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ORIGINAL PAPER

Metabolic parameters, insulin resistance surrogates, and Peyronie's disease: A cross-sectional analysis of disease presence and curvature severity

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Summary

Methods: *This retrospective, cross-sectional study included 317 adult men, comprising 123 patients diagnosed with PD and 192 control subjects without clinical evidence of PD. Demographic data, body mass index (BMI), comorbidities, and fasting laboratory parameters (glucose, total cholesterol, LDL, HDL, and triglycerides) were collected. TG/HDL ratio and TyG index were calculated using established formulas. Between-group comparisons were performed using Mann-Whitney U and chi-square or Fisher's exact tests, with false discovery rate correction for multiple comparisons. Multivariable binary logistic regression analysis was conducted to identify independent predictors of PD presence. Within the PD cohort, associations between penile curvature degree and metabolic parameters were evaluated using Spearman's correlation analysis.*

Results: *Patients with PD had a significantly lower median BMI compared to controls (25.0 vs. 27.3 kg/m², $p < 0.001$). LDL-cholesterol and total cholesterol levels were lower in the PD group on univariable analysis; however, these differences did not remain significant after correction for multiple testing. No significant differences were observed between groups for fasting glucose, triglycerides, HDL, TG/HDL ratio, or TyG index. In multivariable analysis, BMI emerged as the only independent predictor of PD presence (OR 0.83 per kg/m² increase, 95% CI 0.76-0.90; $p < 0.001$). No metabolic parameter, including insulin resistance surrogates, was independently associated with PD. Among PD patients, penile curvature degree showed no significant correlation with BMI, lipid profile components, TG/HDL ratio, or TyG index.*

Conclusions: *In this cohort, BMI – but not lipid profile components or insulin resistance surrogate markers – was independently associated with the presence of Peyronie's disease, while metabolic factors were not related to curvature severity. These findings suggest that systemic metabolic dysregulation may play a limited role in PD development and phenotypic expression, highlighting the importance of local tissue-specific mechanisms in disease pathogenesis.*

KEY WORDS: *Peyronie's disease; Body mass index; Metabolic parameters; Insulin resistance; Lipid profile.*

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INTRODUCTION

Peyronie's disease (PD) is a localized fibrotic disorder of the tunica albuginea characterized by penile plaque formation, curvature, pain, and varying degrees of sexual dysfunction (1). Although its prevalence is reported to range widely from 0.4% to over 20%, this variability largely reflects differences in study populations and diagnostic approaches (2). Despite being recognized for nearly three centuries, the precise pathophysiology of PD remains incompletely understood (3).

The most widely accepted hypothesis suggests that repetitive microtrauma to the tunica albuginea, occurring in genetically or biologically susceptible individuals, initiates an aberrant wound-healing response (4). This process is characterized by inflammation, oxidative stress, dysregulated cytokine signaling, and excessive collagen deposition, ultimately leading to fibrosis and plaque formation (5). In this context, systemic conditions associated with endothelial dysfunction and impaired tissue repair, such as *diabetes mellitus* (DM), obesity, and dyslipidemia, have been proposed as potential contributors to PD development (4).

Several epidemiological studies have reported associations between PD and metabolic comorbidities, particularly DM and advancing age (6). Poor glycemic control has been linked to increased PD prevalence and more severe deformities, suggesting that chronic hyperglycemia and insulin resistance may exacerbate fibrotic processes (7). However, the role of other metabolic parameters, including lipid profile abnormalities and obesity, remains controversial (8). While some studies have suggested a positive association between dyslipidemia and PD, others have paradoxically reported lower lipid levels among PD patients or failed to demonstrate an independent relationship after multivariable adjustment (9).

More recently, attention has shifted toward surrogate markers of insulin resistance and metabolic dysfunction, such as the *triglyceride-to-high-density lipoprotein cholesterol ratio* (TG/HDL) and the *triglyceride-glucose* (TyG) index (10, 11). These indices have been shown to correlate with endothelial dysfunction, subclinical inflammation, and cardiovascular risk, all of which are biologically plausible mechanisms in PD pathogenesis (12).

Nevertheless, data regarding their association with PD are limited, and available studies are often heterogeneous in design, patient selection, and statistical methodology (4). Beyond disease presence, the potential relationship between metabolic status and disease severity, commonly

expressed as penile curvature degree, remains even less well defined (13). Although severe deformity has been hypothesized to reflect a more pronounced inflammatory or fibrotic milieu, evidence linking curvature severity to metabolic or insulin resistance markers is sparse and inconsistent (9).

