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Relationship Between the Visceral Adiposity Index and Peyronie's Disease

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What's known on the subject? and What does the study add?

Peyronie's disease (PD) is an acquired benign localized connective tissue disease. Abnormal healing pattern and excessive fibrosis development in the tunica albuginea secondary to penile microtrauma is the most accepted mechanism. Clinical conditions, including hypertension, hyperlipidemia, and abnormal glucose metabolism, can increase PD by creating a hypoxic microenvironment in erectile tissues. The visceral adiposity index (VAI), defined as a marker of adipose tissue dysfunction, is a beneficial mathematical model based on anthropometric and functional parameters. This study is the first one ever to define VAI as a new independent risk factor for PD. We think that considering VAI in the follow-up and treatment protocols of PD will offer important innovations in clinical practice.

Abstract

Objective: We aimed to investigate the relationship between Peyronie's disease (PD) and the visceral adiposity index (VAI), which is thought to predict visceral obesity homogeneously.

Materials and Methods: We included 102 healthy volunteers (Group 1) and 89 patients with PD (Group 2) in this retrospective study. We recorded demographic, anthropometric, and clinical data, including age, comorbidity, International Index of Erectile Function (IIEF) score, waist circumference (WC), body mass index (BMI), visceral adiposity index testosterone (VAI), serum fasting glucose, high-density lipoprotein (HDL), and triglyceride (TG). For Group 2 participants, plaque size, duration of symptoms, and degree of penile curvature were recorded.

Results: The mean ages of Group 1 and Group 2 were 55.12±9.51 years and 54.79±9.99 years, respectively ($p>0.05$). The mean BMI, WC, VAI, fasting glucose, and TG values were significantly higher in Group 2 ($p<0.001$, $p=0.004$, $p=0.001$, $p=0.001$, and $p=0.003$, respectively). The mean HDL values between the groups were similar ($p>0.05$). The mean IIEF score was lower in Group 2 than in Group 1 ($p=0.008$). An increase of 1 unit in the VAI value increases the probability of having PD 1.2 times ($p=0.001$). Each VAI integer increase decreased 1.25 points in the IIEF score, a 1 mm increase in plaque size, and a 1.98-degree increase in curvature.

Conclusion: Our study has shown that VAI can be used as a reliable, independent risk factor for plaque size and penile curvature in patients with patients with PD.

Keywords: Peyronie's disease, visceral adiposity index, men, penile curvature

Introduction

Peyronie's disease (PD) is an acquired benign localized connective tissue disease characterized by fibrous collagen plaque formation in the tunica albuginea of the penile corpus cavernosum (1,2). Penile plaques can be palpated when the penis is flaccid. PD can cause impotence, painful erection, and penile deformities such as narrowing, contraction, and shortening (3). As PD progressed, severe sexual dysfunction may occur (1,4). The incidence of PD

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is reported to be 26 per 100.000 with a prevalence of 389 per 100.000, and it varies between geographies (3). PD is a clinical condition whose pathophysiology has not been sufficiently elucidated to date. Abnormal healing pattern and excessive fibrosis development in the tunica albuginea secondary to penile microtrauma are the most accepted mechanism. Clinical conditions, including hypertension, hyperlipidemia, and abnormal glucose metabolism, can increase PD by creating a hypoxic microenvironment in erectile tissues (1).

With an increasing prevalence, obesity and obesity-related health problems have become a threatening global problem. Epidemiological studies have shown that the number of overweight people in the world will increase to 1.35 billion in 2030 and the number of obese people to 573 million (5). Obesity may lead to endothelial dysfunction by increasing susceptibility to hypertension and metabolic syndrome. Obesity also causes significant changes in hormonal function (6). Body mass index (BMI) and waist circumference (WC) are commonly used anthropometric measures to assess obesity. However, BMI is not a reliable indicator for estimating body fat distribution due to such factors as age, gender, race, high muscle mass, and fluid intake habits. Similarly, WC also fails to show visceral adipose tissue because it measures the subcutaneous adipose tissue (6,7). It plays an essential role in the physiopathology of disorders secondary to obesity (8).

