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Chapter 9

CURRENT ROLE OF VASCULAR SURGERY (ARTERIAL AND VENOUS) IN ERECTILE DYSFUNCTION

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ABSTRACT

Penile vascular surgery for the treatment of erectile dysfunction (ED) has been extensively studied over recent decades. It is still regarded with caution. We sought to provide an overview the publications and new developments in this field over the last century. Recent studies support a revised model of the tunica albuginea of the corpora cavernosa (CC) as a bi-layered structure with a 360° complete inner circular layer and a 300° incomplete outer longitudinal coat whereby penile erection-related vasculature interact with the tunica albuginea composed of multiple collagen bundles. Furthermore, additional studies demonstrate a more sophisticated venous drainage system than previously understood, and, most significantly, that the emissary veins can be easily occluded by the shearing action elicited by the inner and outer layers of the tunica albuginea. Pascal's Law has been shown to be significant, if not the major factor in the erectile mechanics, with recent hemodynamic studies on fresh and defrosted human cadavers demonstrating rigid erections despite the lack of endothelial activity. Overall, reports on revascularization surgery support its utility in arterial trauma in young males, and with localized arterial occlusive disease in the older male. Penile venous stripping surgery has been shown to be beneficial in correcting veno-occlusive dysfunction, with outstanding results. The traditional complications of irreversible penile numbness and deformity have been virtually eliminated with the venous ligation technique superseding

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venous cauterly. Penile vascular reconstructive surgery is viable if, and only if, the surgical handling is properly carried out using a sound method. It ought to be promising in the near future.

Keywords: penile arterial insufficiency, penile arterial reconstruction, revascularization, veno-occlusive dysfunction, penile venous stripping, erectile dysfunction

PENILE REVASCULARIZATION SURGERY

Introduction

In the human penis, erectile capability depends on the sinusoids, which are specifically distributed in the glans penis, corpus spongiosum, and corpora cavernosa (CC) independently. Among these CC sinusoids is an exclusive milieu encircled by a bilayered tunica albuginea with a 360° complete inner circular layer and a 300° incomplete outer longitudinal coat, spanning from the bulbospongiosus and ischiocavernosus proximally and extending continuously into the distal ligament within the glans penis (Figure 1) [1]. This fibro-skeleton interacts with erection-related vasculatures, whose peculiar design provides a bony rigidity on full erection. The outer longitudinal layer is seemingly a determined structure for interplaying the erection-related artery and veins [2]. Because the CC arterial supply rate increases from 2-3 ml/min to 60-80 ml/min in flaccid and full erection states, respectively, a healthy erectile function is categorically a result of an unaffected erection-related vascular system. Otherwise an awkward status ensues, which is commonly called erectile dysfunction (ED), defined as persistent inability to attain and maintain an erection sufficient to permit satisfactory sexual performance. It is a common disorder worldwide, afflicting a high percentage of the male population.

This issue is unfortunately still a challenging medical problem, even after the introduction of phosphodiesterase 5 (PDE5) inhibitors, which have become the first-line drugs for ED management since 1998. Previously, the vast majority of cases of ED were thought to be psychogenic in nature. This belief has given way to the realization that ED is etiologically of an organic basis in most patients. While the etiologic contributors of ED are psychological, neurological, hormonal, pharmacological, cavernosal fibrosis, chronic systemic diseases and vasculogenic factors, in this chapter our major interest is the latter of these categories, the vasculogenic origin, which can be divided into arteriogenic, venogenic ED and mixed type. We will concentrate then on penile erectile-functional-reconstructive surgeries including penile arterial revascularization and venous surgery.

It was Leriche who recognized a connection between arterial insufficiency and loss of erection when he observed that endarterectomy of an occluded bifurcation of aorta did not only improve blood flow in the lower extremities but also showed marked improvement of erectility [3]. An increase in the blood flow through the paired cavernosal arteries is the primary mechanism in obtaining an erection. Any arterial lesion that reduces inflow to the penis can lead to ED; this is true for lesions even in smaller vessels such as the penile artery [4].

The prevalence of vascular disease increases with age and is a major cause of organic ED in men over the age of 50. Arteriogenic ED can be due to atherosclerotic or traumatic arterial

occlusive disease. Michal and Ruzbarsky noted that impaired penile perfusion is an indicator of generalized atherosclerotic disease, and that the age of onset of ED and coronary arterial disease (CAD) is often similar [5]. In fact, ED has been shown to be a bellwether for development of CAD in asymptomatic men, [5] and both diseases share the same medical conditions or risk factors—specifically smoking, diabetes, hypercholesterolemia, and hypertension, [6] as well as peripheral vascular disease.

