

## Standard Operating Procedures for Peyronie's Disease

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### ABSTRACT

**Introduction.** Peyronie's disease (PD) refers to a penile deformity that is associated with sexual dysfunction.

**Aim.** To provide recommendations and Standard Operating Procedures (SOPs) based on best evidence for diagnosis and treatment of PD.

**Methods.** Medical literature was reviewed and combined with expert opinion of the authors.

**Main Outcome Measures.** Recommendations and SOPs based on grading of evidence-based medical literature.

**Results.** PD is a fibrotic wound-healing disorder involving the tunica albuginea of the corpora cavernosa. The resulting scar is responsible for a variety of deformities, including curvature, shortening, narrowing with hinge effect, and is frequently associated in the early phase with pain. Patients frequently experience diminished quality erections. All of these conditions can compromise sexual function for the affected male. The etiopathophysiology of PD has yet to be clarified and as a result, effective, reliable, mechanistic directed non-surgical therapy is lacking.

**Conclusions.** The management of PD consists of proper diagnosis and treatment, ranging from non-surgical to surgical interventions. The main state of treatment for PD rests at this time on surgical correction that should be based on clear indications, involve surgical consent, and follow a surgical algorithm that includes tunica plication, plaque incision/partial excision and grafting, and penile prosthesis implantation. **Levine LA and Burnett AL. Standard operating procedures for Peyronie's disease. J Sex Med 2013;10:230–244.**

**Key Words.** Peyronie's Disease; Surgical Straightening of Penis; Plication Procedures; Plaque Incision or Excision with Grafting; Penile Prosthesis

### Introduction

Peyronie's disease (PD) specifies a condition of penile deformity characterized by the presence of a fibrous inelastic scar of the tunica albuginea of the corpus cavernosum. Observed deformities include curvature, shortening, narrowing, and hinge effects. Erectile dysfunction (ED) is a frequent manifestation of the clinical condition. Penile pain is also a common feature, although this phenomenon resolves in most patients within 6–18 months after onset. Pain and deformity progression are features of the early stages of the condition, whereas pain resolution with either deformity regression or stabilization characterizes its late stages.

### Epidemiology

PD is common, with a prevalence that is in the range of 3–9% of adult men [1,2]. The condition

exacts emotional and psychological consequences on the patient and partner. Dupuytren's disease is an associated collagen disease. Other comorbid conditions which have been reported to occur in the man with PD include diabetes mellitus, hypertension and dyslipidemia, and hypogonadism [1–3].

### Pathophysiology

According to current thought, PD is considered a wound-healing disorder that occurs in genetically susceptible individuals following penile trauma [4]. An inflammatory component develops in the early stages of the condition, and this biological process is associated with the subjective pain complaint. Multiple molecular factors are known and are under study that account for the pathologic transformation, including various cytokines and free radicals that lead to unregulated deposition of

extracellular matrix (e.g., fibronectin, collagen) resulting in plaque formation. The normal distribution of elastin within the tunic is also disrupted, contributing to the inelastic nature of the scar tissue (plaque).

### Clinical Diagnosis

There is neither an established, internationally accepted standard evaluation for PD nor is there an accepted norm for reporting on treatment outcomes. Levine et al. suggested a standardized form of evaluation that addressed history, physical examination, diagnostic imaging, and non-validated questionnaires [5]. Although no validated questionnaire currently exists, there is one which is in the final phase of the validation process. In general, questionnaires should address deformity, sexual function, impact of disease, as well as treatment satisfaction. The current domains of the patient reported outcome PD questionnaire being developed by Auxilium Pharmaceuticals Inc. (Malvern, PA, USA) for Xiaflex (clostridial collagenase product) include: psychological and physical symptoms, penile pain, and PD symptom bother [6].

*History* should address the estimated time of onset, what the initial presenting symptoms were and how they presented, including: pain, deformity, and/or palpable lump. The patient should be asked about any recognized penile trauma that may have preceded the onset of symptoms by days to months. Remote injuries are unlikely to activate recent scarring. Expert opinion has indicated that no more than 20–30% of patients presenting with PD recall any specific event where the penis was injured, most commonly occurring during intercourse, but may occur following blunt trauma to the flaccid penis as well. Determining whether there is a family history of PD disease or other fibrotic disorders such as Dupuytren's is also useful to obtain. Although no clear genetic predisposition has been identified, it does appear to occur more frequently amongst males in the same family and through generations. The patient should be queried as to whether they have had any other treatment for the PD.

Importantly, questions regarding their current and pre-PD erectile status are useful. Therefore, the patient should be asked to grade his erection (0–10 scale recommended) before they developed PD, and what their current rating of rigidity would be at presentation. It is not uncommon to find diminished rigidity in a large proportion of

patients with PD, but full ED is unusual when there were good pre-PD erections. Diminished rigidity may be associated with a variety of underlying medical conditions which are also found with ED, including: diabetes, hypertension, dyslipidemia, and a history of smoking, but may also be of psychogenic etiology given the devastating effects that PD has psychologically on the affected individual [7,8]. Further questions should address other areas of sexual dysfunction including: ejaculation, orgasm, and change in sensation.

It is useful to ask the patient to estimate the degree and direction of penile curvature when erect. It has also been reported that patients with PD tend to overestimate their degree of curvature, making objective measures necessary to properly counsel patients [9]. Indentation, hinging, or buckling of the erect penis when axial forces are applied, as well as shortening, should also be determined. Shortening appears to occur in 70% of patients presenting with PD, which can be less than a centimeter to as much as 10 cm [10]. Although curvature is considered the most common presenting complaint to the physician, penile shortening tends to be one of the most devastating complications to the patient.

