



Peyronie's disease in men under age 40: characteristics and outcome

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Peyronie's disease is most commonly seen in the fifth decade of life. However, a wide range of age (20–83 y) is reported. During a 6-year period, men with Peyronie's disease presenting under the age of 40 were reviewed retrospectively and followed-up. The prevalence of Peyronie's patients presenting under age 40 was 8.2%. Their mean age was 32.47 ± 5.37 (range: 23–39) y and 78.9% of them presented during the acute phase of the disease. Pain on erection was a part of presenting symptom complex in 52.6% and the majority (84%) had a degree of penile curvature $<60^\circ$. Erectile dysfunction (ED) was present in 21% of patients, who responded well to intracavernous injection test. After a minimal 2-year follow-up, improvement in penile deformity was observed in 36.8%, and 42.1% had stable disease while 21% experienced deterioration of the penile curvature. The onset of Peyronie's disease is clinically more noisy and acute in patients presenting under age 40 and this forces the physicians to treat them more vigorously. *International Journal of Impotence Research (2001) 13, 18–23.*

Keywords: Peyronie's disease; symptoms; treatment; outcome; colchicine; venous grafting

Introduction

Peyronie's disease is an idiopathic connective tissue disorder of the penis characterized by an initial inflammatory reaction followed by fibrous inelastic scar formation involving the tunica albuginea of the corpora cavernosa and adjacent erectile tissue.^{1,2} Patients with Peyronie's disease present at different stages of progression, with a variety of symptoms and signs. The acute inflammatory phase usually lasts about 12–18 months and clinical hallmarks are unstable penile deformity and pain on erection.³ The chronic or stable phase begins when the acute phase subsides and it is characterized by stable penile deformity. During the acute phase, lesions on the tunica albuginea show inflammatory infiltrate while those of long duration exhibit fibrosis, calcification and sometimes ossification.^{4–7} Although complete resolution has been reported to occur without treatment in up to 13% of cases, it often takes several years.⁸ Peyronie's disease is easily differentiated from congenital curvature of the penis, but the plaque may mimic, albeit rarely, a

more serious condition such as epithelioid sarcoma of the penis.⁹

Although it was once considered a rare condition, 1–2% incidence of symptomatic Peyronie's disease was found in different populations of male physicians.^{10,11} The disease affects approximately 10% of men presenting with erectile dysfunction (ED) and is most commonly seen in the fifth decade of life.¹⁰ However, a wide range of age, between 20 to 84 y, appears in the literature with the youngest affected being 19 y.^{10–18} An average age-adjusted annual incidence rate of 25.7 and a prevalence rate of 388.6 per 100 000 male population were noted in an epidemiological study by Lindsay *et al*, from Rochester, Minnesota.¹¹ In the same study, the prevalence of patients, presenting under 40 y of age, was also observed to be 9.9% ($n=10$) among 101 men with Peyronie's disease.¹¹

Since the natural history of Peyronie's disease is still obscure, and detailed epidemiological studies are lacking, the aim of the study is to identify the characteristics of men with Peyronie's disease presenting under age 40 and give the results of their long-term follow-up.

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Materials and methods

During a 6-year period, 231 men with Peyronie's disease were seen at our institution. Their age

ranged between 23 and 76 y with a mean age of 54.3 ± 13.2 y (median age: 53 y). We retrospectively reviewed the charts of cases presenting under age 40, and they were further followed-up with regular visits.

Diagnostic evaluation

All cases underwent a basic evaluation concerning ED. The first part of this evaluation was directed toward a detailed history. Age at presentation was recorded. Duration of the disease (ie the interval between onset of the disease and presentation to our institution) and presenting symptoms were specially assessed by a structured questionnaire. Presence of risk factors for ED as well as for systemic vascular diseases, such as smoking, insulin dependent diabetes mellitus (IDDM), non-insulin dependent diabetes mellitus (NIDDM), hypertension and serum lipid abnormalities were recorded.^{13,15} Physical examination focused on abnormalities of the genitalia and extent of the palpable plaque on the penis. A clear differential diagnosis with congenital penile curvature was made by an experienced urologist (AK).