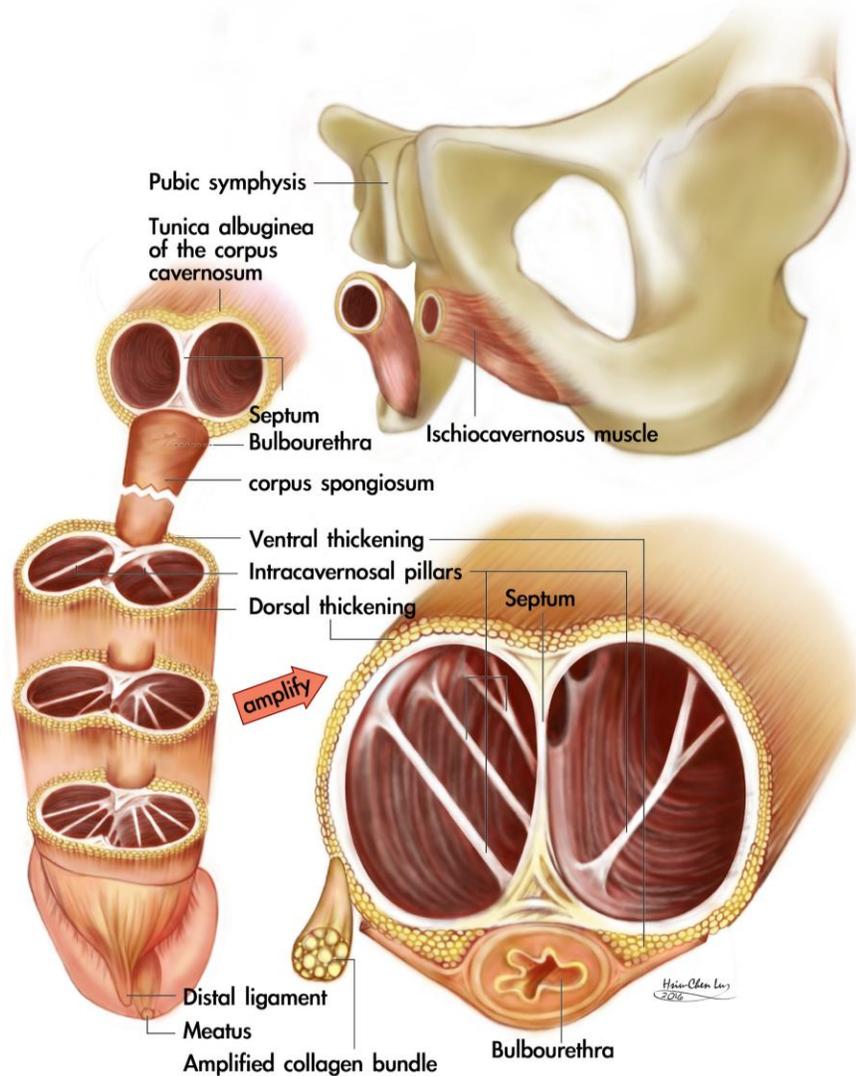


Figure 1. Schematic illustration of the fibroskeleton in the human penis. The tunica albuginea of the corpora cavernosa is an exclusively bilayered structure in the human penis. The inner circular layer completely contains and, together with the intracavernosal pillars, supports the sinusoids. There is a paucity of outer layer bundles at the region between the 5 and 7 o'clock positions where there is close contact with the corpus spongiosum. Distally, they are grouped into the glans penis forming the distal ligament, located at the 12 o'clock position of the distal urethra. This previously overlooked tissue is an indispensable supporter for glans penis. The median septum is incomplete with dorsal fenestration at the pendulous portion of the penis and is merely complete where the penile crura are nearly formed.

In arteriogenic ED, the corpora cavernosa demonstrate lower oxygen tension [7] which may result in a decreased volume of sinusoidal smooth muscle and subsequent venous leak [8]. In an experimental animal model, rabbits with iatrogenic iliac atherosclerotic disease demonstrated alterations in their downstream penile arteries and a reduction in cavernosal smooth muscle content [9]. The pathogenesis of ED in these patients appears, in part, to be linked to endothelial dysfunction. These alterations were associated with decreased nitric oxide synthase (NOS)- and NO-mediated relaxation of corpora cavernosal tissue [10]. In erectile dysfunction due to traumatic stenosis of cavernous or pudendal arteries noted in young men with pelvic trauma, [11] as well as in long-distance cyclists, [12] the ultimate goal of the surgery is to provide an alternative arterial pathway to bypass arterial lesions that cause obstruction in the hypogastric-cavernous arterial bed, which offers an option for a potential cure.

A Historical Overview – Penile Revascularization

Penile revascularization has undergone many refinements since its first description by Vaclav Michal and associates in 1973, who described a direct anastomosis of an arterial donor vessel to the corpora cavernosa of the penis [13]. Another proposal of his method (Michal II) was to anastomose the inferior epigastric artery (IEA) with one of the dorsal arteries of the penis in an end-to-side fashion [14]. Over the years, alterations to Michal's techniques have been reported, all of which share the common goal of restoring arterial inflow and perfusion pressure to the corpora cavernosa [15-19]. However, proposals for an anastomosis of the IEA with the deep artery of the penis published a little later were equally unsuccessful [20-22].

In 1981, Virag and colleagues described a procedure (Virag I) in which the IEA was anastomosed directly to the deep dorsal vein (DDV) with the proximal vein not ligated, introducing the concept of venous arterializations [23]. Later, Virag described modifications of his techniques (Virag II-VI) [24-26]. In Virag II, the proximal DDV was ligated. In Virag III, the anastomosis between the IEA and the DDV was fashioned in an end-to-end maneuver. In Virag procedures IV, V and VI, a direct shunt between the DDV and the tunica albuginea of the corpus body was added to the Virag I, II and III procedures. A number of other investigators have described other variations on this basic procedure. In 1986, Hauri advocated the so-called three-vessel anastomosis with direct arterial anastomosis of the IEA to the dorsal artery, but additionally incorporating the DDV into the anastomosis. In principle, arterialization of the dorsal vein would improve arterial flow to the corpora cavernosa in a retrograde manner via the emissary veins [27, 28]. Furlow and Fisher have proposed anastomosis of IEA to DDV with ligation of the proximal and distal DDV in addition to all the contributing circumflex veins and small branches [29]. In 1994, Shah developed a new procedure that permits antegrade arterialization of the dorsal vein (Parulkar-Shah ADVA procedure), in which the distal half of the dorsal vein was completely mobilized, divided near the glans and then flipped to lie upon the symphysis pubis where it was anastomosed end-to-end to the IEA [30]. This procedure employed the same principle as the Virag procedure, with the advantage that the flow of blood is in the direction of the venous valves, which may be left intact. As the principles of revascularization consisted of distal or proximal ligation of the arterialized vein, windows between the artery and vein, and ligation of the circumflex vessels

and destruction of the valves in the dorsal vein, many other variations have been proposed [31-36].

Additionally, in 1982, Crespo described a procedure in which the femoral artery was anastomosed to the cavernous artery or dorsal penile artery with an autologous saphenous vein graft interposed between the two vessels [37]. MacGregor and Konnak reported on a variant, in which they anastomosed IEA, instead of the reversed saphenous vein, directly to the cavernous artery [38]. These procedures required the surrounding erectile tissue to be dissected to obtain control of the cavernosal artery. Fibrosis of the transplanted artery at the entrance into the tunica eventually causes abandonment of that approach to revascularization. DePalma in 1988 attempted to restore penile erections in cases of vasculogenic impotence by utilizing aorto-iliac reconstruction [39]. Shafik in 1994 performed pudendal canal decompression through a perineal approach, and reported an improvement in 80% of cases with narrowing or obstruction of the distal part of the internal pudendal artery on both sides with poorly or non-visualized penile arteries [40].

There have been no further revolutionary changes in the realm of penile revascularization surgery, nor does consensus exist among experts with regard to the definitive technique. In addition, endovascular management of focal arterial occlusion has also been studied. The majority of the reports published in the 1980s used balloon angioplasty without stenting [41]. Results are variable and poorly defined.

