (mean ± SD)	P value
Age (years)	47.14 ± 11.70	34.51 ± 9.45	0.001
BMI (kg/m^2)	27.88 ± 3.49	26.85 ± 2.09	0.036
Fasting Blood Glucose (FBG) (mg/dL)	116.21 ± 64.79	87.59 ± 20	0.003
Glycolyzed Hemoglobin (HbA1c) (%)	6.15 ± 1.68	5.39 ± 0.43	0.002
Triglyceride (mg/dL)	164.52 ± 101.61	138.35 ± 113.35	0.172
Total Cholesterol (mg/dL)	184.19 ± 38.27	194.24 ± 40.52	0.155
HDL Cholesterol (mg/dL)	41.56 ± 9.63	46.99 ± 9.90	0.002
LDL Cholesterol (mg/dL)	111.82 ± 34.91	122.76 ± 37.35	0.092
Total Testosterone (ng/dL)	471.43 ± 153.21	464.39 ± 159.52	0.797
hemoglobin (g/dL)	15.15 ± 1.14	15.19 ± 0.91	0.836
Leukocyte (mcL)	7.80 ± 2.02	7.11 ± 1.78	0.053
Neutrophil (mcL)	4.51 ± 1.47	4.19 ± 1.36	0.224
Lymphocyte (mcL)	2.42 ± 0.67	2.22 ± 0.57	0.091
Monocyte (mcL)	0.51 ± 0.15	0.47 ± 0.12	0.155
Monocyte/HDL ratio	0.0131 ± 0.005	0.0106 ± 0.004	0.009

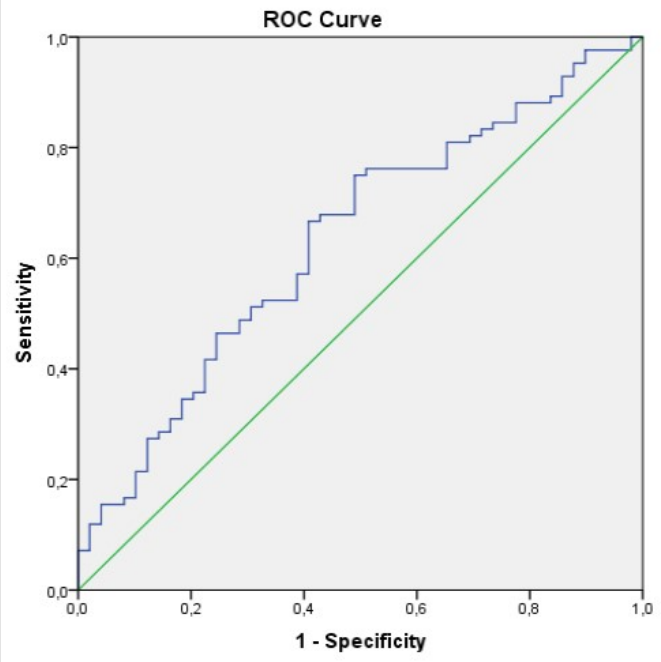

Figure 1: ROC curve of MHR in predicting ED.

Discussion

The main aim of this retrospective study was to investigate whether MHR was associated with ED. As a result of our analyses, we found that MHR had a relationship with ED and MHR was significantly higher in the ED group. In addition, other main findings we obtained were that age, BMI, FBG and HbA1c were significantly higher in ED patients. HDL cholesterol was found to be significantly lower in the ED group. Inflammation and oxidative stress are well recognized mechanisms in the development and progression of atherosclerosis [7]. Monocytes play a critical role in this process. Activated monocytes interact with the endothelium, causing overexpression of proinflammatory cytokines. Monocytes then differentiate into macrophages that digest oxidized LDL cholesterol and form dangerous foam cells [13]. On the contrary, HDL molecules inhibit the migration of macro-

phages and stimulate the outflow of oxidized cholesterol from these cells [13]. Monocytes exert proinflammatory and prooxidant effects, whereas HDL-C acts as an anti-inflammatory and antioxidant factor that reverses these processes [7,12]. Canpolat et al. showed that higher MHR levels were significantly and independently associated with the presence of SCF in Coronary Slow Flow Phenomenon (SCF) associated with inflammation, oxidative stress, and endothelial dysfunction [7]. Kanbay et al. reported that MHR increased during decline in the glomerular filtration rate and was associated with a worse cardiovascular profile and was an independent predictor of major cardiovascular events during follow-up in their study with patients with chronic renal failure.

