ORIGINAL RESEARCH—PEYRONIE'S DISEASE

Peyronie's Disease Plaque Calcification—Prevalence, Time to Identification, and Development of a New Grading Classification

Laurence Levine, MD,* James Rybak, MD,* Christopher Corder, MD,† and Michael Ryan Farrel, MS, MPH†

*Department of Urology, Rush University Medical Center, Chicago, IL, USA; †Rush University School of Medicine, Rush University Medical Center, IL, USA

DOI: 10.1111/jsm.12334

ABSTRACT

Introduction. Peyronie's disease (PD) is a connective tissue disorder of the penis in which a fibrous scar in the tunica albuginea can result in multiple penile deformities.

Aim. The study aims to investigate the prevalence and time to identification of plaque calcification (PC) in our PD patient population and whether stratification of calcification based on severity seen on ultrasound would serve as a predictor of treatment progression to surgery.

Methods. A retrospective review of 1,041 men presenting with PD from 1993 to 2009 was performed. Eight hundred thirty-four underwent penile duplex ultrasound.

Main Outcome Measures. PC was graded as: grade 1 (<0.3 cm), grade 2 (>0.3 cm, <1.5 cm), grade 3 (>1.5 cm; or ≥2 plaques >1.0 cm). A matched control group with noncalcified plaques (n = 236) was selected for comparison.

Results. Two hundred eighty-four men (34%) were found to have PC noted on ultrasound, and 98 had fully documented dimensions of the PC. Forty-one percent were found to have grade 1, 28% grade 2, and 32% grade 3. When analyzed by grade and progression to surgery, 23% of grade 1, 32% of grade 2, and 55% of grade 3 patients had surgery. Those with grade 3 PC were more likely to undergo surgical intervention for PD (OR 2.28 95% CI 1.07–4.86) and more likely to undergo a grafting procedure than control patients ($P < 0.0001$).

Conclusions. Men with PC are not more likely to undergo surgery than those without PC (OR 0.95, 95% CI 0.58–1.57). PC is not uncommon, as it was found in 34% of our cohort. PC does not appear to be an indication of mature or stable disease, as it was identified by ultrasound in 37% of patients less than 12 months after onset of symptoms. Men with grade 3 PC have an increased likelihood of progression to surgical intervention and a higher likelihood of undergoing a grafting procedure. **Levine L, Rybak J, Corder C, and Farrel MR. Peyronie's disease plaque calcification—prevalence, time to identification, and development of a new grading classification. J Sex Med 2013;10:3121–3128.**

Key Words. Calcification; Prevalence; Incidence; Severity; Mature Disease; Tunica Albuginea Deformity

Introduction

Peyronie's disease (PD) is an acquired connective tissue disorder affecting the tunica albuginea of the corpus cavernosum. PD is a member of the class of diseases termed fibrotic disorders [1].The prevalence of PD has been reported to be up to 8.9% in recent demographic surveys [2]. It typically affects males between the ages of 45 and 60 years; however, men as young as 15 years have been reported [3]. The pathophysiology of PD remains unclear, although multiple pathways may be responsible for the fibrotic changes. Studies have demonstrated that an overabundance of myofibroblasts in the damaged tunica may lead to plaque formation, and that progression of these plaques may lead to calcification or ossification [4]. The exact mechanism by which tissue mineralization occurs remains largely unknown. Development of a fibrous scar in the tunica albuginea can result in multiple deformities of the penis including curvature, narrowing, indentation, hinging,

and loss of penile length [5]. In addition to the morphological changes, PD plaques can also cause significant pain, psychological distress, and often results in sexual dysfunction [6,7].

While history and physical exam are generally sufficient to provide a diagnosis, multiple imaging modalities have been described in the literature. Visualization of the tissues has been performed using plain film radiography (X-ray), computerized tomography, magnetic resonance imaging, and ultrasonography. More recently, penile duplex ultrasonography (PDU) has emerged as the preferred method of examination [8–12]. This modality provides an image of the penile tissues along with the ability to detect areas of calcification, as well as evaluate hemodynamic parameters [11].

