ORIGINAL RESEARCH—PEYRONIE'S DISEASE

A Cross-Sectional Study for the Analysis of Clinical, Sexual and Laboratory Conditions Associated to Peyronie's Disease

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ABSTRACT

Introduction. Although Peyronie's Disease (PD) was first described over 250 years ago, its precise etiology remains obscure.

Aim. Analyze a variety of potential associated factors with PD, including erectile dysfunction.

Materials and Methods. This cross-sectional study included 83 consecutive men with PD and 252 age-matched controls. All men completed the International Index of Erectile Function (IIEF) and were evaluated regarding their clinical and demographic characteristics, comorbidities, and used medications. Anthropometric measures included body mass index and waist circumference (WC). Fasting blood glucose, lipid profile, total testosterone, and dehydroepiandrosterone-sulfate were determined.

Main Outcome Measures. Clinical and laboratory characteristics associated to PD.

Results. The mean age was 59.2 ± 10 years in the cases and 59.7 ± 12 years in the controls. Marital status, current smoking, and excessive consumption of alcoholic beverages were similar between groups ($P > 0.05$). PD was more common among white skin color males ($P = 0.001$). The mean score for each IIEF domain and the androgen levels were similar in the two groups. Thiazides were the only medication associated to PD ($P = 0.03$). Dupuytren's disease was more frequent among individuals with PD ($P = 0.001$). The distribution of all other comorbidities investigated was similar between groups ($P > 0.05$). The characteristics WC > 102 cm and levels of low-density lipoprotein (LDL) > 130 mg/dL were more prevalent in the controls ($P < 0.05$). After multivariate analysis, white skin color (OR: 8.47, 95%CI: 1.98–36.24) and thiazide use (OR: 2.29, 95%CI: 1.07–4.90) were associated to PD, and LDL > 130 mg/dL (OR: 0.55, 95%CI: 0.32–0.92) and WC > 102 cm (OR: 0.53, 95%CI: 0.29–0.96) were inversely associated to PD.

Conclusions. In this study, PD was more common among white skin colored males. An inverse relationship with the presence of elevated serum levels of LDL and WC was observed. We found no association with medications other than thiazides and comorbidities other than Dupuytren's disease. Androgen serum levels and sexual dysfunction had also no association to PD. **Rhoden EL, Riedner CE, Fuchs S, Ribeiro EP, and Halmenschlager G. A cross-sectional study for the analysis of clinical, sexual and laboratory conditions associated to Peyronie's disease. J Sex Med 2010;7:1529–1537.**

Key Words. Peyronie's Disease; Erectile Dysfunction; Comorbidities in Peyronies Disease; Obesity; Dyslipidemia; Associated Factor

Introduction

Peyronie's disease (PD) is an acquired localized connective tissue disorder that affects the tunica albuginea of the penis of individuals aged 40 to 70 years. Normal elastic fibers are replaced by a fibrous scar tissue, which causes a characteristic penile deformity that is most evident during erection (curvature, indentation, hourglass deformity, and/or shortening). Although its prevalence has been previously described, ranging from 0.39% [1] to 3.7% [2], it might reach 6.5% of males aged between 70–79 [3], and 18.5% of men with diabetes mellitus [3]. Besides, there is some concern that the true prevalence of PD has been underestimated [4].

Although the first PD cases were reported in 1743 by Francois Gigot de la Peyronie [5], the etiology of the disease is still not fully understood [6,7]. Repetitive minor trauma to the penile tunica albuginea during sexual intercourse, followed by abnormal wound healing and scar formation, has been implicated as a mechanism of plaque formation [4].

Minor penile traumas are common in men with erectile dysfunction (ED), which in turn makes the penis more susceptible to flex during penetration [8]. ED has been associated to PD in 20% to 54.4% of cases [5,9], being more prevalent among men with other comorbidities [7]. In this scenario, systemic disorders such as diabetes mellitus, hypercholesterolemia, hyperlipidemia, and hypertension may play a role in the pathogenesis of PD [6,7,10]. In addition, a variety of clinical conditions have also been linked to PD etiology, including Dupuytren's contractures, plantar fascial contractures, tympanosclerosis, urethral instrumentation, gout, Paget's disease, and the use of beta-blockers [10].

The aim of the present study was to investigate the association of PD with different clinical and laboratory characteristics, particularly obesity, diabetes mellitus, sexual dysfunction, use of medications, and serum androgen levels.

