Peyronie's Disease

6

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6.1 Introduction

Peyronie's disease (PD), also known as *induration penis plastica* (IPP), is a clinical condition characterized by the formation of fibrotic plaques onto the tunica albuginea of the penis, which may result into abnormal penile curvature and deformity, erectile dysfunction (ED), and loss of penile length. The combination of these events may result in the impossibility of performing penetrative intercourse [1].

PD is thought to be a form of connective tissue disease deriving from excessive scarring of the tunica albuginea or of the septum of the corpora cavernosa as a reaction to penile trauma; nevertheless, not all patients recall such episodes when reporting their clinical history [2]. Patients suffering from PD most commonly present diabetes, hypertension, hyperlipidemia as comorbidities and smoking, sexually transmitted diseases, and genital tract surgery as risk factors [3].

PD is not rare even though its occurrence is probably underreported. Indeed, its prevalence has been reported ranging between 0.4% and 7% [4] and up to 16% in the subset of patients undergone radical prostatectomy [5]. PD may be an incidental finding in asymptomatic patients or diagnosed in patients with acquired penile curvature or/and ED, taking a complete medical and andrological history and a focused physical examination of the penile shaft. The correct assessment of the entity of the penile curvature and deformity, as well as of erectile function, especially prior to a planned surgical treatment, requires the evaluation of the penis during erection. So, intracavernous injection and penile Doppler ultrasonography (PDUS) [6] represent the gold-standard diagnostic evaluation.

6.2 Pathophysiology

Although PD was first described by the French surgeon Francois Gigot de la Peyronie in 1743 [7], its pathophysiology remains under investigation. The progression of the disease seems to reflect an alteration of the physiological balance between fibrosis and fibrinolysis in tissue repair processes, resulting in the formation of fibrotic

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plaques [8]. The underlying mechanisms are thought not to be exclusive to PD, given a significant overlap in pathology, occurrence, and epidemiology between PD and other localized fibrosing afflictions such as Dupuytren and Ledderhose disease [9].

PD evolution includes two distinct phases: the acute phase is defined by the presence of inflammation and pain, while the chronic phase mainly leads to fibrosis and calcification, with resolution of pain and stabilization of penile deformity [10].

The acute phase is believed to be triggered by microtrauma delivered to the penile tunica albuginea, most commonly during sexual activity. The structure of the tunica albuginea is damaged through delamination of fascial layers. This results in a release of pro-inflammatory mediators (TGF-β, IL-1, FGF, PDGF, PAI-1 as well as reactive oxygen species) involved in wound healing which generate platelet aggregation, clot formation, and local recruitment of inflammatory cells [11]. Alterations in the levels of growth factors and cytokines released in these instances are responsible for the imbalance between extracellular matrix (ECM) deposition, myofibroblast proliferation, and myofibroblast apoptosis which is at the core of this phase [12].

The altered repair processes of the first phase result in the formation of dense fibrotic plaques which may also progress to calcification, stabilizing, or worsening the penile curvature [13]. The bone-like nature of the calcified tissue is thought to be due to the recruitment of osteoblast-like cells from the vascular lumen or to the upregulation of the osteoblast-specific factor 1 gene [14, 15]. Cavernosal hypoxia is also considered as a possible explanation for the aberrations in local collagen deposition, such as those found in patients who underwent radical prostatectomy and developed PD afterwards [16].

Current knowledge on the matter of molecular pathways of inflammation and fibrosis still seems not enough clear. Indeed, penile trauma does not always result in PD [17], and PD patients do not always have a history of penile trauma. This fact, along with an uneven prevalence across ethnicities and the noted correlations with other fibroproliferative diseases, has prompted research in genetics, mainly in the fields of HLA group antigens, autoimmunity, single nucleotide polymorphisms and karyotype aberrations. Nevertheless, results in this field have been inconclusive [18].