To date, several studies have aimed to describe the Peyronie's patient with plaque calcification [8–10,13,14] The incidence of calcification is currently estimated at 20% to 25%, although it has been reported as high as 88% in one series [8,11] Most of these articles assert that plaque calcification is indicative of "mature," "advanced," "severe," or "chronic" disease [9,10,15] Current clinical opinion holds that patients with calcified Peyronie's plaques are less responsive to nonsurgical therapies [5,8,10,16,17]. Most of the published literature focusing on ultrasound evidence of plaque calcification is observational. We endeavored to compare the patients with calcification vs. those without calcification. This study analyzes a large cohort of patients with evidence of plaque calcification, from a single center specializing in PD. We investigated the prevalence, detection time of calcification by PDU from onset of symptoms, and whether stratification of calcification based on mineral burden, rather than presence or absence of calcification alone, would serve as a predictor of progression to surgery. Our overall aim is to offer a better understanding of the significance of plaque calcification in the hopes of providing prognostic information to PD patients with plaque mineralization.

Materials and Methods

We conducted a retrospective study of our PD database comprised of 1,041 patients presenting to a single clinical practice between July 1993 to July 2009. A cohort of these men (N = 834) underwent PDU conducted by a single urologist documenting the presence or absence of calcification in the Peyronie's lesion (Figure 1). Areas of calcification were defined as hyperechoic regions with the presence of acoustic shadowing [14]. Each patient underwent physical examination and completed a nonvalidated, but published, PD specific questionnaire detailing medical, social and sexual history, family history of any fibrotic disease, treatment history for PD, and subjective analysis of erectile function, disease progression, and psychological status [12].

Duplex ultrasonography was conducted with the patient in the supine position in both transverse and longitudinal orientations. Injections with papaverine, alprostadil, or Tri-Mix were used to achieve a full erection equal to or better than their sexually induced erection. Additional dosing as well as manual stimulation was used as needed to accomplish this goal. Examinations were performed in both the flaccid and erect states. Doppler studies were used to evaluate vascular parameters including peak systolic velocity, end-diastolic velocity, and calculated resistive index. Plaque size, location, echogenicity, and presence

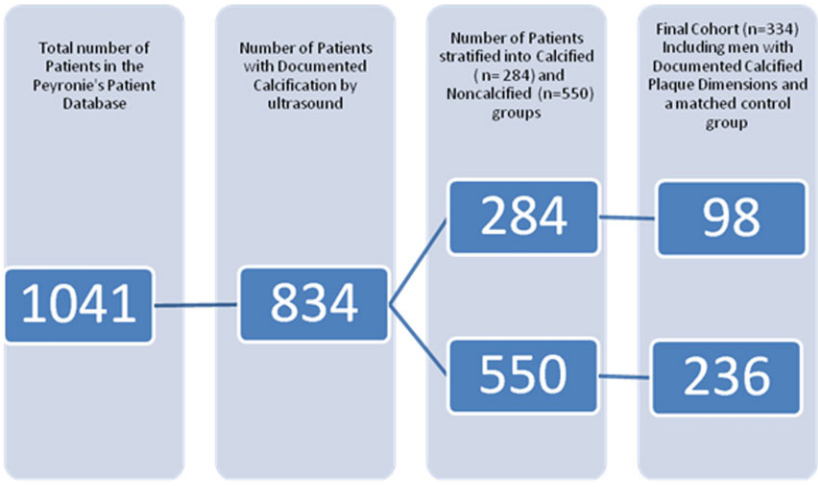

Figure 1 Patient demographics.

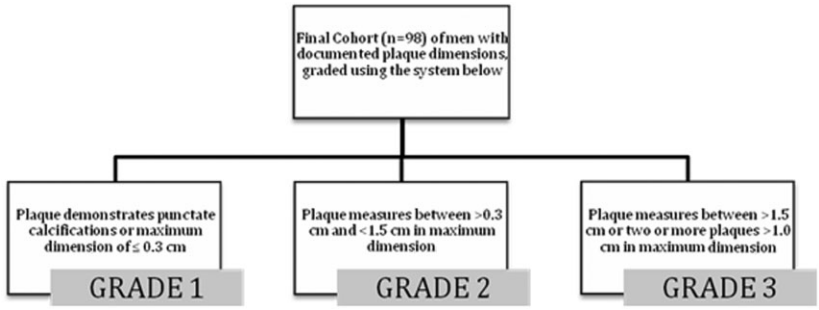

Figure 2 Grading classification.

of acoustic shadowing were recorded. In a smaller population (N = 98), the maximum dimensions of the calcified plaque were recorded in the transverse and longitudinal axis.