Selection of Patients with Suspected Arteriogenic ED

Patient selection for surgery is crucial. Prior to embarking on this procedure, other organic causes of ED need to be excluded. A Rigiscan study may be considered in young patients with suspected arterial injury. Selective internal pudendal angiography and penile arteriography are the gold standard in assessing patients' eligibility for arterial reconstructive surgery (Figures 2 and 3). Such patients have pure arterial insufficiency, without corporal veno-occlusive dysfunction (CVOD), arterial occlusive pathology in the distal internal pudendal, common penile or proximal cavernosal artery secondary to focal injury from blunt pelvic, perineal or penile trauma, as well as at least one patent IEA of sufficient length to serve as a donor artery.

Irrespective of the anatomic details of arteriography, the results must be interpreted in conjunction with the functional results obtained on penile duplex Doppler ultrasound (PDDU) and/or dynamic infusion cavernosometry and cavernosography (DICC). A PDDU study confirms vascular insufficiency and documents any venous leak. Concomitant corporeal veno-occlusive dysfunction should be excluded by preoperative DICC, as this may further predict postoperative success [42]. However, it is noteworthy that almost half of patients who seek a second opinion regarding penile revascularization had a significant discrepancy between erectile hemodynamics using PDDU and/or cavernosometry and penile arteriography [43]. Of these, 73% had normal repeat studies, making them no longer candidates for penile revascularization.

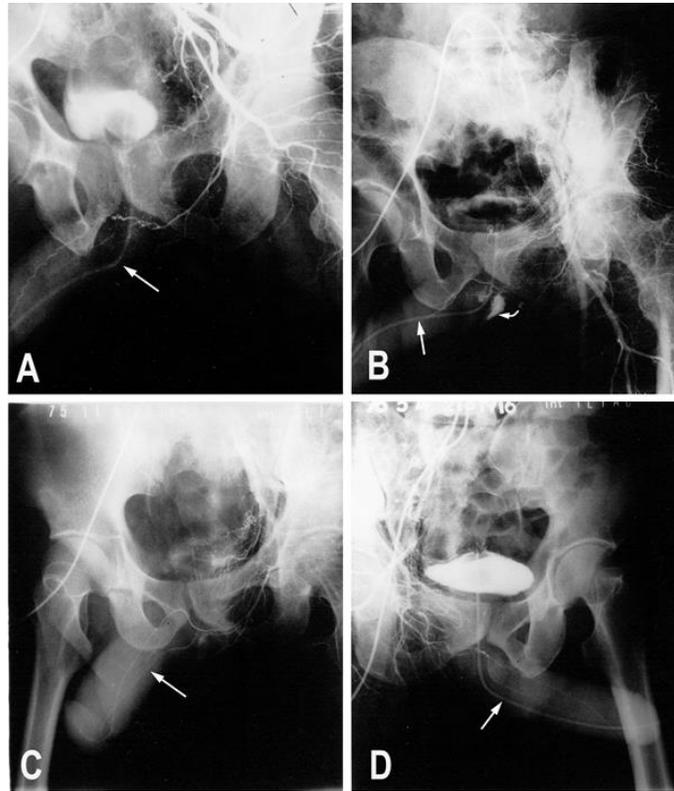


Figure 2. Selective internal iliac arteriography. A. After papaverine 60mg intracavernous injection, this arteriogram clearly demonstrated both dorsal artery and cavernosal artery. Note the Foley catheter in situ (arrow). B. A similar phase arteriogram showed a blockage of penile dorsal and cavernosal artery, whereas the spongiosal artery appeared diffusely profuse to the corpus spongiosum after a straddle injury in a 32-year-old man. Is it similar to an arterio-venous malformation? The Foley catheter (arrow) was clamped. C. Left side pudendal artery was clearly shown and the dorsal artery could be presented travelling into the glans penis. Unfortunately his fellow side artery failed to present (not shown). D. In another patient the right pudendal artery was clearly seen despite a latter phase arteriogram having been undertaken.

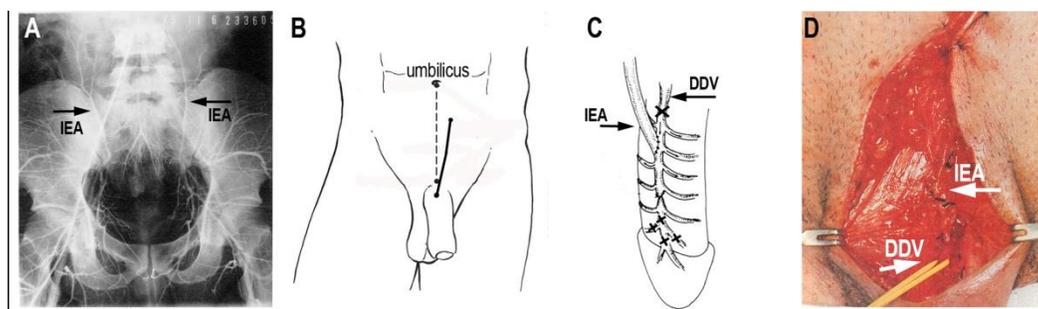


Figure 3. Selection of an inferior epigastric artery (IEA) as a donor artery. (A) Bilateral inferior epigastric artery was well identified (arrows). Left IEA looked straighter, implying a better candidate for donor was determined. (B) An imaging line was referenced between the umbilicus and the point of central pubic region (dotted line). A para-rectal skin incision (dark line) was marked. (C) Illustration of ongoing penile deep dorsal vein (DDV) arterializations with IEA. Note that the DDV was ligated proximally and at lateral margins of circumflex veins (cross marks). (D) Photo of a DDV (yellow traction) arterializations was made with IEA.