The erectile status of patients was investigated by a detailed history, combined injection and stimulation (CIS) test in all patients with penile color Doppler ultrasonography (CDU) in selected cases.¹⁹ Patients with consistent inability to achieve and maintain erection of sufficient rigidity and duration to permit satisfactory sexual performance were considered to have erectile dysfunction (ED).²⁰ All patients were given an intracavernous injection of 60 mg papaverine combined with manual stimulation (CIS test) to assess the degree of tumescence, location and degree of the curvature.¹⁹ Criteria for positive erectile response to CIS test were determined as occurrence of erection (buckling pressure >500 gr, measured by a bucklometer) within 10 min, and duration of this state for at least 10 min.¹⁹ The degree of penile deformities were measured by a protractor during erection obtained by intracavernous injection (CIS) test. The deformities were also documented by photography or drawing, and modified Kelami's classification was used in order to stratify the cases as follows; grade I was curvature of 30 degrees or less, grade II was a curvature between 30 and 60 degrees, and grade III was a curvature greater than 60 degrees.¹⁸

In cases during the chronic phase of disease or stating a stable penile deformity for at least 6 months, penile CDU examination (ATL, Ultramark 9) was performed as thoroughly described elsewhere.²¹ Briefly, diameters of right and left cavernous arteries before and after intracavernous injection (ICI) of 10 µg prostaglandin E-1 (PGE-1), peak systolic velocity (PSV), end diastolic velocity (EDV) and resistance index (RI), calculated as PSV-

EDV/PSV, were measured. The cut-off value was >35 cm/s for a normal PSV, values below were considered to be diagnostic penile arterial disease.^{15,19,22} Cases with full erectile response to ICI and self-stimulation, almost always had an EDV >5 cm/s and were considered to have an intact veno-occlusive system. Diagnosis of veno-occlusive dysfunction (VOD) was concluded in patients with both EDV >5 cm/s and RI <0.9.^{15,22} Patients were considered as having mixed (arterial+venous) vascular disease when there was evidence of both arterial insufficiency and VOD on CDU.

Treatment strategy

Patients were treated according to recently published algorithms.^{3,13,14,18} Briefly, medical treatment was initiated in patients presenting during the acute phase of the disease (duration <12 months). All patients enrolled in the study were previously untreated. Colchicine was our choice of medical treatment and was administered orally.²³⁻²⁵ Initial doses ranged from 0.5 to 1.0 mg daily during the first week and were increased gradually until the maximum dose of 2.0 mg daily was reached.²⁵ Three to 6 months of treatment was recommended.²⁵ Complete blood count was obtained prior to therapy and every 2 months during therapy. The success of the treatment was based on the criteria such as decrease in pain on erection and decrease of the degree of penile curvature, while improvement of the curvature was defined as straightening of the penis or significant decrease in the penile curvature, permitting sexual intercourse possible, if previously not.

Surgical treatment was considered in patients during their stable phase with the duration of disease longer than 12 months. Plaque incision with venous grafting, as a reconstructive procedure, was our choice of surgical treatment for potent patients or for those with erectile dysfunction by history but responding well to intracavernous injection of vasoactive (ICI) agents and/or vacuum erection device (VD).¹³ Implantation of penile prosthesis was considered for those with erectile dysfunction and non-responding to ICI and/or VD.¹³

Follow-up

The outcome, either natural or after treatment, was determined by regular visits, every 3 months for at least 2 y. A structured questionnaire, concerning the alterations in penile deformity, pain, and erectile function, was used for the follow-up of cases in their acute, unstable phase of disease. On the other hand, those stating a stable deformity for at least 6 months

were asked to provide a self-photo during erection, or undergo CIS test. In addition, penile CDU was performed in those candidates for surgery (ie cases with penile stable deformity disabling sexual intercourse) in their follow-up.

Results

Out of 231 men with Peyronie's disease, 8.2% ($n=19$) were identified to present under age 40. The mean age of this group was 32.47 ± 5.37 (range: 23–39) y and the median duration of Peyronie's disease was 3 months (mean: 11.2 ± 6 months and range: 1 week–90 months). Fifteen of the cases (78.9%) presented in their acute phase of the disease (duration <12 months) and out of these 15 cases, 8 (42.1%) stated that the deformity developed in an hyper-acute fashion in less than 1 month. Only four cases (21%) were diagnosed in their chronic and stable phase (Table 1).