### Physical Examination

The critical part of the *physical examination* is of the phallus. It should be noted whether the penis is circumcised or not. Stretched penile length is useful to obtain because of the concern of further shortening that may occur with this disease and/or as a result of treatment. A variety of techniques of flaccid stretched length assessment have been reported. We recommend the technique described by Wessels et al. where the patient is evaluated in the supine position. The glans is grasped and pulled to full stretch at 90 degrees from the plane of the body [11]. A rigid ruler can be used to press down on the fat pad to the pubic bone, and then the penis is measured dorsally to the corona or meatus depending on physician preference. The patient should also have the hands and feet examined for evidence of Dupuytren's contracture and Ledderhose nodules. Common co-morbidities should be assessed, including: hypertension, diabetes, and hyperlipidemia. Recently, low testosterone has been found to be associated with PD in up to 70% of men [12], but several unpublished reports have not found a significant correlation [13].

Although no standard evaluation for assessment of penile sensitivity has been established, light

touch and biothesiometry can be used. Biothesiometry has been suggested to be an indirect measure of penile sexual sensation, as the vibratory nerves travel with the unique penile sexual sensory nerves. Therefore, an intact vibration sensation should correlate with intact sexual sensation and vice versa. Plaque location should be noted, but measurements of size have proven to be extremely inaccurate with any technique, and rarely have an impact in terms of treatment outcome. Therefore, plaque size assessment is not recommended other than obtaining measures of maximum length and width. Penile imaging with MRI can identify the location and thickness of the plaque, but this study is expensive and at this time there does not appear to be any clinically useful reason to order this test.

#### *Deformity Assessment*

The most important part of the clinical diagnosis is to visually evaluate the penis in the erect state so that objective measures can be made of the deformity. It appears that the most reliable technique is the vasoactive injection-induced erection, as defined by Ohebshalom et al. compared to vacuum-induced or a photographed office or home erection [14]. Duplex ultrasound may also be incorporated into the diagnostic algorithms, as this can be used in the initial evaluation of the flaccid condition looking for corporal fibrosis and plaque calcification [15,16]. Recent reports have suggested that up to 30% of men will have plaque calcification, which, contrary to previous reports, can occur early after initial onset of the plaque and therefore is not an indicator of mature disease, as previously thought [17]. Once an erection is created with a variety of vasoactive agents, including papaverine alone, Tri-Mix (papaverine, phenolamine, and prostaglandin E1), or prostaglandin alone, this will allow assessment of penile vascular integrity as well as determine erectile response to the injected drug. Audio/visual erotic and/or manual stimulation may be used to augment the erectile response. If a full erection does not occur as a result of injection, redosing is recommended to try to obtain an erection that is equal to or better than that which can be obtained at home with sexual stimulation. If necessary, pressure at the base of the penis can be used to enhance rigidity, as some individuals experience significant psychogenic inhibition during direct observation. Curvature is best measured with a goniometer, and a simple string can be used to measure girth at the base, subcoronal area, and any area of indentation or hourglass narrowing.

## **Treatment**

### *Non-Surgical Therapy*

A spectrum of nonsurgical options comprises current management for PD [18–21]. Their success rates are variably known because of several factors. A major confounding issue is the variability in the natural history of the disease with its occasional spontaneous improvement at times such that outcomes are difficult to interpret and generalize. Another limitation is the inconsistent determination of therapeutic success in this field. Well recognized is the fact that purported therapies exert divergent effects on objective measures, including penile curvature stabilization, as well as subjective measures, including penile pain resolution, sexual performance, and interpersonal satisfaction. Further, owing to the incomplete knowledge of the pathophysiology of the disease, the application of rational mechanism-based therapy is restricted. Even for therapies that seem plausible, they are often not supported by rigorous clinical trials that definitively establish their therapeutic success. Quite commonly, clinical trials in this field are compromised by study design limitations including small numbers of subjects, brief follow-up, and lack of a standardized approach for the evaluation and inclusion of patients. As such, definitive conclusions in many aspects surrounding the treatment of this condition are necessarily limited. Notwithstanding these shortcomings, it is reasonable to present here briefly the various purported nonsurgical therapies, i.e., oral, intralesional, and external energy, employed in the management of PD. Recommendations for their applications in clinical practice are appropriately based on clinical evidence or consensus opinion in support of their clinical roles.

Appropriate therapy is considered based on assessments of the patient's erectile status, the presence of bothersome symptoms such as pain, the patient's motivation for treatment, and the patient's overall psychological status [18,19]. The duration of the condition impacts clinical decision-making, and management is often assigned according to whether the condition is evaluated to be in early (<12 months) or late stages after onset. Conservative management is commonly applied for early presentations of PD, taking into account that the condition has a variable natural history and may resolve in some individuals. Historically, spontaneous improvement rates have been reported to be up to 39%, but more recent natural history studies have indicated