Given these uncertainties, the present study aimed to comprehensively evaluate the association between metabolic parameters, lipid profile components, and insulin resistance surrogates with Peyronie's disease in a well-characterized cohort. Additionally, we sought to explore whether these metabolic factors were associated with penile curvature severity among patients with PD. By applying a structured analytical approach incorporating univariable comparisons, multivariable logistic regression, and correlation analyses, this study aims to clarify the extent to which metabolic dysregulation contributes to the presence and phenotypic expression of Peyronie's disease.

This manuscript is written following the STROBE checklist.

Methods

Study design and population

This retrospective, cross-sectional study was conducted to investigate the association between metabolic parameters, insulin resistance surrogates, and PD, as well as the relationship between metabolic status and penile curvature severity among affected patients. Clinical and laboratory data were obtained from patients evaluated at a tertiary referral urology center during routine outpatient assessment.

Patients diagnosed with PD were identified based on established clinical criteria, including the presence of a palpable penile plaque and/or documented penile deformity, confirmed by physical examination by experienced andrologist (HLC).

Penile deviation (curvature) degree was assessed during spontaneous or pharmacologically induced erection using a standardized goniometric method, with the angle measured between the proximal and distal straight segments of the penile shaft at the point of maximal curvature. The control group comprised men without clinical evidence of Peyronie's disease who were evaluated during the same period for non-inflammatory urological conditions, including lower urinary tract symptoms suggestive of benign prostatic hyperplasia, erectile dysfunction without penile deformity, urolithiasis follow-up, and routine urological assessments. Patients with active malignancy, acute inflammatory urological diseases, or systemic inflammatory and autoimmune conditions were excluded to minimize potential confounding effects on metabolic parameters. No formal age-matching or propensity score matching was performed; instead, both the PD and control groups were recruited consecutively from the same outpatient population during the same study period. Accordingly, the similar mean age observed between groups reflects the natural age distribution of men presenting to a tertiary urology clinic rather than deliberate matching. Age was assessed in preliminary analyses but was not included in the final multivariable model to avoid overadjustment and because no clinically meaningful between-group age imbalance was identified.

Data collection and analysis were performed retrospectively using anonymized records, in accordance and approval (KAEK/08.01.2025.12) with institutional and international ethical standards.

Inclusion and exclusion criteria

Adult male patients with available demographic data, anthropometric measurements, and fasting laboratory results were eligible for inclusion. Patients were excluded if they had acute infectious or inflammatory conditions, known chronic inflammatory or autoimmune diseases, active malignancy, or incomplete metabolic data that could bias lipid or glucose measurements, in line with previously published methodologies (8).

Clinical and Laboratory evaluation and Metabolic indices

Age, *body mass index* (BMI), and comorbidities including DM and hypertension were recorded. Venous blood samples were collected after an overnight fast. Laboratory parameters included fasting plasma glucose, total cholesterol, *low-density lipoprotein cholesterol* (LDL), *high-density lipoprotein cholesterol* (HDL), and triglycerides, measured according to standardized in-house laboratory protocols.

To assess insulin resistance and metabolic dysregulation, the following indices were calculated using established formulas:

TG/HDL ratio = triglycerides / HDL (10)

TyG index = ln [triglycerides (mg/dL) × fasting glucose (mg/dL) / 2] (11)

Statistical analysis

All statistical analyses were performed using Statistical Package for Social Sciences (*SPSS, version 21, Chicago, IL, USA*). Continuous variables were assessed for normality using visual inspection and the Shapiro–Wilk test. As most metabolic parameters demonstrated non-normal distributions, data are presented as median and *interquartile range* (IQR), while categorical variables are presented as frequencies and percentages.

Comparisons between PD patients and controls were conducted using the Mann-Whitney U test for continuous variables and the chi-square test or Fisher's exact test for categorical variables, as appropriate. Effect sizes for non-parametric comparisons were estimated using Cliff's delta. To control for multiple comparisons across metabolic parameters, false discovery rate correction according to the Benjamini-Hochberg method was applied.

Binary logistic regression analysis was performed to identify independent predictors of PD presence. PD status was used as the dependent variable. Based on clinical relevance and prior univariable findings, the multivariable model included BMI, DM status, fasting glucose, total cholesterol, LDL, HDL, triglycerides, TG/HDL ratio, and TyG index, while age and hypertension were intentionally excluded from the final model to avoid overadjustment. Results are reported as *odds ratios* (ORs) with 95% *confidence intervals* (CIs).

Within the PD group, associations between penile curvature degree and metabolic parameters (BMI, fasting glucose, lipid profile components, TG/HDL ratio, and TyG

index) were evaluated using Spearman's rank correlation coefficient. Correlation coefficients (ρ), p values are reported.

All statistical tests were two-sided, and a p value < 0.05 was considered statistically significant.