Patients with measured calcification dimensions were stratified into three groups based on maximum dimension of the hyperechoic area: grade 1 (punctate or ≤0.3 cm), grade 2 (>0.3 cm and <1.5 cm), grade 3 (≥1.5 cm or ≥2 plaques >1.0 cm) (Figure 2). Progression through treatment from noninvasive to surgical was also reviewed (oral medication, traction, and injection therapy vs. surgery). We elected to compare the measured calcified plaque cohort to two noncalcified PD populations (Table 1), including the overall noncalcified cohort (Table 1), as well as a separate group of men with PD who had noncalcified plaques (n = 236) matched for age, disease duration, date of presentation, and mean curvature (Table 2).

Data analysis was conducted using PASW Statistics 18 software (SPSS Inc., Chicago, IL, USA). Continuous independent variables were analyzed using a two-sample *t*-test. One-way ANOVA was used to make comparisons between groups defined by grade of calcification. Associations across categorical independent variables were evaluated using Pearson's chi-squared univariate analysis. For all analyses, variables are considered significant predictors if the *P* value associated with the appropriate test statistic is <0.05.

Results

A total of 1,041 patients with PD were analyzed in this study (mean age 49.9 years ± 11.3 years; range 17–74). Eight hundred thiry-four men who underwent duplex ultrasound were stratified into one of two groups, either calcified (n = 284; mean age 52.1 years; range 20–69) or noncalcified (n = 550; mean age 48.9 years; range 17–74). Subsequent evaluation of the calcified group identified 98 men with fully documented dimensions of the calcified portion of the Peyronie's plaque within the ultrasound report.

In the 834 who underwent PDU (Table 1), mean subjective erect curvature (patient

Table 1 Demographics and patient characteristics of overall cohort undergoing PDU

		Overall (n = 834)	Calcified (n = 284)	Noncalcified (n = 550)	*P* value
Age, mean (SD)			52.20 (8.18)	48.97 (12.41)	0.003
Duration of disease (months), mean (SD)			17.70 (22.27)	33.20 (77.54)	0.011
Subjective Curvature, # (%)	<60°		163 (57.4)	367 (66.7)	0.002
	≥60°		121 (42.6)	183 (33.3)	
Objective Curvature, # (%)	<60°		175 (61.5)	346 (62.9)	0.706
	≥60°		109 (38.5)	204 (37.1)	
Subjective curvature, mean (SD)		48.7 (24.4)	53.0 (25.6)	46.9 (23.6)	0.006
Loss of penile length, mean (SD)		3.7 (2.2)	3.9 (2.0)	3.5 (2.2)	0.125
Penile pain, # (%)	Any pain since onset	366 (43.9)	143 (50.3)	223 (40.5)	0.008
	Pain at inciting event	66 (7.9)	38 (13.4)	28 (5.1)	<0.001
	Pain with erection	165 (19.8)	59 (20.8)	106 (19.3)	0.647
	Pain with intercourse	207 (24.8)	71 (25.0)	136 (24.7)	0.933
	Partner experienced pain	41 (4.9)	12 (4.2)	29 (5.3)	0.613
Lesion Location, # (%)	Dorsal	262 (64.5)	99 (64.7)	163 (64.4)	1.000
	Ventral	24 (5.9)	8 (5.2)	16 (6.3)	0.829
	Lateral	30 (7.4)	6 (3.9)	24 (9.5)	0.049
	Multiple aspects	90 (22.2)	40 (26.1)	50 (19.8)	0.141

PDU = penile duplex ultrasonography

Table 2 Demographics and patient characteristics by grade of calcification compared with control group