Visceral adiposity is closely related to increased adipocytokine production, increased proinflammatory activity, atherosclerosis, hypertension, insulin resistance, glucose, and lipid profile disorders (9). Different medical equipment, such as bioelectrical impedance, magnetic resonance imaging, and dual-energy X-ray absorptiometry are needed to reveal the visceral adipose tissue distribution directly. Since these techniques require specific technological infrastructure and are costly, it is almost impossible to apply them in our daily clinical practice (10). This situation has led researchers to look for easy and practical methods. In this context, the visceral adiposity index (VAI), defined as a marker of adipose tissue dysfunction, has attracted great interest. VAI is a beneficial mathematical model based on anthropometric and functional parameters. Ever since Amato et al. (10) first described the concept of VAI in 2010, numerous studies have been conducted for many conditions such as neurologic, cardiovascular, and metabolic disorders (11). However, as a predictor of adipose tissue function, in Andrology, the VAI has been considered only recently, and few studies have been published (12).

We conducted out this study to show whether the VAI can affect the plaque size and severity of penile curvature in Peyronie's disease. To the best of our knowledge, this is the first study in the English literature that analyzed VAI in patients with PD patients.

Materials and Methods

Patients

Of the 191 participants, 102 were assigned to the control group (Group 1), and 82 patients with PD were to Group 2. We retrospectively analyzed the data of the patients who applied to our clinics between April 2010 and March 2021, and we obtained detailed informed consent from the participants. Patients with PD were defined as Group 1. The patients who applied for routine checks and had no uropathology was determined as Group 2. We recorded their demographic data, comorbidities, clinical complaints, duration of symptoms, physical examination findings, and any history of trauma, pelvic radiotherapy, and genital surgery. The diagnosis of PD was established based on the characteristic symptoms and palpable penile plaque on physical examination.

Plaque size was determined by physical examination. Curvature degree was calculated by reviewing the images taken after intracavernosal injection (1,2). Additionally, the weight, height, and WC of the patients were measured. The erectile function was calculated using the International Index of Erectile Function (IIEF) (6). Fasting morning blood samples were taken between 8:30 and 10:00 in the morning for total testosterone, fasting blood glucose, HDL, and TG.

This study was conducted according to the Declaration of Helsinki Principles. The local ethics committee (Clinical Studies Ethics Committee decision no: 21-KAEK-132, date: 20.05.2021) approved this study.

Measurements of BMI, WC, and VAI

BMI was determined as weight/height^2 (kg/m^2). WC was calculated by measuring the circle's circumference passing through the midpoint of the lines perpendicular to the 10th rib on both sides and the spina iliaca anterior superior. The units for BMI and WC were kg/m^2 and cm, respectively (9). The VAI was calculated according to the male gender-specific formula [WC/39.68 + (1.88xBMI)] [TG/1.03] [1.31/HDL] (10).

Inclusion and Exclusion Criteria

Only the participants with complete data were included in our study. Cases with a history of penile trauma, pelvic surgery, and radiotherapy were excluded.

Statistical Analysis

Statistical analysis of the data was carried out using the SPSS (Version 22, SPSS Inc., Chicago, IL, USA) package Inc..

The normal distribution of the data was evaluated using the Kolmogorov-Smirnov test. Descriptive statistics of continuous variables were presented using mean ± standard deviation or median ± interquartile range (IQR), depending on the data distribution. Categorical variables were presented as number (n) and percentage (%). Student's t-test and the Mann-Whitney U test were used to compare the numerical variables between two independent groups for normally and non-normally distributed data, respectively. Proportion comparisons between categorical variables were performed using the chi-square test or Fisher's exact test. Receiver operating characteristic (ROC) analysis was used to determine whether the AVI scores could be a prognostic indicator for disease prediction. ROC curves and area under the curve (AUC) and 95% confidence intervals (CIs) were also calculated. The AUC values obtained in the analyses were interpreted as 0.9-1: excellent, 0.8-0.9: good, 0.7-0.8: fair, 0.6-0.7: poor, and 0.5-0,6: unsuccessful. The Youden index (maximum sensitivity and specificity) was used to determine the best cut-off point in the ROC analysis. The success of the cut-off points was evaluated using the values of accuracy, sensitivity, specificity, positive predictive value, negative predictive value, and positive likelihood ratio. Pearson correlation coefficients and Univariate linear regression analysis were used to make the correlation analysis between the VAI score and the IIEF score, plaque size, and degree of curvature. Binary logistic regression analysis was used to show the effect of VAI on PD, and the odds ratios were calculated. Statistical significance level was accepted as p<0.05.