**Table 1** Oral therapies

Treatment	Mechanism of action	Adverse effects	Clinical role
Vitamin E	Antioxidant effect; immune modulation	Possible cerebrovascular events, nausea, vomiting, diarrhea, headache, dizziness	No benefit
Colchicine	Inhibition of fibrosis and collagen deposition	Myelosuppression, diarrhea, nausea, vomiting	No benefit
Potassium aminobenzoate	Stabilization of tissue serotonin monoamine oxidase activity; antifibrotic effect (direct inhibitory effect on fibroblast glycosaminoglycan secretion)	Anorexia, nausea, fever, skin rash, hypoglycemia	No benefit
Tamoxifen	Modulation of TGF release from fibroblasts	Alopecia, retinopathy, thromboembolism, pancytopenia	No benefit
Carnitine	Attenuation of collagen fiber deposition and elastogenesis	Seizure, diarrhea, nausea, stomach cramps, vomiting	No benefit
Pentoxifylline	Nonspecific phosphodiesterase inhibition; attenuation of collagen fiber deposition and elastogenesis	Indigestion, nausea, vomiting, dizziness, headache, angina, aplastic anemia, leucopenia, thrombocytopenia	Uncertain benefit

that spontaneous curvature improvement is in the 5–13% range [20]. Beyond surveillance, active nonsurgical therapy is considered adhering to fundamental principles. Indications for nonsurgical therapy include: men with early phase disease (i.e., <12 months in duration) manifest by unstable or progressive deformity and painful erections as well as those not psychologically ready or interested in surgery [21]. Several approaches currently comprise nonsurgical management for PD.

### Oral Therapy

Oral treatments for PD are attractive as non-invasive, simply administered therapy. However, notwithstanding their effecting possible symptomatic benefits, this therapeutic approach has uniformly been unimpressive in addressing penile deformity, the principal outcome variable of the condition. A further difficulty is that the majority of oral agents have been investigated insufficiently, such that further studies are required to substantiate claims of efficacy. The International Consultation on Sexual Medicine has taken a stance in recently published guidelines that oral therapy is not currently proven to be beneficial in the treatment of PD; therefore, this organizational body does not support their clinical use for this condition at the present time [19]. A brief description of the most commonly used oral treatments is provided as follows. Their proposed mechanisms of action, adverse effect profiles, and clinical roles are further summarized in Table 1.

#### Vitamin E

Vitamin E, a fat-soluble vitamin metabolized in the liver, is the most common nonsurgical prescription therapy for PD. Its effect is to limit oxidative stress in tissues and thus a seeming benefit in reducing the actions of reactive oxygen species

known to be increased during the acute and proliferative phases of wound-healing characteristic of PD is presumed. However, recent double-blinded, randomized, placebo-controlled trials showed nonsignificant improvements in pain, curvature, and plaque size [22,23].

#### Colchicine

Colchicine, an anti-inflammatory agent with inhibitory effects on neutrophil microtubules, has been used as primary therapy as well as in combination with other modalities for PD. A randomized, controlled trial showed no improvement in pain, curvature, or plaque size as measured by ultrasound for colchicine as monotherapy [24]. However, colchicine in coadministration with Vitamin E was shown in another double-blinded, randomized trial to induce significant improvements in plaque size, curvature, and pain during the initial phase of PD [25].

#### Potassium Aminobenzoate (Potaba)

Potassium aminobenzoate (Potaba) has been in use for the treatment of PD since 1959, with a putative mechanism of action that is both anti-inflammatory and antifibrotic. Beyond initial reports touting its symptomatic benefits, a more recent study that was double-blinded, randomized, and placebo-controlled suggested that Potaba protects against progression of penile curvature (although it does not improve pre-existent curvature) [26].

#### Tamoxifen Citrate

Tamoxifen citrate is a selective estrogen receptor modulator with either agonist or antagonist effects depending upon tissue-specific estrogen receptor expression. Its additional effect is to work as an antifibrotic agent via direct inhibition of TGF-

**Table 2** Intralesional therapies

Treatment	Mechanism of action	Adverse effects	Clinical role
Corticosteroids	Anti-inflammatory effect, inhibition of phospholipase A <sub>2</sub> , immune suppression	Local tissue atrophy, thinning of the skin, uncommon systemic effects	No benefit
Collagenase	Degradation of interstitial collagens	Injection-site pain, ecchymosis, corporal rupture	Possible benefit
Calcium Channel Blockers	Inhibition of calcium-dependent transport of extracellular matrix molecules (collagen, fibronectin, glycosaminoglycan); collagenase activation; modification of inflammatory response; inhibition of fibroblast proliferation	Nausea, lightheadedness, penile pain, ecchymosis, no cardiovascular adversity	Possible benefit
Interferons	Regulation of immune responses; inhibition of fibroblast and collagen production	Myalgia, arthralgia, sinusitis, fevers, flu-like symptoms	Possible benefit

receptors in fibroblasts. Despite initial enthusiasm for this treatment in studies based on apparent improvement in penile pain, curvature, and plaque size, more recent work involving controlled investigation failed to corroborate these findings [27].

### Carnitine

Carnitine is a naturally occurring metabolic intermediate, which facilitates the entry of long-chain fatty acids into muscle mitochondria. Its hypothesized role to inhibit acetyl coenzyme-A is linked with the repair of damaged cells. A double-blinded, randomized, controlled trial evaluating this therapy alone or in combination with Vitamin E failed to demonstrate improvement in pain, curvature, or plaque size [23].

### Pentoxifylline

Pentoxifylline is a nonspecific phosphodiesterase inhibitor, which exerts anti-inflammatory and antifibrogenic effects by downregulating TGF- $\beta$  and increasing fibrinolytic activity. A report of a double-blinded, placebo-controlled study indicated that the therapy was associated with improvement in penile curvature and plaque volume [28]. This study will require further confirmation.

### Phosphodiesterase Type 5 Inhibitors

Of note, there have been several unpublished reports on the use of daily phosphodiesterase type 5 inhibitors including tadalafil indicating the potential benefit of these agents as antifibrotic drugs reducing progression during the acute phase and possibly reducing curvature in those with a stable deformity [29,30]. Further placebo-controlled trials are necessary before this class of drugs is recommended to treat men with PD.

