Peyronie's Disease: Nonsurgical Therapy Options

Franklin E. Kuehhas, MD,[1] Peter Weibl, MD,[1] Tosev Georgi, MD,[2] Nenad Djakovic, MD,[3] Ralf Herwig, MD[1]

[1]Department of Urology, Medical University of Vienna, Vienna, Austria; [2]Department of Urology, Medical University of Heidelberg, Heidelberg, Germany; [3]Department of Urology, Clinic Altoetting, Altoetting, Germany

Peyronie's disease (PD) is a fibrous inelastic scar of the tunica albuginea, leading to penile deformity, penile curvature, shortening, narrowing, and painful erections that subsequently lead to painful or unsatisfying sexual intercourse. No consensus exists yet on the ideal management of PD. This fact is a result of our limited knowledge of its etiology and causative factors. The acute presentation of PD is treated conservatively, and surgical approaches are only attempted if severe curvature, narrowing, or indentation persists for more than 1 year; PD stability exists for at least 3 months; curvature impedes sexual intercourse; and severe penile shortening occurs. This review focuses on new developments for conservative treatment strategies for PD.
[Rev Urol. *2011;13(3):139-146 doi: 10.3909/riu0528*]

Key words: Peyronie's disease • Nonsurgical therapy • Oral medication • Intralesional therapy • Extracorporeal shock wave therapy • Iontophoresis • Penile traction systems

Peyronie's disease (PD) manifests as a fibrous inelastic scar of the tunica albuginea, leading to penile deformity, penile curvature, shortening, narrowing, and painful erections that subsequently lead to painful or unsatisfying sexual intercourse. It was first described by François Gigot de la Peyronie, the personal physician of King Louis XVI of France in 1743.[1] The prevalence of PD is still under debate. Some studies have shown prevalence rates ranging from 1% to 4%[2]; autopsy studies have even gone so far as to state that 22% of men have some lesions on the penile tunica albuginea.[3]

No consensus exists yet on the ideal management of PD. This is a result of our limited knowledge of its etiology and causative factors. PD has a multifactorial etiology. Young men often present with a history of trauma during sexual intercourse. Repetitive microtrauma of the penile tissue during sexual intercourse is thought to be the initiator of a local autoimmune reaction in genetically susceptible individuals. This leads to abnormal healing and consecutive development of PD. Casabé and colleagues recently showed that erectile dysfunction (ED) and coital trauma are independent risk factors for the development of PD.[4] Studies have shown altered composition of certain tissue proteins in the tunica albuginea of men—such as decorin, biglycan, fibromodulin, gelatinase A, collagenase II—suggesting an abnormal remodeling process following the microtrauma.[5]

The acute presentation of PD is treated conservatively, and surgical approaches are only attempted if the following four criteria are met[6]: (1) severe curvature, narrowing, or indentation for more than 1 year; (2) PD stability for at least 3 months; (3) curvature that impedes sexual intercourse; and (4) severe penile shortening.

It is important, however, to keep in mind that many patients with PD may not have any symptoms and if they seek urological council because of palpable lesions it is therefore sufficient to reassure them that these lesions are not cancerous. Current data indicate that there is no standard surgical procedure in the treatment of PD. Three main surgical categories are being used as therapy modalities including plication/wedge resection procedures to shorten the convex side of the tunica, lengthening of the concave side with graft material, or implantation of penile prosthesis for men with severe ED caused by PD.

New Developments in the Diagnosis of PD

Diagnosis and treatment plans for PD have been based on patient history and physical examination of the penis. In the past, penile ultrasound was used to localize and measure plaques, exclude patients with calcifications from clinical trials, and assess vascular status before penile surgery.[7]

In recent years, penile ultrasound has gained widespread acceptance as a valuable tool for the diagnosis of PD. Recent studies describe clinical characteristics of PD and the relation to penile ultrasound findings.[8,9] Bekos and colleagues demonstrated that corporal ultrasonography in patients with PD allows objective evaluation and classification of PD. It was shown that a solitary hyperechoic lesion without acoustic shadow stands for the acute phase of PD. Multiple moderate hyperechoic lesions with acoustic shadows represent an intermediate phase of the course of PD. Dense calcified hyperechoic plaques with acoustic shadows were a clear sign for the chronic phase of PD. The authors concluded that the density of echogenic areas and the presence of acoustic shadows are predictors of disease stability.[9] Breyer and associates tried to investigate the correlation between several factors and progression to surgical intervention in men with PD. They concluded that the presence of sonographically detected subtunical calcifications during the initial office evaluation was independently associated with subsequent surgical intervention.[10] Current data suggest that surgical correction of penile deformity should be offered as soon as prominent calcifications are visible in penile sonography, because these calcifications represent a chronic mature disease phase that is refractory to any kind of medical intervention.[8-10] These findings may help to counsel patients on the optimal time for surgery.