Results

The mean ages were 55.12±9.51 years and 54.79±9.99 years in Groups 1 and 2, respectively (p>0.05). The mean symptom duration of the patients in Group 2 was 17.1±4.1 months. The mean penile curvature degree and plaque size of the patients in this group were 47.83±12.79° and 16.1±4.9 mm. Patients with PD had a higher rate of Dupuytren's contracture, hyperlipidemia, and smoking than Group 1 (p<0.05). Both groups had similar rates of coronary artery disease (p=0.074) (Table 1).

Group 2 patients had higher BMI and WC than Group 1 (p<0.001 and p=0.004). When blood biochemical analyses were examined, the mean fasting glucose and TG levels in Group 2 were found to be 100±30 mg/dL and 155±84 mg/dL, respectively. These values were significantly higher than Group 1 (p=0.001 and p=0.003, respectively). Conversely, total testosterone levels were significantly lower in Group 2 than in Group 1 (p=0.002). HDL values were similar in Groups 1 and 2 (p>0.05). Mean VAI values in Groups 1 and 2 were recorded as 3.83±1.79 and 5.72±4.62, respectively. These values were significantly higher in Group 2 (p=0.001). While erectile dysfunction was observed in only 20 (19.6%) cases in Group 1, it was detected in 44 (49.4%) patients in Group 2 (p<0.001), and the IEFF score in Group 2 was recorded to be significantly lower than Group 1 (p=0.008) (Table 2). The distribution of VAI and IIEF scores among the groups is documented in Figure 1.

The results of the linear regression analysis showed that each integer increase in VAI increased the probability of having PD 1.2 times (CI: 1.07-1.35), decreased the IIEF score by 1.25 points (CI: 1.03-1.47) (R2=0.4, p<0.001), increased plaque diameter by

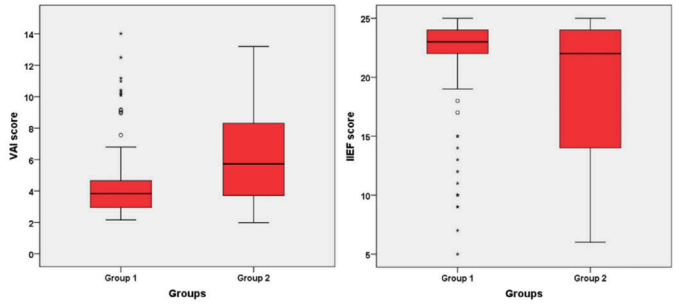

Figure 1. Boxplot of the distribution of VAI and IIEF scores among the research groups

VAI: Visceral adiposity index, IIEF: International Index of Erectile Function

Table 1. Distribution of the study population by comorbidity

Comorbidity	Group 1 (n=102)	Group 2 (n=89)	p-values
Diabetes mellitus	9 (8.8%)	17 (19.1%)	**0.039**[a]
Hypertension	6 (5.9%)	13 (14.6%)	**0.044**[a]
Hyperlipidemia	15 (14.7%)	32 (36%)	**0.001**[a]
Coronary artery disease	3 (2.9%)	8 (9%)	0.074[a]
Smoking	34 (33.3%)	46 (51.7%)	**0.010**[a]
Dupuytren's contracture	2 (2%)	8 (9%)	**0.047**[b]

[a]Chi-square test, [b]Fisher exact test

Table 2. General characteristics of Groups 1 and 2

Characteristics	Group 1 (n=102)	Group 2 (n=89)	p-values
Age (years)	55.12±9.51	54.79±9.99	**0.816**[b]
WC (cm)	95.6±12.3	101.8±16.3	**0.004**[a]
BMI (kg/m^2)	26.23±3.65	28.50±4.61	**<0.001**[a]
TG (mg/dL)	142.5±65.75	155±84	**0.003**[b]
HDL (mg/dL)	50±13.25	45±26	0.185[b]
Testosterone (ng/dL)	456±33	308±300	**0.002**[b]
Glucose (mg/dL)	95±19.25	100±30	**0.001**[b]
VAI	3.83±1.79	5.72±4.62	**0.001**[b]
IIEF score	23±2	22±10	**0.008**[b]

[a]Student's t-test with mean ± standard deviation
[b]Mann-Whitney U test with median ± interquartile range (IQR), WC: Waist circumference, BMI: Body mass index, TG: Triglyceride, HDL: High-density lipoprotein, VAI: Visceral adiposity index, IIEF: International Index of Erectile Function

1 mm (CI: 0.07-0.13) (R2=0.31, p<0.001), and penile curvature by 1.98 degrees (CI: 1.14-2.82) (R2=0.2, p<0.001) (Figure 2) (Table 3).