Table 1 Summary of characteristics of patients with Peyronie's disease under age 40

	n
Phase of the disease at presentation	
Acute phase (<12 months)	15 (78.9%)
Hyperacute phase (<1 month)	8 (42.1%)
Chronic phase (>12 months)	4 (21.1%)
Presenting symptoms	
Penile deformity	19 (100%)
Dorsal curvature	8 (42.1%)
Lateral curvature	8 (42.1%)
Ventral curvature	3 (15.8%)
Notching	2 (10.5%)
Pain on erection	10 (52.6%)
Degree of penile deformity (Modified Kelami's classification)	
<30 degrees	9 (47.4%)
30–60 degrees	7 (36.8%)
>60 degrees	3 (15.8%)
Presence of risk factors for vascular disease	
At least one risk factor	11 (57.9%)
Smoking	7 (36.8%)
Hypercholesterolemia	6 (31.6%)
Diabetes Mellitus (IDDM/NIDDM)	4 (21%)
Hypertriglyceridemia	4 (21%)
History of genitourinary trauma	2 (10.5%)
Frequent masturbation	2 (10.5%)
Previous urological surgery	2 (10.5%)
Erectile status	
Erectile dysfunction by history	4 (21%)
CIS test (+)	14 (73.6%)
(–)	4 (21.1%)

Penile deformity was the main presenting symptom in all cases with pain on erection in 52.6% of patients (Table 1). Dorsal penile curvature was the most common type of deformity and was observed in eight (42%) cases. The second most common type of deformity was lateral curvature, that was to the left side in seven cases (36.8%) and right side in one case (5.2%). The remaining three cases (15.8%) had ventral curvature and two cases (10.5%) had notching on the shaft of penis.

According to modified Kelami's classification, nine cases (47.4%), including those two cases with notching deformity, had grade I deformity (ie <30° of penile curvature), seven (36.8%) had grade II and three (15.8%) had grade III penile deformities (Table 1).

At least one risk factor for erectile dysfunction could be identified in 57.9% ($n=11$) of patients (Table 1). Smoking and hypercholesterolemia, observed in 36.8% ($n=7$) and 31.6% ($n=6$) cases, respectively, were the most common risk factors. Four patients had diabetes mellitus (IDDM in 3, NIDDM in 1) and four had elevated serum triglyceride levels. A history of genitourinary trauma was suspected in two cases, and two patients had undergone urological surgery (1 distal hypospadias repair, 1 ureteroneocystostomy) in their childhood, while frequent masturbation was noted in two patients (Table 1).

By history, 42.1% ($n=8$) of patients stated that they were able to attain and maintain rigid erection, sufficient for sexual intercourse, despite their penile deformity. Difficulty with intromission due to severe penile deformity and pain, despite rigid erection, was a complaint in seven cases (36.8%) and their median degree of penile curvature was 65°. By history, four patients (21.1%) complained of ED by history but all of these four cases had positive response to CIS test and had a median degree of deformity of 25° (Table 1). Of these four cases with ED by history, two had no risk factor for ED, while one had IDDM for over 10 y and the other had elevated serum lipid levels.

Overall, 73.6% had positive response to CIS test while one patient refused this test because of severe pain on erection.

Penile CDU was performed in five cases, who were candidates for surgery, in their chronic phase of Peyronie's disease and revealed normal penile vascular system in two and slight veno-occlusive dysfunction in three cases.

Table 2 The outcome of the deformity after a minimal 2-year follow-up

	Improvement	Stable or Slight improvement	Deterioration
No treatment ($n=5$)	—	60% ($n=3$)	40% ($n=2$)
Medical treatment ($n=11$)	36.3% ($n=4$)	45.5% ($n=5$)	18.2% ($n=2$)
Surgical treatment ($n=3$)	100% ($n=3$)	—	—
Total ($n=19$)	36.8% ($n=7$)	42.1% ($n=8$)	21.1% ($n=4$)

Five cases did not receive any treatment. Three of them refused any treatment. The remaining two cases had minimal notching on the shaft of penis that did not interfere with sexual intercourse. In this group of cases with no treatment, three (60%) had a stable disease while two experienced deterioration of their penile deformity (Table 2).