Current data suggest that surgical correction of penile deformity should be offered as soon as prominent calcifications are visible in penile sonography, because these calcifications represent a chronic mature disease phase that is refractory to any kind of medical intervention.

Update on Nonsurgical Therapy Options for PD

The acute painful phase of PD should be treated conservatively. Several therapy regimens are available that may stabilize or reduce penile deformity and improve sexual function. The evaluation of conservative therapy modalities is difficult because PD has a spontaneous improvement rate of 5% to 12%.[11] Furthermore, the lack of validated questionnaire and the fact that most trials are small in size and lack placebo control, do not help to clarify treatment enigmas of PD. Nonsurgical treatment options include oral, topical, intralesional, external energy, and combination therapies.

The evaluation of conservative therapy modalities is difficult because PD has a spontaneous improvement rate of 5% to 12%. Furthermore, the lack of validated questionnaires and the fact that most trials are small in size and lack placebo control, do not help to clarify treatment enigmas of PD.

Oral Medication

Vitamin E, with its antioxidant properties, was extensively investigated for the potential use in the treatment

of PD. Gelbard and associates[12] already showed that vitamin E does not have an impact on the natural history of PD. Safarinejad and colleagues[13] compared the efficacy and safety of oral vitamin E and propionyl-L-carnitine, separately, or in combination, for the treatment of PD. A total of 236 men with PD were randomly assigned to four groups. Group 1 (58 men) received vitamin E, 300 mg, orally twice daily. Group 2 (59 men) received propionyl-L-carnitine, 1 g, orally twice daily, and Group 3 (60 men) received vitamin E, 300 mg, and propionyl-L-carnitine, 1 g, orally twice daily. Group 4 (control group, 59 men) received a similar regimen of placebo during the 6-month treatment period. Pain decreased in 60.4%, 63%, 62.3%, and 59.2% of the patients treated with vitamin E, propionyl-L-carnitine, vitamin E plus propionyl-L-carnitine, and placebo, respectively ($P = .1$). After therapy, a reduction in penile curvature was observed by 18.9%, 20.4%, 22.6%, and 18.4% of the patients in groups 1, 2, 3, and 4, respectively ($P = .09$), and a decrease in plaque size was noted in 11.3%, 12.9%, 13.2%, and 11.1%, respectively ($P = .1$). Clearly, these results showed no improvement in patients with PD treated with vitamin E, propionyl-L-carnitine, or vitamin E plus propionyl-L-carnitine compared with those treated with placebo.[13]

In 2004, Safarinejad showed that colchicine, an antigout agent that inhibits fibrosis and collagen deposition by inhibiting neutrophil microtubules, did not have a more beneficial effect than placebo on patients suffering from PD.[14]

Another substance which has been under investigation was potassium aminobenzoate (Potaba®, Glenwood, LLC, Englewood, NJ). Potassium aminobenzoate is believed to increase the activity of monoamine oxidase in tissue, thereby decreasing local levels of serotonin and therefore, possibly decreasing fibrogenesis. In 2005, Weidner and colleagues indicated that the use of potassium aminobenzoate may have a protective effect against progression in PD plaques. However, due to severe gastrointestinal side effects and its relatively high cost, it is not recommended as a standard therapy modality.[15] Furthermore, no study until now could definitively show a significant benefit for potassium aminobenzoate.

Tamoxifen citrate has been used as a therapy option because it blocks the transforming growth factor (TGF) receptors and thus potentially reduces fibrogenesis. Again, studies could not confirm this theory.[16]

Pentoxifylline, a nonspecific phosphodiesterase (PDE) inhibitor has also been tested as a potential solution. An initial promising report from Brant and colleagues reviewed a successful treatment of one patient with pentoxifylline[17] that was recently confirmed by Safarinejad and associates.[18] This group of authors showed a moderate reduction in plaque size and penile curvature under a dose of pentoxifylline, 400 mg, twice daily over placebo. However, further studies are needed to better elucidate the beneficial effects of pentoxifylline.