ROC analysis was performed to determine the success of VAI scores in predicting PD. AUC values, accuracy, sensitivity, selectivity, positive-negative predictive values, and likelihood ratio (+) values together with the 95% confidence intervals calculated because of the ROC analysis are shown in Table 4. The ROC curve is documented in Figure 3. ROC analysis showed a statistically significant difference between the VAI scores of Groups 1 and 2 [AUC=0.640 (0.559-0.721); p=0.001]. In terms of the AUC value, the discrimination power of VAI was weak. The cut-off point for the VAI score was found to be 5.43. For this cut-off point, classification success was determined as: 55.1% sensitivity and 80.4% selectivity.

Table 4. ROC analysis results and sensitivity, specificity, PPV, NPV, and likelihood ratio (+) values of VAI score in disease prediction

	VAI
AUC (95% CI)	0.640 (0.559-0.721)
P values	0.001
Cut-off	≤1.43
Accuracy	68.6% (131/191)
Sensitivity (95% CI)	55.1% (44.1-65.5) (49/89)
Specificity (95% CI)	80.4% (71.1-87.3) (82/102)
PPV (95% CI)	71% (58.7-81) (49/69)
NPV (95% CI)	67.2% (58-75.3) (82/122)
LR+ (95% CI)	2.81 (1.82-4.34)

ROC: Receiver operating characteristic, PPV: Positive predictive value, NPV: Negative predictive value, AUC: Area under the curve, CI: Confidence interval, VAI: Visceral adiposity index, LR: Likelihood ratio

Discussion

To the best of our knowledge, this study is first ever to define VAI as a new independent risk factor for PD. Each integer increase in the VAI value increases the probability of having Peyronie's disease 1.2 (1.07-1.35) times. Each VAI integer increase decreased 1.25 (CI: 1.03-1.47) points in the IIEF score, an increase of 1 mm (CI: 0.7-1.3) in plaque diameter, and an increase of 1.98 degrees (CI: 1.14-2.82) in curvature.

Table 3. Correlation analysis results between the VAI score and IIEF score, plaque size, and curvature degree in Group 2

		IIEF score	Plaque size (mm)	Curvature degree
VAI	r	-0.610*	0.557*	0.449*
	P values	<0.001	<0.001	<0.001
	N	89	89	89

*Pearson correlation coefficient (statistically significant p<0.001), VAI: Visceral adiposity index, IIEF: Index of Erectile Function