The indication of pelvic trauma for penile revascularization is controversial. Several authors describe men with such a medical history as ideal candidates [44], while others exclude these cases from surgery due to the possible influence of severe neurogenic aspects on impotence [45]. A list of criteria has been developed that the patient and surgeon must meet to ensure optimum results. The criteria include: (1) patient must have strong sex drive; (2) patient must experience a consistent reduction in erectile hardness during sexual activity; (3) normal hormonal evaluation; (4) normal neurologic evaluation; (5) arterial insufficiency on vascular testing; (6) arterial blockage located in the common penile artery or cavernosal artery; (7) the presence of a donor (inferior epigastric) artery of sufficient length; and (8) the surgeon must be trained in microvascular surgery. Based upon the literature [42, 46-48], the following appear to be inclusion criteria in selecting patients for arterial surgery: [49]

- Age less than 55 years
- Non-smoker
- Non-diabetic
- Absence of venous leakage
- Stenosis of the internal pudendal artery

Surgical Technique

General endotracheal or regional anesthesia may be used for the procedure. One dose of intravenous broad-spectrum prophylactic antibiotic is administered prior to the operation. The patient is positioned supine on the operating table with the legs spread in a frog-leg orientation. Once the patient has been prepared and draped, a sterile 16Fr Foley catheter is inserted into the bladder and left to closed drainage. The operative procedure involves three steps:

Scrotal Exploration and Dorsal Artery Dissection

An inguinal-scrotal incision is made on the side opposite the donor IEA harvest. The arterial anastomosis is performed at the penile base. Penile inversion and elevation of the fundiform ligament (exposed under the back of vascular tissue forceps) with hooks during surgery reduces the risk of fundiform ligament injury so the penis maintains elasticity during postoperative penile erection [50]. Alternatively, our preference would be a longitudinal incision performed on penile base and extended paramedially to 3-5cm below umbilicus level (Figure 3).

IEA Harvesting

A preoperative Doppler localization mark is helpful, although an appropriate IEA has been identified as an ideal donor vessel by arteriography (Figure 3A). A pararectal or oblique incision in Langer's lines is made to expose the rectus muscle, which is reflected medially over the lower abdomen. Alternatively, a midline abdominal incision will allow access to both arteries in case the first is not suitable for the surgery (Figure 3B). The IEA is identified and then mobilized from its origin near the femoral artery to a point near the umbilicus, where it is transected. It is then transferred from the internal ring, through the inguinal ligament, out

of the external ring, and under the fundiform ligament to lie onto the dorsum of the penis. Papaverine hydrochloride is applied topically to reduce arterial spasm as needed [50].

To obviate the wide incision, pararectal or transverse abdominal, laparoscopic mobilization of the inferior epigastric vessels has been introduced [51-53]. A balloon-tipped Hassan cannula is placed in the midline just below the umbilicus, and pneumoperitoneum is created. Two additional trocars are positioned laterally in a triangular fashion. The inferior epigastric bundle is identified below the arcuate line and dissected cephalad en bloc near the umbilicus, where it is transected, and dissected caudally to its origin from the external iliac artery. It is then delivered at the base of the penis for subsequent microvascular anastomosis. Recently, the robot-assisted approach to inferior epigastric vessel harvesting has been introduced as an ideal minimally-invasive complement to penile revascularization, negating the need for a large incision and shortening recovery time [54].

Microsurgical Anastomosis

Three principal procedures of penile revascularization and arterializations surgery in clinical practice are based upon the following techniques: [55]

- Anastomosis of the IEA to dorsal penile arteries end to end [13], or end to side [14], (true revascularization).
- Anastomosis of the IEA to the deep dorsal vein with additional proximal and/or distal vein ligation (venous arterializations, Figure 3C) [56, 57].
- Anastomosis of the IEA to the deep dorsal vein and artery (arterial-venous shunt) [27].

The operating microscope is introduced to perform the anastomosis between the IEA and the recipient dorsal artery or vein of penis using 10-0 nylon interrupted microsutures (Figure 3D). After careful and thorough removal of the vessel adventitia, the initial suture is typically passed from the outside of the IEA into the lumen, and then from inside the lumen to the outside of the recipient vessel. After completion of the anastomosis with meticulous hemostasis has been achieved, the penis is replaced into its anatomic position and the wound is closed.

In clinical practice, abstention from sexual activities involving an erect penis is recommended for at least 6 weeks postoperatively. Anticoagulants, usually aspirin, are recommended for 6 months after the operation. A patent microvascular anastomosis can be documented postoperatively by selective internal iliac arteriography.

Outcomes of Revascularization

During the 1970s and 1980s, surgery for arteriogenic ED was routinely performed. The efficacy of this surgery is unproven and controversial, largely because of lack of standardization in patient selection, hemodynamic evaluation, surgical technique, and limited long-term outcome data using validated instruments. In 2005, the members of the Erectile Dysfunction Guideline Update Panel reviewed the available publications, and concluded that only four of 31 manuscripts with a total of 50 patients enrolled met the strict inclusion criteria for the Arterial Occlusive Disease Index Patient [33, 58-60]. Of the 50 patients, 42 had an

anastomosis of the IEA to the dorsal penile artery (dorsal artery arterialization) and eight had an anastomosis of the IEA to the dorsal penile vein. Reported successful outcomes were 36-80% and 91% for IEA to dorsal vein and IEA to dorsal artery revascularization, respectively. The total studied population with reported outcome was considered too small to determine whether or not the surgery is effective [61].

In the second Paris consultation in 2003, the literature from 1993 to 2003 was evaluated [62]. They compared the sexual satisfaction rate in 130 patients with arterial and/or venous impotence treated with four surgical techniques with long-term follow up. Arterialization of the deep dorsal penile vein was performed in 39 (30%) and 78 (60%) were treated with penile implants. There was no identified difference in success among the different technique. Sexual satisfaction rate was 12% for arterialization, compared to 93% for penile prosthesis. The success rate for young patients with traumatic arterial lesions was 100%. It is apparent that patient outcome is poor in men undergoing arterialization compared to other treatment modalities [49].

Despite the negative opinion of the AUA consensus panel on penile revascularization surgery, some recently published papers have supported the efficiency of penile revascularization surgery in carefully selected healthy patients [19, 48, 63-66]. Among these studies, subjective success rates vary by the type of revascularization procedure, definition of successful outcome, and patient population, but range from 50% to 82%.

More recently, Babaei performed a meta-analysis and systematic review to determine the subjective and objective outcomes of penile revascularization surgery in patients with arteriogenic ED [67]. The impact of age on postoperative success was most prominent, followed by the presence of venous leak, smoking, and the type of operative procedures employed. Young patients with posttraumatic circumscribed arterial lesions could profit most from penile arterialization. The authors conclude that inconsistent measurements of outcomes limited the findings, and none of the studies were randomized controlled trials.