### Intralesional Therapy

The application of medical treatment directly into penile plaques to induce their regression has represented an alternative non-surgical therapeutic

approach for managing PD. The presumed advantage of intralesional therapy compared with oral therapy is that it permits the direct delivery of a drug to the site of pathology at a higher concentration than that possible by systemic administration. Several drugs have been proposed for this purpose, although much like oral therapeutic considerations for PD affirmation of their optimal clinical roles is awaited. At this time, consensus opinion is that further investigations, principally by way of large-scale, placebo-controlled trials, are required to establish clinical benefit of this therapeutic approach [19]. A brief description of options is provided below, along with a summary of their proposed mechanisms of action, adverse effect profiles and clinical roles (Table 2).

### Corticosteroids

Consistent with the widespread use of corticosteroids in medicine to induce immunosuppressive and anti-inflammatory effects, a role for this treatment for PD would seem plausible. Intralesional dexamethasone was initially used for PD in the 1950s with reports that it decreased plaque size and penile pain. However, subsequent studies did not replicate earlier findings, and investigators determined the effects were either no different than the natural history of the condition or otherwise reflected the mechanical effects of the injection, rather than drug action alone [19]. Additional concerns regarding the local adverse effects of intralesional corticosteroid therapy has diminished support for its use [21].

### Collagenase

Collagenase is a biological agent (also classified as specific matrix metalloproteinase 1, 8, and 13) that enzymatically degrades interstitial collagens. The rationale for its use in PD is to degrade collagen types I and III, which typically occur in PD plaques. An initial report of the use of this agent for the treatment of PD suggested a favorable

alteration of penile plaques and improvement of penile curvature [31], and this success was also observed in another recent uncontrolled study [32]. Intralesional collagenase is currently undergoing investigational trials at a large-scale, multi-institutional level, with aims for governmental regulatory agency approval for PD treatment. The initial reports released by the manufacturer indicate a statistically significant difference with respect to curvature reduction and bothersomeness with the active drug over placebo [33].

#### Calcium Channel Blockers

Calcium channel antagonism as an approach to treat PD is based on the rationale that it regulates calcium-dependent processes associated with fibroblast function and extracellular matrix production, while also exerting anti-inflammatory effects. Levine and colleagues introduced intralesional verapamil therapy in 1994. These uncontrolled trials provided early evidence that verapamil significantly reduces penile curvature [34,35]. However, further investigations have shown less dramatic results [36–39]. Intralesional nifedipine therapy has also been briefly studied, with demonstrated improvement in penile pain and erectile function but no distinct effects on penile curvature [40].

#### Interferons

Interferons are a class of endogenously produced, low-molecular-weight cytokines involved in immune function. Interest in their use for treating PD derives from their potential to regulate fibroblast function and reduce the production of extracellular collagen. In a single-blinded, multicenter, placebo-controlled parallel study, Hellstrom and colleagues demonstrated that intralesional interferon alpha-2B produced significantly improved pain resolution and penile curvature [41]. Importantly, this study demonstrated that saline injection had little evidence of benefit. *In that less than 9% had measured reduction of curvature with a mean improvement of 9 degrees, which is not deemed clinically meaningful.* Another study comparing this treatment with vitamin E in a prospective, randomized trial did not establish therapeutic benefit [42].

#### External Energy Therapies

Several modalities representing energy sources have been introduced as alternative PD treatments. Their purpose relates to a mechanical action that is directed locally at the site of pathology. Several options in this manner have been pro-

posed. However, similar to the aforementioned oral and intralesional treatments, these therapies have not yet been convincingly established to have clinical roles.

#### Iontophoresis

Iontophoresis refers to the use of an external electric force to electromotively induce the passage of ions through tissue. This technique affords a means to enhance the penetration of topical (transdermal) medications, which are unlikely to infiltrate the tunica albuginea [43]. Its appeal for PD follows demonstrations that it more effectively delivers medication into PD plaques than by topical administration alone and in a less invasive manner than by injection. Reduction of penile deformity by electromotive drug therapy with dexamethasone and verapamil was observed in controlled clinical trials by some investigators [44,45] but not others [46].

#### Shock Wave Therapy

Electroshock wave therapy for PD applies shocks to the penis in hopes of reducing PD plaque size, penile deformity, and pain. Despite early enthusiasm for its potential benefit, controlled investigations have not demonstrated significant improvements in penile curvature and otherwise possible reductions in penile pain [47,48].

#### Penile Traction Devices

The application of mechanical strain on biological tissues modulates connective tissue structure and function via mechanically induced signal transduction pathways and gene regulatory mechanisms. A potential benefit to remodel penile deformity has merit. Early small, non-controlled studies have shown reduction of penile deformity and increased penile length [49,50].

#### Radiation Therapy

Radiation therapy has been in use for the non-surgical management of PD since the 1940s [51]. In an uncontrolled trial, therapeutic success has been claimed primarily with respect to decreasing penile pain [52]. Evidence in support of improving penile curvature remains lacking. This therapy cannot be advocated at this time.