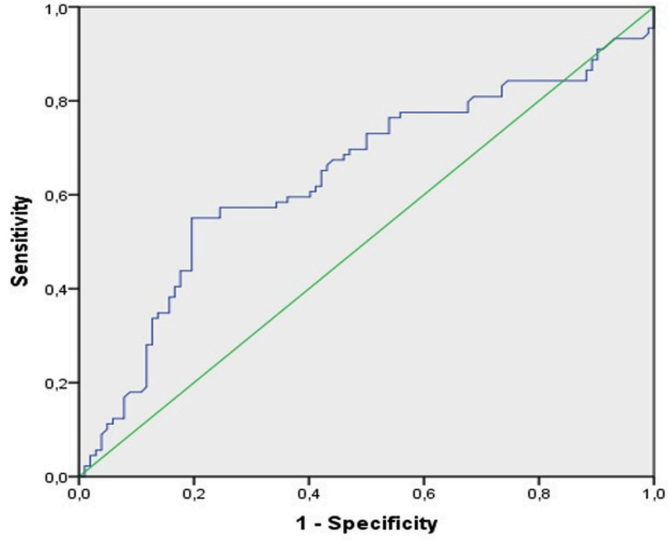

Figure 3. ROC curves for VAI scores in disease prediction

VAI: Visceral adiposity index, ROC: Receiver operating characteristic

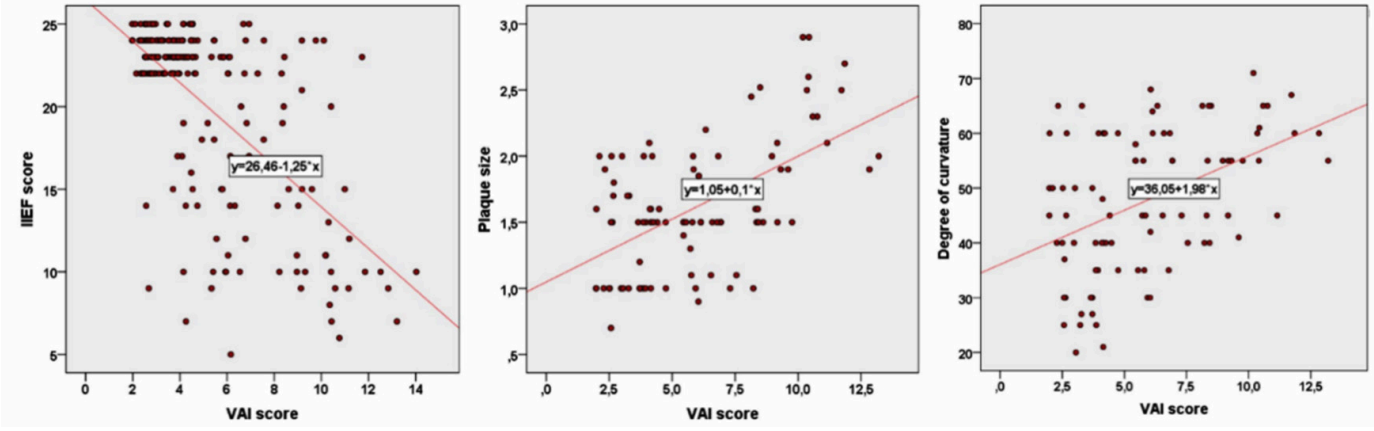

Figure 2. Scatterplots with regression curve for the correlation between VAI score and IIEF score, plaque size, and degree of curvature in the case group

VAI: Visceral adiposity index, IIEF: International Index of Erectile Function

Penile curvature is a common finding of PD. According to the most widely accepted theory, repetitive penile microtraumas stimulate subsequent scar formation in the penile tunica albuginea. Some conditions that accelerate the atherosclerotic process by decreasing tissue oxygenation, such as diabetes mellitus, hyperlipidemia, hypertension, and ischemic heart disease, may play a role in the etiopathogenesis of PD (10,13). One study reported 4.15 times reduced erectile response to combined injection and penile stimulation in patients with PD with type 2 diabetes mellitus (1). Excessive fibrin production and inhibition of fibrinolytic activity at the site of inflammation cause excessive fibrin deposition (14). Neutrophils, macrophages, and mast cells, which have a strong chemotactic effect, increase the production of proinflammatory cytokines such as transforming growth factor beta (TGF-β1) (15,16). The increase in TGF-β1 has a pleiotropic effect on fibroblast functions by increasing the synthesis of tissue collagenase inhibitors, which prevents connective tissue destruction (17). Fibroblasts have the same phenotype as smooth muscle cells and differentiate into myofibroblasts, mesenchymal cells capable of contraction and collagen synthesis (18). Myofibroblasts are the common cell types of all fibrotic diseases (19). Under normal conditions, collagen synthesis increases with the differentiation of fibroblasts to myofibroblasts in wounds, the damage is repaired, and re-epithelialization occurs with the formation of granulation tissue. In the later stages of healing, collagen synthesis is inhibited by apoptosis of myofibroblasts, the fibrinolytic system degrades fibrin, and matrix metalloproteinases remodel collagen fibers. In PD, unlike normal wound healing, myofibroblast production continues, and excess collagen causes tissue contraction, ultimately leading to fibrosis and plaque formation (20). One study reported that 67.5% of patients with PD had at least one risk factor (1). Another study reported that patients with diabetes with PD had much more severe penile deformity (21). Similarly, the rate of diabetes mellitus in this study was two times higher among patients with PD than in the control group.

Some studies have reported that plaque diameter was associated with decreased serum testosterone levels in patients with PD patients, whereas some showed only mild hypoandrogenemia and failed to show a relationship between increased plaque diameter and serum testosterone level (20-25). Based on testosterone levels, our results showed that androgen levels were within normal ranges, but the PD group had a slightly lower testosterone level. Testosterone is an endogenous anabolic hormone and is central to wound healing. Testosterone deficiency results in impaired wound healing and subsequent keloid formation by suppressing the overexpression of TGF-β1 (20,21).