6.3 Epidemiology

PD shows variable rates of occurrence depending on country of origin and age group. Its reported prevalence in general male population ranges between 0.4% and 7%, but is likely to be underestimated due to underreporting [4]. As for ethnic differences, the reported prevalence is 0.4–3.2% of men in the United States [19], as opposed to 0.6% of Japanese men [20]. Indeed, it seems to be more frequent in Caucasians [21].

PD distribution also changes with age. A large study performed in Germany on over 8000 patients by administration of a questionnaire showed that PD prevalence was 1.5% in 30–39 year-old males, 3.0% in 40–59 year-old males, 4.0% in 60–69 year-old males, and 6.5% in men older than 70 years [19]. It is worth mentioning that PD can also occur in teenagers (15–19 years old), often causing high emotional distress levels and more commonly appearing with an increased number of plaques at presentation [22].

Comorbidities associated with PD include diabetes [23], smoking [24], and Dupuytren's disease [25]. Patients suffering from diabetes seem more prone to experience severe PD [23]. Hypertension and hyperlipidemia have been inconstantly associated with PD [24] while there seems to be a strong link between obesity and PD [26]. Penile trauma, both deriving from sexual activity or iatrogenic in nature (catheterization, cystoscopy, and TURP) is the most reported risk factor for PD [24, 27] reaching a 16% incidence in men having undergone radical prostatectomy for prostate cancer (16%) [5].

6.4 Clinical Presentation and Medical Evaluation

PD patients usually seek medical evaluation because of penile pain during the erection, penile bending or complex deformity, loss of penile length, and presence of palpable areas of indura-

tion on the penile shaft [28]. Patients may come to the attention of the specialist during the acute phase, in which penile pain and progressive deformity are the main complaints, or during the chronic phase, in which pain is mostly absent and complaints include penile deformities and the impossibility of having regular penetrative intercourse due to excessive bending or penile structural instability [2]. Erectile dysfunction is also present in up to half of men with PD, though it is still object of debate whether PD is a cause of ED or the other way around [29].

PD may generate a significant psychological distress in the affected patient leading to depression, anxiety, avoidance, and lowered self-esteem in intimate situations, partner and relationship problems, and dissatisfaction with sexual activity [30].

History and physical examination are needed to a correct diagnosis and evaluation of PD [31]. History taking should include past medical occurrences and identification of known PD risk factors such as penile trauma, palmar or plantar fibrosis, diabetes, hypertension, and smoking habit. The patient should be asked about the presence or absence of penile pain, and time of deformity onset or eventual stability in order to initially define whether the disease is in an acute or chronic phase. There are specific questionnaires which may aid the specialist in keeping track of all valuable information, such as the Peyronie's disease questionnaire (PDQ) [32]. Other ancillary questionnaires such as the International Index of Erectile Function (IIEF) or Erection Hardness Score (EHS) may prove useful in objectively assessing the sexual function of the patient [2].

Laboratory testing may turn useful in identifying underlying diseases related to PD and ED; they include a complete blood count, a glucose and lipid profile, and total testosterone [33]. Given the usual patients' age, it is worth assessing also serum Prostate-specific Antigen (PSA).

When performing a physical examination in a patient with suspected PD, the focus should be on the penile shaft with palpatory assessment of deformities and areas of abnormal consistency or plaques. The examination should be carried out along the entire length of the shaft, from the pubis to the glans, and may include a Stretched Penile Length (SPL) measurement in the usual fashion—from the pubis to the coronal sulcus—for future reference [2].

The objective evaluation of the degree and entity of the penile curvature or deformity necessitates measurements to be taken when the penis is erect. Patient-provided self-photographs are a viable solution but the quality of the images may be insufficient, leading to incorrect assessments [34]. This may be of utmost importance in patients seeking active curative interventions, in which accurate evaluation of penile deformity is required to choose the correct therapeutic strategy. In-office intracavernous administration (ICI) of an erectogenic agent allows a specialist to perform objective assessment not only of erectile function but also of penile curvature, for example, with the aid of a goniometer, establishing the point of maximum curvature, the degree of penile torsion, and the presence of indentation, hourglass deformity, or "hinge" effect in the case of a planned surgical intervention [31].