The same group of authors investigated the role of omega-3 fatty acids for the treatment of early stage PD; however, they could not find any beneficial effect on the course of early stage PD.[19]

The newest data focus on the safety and efficacy of coenzyme Q10 as a treatment option for PD.[20] A total of 186 patients were randomly assigned to either coenzyme Q10, 300 mg, daily (n = 93) or a similar regimen of placebo (n = 93) for 24 weeks. The Erectile Dysfunction Inventory of Treatment Satisfaction (EDITS) questionnaire, the International Index of Erectile Dysfunction (IIEF-5) questionnaire, and a visual analog scale (VAS; 0-10) to evaluate pain were used in the course of the study every 4 weeks. After 24 weeks, mean IIEF-5 score, mean VAS score, and mean EDITS score improved significantly in patients receiving coenzyme Q10 (all $P < .01$). Mean plaque size and mean penile curvature degree were decreased in the coenzyme Q10 group, whereas a slight increase was noted in the placebo group (both $P = .001$). Mean index of IIEF-5 in the 24-week treatment period was 17.8 ± 2.7 in the coenzyme Q10 group and 8.8 ± 1.5 in the placebo group ($P = .001$). Of the patients in the coenzyme Q10 group, 11 patients (13.6%) had disease progression versus 46 patients (56.1%) in the placebo group ($P = .01$). These promising results should lead to the further investigation of the role of coenzyme Q10.[20]

In 2001, Biagiotti and Cavallini examined the potential of acetyl-L-carnitine, a naturally occurring metabolic intermediate, which is hypothesized to inhibit acetyl coenzyme A, which is supposed to help in the repair of damaged cells. They showed that men taking carnitine saw an improvement in pain and curvature. The side-effect profile was also acceptable. However, no follow-up study has been published.[21]

Note that no single oral medication should be recommended as a treatment option for patients in the acute phase of PD. Some reports show promising data; however, randomized,

Note that no single oral medication should be recommended as a treatment option for patients in the acute phase of PD. Some reports show promising data; however, randomized placebo-controlled studies showing a clear statistically significant benefit are still missing.

placebo-controlled studies showing a clear statistically significant benefit are still missing.

Topical Therapy

Verapamil is a calcium channel blocker. In vitro studies showed an inhibition of local extracellular matrix production by fibroblasts, a reduction of fibroblast proliferation, an increase of local collagenase activity, and a modification of the cytokine milieu of the fibroblasts induced by verapamil. Examination on its efficacy when administered as a topical agent did not lead to promising results.[22,23]

Intralesional Therapies

The anti-inflammatory effects of steroids led to the examination of the impact of intralesional applied steroids in PD patients. In 1954, Bodner and colleagues reported an improvement in 17 patients treated with intralesional hydrocortisone and cortisone.[24] However, newer data could not confirm Bodner's findings.[25] The application of intralesional steroids cannot be recommended due to the side-effect profile, including local tissue atrophy, fibrosis, immune suppression, and the lack of data showing a clear statistically significant benefit.

The impact of collagenase as an intralesional agent has also been examined. Gelbard and associates were the first to show a positive effect of intralesional collagenase on PD patients. Approximately 64% of patients reported subjective improvement after 4 weeks of treatment.[26] Another study by the same group of authors showed a statistically significant improvement in curvature.[27] Newer data focusing on the safety and efficacy of intralesional clostridial collagenase injections also showed a statistically significant improvement in penile deviation, plaque width, and plaque length.[28] In this study, intralesional clostridial collagenase was generally well tolerated. These data support the initial findings of Gelbard. Larger scale controlled trials of collagenase are currently underway.