Material and Methods

The study population was selected among 966 patients consecutively attended by an urologist (ELR) in an outpatient clinic of the health care system, in the city of Porto Alegre, southern Brazil. All patients seeking routine consultation were screened for PD, regardless of the urologic complaint. Eighty-three men with at least one palpable penile plaque at physical examination were diagnosed with PD and enrolled as cases. Among men without PD (N = 883), stratified by age, a random sample of three controls per PD case was selected from each stratum, resulting in 252 patients enrolled as controls. Therefore, the control group consisted of patients who did not reveal evidence of the disease under investigation, but who would be included in the study as cases if they had indeed been diagnosed. The study was approved by the Ethics and Research Committee of our Institution.

Participants were interviewed using a standardized questionnaire regarding demographic and lifestyle characteristics, comorbidities, and current use of medications (Appendix 1). Sexual function was evaluated by the International Index of Erectile Function (IIEF) questionnaire, in order to obtain information on the five sexuality domains: erection (questions 1 to 5 and 15), orgasm (questions 9 and 10), sexual desire (questions 11 and 12), intercourse satisfaction (questions 6 to 8), and overall sexual satisfaction (questions 13 and 14). The IIEF was fulfilled by participants or, if required, by a certified research assistant. Score of 26 points or over in the erection domain, 9 or 10 in the orgasmic, sexual desire and overall satisfaction domains, and 13 or over in the intercourse satisfaction domain were considered normal (no dysfunction). Patients with ED (score < 26 points) were further classified according to the severity into mild (score 17 to 25), moderate (score 11 to 16), or severe (score ≤ 10). Skin color was self-reported (white or non-white). Marital status was reported as married or living with a partner, or not. Diabetes mellitus was defined as the report of a physician's diagnosis of diabetes, use of medication for diabetes or fasting glucose levels >126 mg/dL. Hypertension was detected by the report of a physician's diagnosis or use of anti-hypertensive medication. Diagnosis of rheumatologic diseases—systemic lupus erythematosus, psoriatic arthritis, rheumatoid arthritis, vasculitis, purpura, scleroderma, dermatomyositis, polymyositis, sarcoidosis, gout, ankylosing spondylitis, and Sjögren's syndrome—were investigated by specific questions. Coronary heart disease was identified by a physician diagnosis of myocardial infarction, angina pectoris, coronary artery bypass surgery or angioplasty, categorized as present or absent. Dupuytren's disease was detected at physical examination. Smoking was evaluated by a single question about current smoking habits. Alcoholic beverage consumption was evaluated considering

the type, quantity, and frequency of each beverage consumed over the previous 12 months. Those who consumed ≥350 g/week of ethanol or 3.5 glasses of wine, 2 bottles of beer or 2 doses of spirits daily were classified as alcoholic abusers [11]. Current use of medication such as oral hypoglycemic drugs, insulin, β-blockers, ace inhibitors, diuretics, calcium-channel blockers, antiarrhythmics, acetylsalicylic acid, nitrates, and anti-depressants was assessed. The size of PD plaque was evaluated by a ruler using a standardized method to determine longitudinal and cross-sectional diameters. The size of the greater plaque was adopted when more than one was present.

All participants were submitted to a second anthropometric evaluation, at the same visit, by an independent physician, blinded for the Peyronie's status, according to standardized procedures and in triplicate. Weight (kg) was measured with the participant in light clothing and barefoot, to the nearest 100 g in the scale (Filizola®, São Paulo, Brazil). Height (cm) was approximated to intervals closer to 0.5 cm on a wall mounted stadiometer. Body mass index (BMI; weight [Kg]/height [m]^2) was calculated, and the cutoff values for obesity (≥30 kg/m^2) and overweight (25.0–29.9 kg/m^2) adopted as indexes of general obesity. Visceral obesity was detected by the waist circumference (WC) measurement (cm), obtained using an inelastic tape at the middle point between the iliac crest and the lower costal margin, taken at a perpendicular plane along the body axis. Values greater than 102 cm were considered as central obesity.