Çetin et al. emphasized that MHR was an independent predictor of the severity of coronary artery disease and future cardiovascular events in patients with ACS in their study, which included 2661 patients with Acute Coronary Syndrome (ACS) and a mean follow-up period of 31.6 months [11]. Bolayır et al. reported in their study including 466 Acute Ischemic Stroke (AIS) patients that MHR was an independent predictor of 30-day mortality in AIS [14]. In our study, the relationship between MHR and ED was investigated and a significantly higher MHR level was found in ED patients compared to the control group. When ROC analysis was performed for MHR, patients with MHR cut-off value above 0.0124 were found to be associated with ED with 47% sensitivity and 76% specificity. The relationship between age and ED, which is one of the important risk factors in the development of ED, has been demonstrated in many studies. In the European Male Ageing Study (EMAS) conducted in 2010 in eight European Union countries with 3369 male participants with an average age of 60±11 years; while the prevalence of moderate or severe ED was reported in 30% of all participants, this rate was reported as 64% in men aged 70 years and over [15]. In a study conducted by Braun et al. in Germany with participants aged 30-80 years, the overall prevalence of ED was 19.2% and increased with age; 2.3% in the 30- 39 age range and 53.4% in the 70-80 age range [16]. In our study, the mean age was found to be significantly higher in the ED group in accordance with the literature.

When the literature is analyzed, it is understood that obesity is among the common causes of ED. Kratzik et al. reported in their study that each 1 kg/m2 increase in BMI, IIEF-5 decrease by 0.141 (p=0.005) regardless of age and that high BMI rates strongly contributed to the development of ED [17]. In a meta-analysis aiming to demonstrate the relationship between BMI and ED, it was found that ED was significantly associated with high BMI ratios [18]. In this context, the present study is consistent with the literature and BMI was found to be significantly higher in the ED group. DM causes sexual dysfunction in both men and women, and ED is the most important dysfunction in men with DM [19]. Epidemiological studies show that the age of onset of ED in diabetic men is on average 10-15 years earlier than in non-diabetic men, and that the duration of DM and ED are closely related [20]. According to a meta-analysis of 145 studies, the overall ED prevalence rate in men with DM was reported to be 52.5% (95% CI, 48.8- 56.2), whereas the prevalence rates in patients with Type 1 and Type 2 DM were 37.5% and 66.3%, respectively [21]. Today, the concept of prediabetes, which is considered as a metabolic state between normoglycemia and diabetes, has emerged [22]. According to the World Health Organization, the definition of prediabetes is defined as a FBG of 110-125 mg/dL and an HbA1c level of 5.7-6.4% [23]. According to the meta-analysis published by Jin et al., compared with normoglycemic men, prediabetic men were reported to have a higher prevalence of ED (OR 1.62; 95% CI 1.28-2.07; p<0.001) [22].

The results reported in various studies support this situation [24,25]. In the present study, in accordance with the literature, mean FBG and HbA1c levels were significantly higher in the ED group compared to the control group. The role of HDL cholesterol in mediating atherosclerotic heart disease is unclear, but results from epidemiological studies suggest that low HDL cholesterol levels are an independent risk factor for atherosclerotic heart disease [26,27]. The MMAS study reported an inverse association between the likelihood of having an ED and HDL cholesterol level [28]. However, high serum total cholesterol and low HDL cholesterol levels have been shown to be associated with an increased risk of ED [29]. In the present study, HDL cholesterol was found to be significantly lower in the ED group compared to the control group and this result supports the studies reporting that HDL cholesterol is protective in terms of ED. Our study has some limitations. Firstly, its design was retrospective, single-centre, cross- sectionally, and the participants did not have specific follow-up periods. In addition, the habits of the participants included in the study, such as smoking/alcohol/nutrition, which may have effect on ED, could not be recorded and analyzed due to lack of data.

Conclusion

In our study aiming to reveal the relationship between ED and MHR, which has a common pathophysiology with atherosclerosis-based vascular diseases, MHR level was found to be significantly higher in ED patients. To the best of our knowledge, this is the first study to demonstrate the relationship between ED and MHR and we think that our study is a valuable contribution to the literature. However, prospective studies with larger participation are needed to support our findings.

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