		All grades (n = 98)	Control (n = 236)	Grade 1 (n = 40)	Grade 2 (n = 27)	Grade 3 (n = 31)	*P* value
Age	Mean (SD)	57 (8.23)	56 (13.07)	55 (10.82)	59 (5.46)	58 (6.23)	0.119[b] 0.449[c]
	Range	25–74	22–83	25–72	51–74	46–68	
Duration of disease (months), mean (SD)		17 (14.88)	26 (69.71)	16 (12.69)	16 (13.73)	22 (18.02)	0.182[b] 0.681[c]
Objective curvature	Mean (SD)	55 (31.7)	50 (27.02)	52 (33.63)	48 (25.32)	63 (34.11)	0.171[b] 0.108[c]
	Range	10–180	15–165	10–150	10–100	15–135	
Subjective curvature	Mean (SD)	53 (26.81)	42 (24.95)	52 (22.57)	50 (21.52)	56 (35.97)	0.690[b] 0.005[c]
	Range	10–150	5–100	5–90	5–90	10–165	
Penile length	SPL (cm), mean (SD)	10.0 (1.5)	11.3 (1.8)	9.9 (1.6)	10.0 (1.6)	10.0 (1.6)	0.955[b] <0.001[c]
	Loss reported, # (%)	85 (86.7)	148 (62.7)	38 (95.0)	23 (85.2)	24 (77.4)	0.092[a]
	Subjective loss (cm), mean (SD)	4.0 (1.5)	3.6 (2.4)	3.4 (1.6)	4.4 (3.0)	4.2 (1.8)	0.123[b] 0.175[c]
Penile pain, # (%)	Any pain since onset	65 (66.3)	148 (62.7)	28 (70.0)	20 (74.1)	17 (54.8)	0.247[a]
	Pain initially	27 (27.6)	28 (11.9)	13 (32.5)	6 (22.2)	8 (25.8)	0.631[a]
	Pain with erection	30 (30.6)	75 (31.8)	12 (30.0)	7 (26.0)	11 (35.5)	0.729[a]
	Pain with intercourse	37 (37.8)	88 (37.3)	16 (40.0)	11 (41.0)	10 (32.3)	0.746[a]
	Partner experienced pain	9 (9.2)	27 (11.4)	4 (10.0)	1 (3.7)	4 (12.9)	0.468[a]
Lesion Location, # (%)	Dorsal	61 (62.2)	122 (51.7)	26 (65.0)	17 (63.0)	18 (58.1)	0.833[a]
	Ventral	5 (5.1)	15 (6.4)	2 (5.0)	2 (7.4)	1 (3.2)	0.770[a]
	Lateral	5 (5.1)	21 (8.9)	3 (7.5)	1 (3.6)	1 (3.2)	0.667[a]
	Multiple aspects	27 (27.6)	78 (33.1)	9 (22.5)	7 (26.0)	11 (35.5)	0.467[a]
Emotional distress, # (%)		79 (80.1)	195 (82.6)	195 (82.6)	22 (81.5)	23 (74.2)	0.516[a]
Reported penile injury, # (%)		34 (34.7)	109 (46.2)	109 (46.2)	8 (29.6)	13 (42.0)	0.575[a]

[a] *P* value compares proportions among grade 1, grade 2, and grade 3
[b] *P* value compares mean value among grade 1, grade 2, and grade 3
[c] *P* value compares mean value among control, grade 1, grade 2, and grade 3
SPL = stretched penile length

estimated) was 48.7 ± 24.4 degrees (range 5–135; CI 47.0–50.4). Mean objective erect curvature measured by goniometry during duplex ultrasound was 50.2 ± 28.5 degrees (range 5–150; CI 48.2–52.0). Loss of penile length was reported by 427 (51.2%) patients. Mean self-reported estimated length loss in the entire cohort was 3.7 cm ± 2.2 cm (range 0.6–9.5 cm). Pain since disease onset was reported by 366 of 834 men (43.9%). Of those reporting penile pain, the distribution of pain was reported as follows: pain at inciting event in 66 men (18.0%); with erection in 165 men (45.1%); with intercourse in 207 men (56.6%); and complaint of pain during coitus by the sexual partner in 41 (11.2%).

Erect deformity was located in the dorsal, ventral, and lateral direction in 262 (31.4%), 24 (2.9%), and 30 (3.6%) patients, respectively. The remainder of the population (n = 518, 62.1%) had curvature affecting more than one aspect of the penis (dorsolateral or ventrolateral). Emotional distress was noted from the patient questionnaire in 416 (49.9%) [18]. These patient-specific characteristics are summarized in Table 3. Medical history revealed risk factors for cardiovascular disease (diabetes mellitus, hyperlipidemia, hypertension, or smoking) in 693 (83.1%) men (Table 3). Penile trauma within 2 months of onset of PD was noted by 288 men (36.3%), including specifically trauma with intercourse in 114 (13.7%) men. Time between disease onset and presentation to clinic with duplex ultrasonography was ≤6 months in 149 men (17.9%), >6 months and ≤12 months in 166 men (19.9%), and >12 months in 519 (62.2%) men (Table 4). Mean duration to presentation was 28 months (range 1.5 to 68). In this series, patients presented as early as 6 weeks from first recognizing the cardinal symptoms of pain, palpable lump, and/or penile deformity. Furthermore, 17.2% of men with a calcified plaque presented to our center within 6 months of first noting the symptoms of PD.