Fasted blood samples were obtained for assessing fasting glucose (≥126 mg/dL), total cholesterol (>200 mg/dL) by colorimetric assay, high-density lipoprotein (HDL) (≤35 mg/dL), LDL (>130 mg/dL), LDL-cholesterol (>130 mg/dL), triglycerides (>150 mg/dL), dehydroepiandrosterone sulfate (SDHEA) (chemiluminescence, normal range: 80 to 560 μg/dL, cutoff <80 mg/dL), and total testosterone (radioimmunoassay, normal range: 300–1,000 ng/dL, cutoff <300 ng/dL), all in the same laboratory.

To examine potential characteristics associated with PD, we calculated proportions for categorical variables and means and standard deviation for continuous variables according to PD status. These analyses were conducted using Pearson chi-square test for proportions, Student's *t*-test for normal distribution continuous variables and Mann–Whitney test for asymmetric distribution

continuous variables. $P < 0.05$ was considered statistically significant. All variables associated to PD, identified at univariate analysis ($P < 0.05$), were subsequently included in a multivariate logistic regression model. The score for erectile domain of the IIEF was also included in the modeling as a continuous variable on the basis of the extensively described association between ED and PD. Statistical Package for Social Sciences (SPSS®, *version* 14, Chicago, IL, USA) was used for all the analyses.

Results

Sociodemographic, behavioral, and clinical characteristics of the 335 men evaluated are described in Table 1. Median age was 60 (21 to 90) years old. Most participants were caucasian (87.5%), 91% were married, 20.6% reported current smoking, and 7.8% had abusive consumption of alcoholic beverages. Sexual dysfunction was present in 65.4% to 83.6%, depending on the

Table 1 Sociodemographic, behavioral, and clinical characteristics of the study population (335 men)

	N (%), mean ± SD or median (25–75%)
General data	
Age	59.6 ± 11.3
White skin color	293 (87.5%)
Marital status	305 (91%)
Current smoking	69 (20.6%)
Excessive consumption of alcoholic beverages	26 (7.8%)
Obesity status	
Body mass index	26.2 ± 4.6
Waist circumference	97 ± 11.4
Laboratory characteristics	
Fasting blood glucose (mg/dL)	100 ± 46.4
Total testosterone (ng/dL)	434.2 ± 204.1
SDHEA (μg/dL)*	98 (63–180)
Triglycerides (mg/dL)	119.5 (86.7–166.0)
Total Cholesterol (mg/dL)	202 ± 42.9
HDL-Cholesterol (mg/dL)	42 ± 11.8
LDL-Cholesterol (mg/dL)	131 ± 34.9
Comorbidities	
Diabetes mellitus	60 (17.9%)
Hypertension	92 (27.5%)
Dyslipidemia	247 (73.7%)
Rheumatologic disease	2 (0.6%)
Dupuytren disease	5 (1.5%)
Coronary heart disease	26 (7.8%)
COPD	9 (2.7%)
International Index of Erectile Function	
Erectile dysfunction	248 (74%)
Orgasmic dysfunction	219 (65.4%)
Sexual desire dysfunction	255 (76.1%)
Intercourse satisfaction dysfunction	300 (89.6%)
Overall satisfaction dysfunction	280 (83.6%)

*SDHEA = dehydroepiandrosterone sulphate; COPD = chronic obstructive pulmonary disease.

IIEF domain evaluated. ED, described as an IIEF erectile score < 26, was observed in 74% of the individuals.

Patients with PD had a median of one plaque (ranging from one to four) with median size of 2 cm (0.5 to 6.0 cm) longitudinally by 1 cm (0.4 to 3.0 cm) cross-sectionally. Eighty-six percent were located in the dorsal penile shaft. Patients who previously knew they had a penile plaque presented it for a median of 12 months (varying from 1 to 240 months). Interestingly, only 35 (42.2%) patients with PD were aware of having a penile disease prior to the appointment. The others did not have noticed it, and were informed by the urologist after physical examination. Twelve (14.4%) individuals complained of local pain.

There was no general characteristic associated with PD except for having white skin color ($P = 0.001$), as shown in Table 2.

For the potential factors evaluated (Table 3), central obesity was inversely associated with PD ($P = 0.04$); approximately 37% of controls vs. 24% of cases presented it. Controls were also more likely to present with high LDL-cholesterol serum levels (>130 mg/dL) than cases ($P = 0.01$). There was also

a trend for higher prevalence of dyslipidemia in men with no PD (76.2% vs. 66.3% $P = 0.08$).