Possible Complications

Complications of penile revascularization occur in approximately 25% of patients [68, 69]. Postoperative arterial hemorrhage with hematoma formation may result from disruption of the microvascular anastomosis. The potential risks of these techniques, such as spongy necrosis and hyperesthesia of the glans, cannot be ignored. In one study, a complication rate of wound infection, inguinal hernias, loss of penile length, and decreased penile sensitivity was of 2.8, 2.8, 28, and 24.7%, respectively. A penile shortening complication rate of 28% of patients has also been documented [70]. Risk of penile sensation may result from dorsal nerve injury and be diminished by employing an operating microscope for dorsal vessel dissection [71].

The major complications are priapism (after epigastric artery-corpus cavernosum anastomosis) and glans hyperemia (after IEA-dorsal vein anastomosis) [68]. Direct anastomosis to corpus cavernosum was quickly abandoned because most patients developed high-flow priapism with subsequent fibrosis of cavernosal tissue. In a series reported by Manning, glans hyperemia developed in 13% of patients, shunt thrombosis in 8%, and inguinal hernias in 6.5% [46]. To prevent glans hyperemia, all of the venous channels distal to the IEA-dorsal vein anastomosis should be ligated to prevent overperfusion of the glans.

Important Guideline Publications

Penile revascularization is considered to be unproven and controversial. In 1996, the AUA's Clinical Guidelines Panel stated that arterial surgery was considered investigational and not justified to be performed routinely, although arterial revascularization procedures appeared to have the highest efficacy in young men with ED secondary to arterial injury from pelvic or perineal trauma [72]. The 2005 guidelines are based on the 1996 guidelines report following a meta-analysis of this literature [61]. The Panel consensus is that arterial reconstructive surgery is a treatment option only in healthy individuals with recently acquired erectile dysfunction secondary to a focal arterial occlusion, and in the absence of any evidence of generalized vascular disease.

In the Third Paris International Consultation on Sexual Medicine in 2009, it was reported that young men with traumatic arterial lesions appear to have better outcomes compared to elderly patients. There are no comparative prospective randomized studies assessing outcome of penile revascularization surgery for arteriogenic ED. Based on the evidence in the literature, this surgery may be offered to men below the age of 55 who are non-smokers, non-diabetic, show no evidence of venous leakage, and demonstrate an isolated stenosis of the internal pudendal artery [73].

Conclusion

Surgical techniques to correct arterial insufficiency of the corpora cavernosa are based on neoarterialization of the dorsal penile artery, cavernous artery and/or deep dorsal vein. The inferior epigastric artery is generally used as the donor vessel. In theory, penile revascularization improves inflow while reducing venous outflow in some modifications. On paper, these procedures may be attractive, not only in men with pure arteriogenic ED, but also those with a venogenic component. The surgery is one of the treatments with the potential to permanently cure patients, that is, to allow a return of spontaneously developing erections without the necessity for any medications or internal/external devices. The ideal patients for PR surgery are young men with a history of focal stenosis and an absence of systemic endothelial dysfunction, properly diagnosed with arteriogenic ED without venous leak. A large-scale study of penile arterial reconstructive surgery must be performed to determine its effectiveness. The authors hope that revascularization might gain popularity in the future as a third-line treatment option in men failing conservative therapy and for those not desiring penile prosthetic implantation.

PENILE VENOUS SURGERY

Introduction

Erectile dysfunction (ED) is of an etiologically organic basis in most patients. Vascular abnormalities are most common in patients with an organic etiology. Penile corporovenous-occlusive dysfunction (CVOD), synonymous with venous leakage, venous vasculogenic

dysfunction and venogenic ED, is the most common such abnormality [74, 75], and can be identified in up to 85 percent of the men evaluated for ED, regardless of the age of the patient [76].

The venous closure mechanism has been described in anatomical dissections and physiological studies [77]. CVOD is considered to result from an improperly functioning occlusion mechanism. Investigations emphasize the role of the tunica albuginea in the venous occlusion mechanism of the penis during erection [78]. The location and degree of venous leak is variable, and can occur anywhere along the tunica albuginea of the corpus cavernosum in a canine model [79], also demonstrated on ED patients [80].

Recent studies suggest that, in most patients, CVOD is the result of endothelial dysfunction and damage to the trabecular smooth muscle content due to multifactorial degenerative processes [81]. ED patients with a history of vascular risk factors and/or exposure to disorders that induce trabecular structural alterations, such as veno-occlusive priapism, penile irradiation and connective tissue disorders have structurally based CVOD. Others have reported on patients with vasculogenic impotence exhibiting degeneration and atrophy of trabecular smooth muscle cells with increased fibrous connective tissue. The potential causes of CVOD also include congenital vascular anomalies [82], trauma [83], arterial disease (e.g., hypercholesterolemia, arteriosclerosis), alterations in cavernosal smooth muscle, trabeculae, or tunica albuginea, psychogenic causes, postpriapism and unknown origin. While most patients with vascular ED fall into this Venogenic ED group, a minority of especially younger patients may develop ED on the basis of circumscribed acquired or congenital vascular abnormalities. Today, it is a common belief that CVOD is an effect rather than a cause of ED [49, 84].

ED can be due to vasculogenic, neurogenic, hormonal and/or psychogenic factors, as well as alterations in the nitric oxide/cyclic guanosine monophosphate pathway or other regulatory mechanisms, resulting in an imbalance in corporal smooth muscle contraction and relaxation [79]. While there is no doubt that arterial inflow and sinusoidal relaxation are important in the erectile phenomenon, failure to trap the cavernosal blood within the corpora cavernosa is a common cause of ED [78]. The deep dorsal vein has been found to be the major site of venous leakage in more than 75% of cases [77]. Whatever the mechanism, CVOD represents a failure of normal veno-occlusion during the increased arterial inflow of erection, and venous leak surgery is directed at increasing venous resistance. Thus, penile venous surgery may not be acting at the site of the causal veno-occlusive incompetence, but it nonetheless achieves the desired physiological effect.

A Historical Overview – Penile Venous Ligation (PVL) Surgery

In 1873 the Italian physician Francesco Parona injected the dorsal penile vein of an impotent young patient with hypertonic saline in order to cause sclerosis and subsequently reduce the excessive venous outflow. The idea that erectile disorders might be treated surgically by occluding venous channels from the penis was promoted as early as the turn of the twentieth century. This was followed by a large number of surgical procedures. Surgical ligation or resection of the dorsal vein was practiced by several American doctors [85].