Table 3 Cardiovascular risk factors in overall cohort

Risk factor, # (%)	Overall (n = 834)	Calcified (n = 284)	Noncalcified (n = 550)	*P* value
Diabetes	86 (10.3)	40 (14.1)	46 (8.3)	0.012
Hypertension	205 (24.6)	71 (25.0)	134 (24.4)	0.865
Dyslipidemia	178 (21.3)	69 (24.3)	109 (19.8)	0.154
Smoking history	329 (39.4)	114 (40.1)	215 (39.1)	0.8226

Table 4 Duration of PD symptoms prior to presentation in overall cohort

Duration, # (%)	Overall (n = 834)	Calcified (n = 284)	Noncalcified (n = 550)	*P* value
Presented ≤6 months from onset	149 (17.9)	49 (17.2)	100 (18.2)	0.775
Presented ≤12 months from onset	315 (37.8)	105 (37.0)	210 (38.2)	0.763
Presented >12 months from onset	519 (62.2)	179 (63.0)	340 (61.8)	0.763

PD = Peyronie's disease

Our overall group of 834 men who underwent PDU was further divided based on presence or absence of calcification; 284 (34.1%) demonstrated calcification in the Peyronie's plaque. In this population, men with calcification were older than men without calcified plaques (mean age 52.2 vs. 49.0 years, $P = 0.001$). Subjective reports of estimated curvature (mean 53.0° vs. 46.9°, $P = 0.006$), mean duration of disease (17.7 vs. 33.3 months, $P = 0.011$), and any reported pain (50.3% vs. 40.5%, $P = 0.008$) were found to be significantly different between the calcified and noncalcified groups (Table 1). The presence of diabetes (14.1% vs. 8.3%, $P = 0.012$) was found to be significantly different between the calcified and noncalcified groups. Objective measurements, including curvature (mean curvature 53.3 vs. 50.0, $P = 0.88$) and plaque location, were similar between the calcified and noncalcified groups. Reported emotional distress and recollection of a traumatic inciting event were not found to be statistically different between the two groups.

The course of treatment for each patient was analyzed. Progression to surgery occurred in 265 of 834 patients (31.8%). The percentage of men who ultimately progressed to surgery did not differ between the calcified and noncalcified populations (28.9% vs. 33.3%, $P = 0.21$). In our subpopulation of men with measured acoustic shadowing (n = 98), 40 (40.8%) had grade 1 calcification, 27 (27.6%) had grade 2 calcification, and 31 (31.6%) had grade 3 calcification. Characteristics of these patient groups are illustrated in Table 2. When analyzed by grade and subsequent progression to surgery, 23% of grade 1, 32% of grade 2, and 55% of grade 3 patients ultimately had surgery. In the matched control group without calcification (n = 236), 82 men (34.7%) progressed to surgery which was not statistically different from the entire cohort with calcified plaques (OR 0.95 CI 0.58–1.57) (Table 2). In this subpopulation analysis, we once again found that the presence of calcification alone was not a predictor for progression to surgery (OR 0.95, 95% CI 0.58–1.57), but patients with grade 3 calcification were more likely to undergo surgical intervention for PD than their noncalcified counterparts (OR 2.28, 95% CI 1.07–4.86). Furthermore, those who underwent surgery were stratified by grade of calcification and type of surgical intervention. Overall presence of calcification did not predict progression to tunica albuginea plication or partial plaque excision and grafting (PEG) $P = 0.19$. However, 7/11 of those who underwent PEG had a hinge-effect causing buckling of the shaft with application of axial force and the mean curvature was severe at 78 degrees (Table 5). These criteria meet our indications for PEG as long as the patient was capable of a strong preoperative erection and demonstrated a full erection during PDU [1,19,20]. Those with grade 3 calcification were more likely to undergo a PEG compared with the overall noncalcified cohort who underwent PEG ($P < 0.0001$) (Table 5), and trended to have a higher percentage of narrowing and hinge effect.

Discussion

Plaque calcification in PD has been discussed in the literature [8–11,14]. This study reports on one of the largest cohorts of Peyronie's patients with plaque mineralization. The incidence of plaque calcification has been estimated between 20% and 25% of Peyronie's patients [21]. However, Breyer et al. reported an incidence of 31% in a large cohort, suggesting that calcification is not as uncommon as previously suggested [10] Most recently, Chung and associates reported on the largest cohort analysis of men with PD using PDU and found evidence of calcification in 53% [8].

Table 5 Comparison of grade 3 calcification undergoing PEG with those without calcification undergoing PEG

		Noncalcified	Grade 3	*P* value
PEG, # (%)		57 (10.4)	11 (35.5)	<0.001
Patients undergoing PEG	Total curvature (degrees), mean (SD)	70 (25.5)	78 (23.14)	0.326
	Narrowing, # (%)	22 (38.6)	5 (45.5)	0.743
	Hinge, # (%)	24 (42.1)	7 (63.64)	0.322

PEG = plaque excision and grafting

With an incidence of slightly over 34%, our data further support the notion that plaque calcification is not rare and may actually be a common finding.