As for imaging in PD evaluation, PDUS may aid in the detection and measurement of plaques and their size, although it is often inaccurate and operator-dependent [35]. Most importantly, it can be useful prior to treatment in order to assess penile hemodynamics, especially in the presence of ED. Information obtained through PDUS can be useful for the specialist when selecting the best therapeutic approach while correctly managing the patient's expectations [36].

The other available imaging techniques are not suitable for everyday clinical practice and anyway are all considered inferior to in-office US. Computed Tomography (CT) allows for good visualization of calcified penile plaques, but it is less useful in non-calcified plaques and in the evaluation of soft tissue and degree of inflammation. It is also expensive in terms of time and resources. Magnetic Resonance Imaging (MRI) is the best instrument when needing to visualize soft tissue, areas of inflammations, and non-calcified plaques but its high cost of money, time, and resources far outweighs its benefits [37].

6.5 Non-surgical Treatment for Peyronie's Disease

The main objective of conservative treatment is to prevent disease progression and relieve pain in patients in early stage or in patients who decline other treatments during the active phase.

Non-surgical treatments are as follows: oral medications, topical medications, traction therapy, extracorporeal shock wave therapy, electromotive drugs, intralesional injections, and vacuum erection device. There are several studies on conservative treatments and often their results are contradictory, not allowing to provide recommendations in real life.

6.5.1 Oral Medications

6.5.1.1 Phosphodiesterase Type 5 Inhibitors (PDE5is)

PDE5is are thought to reduce collagen deposition and increase apoptotic index through the inhibition of TFG-b1 [38, 39].

In a retrospective study, PDE5is were administered to 65 patients with penile septal scars; the results showed that those who received therapy had improvement in erectile function, in the reduction of the curvature and resolution of scars (69%) [40]. Unfortunately, there is no prospective RCT that compares PDE5is with placebo.

6.5.1.2 Nonsteroidal Anti-inflammatory Drugs (NSAIDs)

NSAIDs should be offered in active phase of PD to manage penile pain.

6.5.1.3 Coenzime Q10

Coenzime Q10 is hypothesized to prevent the accumulation of free radicals and scar formation in acute PD. One RCT compared Q10 with placebo and found a statistically significant improvement in erectile function and reduction in mean plaque size (40%) in patients to whom was administered Q10. The EAU does not support this treatment.

6.5.1.4 Vitamin E

Vitamin E has antioxidant activity and is hypothesized to have antifibrotic effect reducing circulating free radicals. Vitamin E lacks sufficient evidence. One clinical trial compared Vitamin E with placebo: the results indicated that there was no statistically significant reduction in angulation, pain, or plaque size [41]. The EAU Panel does not support it because of its lack of efficacy.

6.5.1.5 Colchicine

Colchicine is thought to have antifibrotic effects by activating collagenase production and preventing collagen synthesis [42]. Unfortunately, the only RCT available that compares colchicine with placebo does not show significant reductions in angulation, pain, or plaque size [43]. The EAU panel does not support it because of its lack of efficacy.

6.5.1.6 Para-aminobenzoacidic Potassium (POTABA)

POTABA has anti-inflammatory and antifibrotic effects [44]. It is suggested that POTABA can reduce collagen formation. There is only one RCT which concluded that POTABA may reduce plaque size compared to placebo, with no improvement in penile curvature [45]. POTABA has a large amount of side effects; the most common is gastrointestinal distress. The evidence of this treatment is weak, in fact the EAU Panel does not support it.

6.5.1.7 Carnitine

Carnitine has an anti-inflammatory and antifibrotic effect. One RCT compared Carnitine with placebo and found no statistical differences in penile angulation, pain, or plaque size. The EAU Panel does not support this oral medication because of its lack of evidence.

6.5.1.8 Tamoxifen

Tamoxifen is thought to reduce fibrogenesis by increasing the TGF-Beta concentration. The only one RCT that compared tamoxifen with placebo found no statistical difference in penile angulation and pain [46]. Because of its lack of efficacy, the EAU Panel does not recommend tamoxifen for PD.