The calcium antagonist verapamil has shown some promising data when used intralesionally. It was first used by Levine and colleagues in 1994 as a treatment option for PD patients.[29] In vitro studies have shown an inhibition of local extracellular matrix production by fibroblasts, a reduction of fibroblast proliferation, an increase in local collagenase activity, and an alteration of the cytokine milieu of fibroblasts.[30] Calcium antagonists modify the release of cytokines, interleukin-6 and -8, and plaque growth factor. Furthermore, it has been shown that they inhibit the inflammation process and the formation of fibrotic tissue.[29] Therefore, it is believed that calcium antagonists have the potential to decrease, inhibit, or invert the plaque formation during PD. Levine and colleagues initially reported on 14 men who underwent a dose escalation trial of biweekly intralesional injections of verapamil for 6 months. Statistically significant improvement of plaque-associated narrowing and curvature was noted.[29]

In a study by Levine and colleagues 156 patients underwent intralesional verapamil therapy. Approximately 60% reported a decrease in penile deviation and 71% had an increase in sexual function.[31] Bennett and associates administered six intralesional injections (10 mg in 5 mL) every 2 weeks to 94 consecutive patients with penile plaque formation and deviation. Follow-up was after completion of the sixth verapamil injection (5.2 months posttreatment). Approximately 18% (n = 17) reported improved curvatures (average improvement, 12°), 60% (n = 56) had stable curvature, and 22% (n = 21) had an increase in curvature (average increase, 22°). All patients with pretreatment pain reported improvement at follow-up. The authors concluded that intralesional verapamil is a useful agent for disease stabilization.[32] Similar findings were reported by Heidari and colleagues, in which they presented an average decrease in plaque size and penile deviation of 30% after 6 months of intralesional verapamil application every 14 days.[33]

Another calcium antagonist that has been under investigation is nicardipine. A recently published study by Soh and associates focused on the impact of nicardipine injections as a conservative treatment modality for PD in the transition period of acute and chronic phase.[34] A total of 86 patients (age range, 38-72 years; mean age, 52 years) were enrolled in this study. A total of 74 patients were randomly assigned to the nicardipine group (n = 37, 10 mg diluted in 10 mL of distilled water) and the control group (n = 37, 10 mL of saline water). A total of six injections were administered biweekly and patients were assessed by the IIEF-5 and the International Pain Scale. The plaque size was measured by ultrasonography after intracavernosal injection of alprostadil (prostaglandin E1), 20 µg. The penile curvature was also measured by taking a photograph at maximum rigidity. The study results showed a reduction of pain score throughout the course of treatment in both groups with a significant difference between the nicardipine and control groups (multiple analysis of variance [ANOVA] test, $P = .19$). Furthermore, a significant improvement of IIEF-5 score was seen only in the nicardipine group at 48 weeks after treatment initiation ($P < .01$). The plaque size was significantly reduced at 48 weeks only in the nicardipine group (12 points, $P = .004$ by paired

t test). The penile curvature was significantly improved in both groups ($P < .01$) without significant difference between them ($P = .14$). There were no severe side effects, such as hypotension or other cardiovascular events. The authors concluded that intralesional nicardipine injections are a viable alternative to verapamil as a treatment option for PD in the transition period of acute and chronic phase.[34]

Initial reports on the impact of interferon (IFN) as treatment modality for PD were encouraging. In 1991, Duncan and associates reported that IFNs decreased the rate of proliferation of fibroblasts in penile plaques, the production of extracellular matrix was also reduced, and collagenase activity was elevated in vitro.[35] In 2006, Hellstrom and associates published their data of a placebo-controlled, multicenter trial of 117 patients. These patients underwent a biweekly injection of 5×10^6 units of interferon-2α (IFN-2α) for a total of 12 weeks. Results showed an average improvement of penile deviation of 13°, versus only 4° in the placebo arm. Approximately 27% of patients in the treatment group reported improvement versus 9% of patients in the saline group. Pain resolution was observed in 67% of the treatment group and in 28% of the patients in the placebo group.[36] However, Wegner and colleagues demonstrated low rates of improvement and a high incidence of side effects, including myalgia and fever.[37,38] Newer data focused on the role of IFNγ.[39] IFNγ is an important agent controlling TGF-β signaling. In the therapy of other fibrotic diseases, such as lung fibrosis, IFNγ is sometimes used. Several studies have described an increased level of TGF-β in the fibrotic plaques of patients with PD. Therefore, Haag and associates examined the effects of IFNγ on TGF-β1–stimulated fibroblasts from patients with PD, searching for a potential antifibrotic effect mediated by IFNγ. They showed an enhancement of the profibrotic effect of TGF-β1 by IFNγ in fibroblasts. An inhibitory effect of IFNγ on the TGF-β pathway could not be found in PD. Therefore, the authors concluded that IFNγ cannot be taken as a useful tool in the therapy of PD.[39]

Overall, a better understanding of the pathogenesis of PD is still required to facilitate the development of new medical treatments.