No marked differences regarding the presence of comorbidities were found, except for Dupuytren's disease, which was more prevalent among the PD group (five patients vs. none in the control group; $P < 0.001$). There was a trend for higher prevalence of hypertension among cases (35% vs. 25% in the no PD group) ($P = 0.08$). Thiazide diuretics were more often used by men with PD (18% vs. 10% $P = 0.03$). There were no differences between cases and controls related to use of any other medication. The prevalence of sexual dysfunctions was also similar between the groups.

Associated factors to PD identified at univariate analysis were subsequently included in multivariate regression models (Table 4). Dupuytren's disease was not included in this analysis because its prevalence in the population was too low. All four variables included maintained their significance after the multivariate analysis, with the white skin color (OR: 8.47, 95%CI: 1.98–36.24) and thiazide diuretic use (OR: 2.29, 95%CI: 1.07–4.90) associated to PD, and LDL-cholesterol serum level

Table 2 General characteristics according to the presence of Peyronie's Disease (N and %, mean ± standard deviation or median [25–75%])

	Peyronie's disease		
	Present absent (N = 83) (N = 252)		*P* value
Characteristics			
Age (years)	59.2 ± 10.0	59.7 ± 11.7	0.7
White skin color	81 (97.6%)	212 (84.1%)	**0.001**
Marital status	77 (92.8%)	228 (90.5%)	0.7
Current smoking	22 (26.5%)	47 (18.7%)	0.16
Abusive consumption of alcoholic beverages	7 (8.4%)	19 (7.5%)	0.8
Obesity status			
Body mass index (kg/m²)	26.1 ± 3.5	26.4 ± 4.9	0.6
Waist circumference (cm)	95.6 ± 10.7	98.0 ± 11.6	0.10
Laboratory characteristics			
Fasting blood glucose (mg/dL)	112.2 ± 37.7	118.2 ± 48.8	0.08
Total testosterone (ng/dL)	476.9 ± 191.8	446.4 ± 207.8	0.12
SDHEA (µg/dL)*	90.7 (65.5–162.2)	100 (58.7–186.7)	0.3
Triglycerides (mg/dL)	126 (83–159)	119 (88–167)	0.9
Total Cholesterol (mg/dL)	195 (176.5–225.7)	203.5 (178–230)	0.19
HDL-Cholesterol (mg/dL)	44 (37–53)	41 (35–50)	0.11
LDL-Cholesterol (mg/dL)	121.5 (108.7–150)	134 (110–160)	0.06
International Index of Erectile Function (IIEF) (points)			
Erectile domain	19.9 ± 7.9	18.5 ± 7.7	0.13
Orgasmic domain	7.3 ± 2.5	7.3 ± 3.1	0.8
Sexual desire domain	7.1 ± 2.1	7.2 ± 1.9	0.6
Intercourse satisfaction domain	8.6 ± 3.2	8.4 ± 3.3	0.5
Overall satisfaction domain	6.2 ± 2.1	6.4 ± 2.1	0.5
Erectile dysfunction**			
No dysfunction (score 26–30)	25 (30.1%)	62 (24.6%)	0.3***
Mild dysfunction (score 17–25)	31 (37.3%)	90 (35.7%)	0.3***
Moderate dysfunction (score 11–16)	10 (12%)	53 (21%)	0.3***
Severe dysfunction (score ≤ 10)	17 (20.5%)	47 (18.7%)	0.3***

*SDHEA = dehydroepiandrosterone sulphate; **by erectile domain of IIEF; ***degrees of freedom = 3.

Table 3 Potential associated factors to Peyronie's disease (N and % or mean ± standard deviation)