6.5.2 Topical Medications

There isn't enough scientific evidence that topical treatments (Verapamil, H-100 Gel) applied to the penile shaft with or without iontophoresis can be absorbed by the tunica albuginea and change the course of PD. The EAU Panel in fact does not support this type of treatment for PD.

6.5.3 Extracorporeal Shock Wave Therapy (ESWT)

The exact mechanism of action of Li-ESWT is not known: it is assumed that shock waves may generate nitric oxide and increase vascular endothelial growth factor (VEGF) [47]. Four RCT and one meta-analysis assessed the efficacy of ESWT for PD: from these studies, the only consistent outcome is improvement in pain [48–51].

6.5.4 Mechanical Devices

6.5.4.1 Penile Traction Therapy

Penile traction therapy (PTT) is based on mechanotransduction, according to which stretching forces cause collagen remodeling through decreasing myofibroblast activity and upregulating matrix metalloproteinase [52, 53]. There are two prospective randomized trials on PTT [54, 55] that found improvements in curvature and in stretched penile length. The treatment can result in discomfort due to use of the device for 2–8 h daily. Side effects are generally mild, including local discomfort or glans numbness. PTT seems to be effective and safe, but it is not possible to give any definitive recommendation because of the heterogeneity of the study designs and nonstandardized inclusion and exclusion criteria that not allow to draw any definitive conclusions.

6.5.4.2 Vacuum Erection Device

Vacuum erection device seems to affect intracorporeal molecular markers like TGF-b1, collagenase, hypoxia-inducible factor-1a, eNOS. There are no randomized controlled trials using VED to treat PD. The limited data available appear to support improvement in penile curvature and stretched penile length, but further investigation is needed [56].

6.5.5 Intraplaque Injection

6.5.5.1 Collagenase Clostridium Histolyticum (CCH)

CCH is a purified bacterial enzyme that degrades collagen that is the primary component of the PD plaque. In 2014, the EMA approved CCH for the nonsurgical treatment of stable phase PD in men with dorsal palpable penile plaque of 30–90°. Two trials, IMPRESS I and IMPRESS II, found improvement in curvature and PDQ scale (used to assess QoL in PD), with no change in pain or erectile function [57]. During these studies, patients underwent two injections 24–72 h apart, repeated in four treatment cycles with penile modeling. The greatest chance of curvature improvement is for curvatures between 30° and 60°, no calcification, IIEF > 17, longer duration of disease [58]. Regarding side effects, the studies have found several common mild or moderate adverse reactions localized to the penis (penile hematoma, penile pain, and penile swelling). Serious adverse events (0.9%) include penile hematoma and corporeal rupture that require surgical treatment; to avoid these adverse events, the patient should be advised to avoid sexual intercourse in the 4 weeks following injection. Recently, the company has withdrawn the product form the European market.

6.5.5.2 Interferon Alpha

IFN-alpha 2b is hypothesized to treat PD through a fibroblast proliferation decreasing. Furthermore, it seems to reduce extracellular matrix and collagen production, increasing collagenase synthesis by fibroblast [59].

One study found greater improvement in curvature and plaque size among men treated with INF-alpha 2 vs placebo [60]. Intraplaque injection with INF-alpha 2b provides a >20% reduction in curvature, regardless of plaque location. The EAU panel recommends this treatment for stable phase PD.

6.5.5.3 Calcium Channel Blockers (Verapamil, Nicardipine)

CCBs is hypothesized to inhibit calcium dependent extracellular collagen transport and to upgrade the collagenase activity [61]. FDA has not approved verapamil in the treatment of PD. One trial exists for nicardipine with promising results.

6.6 Surgical Treatment for Peyronie's Disease

Surgery represents the most effective treatment for severe penile curvature caused by Peyronie's disease. Its aim is to obtain a penis straight enough for a satisfactory intercourse while preserving sufficient rigidity.