In 1902, as a justification for this type of surgery, Joe Wooten put forward the hypothesis of “atonic impotence”, claiming that impotence is the result of the loss of smooth muscle

tonicity in the corpora cavernosa, resulting in dilated veins and sinusoids at that level [86]. In 1908, Frank Lydston published his results on 100 venous ligation procedures, reporting that 50% of his patients had been definitively cured and that the rest showed improved sexual function. Lydston claimed, by way of an explanation for these promising results, that he ligated not only the superficial dorsal vein, but also the deep dorsal vein of the penis, as well as collateral veins, courting penile tumescence, along with a sensation of enlargement of the penis which boosted the psychological confidence of patients in the effectiveness of this technique [87].

Beginning in the 1930s, Oswald Swinney Lowsley combined simple dorsal vein plication with a surgically more advanced perineal crural technique in which he plicated the bulbocavernosus and ischiocavernosus muscles with several mattress sutures. After his initial report in 1935, he was able to follow up 273 of the 1000+ patients operated on in his later publication in 1953. Later, as urologists embraced different techniques of vascular surgery and transplantation, attempts to resolve erectile dysfunction were directed toward the possibility of producing a greater blood supply through arterial revascularization techniques. These techniques of venous surgery disappeared from medical literature until in the 1980s, when CVOD surgery experienced a revival as a result of the new field of erectile physiology [88].

In most patients, multiple venous leak sites can be visualized on cavernosography. The technical goal of therapy addresses the identified penile veins which drain blood from the corpus cavernosa. Over time, the surgical procedure has been expanded from simple deep dorsal vein ligation to extensive surgical exposure and vein ligation, excision, crural plication and spongiolysis, performed either alone or in combination [89]. However, the failures and disappointment caused by the procedure, as well as the absence of effective alternatives, contributed to the fact that penile venous surgery in men with arteriosclerotic disease have been considered investigational and only to be performed in a research setting with long-term follow-up available [72]. CVOD is attributable to an underlying pathologic process that is not generally correctable through venous ligation [49, 90].

More recently, Basche et al. presented a subset of four patients with CVOD, treated by means of retrograde embolization of the internal pudendal vein. Embolization in angiographically-identified pathological venous leakage might have represented a promising alternative to surgical isolation and antegrade embolization of the deep dorsal penile veins [91]. However, the procedure has not prevailed as a routine therapeutic approach, owing to the limited number of patients and the absence of long-term follow-up data.

Selection of Patients with Suspected Venogenic ED

Objective vascular testing that provides a physiologic diagnosis may help direct appropriate therapy, since not all patients respond adequately to oral ED therapy. Erectile hemodynamics is currently evaluated using penile duplex Doppler ultrasound (PDDU) or dynamic infusion cavernosometry. Diagnostic dynamic PDDU can assess arterial function and the presence of significant cavernosal venous leakage by measuring peak arterial flow and the calculated resistive index [92, 93]. Localization and severity of CVOD may be determined by invasive dynamic intracavernosal cavernosometry and cavernosography (DICC) [94].

Surgical treatment for CVOD should be considered when medical treatment fails to provide sufficient erection. Wespes et al. investigated penile ligature-resection of the deep dorsal vein and concluded that resection of the deep dorsal vein can restore penile erection in around 50% of well-selected patients [95]. The best prognostic factors are found in relatively young patients: primary ED with intact arterial flow, normal hormone levels, normal CC-EMG and flow-to-maintain <50 ml/minute by DICC. Surgery for penile venous leakage is not recommended in older men because penile venous leakage often results from atrophy of the intracorporeal muscles or the tunica albuginea [72, 89]. More recently, Cakan et al. concluded that long-term success for unselected patients undergoing deep penile venous ligation is disappointing; however, careful patient selection significantly improves long-term results [96]. Young patients who have normal penile arterial system and no risk factors (such as diabetes) are the best candidates for the improved postoperative outcome.

Surgical Technique for PVL Surgery

General endotracheal or regional anesthesia may be used for the procedure. One dose of intravenous broad-spectrum prophylactic antibiotic is administered prior to the operation. The patient is positioned supine on the operating table with legs spread in a frog-leg orientation. Various surgical procedures have been described to correct the radiographical finding of venous leakage. Mulhall et al. described success using a transscrotal approach [97], for example, while Lue and colleagues favored a 3-inch inguinoscrotal approach [82]. The shaft of the penis is delivered into the operative field in a gooseneck fashion. Buck's fascia is incised over the dorsum of the penis, identifying and isolating the deep dorsal vein. Care should be taken to avoid injury to the paired dorsal arteries and nerves. The deep dorsal vein is stripped from the symphysis pubis to 1 cm proximal to the corona, while its tributaries are transected and ligated. The suspensory ligaments are divided or not [98]. In an effort to correct isolated venous leak from crural veins, ligation (or exclusion) of the proximal corpora with umbilical tape is undertaken. There has been some debate as to whether a standard surgical approach should be used, ligating and excising the deep dorsal vein and its tributaries [88, 99, 100], or whether the procedure should be directed specifically to the site of the leakage identified on cavernosography [101]. Others have routinely performed an even more extensive procedure, ligating the cavernosal and crural veins in addition to the deep dorsal vein and its tributaries. It is likely that all of these methods were based on the traditional concepts of penile venous anatomy, in which a single deep dorsal vein is flanked by a pair of dorsal arteries located between Buck's fascia and the tunica albuginea (Figure 4). After careful completion of the ligation procedure, hemostasis is achieved, the penis is replaced in its anatomic position and the wound is closed. In clinical practice, abstention from sexual activities involving an erect penis is recommended for a period of at least 6 weeks postoperatively.