Results

A total of 317 male patients were included in the study, comprising 123 patients with PD and 192 control subjects without evidence of PD. All participants had available demographic, anthropometric, and fasting metabolic laboratory data.

Between-group comparisons revealed a significant difference in BMI between PD patients and controls. Patients with PD had a lower median BMI compared with controls (25.0 [24.0-27.2] vs. 27.3 [24.8-30.1] kg/m²; p < 0.001). Regarding lipid parameters, PD patients demonstrated lower median levels of LDL and total cholesterol compared to controls (LDL: 101.0 [79.5-130.5] *vs.* 114.0 [90.8-136.0] mg/dL, p = 0.012; total cholesterol: 168.4 [149.3-206.1] *vs.* 187.1 [162.0-216.4] mg/dL, p = 0.014). These differences did not remain statistically significant after correction for multiple comparisons. No significant differences were observed between groups for fasting glucose, triglycerides, HDL, TG/HDL ratio, or TyG index (all p > 0.05).

The prevalence of DM did not differ significantly between PD patients and controls. Hypertension showed a trend toward lower prevalence in the PD group; however, this difference did not reach statistical significance (Table 1).

In multivariable logistic regression analysis, BMI emerged as the only independent predictor of Peyronie's disease presence. Each 1 kg/m² increase in BMI was associated with a 17% reduction in the odds of PD (OR 0.83, 95% CI 0.76-0.90, p < 0.001).

Fasting glucose, DM, lipid profile parameters (total cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides), TG/HDL ratio, and TyG index were not independently associated with PD in the adjusted model (Table 2).

Table 2.
Multivariate logistic regression analysis of Peyronie's disease associated factors.

Variable	OR	95% CI	P value
Body Mass Index	0.83	0.76-0.90	< 0.0001
Diabetes Mellitus	1.48	0.82-2.67	0.190
Glucose	1.00	0.99-1.01	0.502
Total cholesterol	0.96	0.75-1.23	0.768
LDL	1.03	0.80-1.32	0.817
HDL	1.05	0.82-1.34	0.719
Triglycerides	1.00	0.95-1.05	0.963
TG/HDL ratio	1.28	0.93-1.76	0.137
TyG index	1.46	0.48-4.43	0.508

-TyG index: Triglyceride-glucose index, TG/HDL ratio: Triglyceride/HDL cholesterol ratio.

Table 3.
Penile curvature degree association with investigated factors.

Variable	Spearman ρ	P value
TyG index	-0.249	0.0593
Triglycerides	-0.213	0.1082
Glucose	-0.181	0.1750
TG/HDL ratio	-0.150	0.2595
Total cholesterol	-0.111	0.4087
LDL	-0.073	0.5880
HDL	-0.028	0.8332
BMI	-0.011	0.9356

-TyG index: Triglyceride-glucose index, TG/HDL ratio: Triglyceride/HDL cholesterol ratio.

Among PD patients the median penile deviation degree was 45° (IQR 35-60°, range 15-90°). Spearman correlation analysis demonstrated no statistically significant associations between penile deviation degree and BMI, fasting glucose, lipid parameters, TG/HDL ratio, or TyG index (all p > 0.05) (Table 3).

Table 1.
General characteristics according to the presence of Peyronie's disease (N or median [25–75%]).

Variable	Peyronie disease median (Q1-Q3)	Control median (Q1-Q3)	P value
Age (1)	54.00 (45.00-60.00)	52.50 (41.00-61.25)	0.8640
Body Mass Index (1)	25.00 (24.00-27.23)	27.26 (24.81-30.09)	< 0.0001
Diabetes Mellitus (2)	Yes/No: 53/70	Yes/No: 76/116	0.5370
Hypertension (2)	Yes/No: 25/98	Yes/No: 57/135	0.0647
Total cholesterol (1)	168.40 (149.30-206.10)	187.10 (161.98-216.35)	0.0142
LDL (1)	101.00 (79.50-130.50)	114.00 (90.75-136.00)	0.0119
Triglycerides (1)	117.00 (83.50-176.50)	125.00 (88.00-177.25)	0.2490
HDL (1)	43.00 (35.50-48.50)	42.00 (36.00-48.00)	0.6894
Glucose (1)	101.00 (92.00-142.00)	99.00 (91.00-131.00)	0.2690
TG/HDL ratio (1)	2.83 (1.85-4.69)	3.05 (2.04-4.71)	0.2854
TyG index (1)	8.84 (8.38-9.31)	8.83 (8.43-9.30)	0.8906

1: Mann-Whitney U test. 2: Chi-square test.