Surgery is recommended when penile deformity and/or reduced erectile function make intercourse difficult or impossible or painful for the partner (dyspareunia). Surgery should be carried out when the disease is "stable" meaning there has been no change in the curvature over the last 6 months, otherwise the "wait and see" attitude is preferred [62, 63].

As mentioned above, dynamic penile color-Doppler sonography allows proper assessment of the integrity of arterial inflow and veno-occlusive mechanism, site and degree of curvature, penile length, and overall deformity such as hinge or hourglass. All such data are useful in choosing the ideal surgical procedure [36, 64].

Accurate patient counselling is essential to explain potential sequelae such as penile shortening, erectile dysfunction, recurrence of curvature, and palpation of stitches underneath the skin. The patient should also understand that surgery is not meant to fully restore the penis to its original shape and dimension, but rather to allow a return to satisfactory sexual intercourse [65, 66].

Based on clinical data and patient's counselling, surgery may consist in:

- Shortening procedures
- Lengthening procedures with grafting
- Penile prosthesis implant potentially associated to further manoeuvres [67]

The choice between techniques is based on curvature shape and severity as well as erectile function.

6.6.1 Tunical Shortening Procedure

Shortening procedures are offered to patients with a <60° curvature, no hinge or hourglass deformity, no erectile dysfunction, and a penis long enough not to suffer from the expected shortening [67].

Shortening procedures aim at giving the long (convex) side of the penis the same length of its short (concave) side [68].

In 1965, Nesbit described a procedure for the correction of congenital penile curvature based on an elliptical excision of the tunica albuginea of the long side of the penis at the site of the angle of greatest curvature. The tunical defect was closed with permanent sutures and additional absorbable sutures if needed [69].

Yachia proposed a modification whereby Nesbit's elliptical excision was replaced by a full-thickness longitudinal incision of the albuginea, which was then closed horizontally according to the Heineke-Mikulicz procedure. Depending on the degree of curvature, one or more incisions are needed; in any case, the incisions should be shorter than 1 cm to avoid creating a "dog ears" effect [70].

Non-incisional procedures in which tunical shortening is obtained by plication without incision have been developed to avoid any potential damage to the underlying erectile tissue. Essed and Schroder proposed tunical plication by placing non-resorbable figure-of-eight sutures that should reduce the perception of the knots at penile palpation [71]. In 2002, Gholami and Lue introduced the 16-stitch (two pairs) or 24-stitch (three pairs) procedure, depending on the length of the side of the penis and the degree of angulation of the curvature, as a different mean of plicating tunica albuginea. The rationale of this procedure was distributing tension to a greater surface area of tunica albuginea contralateral to the fibrotic plaque. They reported a 96% satisfaction rate and a 93%

straightening rate in 116 patients. In this series, the shortening rate was 41% and the estimated recurrence rate 15% [72].

In 1985, Ebbehoj and Metz proposed a plication technique in which an "introflecting" double cross-over stitch of 2/0 Prolene grasping deep into the tunica in four positions was used. The employment of an introflecting knot greatly reduced the perception of penile shaft knots by the patients: in fact, this principle has been widely adopted in following adaptations of tunical plication techniques [66].

For all procedures, the first step should be exposure of Buck's fascia. Circumcision and degloving are usually preferred but, occasionally, longitudinal penile shaft incisions may be used in patients with minor curvatures who would like to avoid circumcision. For dorsal and ventral curvatures, mobilization of urethra or neurovascular bundle, respectively, are recommended to properly expose the curvature to be treated. Artificial erection is needed throughout the procedure and is usually obtained by injection of saline into the corpora while manually compressing the crura; avoiding the use of a tourniquet at the base of the penis provides a more reliable profile of the erect penis [73].

Compared to lengthening procedures, shortening procedures require less surgical time. Shortening procedures provide good aesthetic results, reduce risk of postoperative stiffness loss, and constitute a simple and safe solution with effective straightening. The overall short- and long-term results of shortening techniques are satisfactory with surgical straightening achieved in 79–100% of patients.