#### Surgical Reconstruction

Indications for surgical reconstruction for men with PD disease include: (i) stable disease, defined as at least 1 year from the time of onset and at least 6 months of no change in the penile deformity; (ii) no penile pain except when there may be a torque-

**Table 3** Indications for surgical correction of Peyronie's disease

- Stable disease (6 months with no pain and stable deformity)
- Compromised or inability to engage in coitus
- Extensive plaque calcification
- Failed conservative treatment
- Wants the most rapid and reliable result

**Table 4** Preoperative surgical consent issues

Set expectations regarding outcome

- **Persistent/Recurrent Curvature-**
  - Goal—"Functionally Straight"—<20°
- **Change in length**
  - More likely shorter with plication vs. grafting
- **Diminished rigidity**
  - ≥5% in all studies—especially with grafting
  - Dependent upon pre-op erectile quality
- **Decreased Sexual Sensation**
  - Common but infrequently reported to compromise orgasm/ejaculation

like pressure pain that occurs in men who have strong erections; (iii) those who are unable to or have compromised ability to engage in coital activity due to deformity and/or inadequate rigidity; (iv) men who have failed conservative therapy and wish to have correction; (v) those who have extensive plaque calcification (recently defined with a new grading system); and (vi) those men who desire the most rapid and reliable result once they have stable disease (Table 3) [19,53]. The preoperative consent is critical, as patients with PD are frequently distressed and emotionally devastated. Therefore, having a frank discussion with the patient is important so that he understands the possible limitations of the operation, and this should also help him set appropriate expectations regarding those outcomes [19,54].

The following items should be discussed while obtaining a preoperative consent, including: (Table 4)

1. *Persistent or recurrent curvature*, which is unusual but has been shown to occur in 6–10% of men [19,55]. The patient should understand that the goal is to make them "functionally straight," which has been loosely defined as a residual deformity of 20 degrees or less. This number has not been globally accepted, but seems reasonable based on expert opinion.
2. There could be a *change in penile erect length*, which is more likely to occur with plication vs. grafting procedures. All surgical correction procedures have been associated with some

length loss, even with grafting. Therefore, the patient should be well aware of the potential for additional length loss, as 70–80% of men with PD initially present with loss of length due to the fibrotic disease process [19,54].

3. *Diminished rigidity* has been reported in at least 5% in all cases, and has a higher probability in those undergoing any type of grafting procedure. More modern studies over the past 10–15 years have suggested that with proper patient selection, up to 30% of men may have some postoperative loss of rigidity, which usually responds to PDE5 inhibitors. Should the patient already have significant ED, then they should be aware that their rigidity will not likely be made better by the procedure and may be made worse, and therefore consideration for penile prosthesis should be discussed as well [19,55].
4. *Decreased sexual sensation* has been examined and reported upon infrequently in the literature, but it does appear that around 20% of men will describe some reduction in penile sensitivity, rarely interfering with orgasm and ejaculation. Typically, sensory change (hypesthesia, hypoaesthesia) may occur in the acute postoperative period, but tends to resolve over the ensuing months [56].

Several surgical algorithms have been published and are summarized as follows [57–59]:

In those men who have rigidity which is adequate for coital activity with or without pharmacotherapy, then: (Table 5)

1. *Tunica plication techniques* are recommended for those who have a simple curve of less than 60–70 degrees, no hourglass or hinge effect, and when the anticipated loss of length would be less than 20% of total erect or stretched length.
2. *Plaque incision or partial excision and grafting* is recommended for those men with more

**Table 5** Peyronie's disease surgical algorithm

- I. When rigidity adequate preoperatively with or without oral pharmacotherapy:
  - A. **Tunica plication when—**
    - i. Curvature <60–70°
    - ii. No destabilizing hour-glass or hinge
    - iii. Predicted loss of length <20% erect length
  - B. **Plaque Incision/Partial Excision and grafting when—**
    - i. Curvature >60–70°
    - ii. Destabilizing hinge
    - II. When rigidity suboptimal
  - A. **Penile prosthesis implantation**

complex curves greater than 60 degrees and have a destabilizing hourglass or hinge effect. Importantly, what has clearly emerged in the literature is that these men should have strong sexually induced rigidity to reduce the likelihood of postoperative ED [60,61].

### Surgical Plication Techniques

Multiple surgical plication techniques have been offered for PD, beginning with the Nesbit procedure, which is a form of excision of tunica on the contralateral side to the curvature [62]. In the circumstance of the man with a ventral curve, once Buck's fascia has been elevated, small wedges of the tunica albuginea are excised, and then the defect is closed, typically with a permanent suture. Variations on this procedure have evolved, including the Yachia technique, which utilizes the Heineke-Mikulicz technique [63]. As an example, in a man with a dorsal curvature, a short full-thickness vertical incision is made on the ventral shaft tunic opposite the area of maximum curvature, which is then closed transversely to shorten the ventral aspect and correct the curvature.

The 16-dot procedure has also been presented where there is no incision but the tunica albuginea is plicated with permanent suture using an extended Lembert-type suture technique [64,65].

Another variation is a modification of the Duckett-Baskin tunica albuginea plication (TAP), which was originally used for children with chordee and has been modified for PD, where a partial thickness incision is made transversely on the contralateral side to the point of maximum curvature [66,67]. A pair of transverse parallel incisions are made from 1–1.5 cm in length down through the longitudinal fibers but does not violate the circular fibers of the tunic. These incisions are separated by 0.5–1.0 cm and the longitudinal fibers between the two transverse incisions are removed so as to reduce the bulk of the plication. This procedure can be done with a combination of permanent and absorbable sutures.

The key is that all plication procedures shorten the long side of the penis and therefore can result in loss of length on that aspect. Studies have examined the loss of penile length using the TAP technique where the factors which predicted loss of length were direction of curvature and degree of curvature [68]. Therefore, those men who have a ventral curvature of greater than 60 degrees tend to have the greatest potential loss of penile length.