Our series demonstrates the calcified population as older (52.2 vs. 49.0) when compared with our overall population of men with PD (Table 1), which is contrary to previous reports [9]. The significance of this finding is unclear, but may suggest that older, less resilient tissues are more prone to dystrophic calcification. The calcified patient's subjective reports of estimated curvature, estimated length loss, and reported pain are all significantly greater than their noncalcified counterparts. While not entirely clear, this observation may represent an increased patient awareness of the lesion and/or possibly indicate the lack of elasticity in the calcified plaque.

Multiple imaging modalities have been used to identify plaque calcification. We agree that ultrasonography is a superior imaging method, as it is relatively inexpensive, noninvasive, and allows for reliable detection of plaque calcification [8–11,16,21,22] In addition, PDU allows for the evaluation of corporal hemodynamics. It is, however, important to recognize its user dependency which may compromise objective measurements. We have attempted to minimize this variation through the use of a single ultrasonographer.

The etiology and pathophysiology of PD plaque calcification are not fully understood at this time. In patients with normal serum calcium and phosphorus, this calcification may be considered dystrophic in nature [23]. By definition, patients with nonmetastatic dystrophic calcification have normal serum calcium and phosphorus [15]. While all of the patients in our study were believed to have normal serum concentrations of these elements, we acknowledge the lack of these values as a limitation of this study.

Trauma has long been suggested as a primary inciting factor for PD, as well as plaque calcification [24] This hypothesis is based partially on the epidemiologic association of PD with some traumatic event. Early studies suggested that vascular trauma leads to osteoid formation via osteoblast-like cells originating from the vascular lumen [24]. These investigators concluded that vascular trauma was in part responsible for the formation of ossified plaques. Our series, however, did not identify a higher occurrence of recognized traumatic events preceding the development of PD in the calcified population. An early study by Gelbard also failed to demonstrate any difference with regard to trauma when comparing a small population of calcified with noncalcified Peyronie's patients [13].

It is our opinion that calcification of the plaque likely has little association with penile trauma; however, it does appear that the propensity of the tunical scar to undergo mineralization likely varies widely between men. These individuals may represent a separate genetic subtype of PD prone to plaque mineralization. Novel research related to gene expression in PD suggests that up-regulation of certain genes (particularly *OSF1*, *osteoblast specific factor 1*) may be in part responsible for plaque calcification [4,25] It is thought that the products of these genes may act as osteoblast recruiters, thus promoting plaque calcification. Our patients with calcification were not repeatedly studied over time to determine whether spontaneous or treatment-related change occurred with mineral burden. This presents a potential area of future research, as interruption of this process may prove useful as a means of preventing plaque mineralization and possibly provide a better response to nonsurgical treatment.

Current clinical opinion suggests that calcification within the Peyronie's plaque is indicative of long-standing or chronic lesions [9–11,13,15,21], This notion has been widely accepted by practicing urologists. In this report, patients with plaque calcification presented as early as 6 weeks from first recognizing the cardinal symptoms of pain, palpable lump, and/or penile deformity. Further, over 17% of men with calcified plaques presented to our center within 6 months of first noting the symptoms of PD, suggesting that calcification can be an early finding in some men with PD. The majority of calcified plaques were identified as they presented over 12 months after onset of symptoms, but this does not mean that mineralization had not been present earlier in the course of the scarring process. Plaque calcification, in our opinion, should no longer be considered an indication of mature, severe, or chronic disease.

It has also been widely accepted among practicing urologists that the presence of plaque calcification would likely indicate a plaque that would not respond to conservative or nonsurgical treatment. For example, intralesional injection of interferon or verapamil is not recommended when extensive plaque calcification is present [1,17,26] Several investigators have reported that plaque calcification is strongly correlated to progression to surgery [8,10,11]. Chung and associates noted that men with large calcified plaques were more

likely to need prosthesis implantation [8]. These investigators did not stratify the calcification burden. On the other hand, we did not find that calcification alone was a predictor of the need to progress to surgery, unless grade 3 calcification was noted on PDU.

Plaque calcification does not appear to have a significant impact on the degree of penile curvature. This finding is important in that it suggests that the calcified variant should not be categorized as a more aggressive or deforming subtype of PD. However, it does appear that it lends itself to increased pain, which we propose is secondary to the decreased compliance of the mineralized tissue.