Medical treatment with oral colchicine was initiated in 11 cases (57.9%). After a minimal follow-up of 2 y, 36.4% ($n=4$) of them noted improvement in their penile deformity, while 45.5% ($n=5$) and 18.2% ($n=2$) reported slight improvement and no improvement, respectively (Table 2). Pain on erection disappeared in 87.5% cases after the same follow-up. No patient had to terminate the treatment due to gastrointestinal or hematological side effects, but the daily dose of colchicine had to be reduced (that is from 2.0 mg/day to 1.0 mg/day) in two cases (18.2%) due to diarrhea, that resolved with this dose adjustment.

Surgical treatment was indicated for four cases (21%) in their chronic phase of disease. Plaque incision and venous grafting technique was performed in three of these cases and after a mean follow-up of 12 months, complete straightening of the curvature was achieved in all of them. Implantation of penile prosthesis was not considered in any case.

Overall, at the end of the follow-up for which was at least 2 y (Table 2), a total of seven cases (36.8%) achieved improvement in their penile deformities, by either surgical ($n=3$) or medical treatment ($n=4$). On the other hand, four cases (21%), two of whom did not receive any treatment, had deterioration and eight cases (42.1%) had stable disease. Erectile function was preserved in all cases during follow-up.

Discussions

To our knowledge, this is the first report characterizing Peyronie's patients presenting under the age of 40. Although it is well known that the disease is most commonly seen among men in their fifties, a wide age range (20–84 y) has been reported in the literature.^{10–18} The age of patients in our series, consisting of 231 cases, similarly ranged between 23 and 76 y. Furthermore, the prevalence of patients with Peyronie's disease presenting under age 40 has been reported to be 9.9% in an epidemiological study by Lindsay *et al*, and this was also similar (8.5%) to our results.¹¹ Therefore, it was of interest to study the characteristics and outcome of young Peyronie's patients since we believed that their presenting symptoms, risk factors, erectile status, therapeutic options as well as their response to treatment and their follow-up would be different.

Our results revealed that all cases with Peyronie's disease under age 40 present with a penile deformity and that more than half (52.6%) of them complain of pain on erection. Furthermore, the majority (85%) present during the acute phase of the disease (duration <12 months) and 42% of them state a 'hyperacute' onset of the symptoms. These data indicate that the onset of Peyronie's disease is clinically more noisy among younger Peyronie's patients, forcing the physicians to treat them more vigorously, since only about 60% of Peyronie's patients in previously published series had penile deformity as a presenting symptom and pain on erection was reported to range between 30 and 40% among these cases.^{8,11,14} On the other hand, the majority (84.2%) of these cases in our series had a degree of penile curvature <60° and the deformities were stratified to be grade I in 47.4%, grade II in 36.8% and grade III in 15.8%, according to modified Kelami's classification. In this classification, we did not take the plaque size into consideration since recent studies have shown that the tunica albuginea is effected as a whole in Peyronie's disease.^{7,13,26}

Sexual dysfunction is reported to be a part of presenting symptom complexes in 4 to 80% of Peyronie's patients in previously published series.^{12,15} Although excessive angulation due to penile curvature, pain on erection, tenderness of the plaque and performance anxiety may all contribute to ED, it has been shown that penile vascular abnormalities are responsible for ED in 61–70% of cases.^{12,27} Veno-occlusive dysfunction (VOD) is reported to be present in 30–86% and the role of arterial disease has also been shown in 44–52% of Peyronie's patients with ED although it is not easy to determine the exact etiologic factor in every case.^{12,27} Furthermore men with Peyronie's disease, presenting most commonly in their fifties, may only reflect the conditions of potency of age matched patients without Peyronie's disease.⁷ Despite the acute and noisy clinical onset of the disease in our patients under age 40, the prevalence of ED by history was 21%. Moreover, all cases with ED by history had a positive response to CIS test. However, 36.8% of cases complained of difficulty with intromission due to their severe penile deformity (median degree of curvature: 60°) and/or pain on erection although they could achieve rigid erection. These results confirm the previously published data suggesting that ED in Peyronie's disease was related to the increased age and contributing risk factors for vascular disease.^{28–31} Supporting our thesis, Kinsey was the first to notice in 1948 the increasing incidence of ED with age and recently this issue was clarified in details by Feldman *et al* in the Massachusetts Male Aging Study (MMAS).^{29,31} Kinsey *et al* observed that the prevalence of ED was 6.7% in men younger than age 45, in the general population.³¹ On the other hand, Feldman *et al* reported the result of a community based, random