The drawbacks of any tunica plication procedure for PD are that it does not correct shortening and potentially may enhance loss of penile shaft length. It does not address hinge or hourglass effect and may exacerbate it, resulting in an unstable penis. In addition, there can be pain associated with the knots and, as noted, a potential for tactile and sexual sensitivity changes [19,56]. Review of the literature over the past 10 years indicates that surgical straightening with a variety of plication procedures can be expected in 85–100% of patients, the risk of new ED is 0–13%, and diminished sensation is reported in 4–21%, with follow-up of up to 89 months.

The International Consultation of Sexual Medicine presented their recommendations regarding plication procedures in July of 2009, and reported that there was “no evidence that one surgical approach provides better outcomes over another, but curvature correction can be expected with less risk of new ED” compared to grafting procedures [19].

### Incision or Partial Excision and Grafting

Indications for incision or partial excision and grafting for surgical correction of PD include most importantly that the patient must have good preoperative erections [60]. This can be determined during the patient interview, where he is asked directly: “if your penis was straight, would the quality of rigidity that you currently have allow intercourse?” Should the patient hesitate, the incision and grafting procedure should not be performed, unless he fully understands the risk of more advanced postoperative ED, which may not respond to oral PDE5 inhibitors or intracorporeal injection therapy, requiring subsequent prosthesis placement to attain adequate rigidity.

Other factors have emerged in the literature as possible predictors of postoperative ED, including age of the patient (>55 years), evidence of corporal veno-occlusive dysfunction on duplex ultrasound analysis, with a resistance index of less than 0.80, ventral curvature, and possibly the severity of the curvature [60,61,69]. These suggestions have been offered for the most part in single-center studies with a limited number of patients in each cohort. Regardless, the most critical indication for incision and grafting appears to be the quality of their preoperative erections [60,61,70].

In addition, a curvature of greater than 60 degrees with or without significant shaft narrowing and hinge effect would also be indications for grafting. Patients with extensive plaque calcifica-

**Table 6** Indications for surgical correction with grafting

- No significant loss of erectile capacity
- Curvature >60–70°
- Severe indentation causing unstable erection (hinge effect)
- Extensive calcification
- Understands increased risk of postoperative erectile dysfunction

tion may also require partial plaque excision and grafting, again, if the erectile quality is satisfactory (Table 6).

Surgical grafting techniques include plaque incision or partial plaque excision. Historically, total excision of the plaque was practiced to “cut out the disease,” resulting in onlays of large grafts with an unacceptably high rate of ED. Therefore plaque incision was introduced, where a modified H or double Y-incision is made in the area of maximum curvature [71]. This allows the tunic to be expanded in this area, thereby correcting the curvature and shaft caliber. Occasionally, multiple incisions with grafting are needed to obtain satisfactory straightening, or plication may be used for optimal correction of deformity.

Partial plaque excision has been also suggested, where the area of maximum deformity, particularly if it is associated with severe indentation, is actually excised, and then the corners of the defect are darted in a radial fashion to enhance correction of narrowing in that area. Geometrical principles have been applied to the grafting technique in an effort to obtain a reliably sized graft, but there have been reports of a higher rate of ED when this technique is used [61,72]. Regardless, it is recommended that the defect should be expanded so as to allow correction of curvature and indentation. The goal of these operations is to limit the trauma to the cavernosal tissue to maintain the veno-occlusive relationship between the cavernosal tissue and the overlying tunic and graft.

The concept of the ideal graft has been debated. At this time, no graft has been identified as perfect. Multiple grafts have been used historically, including fat, dermis, tunica vaginalis, dura mater, temporalis fascia, fascia lata, saphenous vein, crura, and buccal mucosa, which are harvested from the patient [71,73–81]. These have fallen out of favor because of a need for extended surgery to harvest the graft as well as a second incision to close, which has potential complications of healing, scarring, and possible lymphedema. Synthetic grafts were also used historically, including Dacron and polytetrafluoroethylene (PTFE). These are not recommended now, as there is the potential risk of

infection, as well as localized inflammation, fibrosis and reaction to the presence of the synthetic graft [82]. Finally, “off-the-shelf” allografts and xenografts have emerged, including processed pericardium from a bovine or human source, porcine intestinal submucosa, and porcine skin. The two most common grafts currently used are Tutoplast™ (IOP Ophthalmics, Costa Mesa, CA, USA) processed human and bovine pericardium, which has the advantages of being thin and strong, does not contract, and has a virtually absent reported infection or rejection rate, and small intestinal submucosa (SIS) grafts (Surgis ES, Cook Urological, Spencer, IN, USA), which has similar advantages to pericardium, except that it is known to contract in size up to 25% and has been associated with recurrent curvature [56,83–88].

#### *Operative Technique for Grafting*

Once the surgeon has obtained informed consent, the patient is positioned supine on the operating table under general anesthesia. An artificial erection is created with the aid of saline or an intracavernosal injection of a vasoactive agent (papaverine, prostaglandin E1 or TriMix). An infusion pump is also beneficial, as the saline can augment the effects of the vasodilating agent and give a clear view of the deformity in the fully erect state. The penis is then degloved. The most common practice is a subcoronal circumferential incision allowing degloving of the penis to Buck's fascia. Buck's fascia can then be elevated via two techniques. One is by harvesting the deep dorsal vein and then elevating Buck's fascia off of the dorsal aspect of the penis [54]. This approach does not always allow adequate exposure of the ventral-lateral aspect of the shaft, particularly in patients who have severe indentation defects. The more commonly practiced approach is elevating Buck's fascia by making a pair of longitudinal incisions through Buck's fascia and elevating this tissue off of the lateral and dorsal aspect of the penis, leaving the neurovascular bundle intact as a bridge of tissue within Buck's fascia. The deformity can then be thoroughly examined with reinstatement of a full erection with saline infusion if necessary. As noted, a modified H- or double Y-incision can be made with the incision technique or partial plaque excision technique so as to create a rectangular or square defect [72,89]. One of the more critical aspects of the procedure is the careful elevation of the tunica off of the underlying cavernosal tissue. It seems intuitive that excessive damage to this tissue may encourage scarring, which may inter-