The addition of a calcification grading system may assist in the understanding of the natural history of PD. Bekos et al. conducted the first study demonstrating the utility of ultrasound in describing the natural history of PD [11]. Our calcified plaque patients were stratified using the grading system we developed based upon the distribution of calcification in the studied population. Organization by extent of calcification rather than presence or absence alone demonstrated that those patients with a higher mineral burden (grade 3) were more likely to undergo surgical intervention than their counterparts. Stratification by grade of calcification may help prevent premature surgical intervention as it appears that the presence of calcification is not indicative of mature disease. Moreover, it may serve as a clinical tool to appropriately counsel patients on the likelihood of progression to surgery, particularly for those with grade 3 calcification. As our results show, those with grade 3 calcification were statistically more likely to undergo a grafting procedure, as this group was found to have severe deformity (>60° curve ± hinge effect due to indentation which conforms to previously published algorithms [1,19,20]) (Table 5). In addition, the grade 3 population, and those with greater calcification burden, have been found to be less likely to respond to nonsurgical treatment [8,10,17,26]. Yet our statistical analysis has shown that those with grade 3 calcification did not statistically have more severe deformity than the matched control cohort (Table 2).

Conclusions

This study reviews a large cohort of Peyronie's patients with calcified plaques. On the whole, PD patients who have calcified or noncalcified Peyronie's plaques are similar in curvature, plaque location, emotional impact of the disease, and reported penile trauma. Plaque calcification is not an uncommon finding in men with PD, and does not appear to occur exclusively in the setting of chronic or severe PD. Plaque calcification was found as early as 6 weeks following the onset of symptoms, suggesting that it may be a different subtype of PD rather than an indication of plaque maturation. The pathophysiology of calcification remains unclear; however, research on preventing mineralization may prove to be clinically useful. Based upon the findings in this study, patient stratification by degree of calcification, rather than presence or absence alone, appears to be a predictor of progressing to surgery, as 55% of men with grade 3 mineralization underwent surgery. Moreover, those with grade 3 calcification who underwent surgery were more likely to undergo a grafting procedure (PEG), as a larger percentage had evidence of severe deformity with normal erectile capacity ($P < 0.001$).

Corresponding Author: Laurence Levine, MD, Department of Urology, Rush University Medical Center, 1725 W. Harrison, Suite 352, Chicago, IL 60612, USA. Tel: 312-563-5000; Fax: 312-563-5007; E-mail: drlevine@hotmail.com

Conflict of Interest: Dr. Levine has disclosed the following instutional relationships: Auxilium Pharmaceuticals Consultant/Advisor, Meeting Participant/Lecturer; AMS Corp, Consultant/Advisor, Meeting Participant/Lecturer; Coloplast Corp, Consultant/Advisor, Meeting Participant/Lecturer; Absorpiton Pharmaceuticals—Consultant/Advisor, Meeting Participant/Lecturer.

Statement of Authorship

Category 1

(a) Conception and Design
Laurence Levine; James Rybak; Christopher Corder

(b) Acquisition of Data
Laurence Levine; James Rybak; Christopher Corder; Michael Ryan Farrel

(c) Analysis and Interpretation of Data
Laurence Levine; Christopher Corder; Michael Ryan Farrel; James Rybak