Reduction of the final penile length and difficulty in correcting complex curves such as hourglass or hinge curves are considered the main disadvantages. Especially the former can sometimes lead to patients' dissatisfaction, because of subjective comparisons with the size and the shape of their penis as remembered before the development of the Peyronie's disease. Other less common complications include hematoma in up to 9%, decreased sensitivity from 4% to 21%, urethral injury in less than 2%, and phimosis in up to 5% of patients.

Additional penile shrinkage up to 17% has been reported and recurrence of significant penile curvature deformity has been reported up to 12%. In addition, eventual suture granuloma can generate pain at the affected site. The reported risk of new EDs ranges from 0% to 38% and often depends on baseline functional data.

ED can be explained by the fact that the scarring of a healthy tissue may result in anatomical and functional damage to the corpus cavernosum [74–76].

To this day, no technique has been proven clearly superior. The International Consultation on Sexual Medicine (ICSM) of 2010 states, in regard to penile shortening procedures, that there is no evidence that one surgical approach provides better results than another, but curvature correction with less risk of new EDs can be expected compared to grafting procedures [66].

6.6.2 Tunical Lengthening Procedure

Tunical lengthening procedures are suggested in case of severe curvature (>60°) without erectile dysfunction. Their goal is to incise the plaque, lengthen the short or concave side of the penis, and create a defect in the tunica which will be covered by a graft [67].

Tunical lengthening procedures include both plaque incision and graft (PIG) and plaque excision and graft (PEG). Originally, it was thought that plaques could fuel the evolution of disease, so excision was necessary for healing [36, 77]. However, important evidence emerged: the removal of the plaque enhanced the process of fibrosis of the corpora cavernosa and further damaged the delicate mechanism of the veno-occlusive system. Over time, it was realized that these were the two most important factors contributing to postoperative erectile deficit. For this reason, excision and grafting procedures were replaced by new techniques [78].

Plaque excision may be considered in those patients in whom the area of maximum deformity is excised, particularly if it is associated with severe indentation [79].

The area created by the geometric incision of the tunica albuginea should be covered with a graft. The ideal characteristics of the graft should be as similar as possible to the tissue being replaced. Although elasticity and strength summarize the two major capabilities of albuginous tissue, the ideal graft should also be readily available and not very expensive. It should be biocompatible with the target tissue to avoid excessive fibrotic reactions with low risk of infection, antigenicity, and minimal tissue reaction.

It must also be easy to suture, pliable, and compliant, resistant to intracavernous pressures exerted during erections. It should also not be too thick or too thin to avoid bulging or gap formation along the surface of the albuginea with the appearance of new shapes and/or curves after surgery [80, 81].

Several types of grafts have been proposed:

- Heterologous: of human origin but from a deceased donor, including the pericardium, fascia lata, and dura mater
- Biological xenografts: processed bovine pericardium, porcine intestinal submucosa, and porcine dermis and Tachosil® (matrix of equine collagen) [53–58]
- Autologous: taken from the individual himself, they include the dermis, vein, temporalis fascia, fascia lata, tunica vaginalis, tunica albuginea, and buccal mucosa
- Synthetic: Dacron® and Gore-Tex® [67]

Pericardial grafts have adequate thickness, resistance to traction and low risk of contracture, with lower rates of infection and rejection reactions. Many studies evidenced persistent ability to have satisfactory sexual intercourse and poor evidence of insufficient penile straightening [82].

When it comes to biological xenografts, the small intestinal submucosa graft showed similar advantages to the pericardium in terms of sexual satisfaction. This matrix contains angiogenic growth factors that are thought to promote rapid infiltration of host cells and early revascularization, serving as a scaffold for differentiation. In case of large tunica defects, though, decreased stiffness is more common, together with curve recurrence and postoperative complications such as hematomas and infections [67, 83].

Their main disadvantages are due to cost, biocompatibility, possible infection, and immunologic responses. In addition, they may develop excessive scarring retraction with recurvatum or penile shortening and erectile deficiency on a veno-occlusive basis [84, 85].