Extracorporeal Shock Wave Therapy

Extracorporeal shock wave therapy (ESWT) was introduced as therapy modality by Butz and Teichert in 1996. Hauck and colleagues showed in a following study that ESWT led to a significant decrease in penile curvature in patients with PD. A decrease in pain, subjective improvement, and improvement in the quality of sexual intercourse could not be observed in comparison with the case-control group.[40]

The same group of authors reported in a follow-up study that ESWT does not appear to be significantly effective for decreasing penile curvature and plaque size or improving sexual function in PD patients despite improvements in individuals. However, it was shown that penile pain somehow resolved earlier than during the natural course of the disease.[41]

Current data have shown that ESWT is a noninvasive, well-tolerated therapy for PD. However, it cannot be recommended as a standard procedure due to the lack of clear evidence. Literature indicates that ESWT has beneficial effects on painful erections and on sexual function, but it seems to have no significant effect on penile plaque size or penile curvature.[41] Most of the previous studies dealing with ESWT had methodological problems due to the lack of control groups. Recently, the first prospective, randomized, double-blind, placebo-controlled clinical trial for the evaluation of ESWT as a treatment option for PD was published. Palmieri and associates randomly assigned 100 patients to either ESWT (n = 50) or to the placebo group (n = 50).[42] The study evaluated IIEF-5, pain during erection (VAS 0-10), plaque size (cm^2), penile curvature (measured in degrees), and quality of life (QoL) at baseline, 12-week, and 24-week follow-up. After 12 weeks, mean VAS score, mean IIEF-5 score, and mean QoL score ameliorated significantly in patients receiving ESWT. Mean plaque size and mean curvature degree were unchanged in the ESWT group, whereas a slight increase was reported in the placebo group (*P* value not significant vs baseline). After 24 weeks, mean IIEF-5 score and mean QoL score were stable in the ESWT group, whereas mean VAS score was significantly lower when compared with baseline in both groups. Interestingly, after 24 weeks, mean plaque size and mean curvature degree were significantly higher in the placebo group when compared with both baseline and ESWT values. These results may suggest that ESWT has a potential protective effect on disease progression. The authors concluded that ESWT represents a valuable therapy modality for PD patients, leads to pain resolution, and ameliorates erectile function and QoL.[42] The main limitations of the study design were that the QoL questionnaire was not validated, ED was not etiologically characterized, and inclusion criteria were restricted.

Recently, de Berardinis and colleagues published their data on ESWT. The authors described promising findings similar to Palmieri and colleagues.[43] Although current data seem promising, more placebo-controlled trials must be undertaken to gain a

better understanding of the role of ESWT in PD treatment.

Transdermal Electromotive Administration: Iontophoresis

Iontophoresis is the transport of ions through tissue by means of an electric current. Levine and associates noted that verapamil was found within the exposed tunica albuginea from patients after a single intraoperative exposure during plaque incision and grafting surgery.[44] Di Stasi and colleagues reported on a prospective, randomized study of 96 patients treated with verapamil, 5 mg, plus dexamethasone, 8 mg, using iontophoresis versus 2% lidocaine delivered electromotively. Objective improvement of plaque size and penile deviation was noted in 43% of the verapamil and dexamethasone group. Patients in the lidocaine group reported no changes.[45] In 2007, Greenfield and colleagues reported on their experience with the use of verapamil, 10 mg, versus saline iontophoresis. Approximately 65% of the verapamil group and 58% of the saline group reported improvement in curvature (mean 9.1° vs 7.6° in the verapamil and saline groups, respectively). The authors concluded that the electrical current itself might have some beneficial effect on the wound healing. The initial findings have been promising; however, no new data have been published. Further investigation into iontophoresis is needed to clarify its role as a treatment modality for PD.[46]

Penile Traction Systems

Traction therapy is a relatively new therapy option for urological problems. However, it has a long history of use in other areas of medicine such as orthopedics. Initial results on the efficacy and safety of penile traction were first reported in 2001.[47] The penile traction device was used for at least 4 hours per day for a total treatment period of 3 to 6 months. A decrease in mean erect curvature of 14° was seen. The downsides of the study were a small cohort of patients and no control group.