ferre with a proper veno-occlusive mechanism, resulting in diminished postoperative rigidity [90]. The corners are darted in a radial fashion so as to prevent cicatrix contracture and to optimize correction of any girth defects. The defect should be measured on stretch at this point by applying stay sutures at the corners of the defect and also at the mid-point of the transverse aspects, both proximally and distally. If off-the-shelf grafts are used, the tissue is sized after rehydration. The graft is then secured to the defects with running absorbable suture. Once this is complete, artificial erection is again created so as to determine if there is residual curvature, and to close any leaks that may be occurring at the graft/tunic interface. If there is substantial residual curvature (>30 degrees), then the surgeon's choice would be to make another incision requiring grafting, or to perform a plication.

The penis should be measured initially prior to creating the artificial erection. The stretched flaccid length is measured using the Wessells et al. technique noted in the physical examination section. This measurement is then performed again the same way after completing the grafting procedure and during follow-up appointments. Of note, Buck's fascia should also be reapproximated, which acts as a structural and vascular support for the graft as well as to tamponade graft suture line bleeding. For those men who are uncircumcised and have no signs of phimosis whatsoever, it has been suggested that circumcision is not necessary, but the surgeon should be aware that even in this circumstance, paraphimosis can occur, and delayed healing may occur as a result of lymphedema [91]. Various dressings have been recommended, including just a simple gauze, but most commonly a Xeroform™ (Covidien, Mansfield, MA, USA) Vaseline antibiotic impregnated gauze is applied over the suture line and then a Coban™ (3M, St. Paul, MN, USA) elastic dressing is lightly applied to the shaft so as to not cause significant compression which could result in postoperative ischemia. This dressing can be changed daily or left in place for several days and then removed, at which point the patient may shower.

#### *Postoperative Rehabilitation*

The postoperative period is critical. Typically a patient is seen 2 weeks after surgery, at which point massage and stretch therapy is initiated [92]. It is recommended that the patient grasp the penis by the glans and gently stretch it and then with his other hand massage the shaft of the penis for 5

minutes twice per day for 2–4 weeks. The massage and stretch can be performed by the patient's partner for the second 2 weeks if possible. Investigators have recommended the use of nocturnal PDE5 inhibitors so as to enhance postoperative vasodilation, which may help support graft take as well as reduce cicatrix contraction [70]. Finally, external penile stretching devices have been encouraged and have been recently shown to actually enhance the likelihood of further length gain with both grafting and plication procedures, but will at a minimum reduce length loss postoperatively [93,94].

In a review of the published reports on grafting for PD over the past 12 years, satisfactory straightening was found in 74–100% of patients, but postoperative ED, which does not have a uniform definition in the literature, has been reported in 5–53% of patients. There are very few reports that address diminished sensation after grafting, and the majority of reports have a follow-up of less than 5 years [55]. In the few single-center surgical outcome reviews with 5 or more years of follow-up, ED has been reported in up to 22–24%, with recurrent or persistent curvature in the 8–12% range [87,95,96].

#### *Penile Prosthesis for Men with PD*

Published surgical algorithms have indicated that when the man with PD has ED that does not respond to medical therapy, that penile prosthesis placement is the procedure of choice [57,59,97]. This procedure allows for correcting the deformity while addressing the ED as well. This provides the patient with a functional penis both in terms of erect configuration and rigidity. Penile prosthesis placement can be performed without additional straightening maneuvers, especially for men who may have minimal curvature or simply have an unstable penis because of indentation or hourglass deformity. In those who have substantial curvature, the recommended first step is manual modeling, as initially reported by Wilson et al. [98]. If after modeling there is residual curvature in excess of 30 degrees, then an incision in the tunica albuginea overlying the area of maximum curvature can be made, which should correct the residual curvature and likely also correct associated indentation. Although there is no standard here, it has been recommended that if the incisional defect is greater than 2 cm in any dimension, then a biograft should be placed over the defect to prevent cicatrix contracture of the incision or herniation of the prosthesis (Table 7) [97].

**Table 7** Algorithm for prosthesis placement

- 
- Placement of inflatable prosthesis
  - Manual modeling
  - Tunica incision
  - Grafting of incision defect if >2 cm with biograft
- 

An inflatable penile prosthesis appears to be the preferred surgical implant, as the pressure within the cylinders allows for superior correction of curvature with manual modeling, as well as more acceptable girth enhancement [98]. Historically, when malleable prostheses were used for PD, there have been reports of complaints of a narrow, cold, less than natural erection [99].