Among biological xenografts, the novel collagen fleece synthetic graft (Tachosil®) is currently raising scientific interest. The main feature is the ease of use: application is advertised to be suture-less as the graft has self-adhesive properties. This leads to shorter operating time and reduction of the eventual risk of damaging a penile prosthesis in the case of simultaneous implantation. Retraction and scarring also have been reported to be fairly rare occurrences, but randomized comparison trials with other materials are still needed for a conclusive evaluation [67].

Autologous grafts require preparation of a second surgical site intraoperatively for graft harvest and this potentially lengthens operating room time. In addition, harvesting in the same patient is not free from possible side effects in terms of healing, aesthetic results, and lymphedema. In other cases, the extent of the harvest may be limited by the anatomical site, thus reducing the possibility of obtaining enough tissue to cover large defects [67].

Several series have reported excellent results with the use of autologous vein grafting in the short term (1 year) with a 90% satisfaction rate and a curvature correction rate of 59–96%. On the other hand, these results were not confirmed in the long term with a significant decrease in patient satisfaction after 5 years due to erectile dysfunction (22.5%) or penile shortening (35%) [86].

Buccal mucosa as an autologous graft presented extraordinary characteristics, namely, increased elasticity, best enlargement, and elongation coefficient. At an average follow-up of about 3 years, 24 out of 26 patients (92.3%) achieved complete straightening of the penis with a rate of postoperative recurvature and erectile dysfunction as low as 7.7% with a loss of penile

length in 15.4% of cases [87] but plaque excision was carried out. A subsequent study pointed out plaque incision and buccal mucosa grafting was associated with 100% penile straightening, no curvature recurrence or de novo erectile dysfunction, and patient and partner satisfaction of 93.3% and 100%, respectively [88]. A subsequent study from the same authors [90] pointed out that, at mean follow-up of 62.01 ± 34.3 months (range 12-135), all of the 72 patients were able to obtain an erection (SEP-1), 97.1% to penetrate (SEP-2), and 89.7% to successfully complete intercourse (SEP-3); 80.9% of them were satisfied with erection hardness (SEP-4) and 86.8% were overall satisfied (SEP-5), with the main reason for dissatisfaction being expectation of better length and rigidity. Available evidence suggest that buccal mucosa grafting provides excellent long-term results probably due to the typical graft characteristics such as the peculiar blood support that reduces the hypoxia time of the patch. Moreover, the limited loss of elasticity reduces of the risk of fibrosis [89].

Synthetic grafts made of polyethylene terephthalate (PETE, Dacron) and polytetrafluoroethylene (PTFE, Teflon) have been used in the past showing a significant risk of inflammation and subsequent adjacent fibrosis have limited success. The hypoxic environment created inside and around synthetic grafts increases the risk of infection and possible allergic reactions [67, 90].

6.6.3 Penile Prosthesis Implant

Penile prosthesis implantation is typically reserved for the treatment of Peyronie's disease in patients with erectile dysfunction, especially when they do not respond to medical therapy [67].

Although all types of penile prostheses can be used, inflatable penile prosthesis implantation appears to be more clinically feasible in these patients. The pressure within the cylinders allows for superior curvature correction with manual shaping, as well as increased circumference [91].

According to the severity of the curvature, different procedures may take place.

In case of mild to moderate curvature (up to 30°), it may be sufficient to insert two cylinders for an excellent result, without further maneuvers [67].

In cases of severe deformity (>30°), "intraoperative shaping" of the corpora cavernosa on the inflated cylinders has been introduced as an effective treatment and if residual curvature remains, no further treatment is recommended, as the prosthesis will act as an expander leading to progressive straightening in a few months. This approach consists of achieving an erection through the prosthesis to maximum rigidity, evaluating the curvature. The system is then sealed with protected hemostats between pump and cylinders, to protect the pump from the high pressures that can occur during manual modeling. The penis is then bent in the contralateral direction to the curvature for approximately 60–90 s.