In 2008, Levine and associates reported the results of a study of 11 men with PD who underwent penile traction therapy. Patients were instructed to wear the device for a minimum of 2 hours per day but were encouraged to increase the duration of use to a maximum of 8 hours per day. Treatment was continued for 6 months. Every 2 weeks the penile extender rods were lengthened by 0.5 cm and an evaluation of penile length was performed. A total of 10 men completed the study. Improvements in length and curvature were reported from all patients, 0.5 to 2.5 cm and 10° to 45° (mean, 22°), respectively. No side effects were noted. Patients reported a high satisfaction and an improvement of the IIEF score.[48]

On the other hand, Gontero and colleagues published their results with a penile traction device and could not confirm the promising findings that were seen by Levine and associates. The study consisted of 19 patients with less than 50° penile curvature, no penile pain when flaccid, and PD lasting for at least 12 months. Patients were encouraged to use the traction device for at least 5 hours per day up to a maximum of 9 hours. Evaluation took place at months 1, 3, and 6. The treatment finished at month 6 and at month 12 another evaluation took place. Fifteen patients finished the study and reported a median daily use of the penile traction device of 5.5 hours. Penile curvature decreased from a mean of 31° to 27°, which was not statistically significant. Improvements were noted in mean flaccid and stretched penile length: 1.3 and 0.83 cm, respectively. No further changes of curvature or penile length were noted at the last 12-month follow-up.[49]

The investigation of traction devices as therapy tools for PD is still in its infancy. Although no large multicenter, controlled trials have been published to date, initial data seem promising. Combination therapy of penile traction and nonsurgical therapy options may also be a promising alternative.

Conclusions

There is still a great need for further investigation of the pathology of PD to make clear recommendations for patients suffering from penile narrowing, deviation, and painful erections due to PD. Various conservative treatment modalities have been examined, some showed promising data whereas others were not useful at all. There is no gold standard available for the nonsurgical therapeutic approach. The best approach from our point of view is multimodal therapy. Patients who suffer from severe penile deviation, narrowing, or indentation, who report disease stability for at least 3 months, and who specify to have a curvature that impedes sexual intercourse should be advised to undergo surgical correction of PD. ■

References

1. Kendirci M, Hellstrom WJ. Critical analysis of surgery for Peyronie's disease. *Curr Opin Urol.* 2004;14:381-388.
2. Devine CJ Jr. International Conference on Peyronie's disease advances in basic and clinical research. March 17-19, 1993. Introduction. *J Urol.* 1997;157:272-275.
3. Smith BH. Subclinical Peyronie's disease. *Am J Clin Pathol.* 1969;52:385-390.
4. Casabé A, Bechara A, Cheliz G, et al. Risk factors of Peyronie's disease. What does our clinical experience show? *J Sex Med.* 2011;8:518-523.
5. Tunuguntla HS. Management of Peyronie's disease—a review. *World J Urol.* 2001;19:244-250.
6. Hellstrom WJ, Bivalacqua TJ. Peyronie's disease: etiology, medical, and surgical therapy. *J Androl.* 2000;21:347-354.
7. Prando D. New sonographic aspects of peyronie disease. *J Ultrasound Med.* 2009;28:217-232.
8. Smith JF, Brant WO, Fradet V, et al. Penile sonographic and clinical characteristics in men with Peyronie's disease. *J Sex Med.* 2009;6:2858-2867.
9. Bekos A, Arvaniti M, Hatzimouratidis K, et al. The natural history of Peyronie's disease: an