Discussion

In this study, we investigated the relationship between metabolic parameters, lipid profile components, and insulin resistance surrogates with Peyronie's disease, as well as their association with penile curvature severity among affected patients. The main findings were that patients with PD had a significantly lower BMI compared to controls, while other metabolic parameters did not differ significantly after appropriate adjustment. In multivariable analysis, BMI emerged as the only independent predictor of PD presence, and no metabolic parameter was associated with curvature severity.

The association between PD and metabolic comorbidities has been extensively discussed in the literature, particularly in relation to DM and advancing age (13).

Chronic hyperglycemia and insulin resistance have been proposed to exacerbate oxidative stress, endothelial dysfunction, and impaired wound healing, potentially facilitating fibrotic plaque formation (5). However, evidence regarding the role of obesity and dyslipidemia remains inconsistent, with studies reporting positive, negative, or null associations (14). For example, a cross-sectional clinical study reported an inverse association between PD and elevated LDL (and central adiposity by waist circumference), highlighting potential heterogeneity and confounding in metabolic associations (8).Our findings contribute to this debate by suggesting that lipid profile parameters and insulin resistance surrogates are not independently associated with PD when confounding factors are considered.

The most consistent finding of our study was the inverse association between BMI and PD presence. Each unit increase in BMI was associated with a reduced likelihood of PD, independent of other metabolic variables. Although counterintuitive, similar observations have been reported in previous cross-sectional analyses (15). This finding may reflect the limitations of BMI as a marker of metabolic health, as it does not capture body composition, fat distribution, or muscle mass (16). Alternatively, selection bias or behavioral factors influencing healthcare-seeking behavior among leaner individuals cannot be excluded.

Declarations

Ethical approval and consent for participate: *The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.*
The study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments. The study was approved by the institutional ethics committee (KAEK/08.01. 2025.12) and individual consent for this retrospective analysis was waived.

Availability of data and material: *The data used in this study were retrospectively collected from archived medical records of patients who presented to a public (state-run) hospital. Access to and use of these data were conducted in accordance with national regulations governing public healthcare institutions. Data sharing with third parties is subject to governmental approval and is regulated by applicable data protection laws and institutional policies. Accordingly, the dataset is not publicly available but may be accessed upon reasonable request and with appropriate authorization from the relevant authorities.*

Competing interests: *The authors declare that they have no competing interests.*

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Authors' contributions: *(I) Conception and design: AA, EA; (II) Administrative support: AA, HLC ; (III) Provision of study materials or patients: AA, EO, TO, EY, EA, MO; (IV) Collection and assembly of data: AA, EO, TO, EY, EA, MO; (V) Data analysis and interpretation: All authors; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.*

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In univariable analyses, PD patients demonstrated lower LDL-cholesterol and total cholesterol levels compared to controls; however, these differences did not persist after multiple testing correction or multivariable adjustment. This suggests that the observed unadjusted differences may be secondary to confounding factors such as BMI, lifestyle, or pharmacological treatment rather than a direct effect of dyslipidemia on PD development. Furthermore, insulin resistance indices, including the TG/HDL ratio and TyG index, were not independently associated with PD, arguing against a major role for systemic insulin resistance as assessed by these surrogate markers (17).

With regard to disease severity, no significant correlations were observed between penile curvature degree and metabolic parameters, lipid profile components, or insulin resistance indices within the PD cohort. Although a weak inverse association between curvature severity and TyG index was noted, it did not reach statistical significance. These findings suggest that penile curvature severity is likely driven predominantly by local pathological processes, such as plaque composition, inflammatory activity, and biomechanical factors, rather than systemic metabolic status (18).

This study has several limitations, including its retrospective, cross-sectional design, which precludes causal inference, and the lack of detailed data on medication use and body composition. In addition, the outpatient-based selection of the control group may have introduced residual confounding, as some underlying non-inflammatory urological conditions (e.g., benign prostatic hyperplasia or erectile dysfunction) are themselves associated with metabolic dysfunction and cardiometabolic risk (19). Furthermore, waist circumference was not available, precluding calculation of the Visceral Adiposity Index (VAI) (20). Although surrogate metabolic indices such as the TyG index and TG/HDL ratio were used to assess adiposity-glucose-lipid interactions and insulin resistance, these markers do not directly capture central fat distribution; therefore, the role of visceral adiposity in Peyronie's disease may not have been fully characterized. Despite these limitations, the study benefits from a well-characterized cohort and a comprehensive analytical approach.

Conclusions

Our results indicate that BMI, but not lipid profile components or insulin resistance surrogates, is independently associated with the presence of Peyronie's disease, while metabolic factors do not appear to influence penile curvature severity. Future prospective studies incorporating longitudinal metabolic assessment and detailed plaque characterization are warranted to further elucidate the complex pathophysiology of PD.

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