After modeling, additional liquid can be introduced into the system to evaluate the aesthetic result. Then, the procedure can be repeated until a satisfactory correction of the deformity is achieved. a gradual and progressive moderation is preferable rather than rapid and violent, to avoid lesions of the tunic and excessive traction of the neuro-vascular bundle. This is considered a first-line therapy for curvature correction after prosthetic implantation [67, 92].

The main risk is represented by urethral injuries. To reduce the likelihood of injury, the distal end of the penile shaft must be protected by the flexing hand, leaving the glans free. In this way, the apexes of the corpora cavernosa will be protected from excessive traction by the tips of the cylinders. The other hand will grasp the base of the penis to provide support to this area, reducing the likelihood of breaking the suture line.

Published reports on the use of modeling indicated that 86–100% successful straightening can be expected without a higher incidence of device revision; sensory traction deficit of the nerve bundle after manual modeling may occur but remains a potential complication that should be discussed with the patient prior to surgery [92, 93].

An alternative to manual remodeling would be plication of the contralateral tunic to correct curvature prior to prosthesis placement [94].

The tunical incision is performed with the cylinders deflated, using the low power cautery, to

free the tunic with the intent of preserving the cavernous tissue over the implant. Once the incision is made, the cylinders are inflated to evaluate the correction. The modeling procedure can be repeated until the desired result is achieved.

While there is no clearly accepted approach, grafting is recommended if the incisions result in a tunical defect that measures more than 2 cm in any size to reduce scar contracture and cylinder herniation [95].

Synthetic grafts were used in the past, but porcine SIS or pericardium biological grafts are now frequently used, while the use of locally harvested dermal grafts is not recommended, because there is a risk of transferring bacteria to the prosthesis. The frequently encountered post-operative complaint is loss of length. This is particularly disabling in the Peyronie's disease population, who often already have a loss of penis length. To overcome this complication, prolonged post-operative inflation of the cylinder has been recommended to preserve the length of the penis. Furthermore, the inflated prosthesis expands the corpora cavernosa in width and favors the correction of any residual curvatures [67].

Another approach to Peyronie's disease when implanting a penile prosthesis has been proposed by Rolle and is known as "sliding technique." After degloving of dartos and isolation of neurovascular bundle, two longitudinal incisions of the tunica albuginea are carried out on the sides of the two corpora cavernosa: the first incision at 3 o'clock on the left and the second incision at 9 o'clock on the right. A dorsal semicircular incision is made to connect the upper ends of the lateral incisions, and a second semicircular ventral incision is made to connect points of the second incision. After incision and dissection of the tunica albuginea from the cavernous tissue and from the septum, traction is exerted on the glans, thus obtaining a sliding of the distal part of the penis from the proximal one. Two rectangular and bow-shaped defects of tunica albuginea remain: the first, dorsal and proximal and the second, distal and ventral. Then, two cylinders of the prosthesis can be inserted in the two corpora cavernosa and the two losses of substance are covered with two rectangular grafts of porcine small intestinal submucosa [96].

Egydio modified this technique, closing the tunical defects using Buck's fascia rather than a graft and making additional longitudinal tunical incisions to restore penile girth. This has been proven to reduce operative time and improve girth and length, but at the cost of a higher rate of hematoma formation and possible auto-inflation of inflatable prosthesis [97].

An evolution of these approaches has been developed by Egydio himself with the MUST (Multiple-Slit Technique). It consists of performing two longitudinal incisions at 3 and 9 o'clock positions on the tunica albuginea, whose ends are connected with semicircular incisions on the ventral and dorsal part of the penis. Additional semicircular incisions must be placed on the concave penile side, creating multiple small tunica defects. The innovation lies in the fact that the use of grafts to cover large tunical defects is avoided, since the size of the tunical defect is actually distributed among multiple small tunical defects. This seems to help in avoiding potential bulging and gap sensations in the affected areas. Glans necrosis, glans ischemia, and partial loss of sensitivity of glans represent the main complications [98].

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