ultrasonography-based study. *Eur Urol*. 2008; 53:644-650.
10. Breyer BN, Shindel AW, Huang YC, et al. Are sonographic characteristics associated with progression to surgery in men with Peyronie's disease? *J Urol*. 2010;183:1484-1488.
11. Deveci S, Hopps CV, O'Brien K, et al. Defining the clinical characteristics of Peyronie's disease in young men. *J Sex Med*. 2007;4:485-490.
12. Gelbard MK, Dorey F, James K. The natural history of Peyronie's disease. *J Urol*. 1990;144: 1376-1379.
13. Safarinejad MR, Hosseini SY, Kolahi AA. Comparison of vitamin E and propionyl-L-carnitine, separately or in combination, in patients with early chronic Peyronie's disease: a double-blind, placebo controlled, randomized study. *J Urol*. 2007;178(4 Pt 1):1398-1403; discussion 1403.
14. Safarinejad MR. Therapeutic effects of colchicine in the management of Peyronie's disease: a randomized double-blind, placebo-controlled study. *Int J Impot Res*. 2004;16:238-243.
15. Weidner W, Hauck EW, Schnitker J, for the Peyronie's Disease Study Group of German Urologists. Potassium paraaminobenzoate (POTABA) in the treatment of Peyronie's disease: a prospective, placebo-controlled, randomized study. *Eur Urol*. 2005;47:530-535; discussion 535-536.
16. Teloken C, Rhoden EL, Grazziotin TM, et al. Tamoxifen versus placebo in the treatment of Peyronie's disease. *J Urol*. 1999;162:2003-2005.
17. Brant WO, Dean RC, Lue TF. Treatment of Peyronie's disease with oral pentoxifylline. *Nat Clin Pract Urol*. 2006;3:111-115; quiz 116.
18. Safarinejad MR, Asgari MA, Hosseini SY, et al. A double-blind placebo-controlled study of the efficacy and safety of pentoxifylline in early chronic Peyronie's disease. *BJU Int*. 2010;106:240-248.
19. Safarinejad MR. Efficacy and safety of omega-3 for treatment of early-stage Peyronie's disease: a prospective, randomized, double-blind placebo-controlled study. *J Sex Med*. 2009;6:1743-1754.
20. Safarinejad MR. Safety and efficacy of coenzyme Q10 supplementation in early chronic Peyronie's disease: a double-blind, placebo-controlled randomized study. *Int J Impot Res*. 2010;22:298-309.
21. Biagiotti G, Cavallini G. Acetyl-L-carnitine vs tamoxifen in the oral therapy of Peyronie's disease: a preliminary report. *BJU Int*. 2001;88: 63-67.
22. Martin DJ, Badwan K, Parker M, Mulhall JP. Transdermal application of verapamil gel to the penile shaft fails to infiltrate the tunica albuginea. *J Urol*. 2002;168:2483-2485.
23. Fitch WP 3rd, Easterling WJ, Talbert RL, et al. Topical verapamil HCl, topical trifluoperazine, and topical magnesium sulfate for the treatment of Peyronie's disease—a placebo-controlled pilot study. *J Sex Med*. 2007;4:477-484.
24. Bodner H, Howard AH, Kaplan JH. Peyronie's disease: cortisone-hyaluronidase-hydrocortisone therapy. *J Urol*. 1954;72:400-403.
25. Hauck EW, Diemer T, Schmelz HU, Weidner W. A critical analysis of nonsurgical treatment of Peyronie's disease. *Eur Urol*. 2006;49:987-997.
26. Gelbard MK, Lindner A, Kaufman JJ. The use of collagenase in the treatment of Peyronie's disease. *J Urol*. 1985;134:280-283.
27. Gelbard MK, James K, Riach P, Dorey F. Collagenase versus placebo in the treatment of Peyronie's disease: a double-blind study. *J Urol*. 1993;149:56-58.
28. Jordan GH. The use of intralesional clostridial collagenase injection therapy for Peyronie's disease: a prospective, single-center, non-placebo-controlled study. *J Sex Med*. 2008;5:180-187.
29. Levine LA, Merrick PF, Lee RC. Intralesional verapamil injection for the treatment of Peyronie's disease. *J Urol*. 1994;151:1522-1524.
30. Mulhall JP, Anderson MS, Lubrano T, Shankey TV. Peyronie's disease cell culture models: phenotypic, genotypic and functional analyses. *Int J Impot Res*. 2002;14:397-405.
31. Levine LA, Goldman KE, Greenfield JM. Experience with intraplaque injection of verapamil for Peyronie's disease. *J Urol*. 2002;168:621-625; discussion 625-626.
32. Bennett NE, Guhring P, Mulhall JP. Intralesional verapamil prevents the progression of Peyronie's disease. *Urology*. 2007;69:1181-1184.
33. Heidari M, Nejadi JR, Ghate A, et al. Evaluation of intralesional injection of verapamil in treatment of Peyronie's disease. *J Pak Med Assoc*. 2010;60: 291-293.
34. Soh J, Kawauchi A, Kanemitsu N, et al. Nicardipine vs. saline injection as treatment for Peyronie's disease: a prospective, randomized, single-blind trial. *J Sex Med*. 2010;7:3743-3749.
35. Duncan MR, Berman B, Nseyo UO. Regulation of the proliferation and biosynthetic activities of cultured human Peyronie's disease fibroblasts by interferons-alpha, -beta and -gamma. *Scand J Urol Nephrol*. 1991;25:89-94.
36. Hellstrom WJ, Kendirci M, Matern R, et al. Single-blind, multicenter, placebo controlled, parallel study to assess the safety and efficacy of intralesional interferon alpha-2B for minimally invasive treatment for Peyronie's disease. *J Urol*. 2006;176:394-398.
37. Wegner HE, Andresen R, Knipsel HH, Miller K. Treatment of Peyronie's disease with local interferon-alpha 2b. *Eur Urol*. 1995;28:236-240.
38. Wegner HE, Andresen R, Knispel HH, Miller K. Local interferon-alpha 2b is not an effective treatment in early-stage Peyronie's disease. *Eur Urol*. 1997;32:190-193.
39. Haag SM, Hauck EW, Eickelberg O, et al. Investigation of the antifibrotic effect of IFN-gamma on fibroblasts in a cell culture model of Peyronie's disease. *Eur Urol*. 2008;53:425-430.
40. Hauck EW, Altinkilic BM, Ludwig M, et al. Extracorporeal shock wave therapy in the treatment of Peyronie's disease. First results of a case-controlled approach. *Eur Urol*. 2000;38:663-669; discussion 670.
41. Hauck EW, Hauptmann A, Bschleipfer T, et al. Questionable efficacy of extracorporeal shock wave therapy for Peyronie's disease: results of a prospective approach. *J Urol*. 2004;171: 296-299.
42. Palmieri A, Imbimbo C, Longo N, et al. A first prospective, randomized, double-blind, placebo-controlled clinical trial evaluating extracorporeal shock wave therapy for the treatment of Peyronie's disease. *Eur Urol*. 2009;56: 363-369.
43. De Berardinis E, Busetto GM, Antonini G, et al. Extracorporeal shock wave therapy in the