Potential associated factor	Peyronie's disease		P value
	Present (N = 83)	Absent (N = 252)	
Obesity evaluation			
IMC ≥ 25 kg/m²	48 (57.8%)	166 (65.9%)	0.19
IMC 25–30 kg/m²	34 (41%)	114 (45.2%)	0.4*
IMC ≥ 30 kg/m²	14 (16.9%)	52 (20.6%)	0.4*
Waist circumference > 102 cm	20 (24.1%)	92 (36.5%)	**0.04**
Comorbidities			
Diabetes mellitus	13 (15.7%)	47 (18.7%)	0.5
Hypertension	29 (34.9%)	63 (25.0%)	0.08
Dyslipidemia	55 (67.0%)	192 (76.2%)	0.08
Rheumatologic disease	2 (2.4%)	0	0.06
Dupuytren disease	5 (6%)	0	**0.001**
Coronary heart disease	8 (9.6%)	18 (7.1%)	0.5
Chronic obstructive pulmonary disease	3 (3.6%)	6 (2.4%)	0.7
Laboratory characteristics			
Fasting blood glucose > 125 mg/dL	12 (14.5%)	39 (15.5%)	0.8
Fasting blood glucose > 200 mg/dlL	5 (6.0%)	18 (7.1%)	0.7
Total testosterone < 300 ng/dlL	16 (19.3%)	64 (25.4%)	0.3
SDHEA < 80 mg/Dl	33 (39.8%)	89 (35.3%)	0.5
Total Cholesterol > 200 mg/dL	41 (49.4%)	136 (54%)	0.5
LDL-Cholesterol > 130 mg/dL	33 (39.8%)	140 (55.6%)	**0.01**
Triglycerides > 150 mg/dL	28 (33.7%)	81 (32.1%)	0.8
HDL-Cholesterol ≤ 35 mg/dL	15 (18.1%)	64 (25.4%)	0.2
Drug use			
Beta-blockers	10 (12%)	23 (9.1%)	0.4
Angiotensin-converting enzyme inhibitors	12 (14.5%)	21 (8.3%)	0.10
Thiazide diuretics	15 (18.1%)	24 (9.5%)	0.03
Oral hypoglycemic drugs	9 (10.8%)	33 (13.1%)	0.6
Calcium channel blockers	4 (4.8%)	12 (4.8%)	0.9
Salicylic acid	7 (8.4%)	12 (4.8%)	0.2
Antiarrhythmic agents	2 (2.4%)	10 (4.0%)	0.5
Others	5 (6.0%)	17 (6.8%)	0.8
International Index of Erectile Function			
Erectile dysfunction	58 (69.9%)	190 (75.4%)	0.3
Orgasmic dysfunction	56 (67.5%)	163 (64.7%)	0.6
Sexual desire dysfunction	63 (75.9%)	192 (76.2%)	0.9
Intercourse satisfaction dysfunction	73 (88%)	227 (90.1%)	0.6
Overall satisfaction dysfunction	73 (88%)	207 (82.1%)	0.2

*df = 2.

>130 mg/dL (OR: 0.55, 95%CI: 0.32–0.92) and WC > 102 cm (OR: 0.53, 95%CI: 0.29–0.96) inversely associated with the presence of this disease. Finally, a second multivariate analysis including the presence of coronary heart disease has been additionally performed, showing that use of thiazide diuretic was independently associated with PD (OR: 2.22, 95%CI: 1.03–4.76).

Discussion

In this case-control study, we observed the lack of association between PD and comorbidities and use of several medications, including some that have been traditionally inked to PD such as diabetes mellitus, ED, and use of beta-blockers. Nevertheless, we did find an independent association

Table 4 Multivariate logistic regression analysis of Peyronie's disease associated factors

Associated factors	P value	OR (95% CI)†	Adjusted OR (95%CI)*
White skin color	0.006	7.64 (1.80–32.35)	8.47 (1.98–36.24)
LDL-cholesterol > 130 md/dL	0.013	0.53 (0.32–0.87)	0.55 (0.32–0.92)
Waist circumference > 102 cm	0.039	0.55 (0.31–0.97)	0.53 (0.29–0.96)
Thiazide diuretics use	0.038	2.09 (1.04–4.22)	2.29 (1.07–4.90)

*OR was adjusted for the continuous variable erectile function International Index of Erectile Function domain score and for all other variables of the table.
†Reference categories are: non-white skin color, LDL-cholesterol ≤ 130 mg/dL, waist circumference ≤ 102 cm and no use of thiazide diuretics.

between use of thiazide diuretics and PD. In addition, PD prevalence was greater among patients with white skin color, and the few cases of Dupuytren's disease were all presented by patients with PD. Interestingly, independent and inverse associations of PD with abnormal WC (>102 cm) and high LDL-cholesterol (>130 mg/dL) were observed in multivariate model that was also adjusted for skin color, thiazide diuretics use, and erectile function.