Category 2

(a) Drafting the Article
Laurence Levine; James Rybak

(b) Revising It for Intellectual Content
Laurence Levine; James Rybak

Category 3

(a) Final Approval of the Completed Article
Laurence Levine

References

1 Ralph D, Gonzalez-Cadavid N, Mirone V, Perovic S, Sohn M, Usta M, Levine L. The management of Peyronie's disease: Evidence-based 2010 guidelines. J Sex Med 2010;7:2359–74.
2 Mulhall JP, Creech SD, Boorjian SA, Ghaly S, Kim ED, Moty A, Davis R, Hellstrom W. Subjective and objective analysis of the prevalence of Peyronie's disease in a population of men presenting for prostate cancer screening. J Urol 2004;171: 2350–3.
3 Raanan Tal MD, Matthew S, Hall MD, Byron Alex MD, Judy Choi MD, John P, Mulhall MD. Peyronie's disease in teenagers. J Sex Med 2012;9:302–8.
4 Vernet D, Nolazco G, Cantini L, Magee TR, Qian A, Rajfer J, Gonzalez-Cadavid NF. Evidence that osteogenic progenitor cells in human tunica albuginea originate from stem cells: Implications for Peyronie disease. Biol Reprod 2005;73:1199–210.
5 Larsen SM, Levine LA. Peyronie's disease: Review of non-surgical treatment options. Urol Clin North Am 2011;38: 195–205.
6 Nelson C, Diblasio C, Kendirci M, Hellstrom W, Guhring P, Mulhall J. The chronology of depression and distress in men with Peyronie's disease. J Sex Med 2008;8:1985–90.
7 Rosen R, Catania J, Lue T, Althof S, Henne J, Hellstrom W, Levine L. Impact of Peyronie's disease on sexual and psychosocial functioning: Qualitative findings in patients and controls. J Sex Med 2008;5:1977–84.
8 Chung E, Yan H, De Young L, Brock GB. Penile Doppler sonographic and clinical characteristics in Peyronie's disease and/or erectile dysfunction: An analysis of 1,500 men with male sexual dysfunction. BJU Int 2012;110:1201–5.
9 Kalokairinou K, Konstantinidis C, Domazou M, Kalogeropoulos T, Kosmidis P, Gekas A. US imaging in Peyronie's disease. J Clin Imaging Sci 2012;2:63.
10 Breyer BN, Shindel AW, Huang YC, Eisenberg ML, Weiss DA, Lue TF, Smith JF. Are sonographic characteristics associated with progression to surgery in men with Peyronie's disease? J Urol 2010;183:1484–8.
11 Bekos A, Arvaniti M, Hatzimouratidis K, Moysidis K, Tzortzis V, Hatzichristou D. The natural history of Peyronie's disease: An ultrasonography-based study. Eur Urol 2008;53: 644–50.
12 Levine LA, Greenfield JM. Establishing a standardized evaluation of the man with Peyronie's disease. Int J Impot Res 2003;15(suppl 5):S103–12. Review.
13 Gelbard MK. Dystrophic penile calcification in Peyronie's disease. J Urol 1988;139:738–40.
14 Chou YH, Tiu CM, Pan HB, Lin SN, Hsu CC, Wu CC, Chang T. High-resolution real-time ultrasound in Peyronie's disease. J Ultrasound Med 1987;6:67–70.
15 Vande Berg JS, Devine CJ, Horton CE, Somers KD, Wright GL Jr, Leffell MS, Dawson DM, Gleischman SH, Rowe MJ. Mechanisms of calcification in Peyronie's disease. J Urol 1982;127:52–4.
16 Chung E, De Young L, Brock GB. Penile duplex ultrasonography in men with Peyronie's disease: Is it veno-occlusive dysfunction or poor cavernosal arterial inflow that contributes to erectile dysfunction? J Sex Med 2011;8:3446–51.
17 Levine LA. Treatment of Peyronie's disease with intralesional verapamil injection. J Urol 1997;158:1395–9.
18 Smith JF, Walsh TJ, Conti SL, Turek P, Lue T. Risk factors for emotional and relationship problems in Peyronie's disease. J Sex Med 2008;5:2179–84.
19 Levine LA, Lenting EL. Experience with a surgical algorithm for Peyronie's disease. J Urol 1997;158:2149–52.
20 Levine LA, Burnett AL. Standard operating procedures for Peyronie's disease. J Sex Med 2013;10:230–44.
21 Smith JF, Brant WO, Fradet V, Shindel AW, Vittinghoff E, Chi T, Huang YC, Davis CB, Conti S, Lue TF. Penile sonographic and clinical characteristics in men with Peyronie's disease. J Sex Med 2009;6:2858–67.
22 Balconi G, Angeli E, Nessi R, de Flaviis L. Ultrasonographic evaluation of Peyronie's disease. Urol Radiol 1988;10:85–8.
23 Majno G, Joris I, eds. Chapter 6. Pathologic calcification. In: Cells, tissues, and disease: Principles of general pathology. 2nd edition. New York, NY: Oxford University Press; 2004: 248–58.
24 Devine CJ Jr. Introduction to the international conference on Peyronie's disease. J Urol 1997;157:272–5.
25 Cadavid-Gonzalez NF, Magee TR, Ferrini M, Qian A, Vernet D, Rajfer J. Gene expression in Peyronie's disease. Int J Impot Res 2002;14:361–74.
26 Andresen R, Wegner HE, Banzer D, Miller K. Ultrasound and soft-tissue radiography to monitor local interferon-alpha 2B treatment in Peyronie's disease. Acta Radiol 1996;37(3 Pt 1): 352–6.