A reason for decreased testosterone levels is the increased BMI (5). Adipose tissue dysfunction reduces adiponectin production decrease and increases proatherogenic, proinflammatory, and prediabetic adipocytokines (26). It is widely accepted that adipose tissue dysfunction is a critical process in the pathophysiology of obesity-related disorders by negatively affecting oxygenation (27). Adipose tissue, also known as fuel storage, supports the internal organs, which play an essential role in maintaining homeostasis via many bioactive mediators such as leptin, estrogen, resistin, and tumor necrosis factor-alpha (26). The distribution of adipose tissue may show individual heterogeneity. The adipose tissue is mainly localized in the superficial subcutaneous region and deep areas surrounding the internal organs. These components have different metabolic properties depending on tissue-specific gene expression, vascularization, and anatomical location. Visceral adiposity content is the most effective component of the pathophysiologic process (28).

Previous studies have showed obesity-associated decreases in testosterone levels secondary to decreased sex hormone-binding globulin, increased insulin resistance, and suppression of the hypothalamic-pituitary-testicular axis (5). Wang et al. (29) reported that obesity is closely related to hypogonadism. That study reported a high VAI level with high FSH and LH levels in response to hypogonadism.

Erectile dysfunction is a prevalent clinical condition in patients with PD. Erectile dysfunction in patients with PD is closely related to penile deformity, vascular dysfunction, or psychological reasons (30). Previous studies have reported the prevalence of erectile dysfunction in patients with PD patients ranging between 20% and 54.4% (31). Increased penile deformity may mechanically challenge the movement of the penis within the vagina, resulting in unsuccessful sexual intercourse. Patients may suffer from impaired body perception, leading to performance anxiety (32). Tunica albuginea is an essential part of penile erection where the veno-occlusive mechanism is provided. Irreversible structural changes within the penile tunica albuginea may potentialize the underlying ED (30,32). Indeed, previous reports showed that 30-86% of patients with PD had veno-occlusive dysfunction, and 44-52% had arterial insufficiency (30). We found that VAI increase was related to erectile dysfunction (1.25 odds ratio, CI: 1.03-1.47). Recent studies have showed similar odds ratios for erectile dysfunction ranging between 1.21 and 3.0 (33,34). The vascular endothelium is a sensitive part of the vascular system which can be negatively affected by inflammatory products including cytokines, adipokines, and fatty acids, in obese and dyslipidemic individuals (23). A subsequent decrease in nitric oxide release resulted in erectile dysfunction.

These factors are the potential contributing risk factors causing hypooxygenation at the level of the penile microenvironment (35). In addition, patients with PD younger than 40 years had a two-fold higher incidence of hypertension and hyperlipidemia

than those in the control group (36). Contrary to these reports, conflicting reports exist that show no relationship between PD and these comorbidities (31,37). Our results also showed no relationship between PD and ischemic heart disease.

In their study evaluating 1,833 cases, 319 of which were patients with PD, Habous et al. (38) found no relationship between PD and metabolic syndrome. They did report, however, that the incidence of PD increased in cases with uncontrolled diabetes (38). We examined the physiopathology of PD from a broad perspective in our study by analyzing VAI, which is closely related to a wide range of pathologies such as ischemic heart disease, hypertension, insulin resistance, pre-diabetes, diabetes mellitus, dyslipidemia, and hormonal disorders.

Study Limitations

The main limitation of our study is that it was conducted retrospectively with a limited number of cases. The lack of a quantitative analysis investigation of the abovementioned cytokines that are involved in the inflammatory process is another limitation.

Conclusion

This study has shown that as a predictor of visceral adipose dysfunction, VAI can be used as a reliable, independent risk factor for plaque size and penile curvature in patients with patients with PD. That being said, further evidence-based, comprehensive studies are needed to support our data.

Ethics

Ethics Committee Approval: This retrospective study involving human participants was in accordance with the ethical standards of the Institutional and National Research Committee; and with 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Gaziosmanpasa University Clinical Studies Ethics Committee approved this study (decision 21-KAEK-132, date: 20.05.2021).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: E.K., M.S.B., M.D., K.S., H.S., Concept: E.K., M.S.B., M.D., K.S., Design: E.K., M.S.B., M.D., Data Collection or Processing: E.K., M.D., K.S., Analysis or Interpretation: E.K., M.D., K.S., Literature Search: E.K., M.S.B., H.S., Writing: E.K., M.S.B., M.D., K.S., H.S.