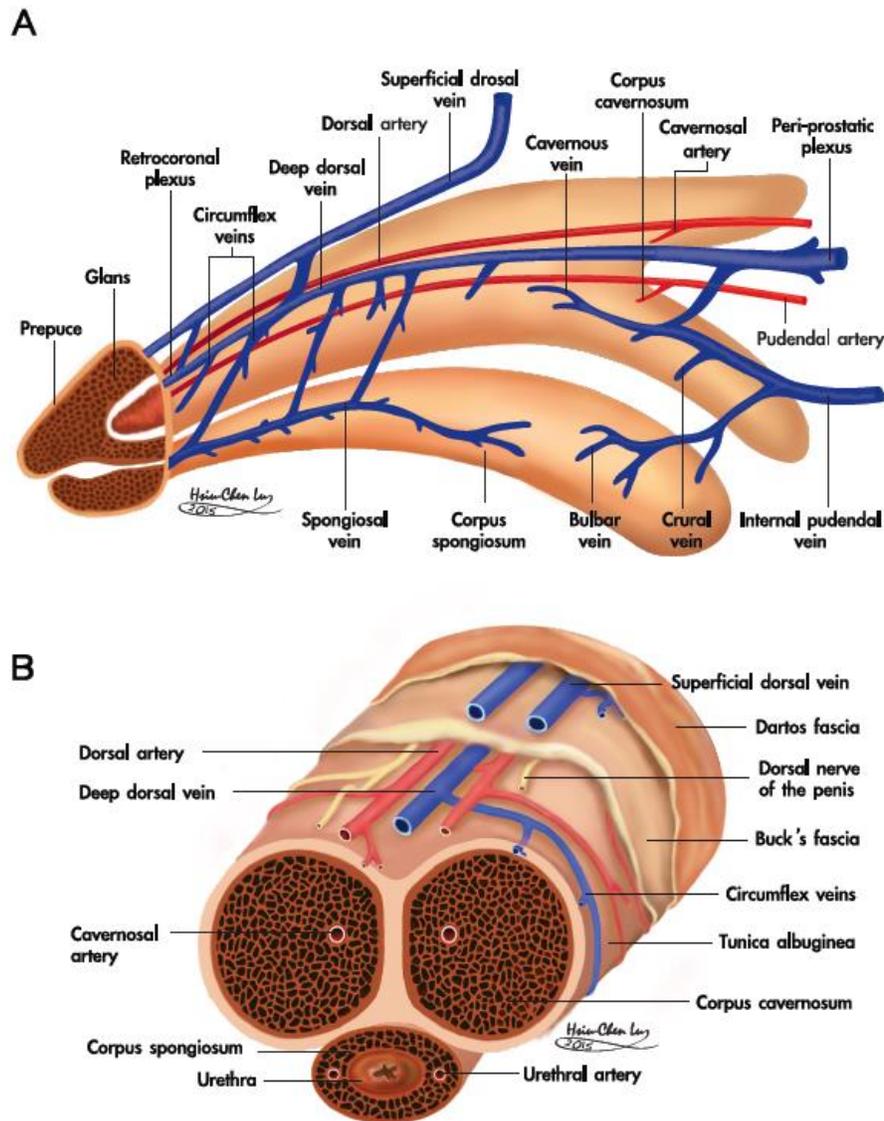


Figure 4. Schematic illustration of the conventional penile tunical and venous anatomy. (A) Lateral aspect. The glans penis is exclusively composed of uniform sinusoids only.? The deep dorsal vein (DDV) is flanked by a pair of dorsal arteries (DA).? Thus the 2:1 ratio of arteries to veins is the same as that in the umbilicus vessel. (B) Cross-section of a pendulous portion in the human penis. The tunica albuginea of the corpora cavernosa is consistently described as a one-layered coat with uniform thickness and strength.? The median septum is complete.? There is one single DDV and two DAs between the Buck's fascia and tunica albuginea.? Thus the penile vascular system still complies with the general anatomical rule that veins number more than arteries in the body as a whole (Figure 1 from *Med Sci Monit.* 18(7): RA118-125, 2012, reproduced with permission).

Recently, a new extraperitoneal laparoscopic approach to venous ligation has been suggested. With this approach, it is easy to gain access to the deep dorsal vein complex overlying the anterior prostatic surface. Suture ligation can be performed without damaging

the dorsal penile structures. However, no long-term success data are available for this new approach to penile venous ligation [102].

Outcome of PVL Surgery

Most studies presented here are retrospective analyses, relying on the patient's report of his sexual functioning. No study has reported the use of standardized questionnaires for subjective improvement, nor has improvement in quality of life as a result of the surgical intervention been reported. Generally speaking there are no postoperative quantitative vascular assessments, except in cases of poor response to the intervention.

Initial reports with short-term results were promising [88, 99, 100, 103], but later publications reporting results from diverging follow-up or patient population did not reflect this high level of success. Success rates within the first year range from 23 to -80%, but consistently decline on longer follow-up [96, 98, 104]. There is a time-related decline in successful function, presumably through incomplete ligation, recanalization, cavernosa-spongiosum leak, inadequate selection of patients, unrecognized presence/progression of arterial pathology, and/or smooth muscle dysfunction [88, 99, 100, 105, 106]. However, it is noteworthy that some surgical failures can be rescued with the intracavernosal administration of vasoactive agents to which patients were unresponsive prior to the operation [106]. In rare cases of isolated venous leaks due to congenital or posttraumatic lesions, targeted ligation of these venous outflow channels may have its place [107].

Possible Complications

Generic complications that may be encountered in the post-operative period include hematoma formation, wound infection, and skin necrosis. Possible specific complications include penile curvature, painful erections, postoperative shortening of the penis, penile deformity, transient or irreversible penile numbness, lymphedema, or ligation of the penile artery in error [105, 108]. Berardinucci et al. reported complication rates of 15%, including temporary paresthesia of the penis (12%) and adhesions between the skin and the penis, thus resulting in variable degrees of penile deviation during erectile episodes [98]. Freedman et al. described complications including excessive penile edema (33%), hematoma (15%), excessive pain (17%), scarring requiring revision (2%), penile shortening (43%) and hypoesthesias (20%) [101]. Extension of surgery to include the crural veins, spongiolysis, and closure of spongoicavernosal shunts showed no additional advantages but higher morbidities.

Important Guideline Publications

The diagnosis and treatment of venous insufficiency has increasingly been called into question, since it appears that "leakage" is a misnomer and represents an erroneous interpretation of a more fundamental problem related to alterations of the cavernosal tissue and the tunica albuginea rather than a primary venous disease [109].