sample observational survey of non-institutional men 40–70 y old and concluded that the combined prevalence of minimal, moderate and complete ED was 52%.²⁹ Additionally, in a study by Donatucci and Lue among cases with ED under age 40, the authors underlined that contributing medical conditions were present in 76% of these cases.³⁰ They also concluded that 72% of these cases had penile vascular pathologies.³⁰ All these data suggest that, Peyronie's disease and ED, are two different clinicopathologic entities, especially among cases under the age of 40.

Risk factors for ED, such as smoking, hypertension, diabetes mellitus and serum lipid abnormalities, could be identified in 57.9% of cases presenting under age 40 in our series. Smoking was the most common risk factor and this was attributed to the high smoking prevalence in our population. Serum lipid abnormalities and diabetes mellitus were other risk factors and their relation with the pathophysiology of Peyronie's disease needs to be clarified by further studies.

According to previously published algorithms for the treatment of Peyronie's disease, medical treatment was indicated in 85% cases presenting under age 40 since they presented during their acute phase of disease, usually accompanied with pain.^{3,13,14,18} With its well-known activity to induce collagenase activity and decrease collagen synthesis and our previous experience, colchicine was our choice for medical treatment.^{23–25} Most of the cases (87.5%) stated disappearance of painful erections and 36% reported improvement of the penile curvature after medical treatment. Only five cases in this series did not receive any treatment. Since the characteristics (that is the severity of penile deformity, duration of disease, presence of risk factors and ED) of men in medical treatment and no treatment groups were different, and the number of cases in each group was too small, comparison of their outcome would be non-logic.

Although colchicine has been reported to cause gastrointestinal side effects and bone marrow suppression in up to 50% of cases by other authors, we did not encounter such a serious side effect to terminate the treatment in this study.²³ But it has to be underlined that the daily dose of colchicine had to be reduced (ie from 2.0 to 1.0 mg/day) in two cases (18.2%) due to diarrhea, that resolved with this dose adjustment. This low prevalence of side effects among young men in this study is compatible with long-term results of our own previously published series, in which only 1.7% terminated colchicine treatment due to severe side effects.²⁵

Surgical treatment can also be considered among patients with Peyronie's disease presenting under age 40 y when the acute phase resolves.^{3,13,14,18} According to the algorithm, generally accepted as a consensus by several authors, reconstructive surgery should be preferred for these young patients since

they are all potent or have a positive response to CIS test.^{17,32} Our choice of surgical treatment modality was plaque incision and venous grafting technique with its several outstanding advantages such as its high success rate, low risk for loss of erectile function and restoration of the neurovascular bundle which is dissected free from fibrous extensions during this procedure.¹³ We achieved complete straightening of the curvature in all cases ($n=3$) under age 40 after plaque incision and venous grafting technique. Indications of implantation of penile prosthesis (ie presence of erectile dysfunction with no response to ICI and/or VD) should be carefully re-evaluated in these young patients with the attended risks such as malfunction and infection.¹³ Supporting this issue, implantation of penile prosthesis was considered neither in our series, nor in their series consisting of cases with ED under the age of 40 by Donatucci and Lue.³⁰

Conclusion

About 8–10% of men with Peyronie's disease present under age 40. Although they seem to be the subset of the whole, they have strikingly different characteristics such as clinical hallmarks and outcome. The majority of them (79%) present during acute phase of disease usually concomitant with pain on erection and medical treatment is indicated in most of them. Despite this acute and noisy presentation, more than 80% have a degree of penile curvature $<60^\circ$ and ED by history is present in only 21% of them. Furthermore CIS test is positive in all cases with ED. Medical treatment with oral colchicine, with its minimal side effects, was the treatment of choice in the majority of cases (73.6%). Although surgical treatment is considered less among younger patients, it must be noted that plaque incision and venous grafting technique, with its important advantages such as restoration of the neurovascular bundle and its satisfactory results, can be preferred. Overall, with or without treatment, the penile deformity improved in 36.8%, was stable in 42.1% and deteriorated in 21% of cases after a minimal 2 years of follow-up.

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