Manual modeling via the penoscrotal approach is recommended with a high-pressure inflatable cylinder, but all available three-piece and two-piece devices have been used successfully to correct deformity. The prosthesis cylinders should be placed first. The surgeon may choose to close or leave the corporotomies open during the modeling process. Using a surrogate reservoir attached to the pump tubing, the prosthesis can be filled to full rigidity, which will allow visualization of the deformity. To protect the pump from the high pressures that may occur during manual modeling, shodded hemostat clamps can be applied to the tubing between the pump and the cylinders. The penis is then bent in the contralateral direction to the curvature. It is recommended to try to hold the penis in this position for 60–90 seconds, but experience has suggested that around 30 seconds may be all that is possible. Regardless, once the modeling is performed, the penis can be reassessed by inflating more fluid, reapplying the hemostats, and then performing the modeling procedure repeatedly until satisfactory curvature correction is attained. The modeling technique should be a gradual bending rather than a violent maneuver, as this will reduce the likelihood of inadvertent tearing of the tunica or injury to the overlying neurovascular bundle. Wilson has demonstrated in two published articles that urethral injury can occur with this technique [98,100]. This appears to be associated with distal extrusion of the prosthetic cylinders at the fossa navicularis. To reduce the likelihood of this, the bending hand should be not positioned on the glans, but rather on the shaft, to avoid downward pressure on the tips of the cylinders. The other hand should be grasping the base of the penis with pressure over the corporotomies, which will provide support to this area and reduce the likelihood of disruption of the suture line.

Published reports on the use of modeling have indicated that sensory deficits after manual modeling are rare, but are a potential complication that should be discussed with the patient preoperatively [101]. Although it would appear that for more severe curvature that more advanced techniques will be necessary, published experience has suggested that curvature correction may be obtained using manual modeling regardless of the curvature. Therefore modeling should be used as first-line therapy for correction of curvature. An alternative to this would be to perform a tunica plication such as the 16-dot suture technique contralateral to the curvature before placement of the prosthesis so as to correct curvature [102].

When there is residual curve of greater than 30 degrees or residual indentation causing the inflated cylinder to buckle, tunical incision is recommended after elevating Buck's fascia in that area. The transverse penoscrotal incision will allow access to virtually the entire shaft, so degloving the penis is rarely necessary. The incision is made with the cylinders deflated, using the cautery to release the tunica, but with an effort to preserve the cavernosal tissue over the implant. When Coloplast™ cylinders are used, the energy should be less than 30 watts to reduce potential injury to the polyvinylpyrrolidone Bioflex® cylinders (Coloplast, Minneapolis, MN, USA) [103]. Once the incision is made, the cylinders are re-inflated and further modeling can be performed to optimize deformity correction. Although there is not a clearly accepted approach, grafting over the defect is recommended when the defect is greater than 2 cm in any dimension. This is to reduce the likelihood of cicatrix contraction or cylinder herniation [97]. Historically, synthetic grafts were used, but currently biografts of pericardium or porcine SIS are recommended. Use of locally harvested dermal grafts are not recommended, as there is risk of transferring bacteria to the prosthesis.

Although there have been limited publications looking at long-term results with regard to outcomes and satisfaction with inflatable penile prostheses in men with PD and drug-refractory ED, recently Levine et al. reported on 90 consecutive men undergoing placement of an inflatable penile prosthesis, with 4% having satisfactory straightening with prosthesis placement alone, 79% having satisfactory curvature correction with modeling only, but 4% required a tunical incision, and 12% had incision and grafting for correction of curvature [101]. It did not appear that the additional maneuvers increased the rate of mechanical failure

of the prosthesis or infection. In the non-validated questionnaire used in this study, overall satisfaction was 84%, whereas only 73% were satisfied with curvature correction. This may indicate a flaw in the design of the questionnaire, but may also reflect the general disappointment and frustration of patients with PD, in that obtaining the desired outcome may not be attainable, and therefore setting appropriate expectations preoperatively, as with any prosthesis placement, is critical [104]. It is recommended that discussion is also focused on the goal of obtaining "functional straightness," in which a residual curvature of 20 degrees or less in any direction would likely not compromise sexual activity.

On the other hand, penile prosthesis placement has been reported to be associated with length loss. This is clearly the most common postoperative complaint heard in men who undergo penile prosthesis placement [105]. As the majority of men with PD do lose length, any additional length loss due to the implant may be distressing to the patient and should be discussed preoperatively. For those men who cannot tolerate any further length loss, daily vacuum therapy for several months before inflatable penile prosthesis (IPP) placement has been reported but not yet published. A recent small pilot study using traction therapy before penile prosthesis placement in men with PD as well as other disorders causing penile shortening (e.g., prosthesis explant, radical prostatectomy) did demonstrate that after 3–4 months of daily traction for an average of 3 hours or more per day, that there was no further length loss after prosthesis placement, but the majority had gained some length (0.5–2.0 cm) compared to their pre-traction stretched length [106].

In conclusion, surgical correction of PD with or without prosthesis remains as the gold standard to correct deformity, and in those men with drug-refractory ED, a prosthesis will provide adequate rigidity as well. These men need to undergo a detailed and comprehensive consent process so that the patient will be more understanding of the limitations of the surgery and hopefully more satisfied with their outcome. For those men who have satisfactory preoperative rigidity but who have curvature of less than 60–70 degrees without significant indentation, then some form of tunica plication is indicated. There does not appear to be any one plication technique which has been demonstrated to be superior to others, as no head-to-head comparative trial has been published. In addition, for those men who have more severe,

complex deformity, but who have strong preoperative erectile function and no evidence of venous insufficiency on duplex ultrasound flow analysis, these men should be considered candidates for straightening with plaque incision or partial excision and grafting. The complications associated with these operations include incomplete straightening, recurrent curvature, shaft shortening, diminished penile sexual sensation, and ED. Finally, for those men who have inadequate rigidity and PD, penile prosthesis placement with straightening maneuvers as necessary should be considered first-line surgery.

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