Conflict of Interest: No conflict of interest was declared by the authors.

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References

1. Kadioglu A, Tefekli A, Erol B, Oktar T, Tunc M, Tellaloglu S. A retrospective review of 307 men with Peyronie's disease. J Urol 2002;168:1075-1079.
2. Culha M, Alici B, Acar O, Mutlu N, Gökalp A. The relationship between diabetes mellitus, impotence and veno-occlusive dysfunction in Peyronie's disease patients. Urol Int 1998;60:101-104.
3. Levine LA, Estrada CR, Storm DW, Matkov TG. Peyronie disease in younger men: characteristics and treatment results. J Androl 2003;24:27-32.
4. Ateş E, Gökçe A. The pathophysiology of peyronie's disease. Androl Bul 2019;21:161-169.
5. Fui MN, Dupuis P, Grossmann M. Lowered testosterone in male obesity: mechanisms, morbidity and management. Asian J Androl 2014;16:223-231.
6. Bolat MS, Kocamanoglu F, Ozbek ML, Buyukalpelli R, Asci R. Can High Visceral Adiposity Index Be a Risk Factor for Sexual Dysfunction in Sexually Active Men? J Sex Med 2020;17:1926-1933.
7. Nusrianto R, Tahapary DL, Soewondo P. Visceral adiposity index as a predictor for type 2 diabetes mellitus in Asian population: A systematic review. Diabetes Metab Syndr 2019;13:1231-1235.
8. Eren H, Horsanlı MO, Dil E, Özbek E. Visceral Adiposity Index and Overactive Bladder in Postmenopausal Woman: A Novel Predictive Risk Factor. Kocaeli Med J 2019;8:84-89.
9. Karabay E, Karsiyakali N, Kayar K, Verim L, Tosun C, Yucebas OE. Evaluation of the relationship between visceral adiposity index and overactive bladder symptoms in females. Endourol Bull 2020;12:150-156.
10. Amato MC, Giordano C, Galia M, Criscimanna A, Vitabile S, Midiri M, Galluzzo A; AlkaMeSy Study Group. Visceral Adiposity Index: a reliable indicator of visceral fat function associated with cardiometabolic risk. Diabetes Care 2010;33:920-922.
11. Li R, Li Q, Cui M, Ying Z, Li L, Zhong T, Huo Y, Xie P. Visceral adiposity index, lipid accumulation product and intracranial atherosclerotic stenosis in middle-aged and elderly Chinese. Sci Rep 2017;7:7951.
12. Bolat MS, Ozbek ML, Şahin B, Yılmaz M, Kocamanoglu F, Buyukalpelli R, Sunter AT, Asci R. Impact of high visceral adiposity index associated with metabolic syndrome on erectile function in sexually active men: Results of a cross-sectional study. Int J Clin Pract 2021;75:e14111.
13. Pryor J, Akkus E, Alter G, Jordan G, Lebret T, Levine L, Mulhall J, Perovic S, Ralph D, Stackl W. Peyronie's disease. J Sex Med 2004;1:110-115.
14. El-Sakka AI, Salabas E, Dinçer M, Kadioglu A. The pathophysiology of Peyronie's disease. Arab J Urol 2013;11:272-277.
15. Garaffa G, Trost LW, Serefoglu EC, Ralph D, Hellstrom WJ. Understanding the course of Peyronie's disease. Int J Clin Pract 2013;67:781-788.
16. Wynn TA, Vannella KM. Macrophages in Tissue Repair, Regeneration, and Fibrosis. Immunity 2016;44:450-462.
17. Diegelmann RF. Cellular and biochemical aspects of normal and abnormal wound healing: an overview. J Urol 1997;157:298-302.
18. Ryu JK, Kim WJ, Choi MJ, Park JM, Song KM, Kwon MH, Das ND, Kwon KD, Batbold D, Yin GN, Suh JK. Inhibition of histone deacetylase 2 mitigates profibrotic TGF-β1 responses in fibroblasts derived from Peyronie's plaque. Asian J Androl 2013;15:640-645.
19. Cannito S, Novo E, Parola M. Therapeutic pro-fibrogenic signaling pathways in fibroblasts. Adv Drug Deliv Rev 2017;121:57-84.
20. Ilg MM, Mateus M, Stebbeds WJ, Milenkovic U, Christopher N, Muneer A, Albersen M, Ralph DJ, Cellek S. Antifibrotic Synergy Between

Phosphodiesterase Type 5 Inhibitors and Selective Oestrogen Receptor Modulators in Peyronie's Disease Models. Eur Urol 2019;75:329-340.