Mulhall [12] has proposed a unique theory to explain the pathogenesis process for the development of plaque in PD. Penile trauma in genetically susceptible males causes a biological transformation of the cells within the tunica albuginea with cytokine over expression. The resulting free radicals overproduction and cytogenetic changes leads to unregulated extracellular matrix deposition (fibrin and collagen). Transforming growth factor beta 1 (TGF-β1), which is over-expressed in PD [13], has been described as having a central role in the disease process, producing histological alterations such as chronic cellular infiltration, focal and diffuse elastosis and collagen bundles thickening, disorganization, and clumping [12].

Microvascular injury, subsequent to trauma, may be the triggering event to the Peyronie's plaque formation [14]. By this concept, premature atherosclerosis may promote the vasculitis that occurs in the initial stages of the disease [15]. Moreover, it may be possible that vascular insufficiency due to the presence of vascular risk factors results in a hypoxic microenvironment in the erectile tissue, leading to exaggerated activation of TGF-β and aggravation of the fibrotic cascade [7,16].

The potential involvement of vascular dysfunction in the origin of PD was also suggested by Agrawal et al. [6], who demonstrated that the association between PD and endothelial dysfunction persisted even after adjusting for the presence of various vascular disease risk factors; that this association could potentially link the PD origin to other endothelial diseases including ED is a reasonable hypothesis. In this scenario, El-Sakka & Tayeb [17] verified that diabetic men with PD have significant lower Doppler parameters in penile vasculature during erection when compared with diabetic men without PD, that are parallel to the showed lower IIEF-scores. Based in these concepts, studies designed to search for potential factors associated to PD should always evaluate the erectile function status. After all, less rigid erections during sexual intercourse might be responsible for the trauma initiating the PD scar process. This trauma associated to less rigid erections are typically minor, and the history of a significant trauma is reported to be more common in young (18%) than older men (5%) [18].

ED has been described to be present in a high percentage of men with PD, rates from literature varying from 20% to 54% [5,9]. Notwithstanding, in the current study, using the IIEF questionnaire, we were not able to find an association between ED and PD. It could be argued that our population included men who attended in a urologic clinic and are not representative of men from the general population. This might be a reasonable explanation for the high rate of ED, almost 70% among the PD group. Nevertheless, controls were selected from the same population where the cases were originated, and should they have PD they could be enrolled in the study as cases. It assures the lacking of selection bias, a major concern in the case-control study.

As the absence of significant influence of PD in ED, we also did not observe different levels of androgens among cases and controls. The last observation is contrary to the one suggested by a recent pilot study [19], and endorse the necessity of other studies to confirm or refute this evidence.

Kadioglu et al. [16] has identified at least one major known vascular disease risk factor in 67.5% of patients with PD. In their series, hypercholesterolemia (43%) and diabetes mellitus were the most prevalent conditions observed in men with PD. In the same way, a multicenter study from Italy described an odds ratio of 4.6 for tobacco smoking [20].

Although particularly appealing, the theory linking endothelial dysfunction to PD has not been universally corroborated. Usta et al. [7] described lower rates of vascular disease risk factors in PD patients. In their study, hypertension, which was the most prevalent clinical condition associated to PD, was present in 27% of the cases, followed by smoking in 26%, hypercholesterolemia in 18%, and diabetes mellitus in 17%. These rates were quite similar to those observed in our study, except for hypercholesterolemia, which were higher and similar to those found by Kadioglu et al. [16]. The inverse relationship observed in our study between central obesity or high LDL cholesterol and PD were unique findings when compared with previous reports. These were unexpected findings that need to be confirmed by further studies. Except for these two associations, our results regarding the relationship of vascular

risk factors and PD are similar to those found by Usta et al. [7]. Also, both PD and ED prevalence increases with aging, as do most vascular disease risk factors, a fact that should produce misleading conclusions if not carefully observed. To limit this potential bias, we have stratified the control group by age.

Different medications have been suggested as having a role in the etiology and pathophysiology of PD. Beta-blockers, particularly propranolol, have been reported as an independent risk factor for PD [10]. Nevertheless, the evidence supporting these findings is rather weak, based on case reports and one case-control study. Recently, a causal association between PD and carvedilol has been suggested, based in a description of a case report [21]. Bjekic et al. [10] evoked the possibility that beta-blockers are associated to PD by an indirect pathway, emphasizing again the role of cardiovascular diseases in this association, conditions in which these drugs are frequently employed. This theory cannot be corroborated by the present evaluation, since the rates of cardiovascular diseases were not greater among men with PD. Nevertheless, it is interesting to observe that in the present study, even after the control for coronary heart diseases, thiazide diuretics remained associated with PD.