Main Points

- The acute presentation of Peyronie's disease (PD) is treated conservatively, and surgical approaches are only attempted if the following four criteria are met: (1) severe curvature, narrowing, or indentation for more than 1 year; (2) PD stability for at least 3 months; (3) curvature that impedes sexual intercourse; and (4) severe penile shortening.
- There is no standard surgical procedure in PD treatment. Surgical categories being used as therapy options include plication/wedge resection procedures to shorten the convex side of the tunica, lengthening of the concave side with graft material, or implantation of penile prosthesis for men with severe erectile dysfunction caused by PD.
- The acute painful phase of PD should be treated conservatively. Several therapy regimens are available that may stabilize or reduce penile deformity and improve sexual function. Nonsurgical treatment options include oral, topical, intralesional, external energy, and combination therapies.
- The best approach for PD treatment from our point of view is multimodal therapy. Patients who suffer from severe penile deviation, narrowing, or indentation, who report disease stability for at least 3 months, and who specify to have a curvature that impedes sexual intercourse should be advised to undergo surgical correction of PD.

treatment of Peyronie's disease: long-term results. *Arch Ital Urol Androl*. 2010;82:128-133.
44. Levine LA, Estrada CR, Shou W, Cole A. Tunica albuginea tissue analysis after electromotive drug administration. *J Urol*. 2003;169: 1775-1778.
45. Di Stasi SM, Giannantoni A, Stephen RL, et al. A prospective, randomized study using transdermal electromotive administration of verapamil and dexamethasone for Peyronie's disease. *J Urol*. 2004;171:1605-1608.
46. Greenfield JM, Shah SJ, Levine LA. Verapamil versus saline in electromotive drug administration for Peyronie's disease: a double-blind, placebo controlled trial. *J Urol*. 2007;177:972-975.
47. Greenfield JM. Penile traction therapy in Peyronie's disease. *F1000 Med Rep*. 2009;May 8;1. Piii: 37.
48. Levine LA, Newell M, Taylor FL. Penile traction therapy for treatment of Peyronie's disease: a single-center pilot study. *J Sex Med*. 2008;5: 1468-1473.
49. Gontero P, Di Marco M, Giubilei G, et al. Use of penile extender device in the treatment of penile curvature as a result of Peyronie's disease. Results of a phase II prospective study. *J Sex Med*. 2009;6:558-566.