21. Tefekli A, Kandirali E, Erol B, Tunc M, Kadioglu A. Peyronie's disease: a silent consequence of diabetes mellitus. Asian J Androl 2006;8:75-79.
22. Cavallini G, Biagiotti G, Lo Giudice C. Association between Peyronie disease and low serum testosterone levels: detection and therapeutic considerations. J Androl 2012;33:381-388.
23. Nam HJ, Park HJ, Park NC. Does testosterone deficiency exaggerate the clinical symptoms of Peyronie's disease? Int J Urol 2011;18:796-800.
24. Moreno SA, Morgentaler A. Testosterone deficiency and Peyronie's disease: pilot data suggesting a significant relationship. J Sex Med 2009;6:1729-1735.
25. Kirby EW, Verges D, Matthews J, Carson CC, Coward RM. Low testosterone has a similar prevalence among men with sexual dysfunction due to either Peyronie's disease or erectile dysfunction and does not correlate with Peyronie's disease severity. J Sex Med 2015;12:690-696.
26. Hajer GR, van Haeften TW, Visseren FL. Adipose tissue dysfunction in obesity, diabetes, and vascular diseases. Eur Heart J 2008;29:2959-2971.
27. Goossens GH, Blaak EE. Adipose tissue dysfunction and impaired metabolic health in human obesity: a matter of oxygen? Front Endocrinol (Lausanne) 2015;6:55.
28. Mittal B. Subcutaneous adipose tissue & visceral adipose tissue. Indian J Med Res 2019;149:571-573.
29. Wang N, Zhai H, Han B, Li Q, Chen Y, Chen Y, Xia F, Lin D, Lu Y. Visceral fat dysfunction is positively associated with hypogonadism in Chinese men. Sci Rep 2016;6:19844.
30. Carson C. Peyronie's disease: new paradigm for the treatment of a unique cause of erectile dysfunction. Postgrad Med 2020;132(sup4):4-8.
31. Usta MF, Bivalacqua TJ, Jabren GW, Myers L, Sanabria J, Sikka SC, Hellstrom WJ. Relationship between the severity of penile curvature and the presence of comorbidities in men with Peyronie's disease. J Urol 2004;171:775-779.
32. Gholami SS, Gonzalez-Cadavid NF, Lin CS, Rajfer J, Lue TF. Peyronie's disease: a review. J Urol 2003;169:1234-1241.
33. Akdemir AO, Karabakan M, Aktas BK, Bozkurt A, Ozgur EG, Akdogan N, Yarıs M. Visceral adiposity index is useful for evaluating obesity effect on erectile dysfunction. Andrologia 2019;51:e13282.
34. Dursun M, Besiroglu H, Cakir SS, Otunctemur A, Ozbek E. Increased visceral adiposity index associated with sexual dysfunction in men. Aging Male 2018;21:187-192.
35. Kadioglu A, Dincer M, Salabas E, Culha MG, Akdere H, Cilesiz NC. A Population-Based Study of Peyronie's Disease in Turkey: Prevalence and Related Comorbidities. Sex Med 2020;8:679-685.
36. Tefekli A, Kandirali E, Erol H, Alp T, Köksal T, Kadioğlu A. Peyronie's disease in men under age 40: characteristics and outcome. Int J Impot Res 2001;13:18-23.
37. Casabé A, Bechara A, Cheliz G, De Bonis W, Rey H. Risk factors of Peyronie's disease. What does our clinical experience show? J Sex Med 2011;8:518-523.
38. Habous M, Malkawi I, Han E, Farag M, Muir G, Abdelwahab O, Nassar M, Mahmoud S, Santucci R, Binsaleh S. Peyronie's Disease is common in poorly controlled diabetics but is not associated with the Metabolic Syndrome. Urol Ann 2019;11:252-256.