It is widely accepted that systemic diseases such as diabetes mellitus, dyslipidemia, chronic renal failure and hypertension have negative impact on erectile function [22]. In fact, as these risk factors have been more related to ED than PD [7], they might be a source for potential bias when evaluating the association of different clinical conditions and PD [23,24]. In the present study, this consideration is particularly important since there was high prevalence of ED among cases. For this reason, we decided to include the erectile function IIEF domain score in the final logistic regression model altogether with other factors associated with PD. This evaluation confirmed that white skin color was an independent associated factor for PD, which endorses our previous report that the majority of PD cases occurred among Caucasians individuals [2]. All other factors found to be related to PD in the isolated evaluation confirmed to be independent associated by the multivariate analysis. Finally, Dupuytren's disease was a significantly associated to PD, which endorses the large evidence in the literature [25].

One limitation of this study that should be addressed is that tobacco consumption has not been fully examined since only the current smoking status has been investigated. This might explain why we were not able to confirm the findings of a positive association between tobacco use and PD which have been previously described [20]. Hypertension was measured with similar accuracy (self-reported) for cases and controls and its association with PD reached only a borderline significance, which might have minimized the potential role of vascular factors in the genesis of ED and PD. The self-reported hypertension led to an underestimate of the true rate of patients with this important risk factor, resulting in a potential bias, but a conservative one. Since the cases and controls were selected from the same population and all patients were seeking a consultation, we believe that they had similar stimulus to recall a previous diagnosis of hypertension. Finally, a potential major limitation are eventual differences in urologic complaints in cases and controls, with possible influences in the observations of the study. This is minimized by the random selection of controls from the same population of cases, stratified by age decade. Certainly, future studies need to be designed to considerer these complaints and to endorse the evidences observed in the current evaluation.

In conclusion, the present study showed that, in the studied population, PD was more frequently detected among white skin color males and it had an inverse association with LDL and WC. We found no association with medications other than thiazide diuretics, and comorbidities other than Dupuytren's disease. The different IIEF domain scores were all similar among individuals with and without PD.

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Appendix 1

Peyronie's Disease Questionnaire

1. Name: _____ 2. Number: _____
3. Age: ___years   4. Skin color: (   ) white   (   ) non-white
5. Marital Status: (   ) Married   (   ) Not married
6. Alcoholic intake: (   ) daily   (   ) 3 times a week   (   ) on weekends
                (   ) ≤2 bottles of beer, 3.5 glasses of wine or 2 doses of spirits
                (   ) > 2 bottles of beer, 3.5 glasses of wine or 2 doses of spirits
7. Tobacco consumption: (   ) current smoker   (   ) current non-smoker
8. Diabetes mellitus: (   )   9. Hypertension: (   )
10. Dyslipidemia: (   )   11. Rheumatoid Arthritis: (   )
12. Systemic Lupus Erythematosus: (   )   13. Psoriatic arthritis: (   )
14. Purpura: (   )   15. Vasculitis: (   )
16. Dermatomyositis: (   )   17. Scleroderma: (   )
18. Sarcoidosis: (   )   19. Polymyositis: (   )
20. Ankylosing spondylitis: (   )   21. Gout: (   )
22. COPD: (   )   23. Sjogren's Syndrome: (   )
24. Dupuytren's disease: (   )   25. Ischemic heart disease: (   )
26. Current Medications: _____
      _____
27. Weight: ____ Kg   28. Heigh: ____ cm   29. Waist: ____ cm   30. Hip: ____ cm
31. Arterial pressure: ____×____ mm Hg
32. Total Testosterone: _____   33. SDHEA: _____
34. Total cholesterol: _____   35. Triglycerides: _____
36. HDL: _____   37. Calculated LDL: _____

38. Fasting glucose: _____
39. Peyronie (Yes)   (No)
40. Plaque location: 40.1 Dorsal (   )   40.2 Ventral (   )   40.3 Lateral (left) (right)
41. Number of plaques: (   )
42. Biggest plaque size: (   ) cm × (   ) cm
43. Pain: (Yes)   (No)
44. Angle: (   ) degrees
45. Curvature: (left)   (right)   (upward)   (downward)
46. Painfull/bothersome to the partner: (Yes)   (No)

DATE: _____