Previously, the NIH Consensus Development Conference Statement and the Clinical Guidelines Panel on ED of the American Urological Association (AUA) concluded that the use of penile ligation and penile revascularization should be performed in a research setting with long-term follow-up available [72, 110]. In 2005, the ED guidelines update panel of the AUA further proclaimed that sufficient evidence to support a routine surgical approach in the management of veno-occlusive ED has not been published. Surgeries performed with the aim of limiting the venous outflow of the penis are not recommended [61]. The first European Association of Urology (EAU) Guidelines on Erectile Dysfunction were published in 2000, with subsequent updates, and the renamed Guidelines on Male Sexual Dysfunction: Erectile Dysfunction and Premature Ejaculation in 2014 also rejected venous ligation procedures of the penis as an option for management of ED, given the poor overall outcomes [111].

***De Novo* Discovery of Penile Venous Anatomy**

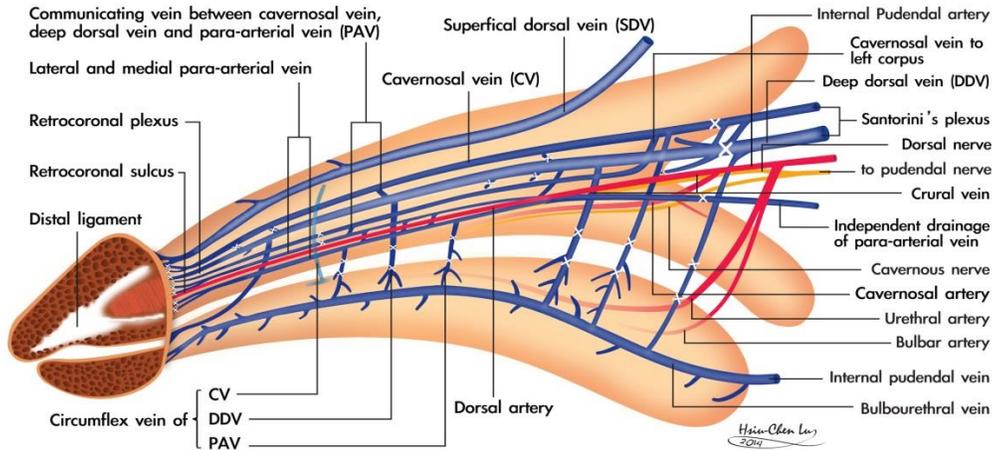
The venous system of the human penis has been widely studied, and traditionally considered to be a single deep dorsal vein located between Buck's fascia and the tunica albuginea [112, 113]. In tandem with surgical assessment, clinical imaging and human cadaveric study, a *de novo* discovery of penile erection-related veins was made, which comprised a deep dorsal vein (DDV), a pair of cavernosal veins (CVs), and two pairs of para-arterial veins (PAVs) in between the tunica albuginea and Buck's fascia instead (Figure 5) [114].

The DDV serves as a common vessel receiving blood drained from the corpora cavernosa through numerous emissary veins and from the corpus spongiosum via a number of circumflex veins. The cavernosal veins are found coursing along each corpus cavernosum extending distally to the glans and situated between the dorsal artery and the deep dorsal vein, but deeper than the latter one and within a different perivascular sheath, lying intimately on the tunica albuginea and receiving direct emissary venous drainage. The cavernosal veins are asymmetrical bilaterally, both in size and course, constituting an independent drainage directly into the Santorini's plexus. Two sets of para-arterial veins were found accompanying the dorsal arteries. These veins are quite prominent distally, with the medial one receiving emissary drainage from the corresponding corpus cavernosum and the lateral one occasionally having its own circumflex vein from the corpus spongiosum. The para-arterial veins either drain into the DDV close to the infrapubic angle or enter the pelvis independently. The drainage proportion of the corpora cavernosa was 60.5 (50.3-69.7)%, 11.9 (5.8-22.9)% and 11.4 (5.2-15.0)% via the DDV, CVs, and PAVs, respectively [115]. This innovation is by no means an abrupt event, but rather a protracted research journey inspired by those who had undertaken PVL elsewhere (Figure 6). It raises the hypothesis that the conventional description of the penile erection-related vein is too simplistic, leading to investigation of this sophisticated venous anatomy. Furthermore, in order to negate the psychogenic influence on the human erection, studies conducted on fresh and defrosted human cadavers arrived at the conclusion that penile veins play a pivotal role in determining a rigid erection [116-118].

The innovation of penile venous anatomy has enabled the development of refined penile venous stripping surgery, an even more radical procedure, routinely performed under local

anesthesia on an outpatient basis [119, 120], as well as being the ultimate in USPTO patent [121].

A



B

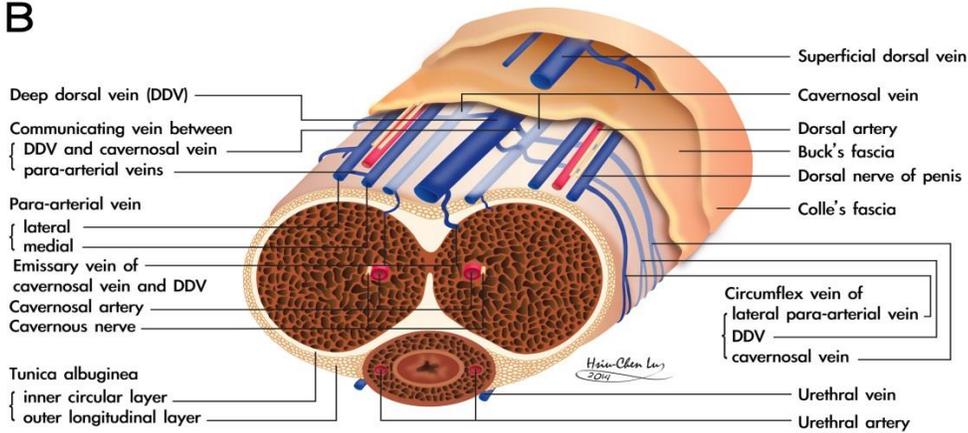


Figure 5. Schematic illustration showing an innovative penile venous anatomy in the human penis. (A) Lateral view: The deep dorsal vein is consistently distributed in the median position and receives blood from the emissary veins draining the corpora cavernosa and the circumflex vein communicating with the corpus spongiosum. It is flanked by bilateral cavernosal veins, although these lie at a deeper position in specific venous sheath. Bilaterally, each dorsal artery is sandwiched between its corresponding medial and lateral para-arterial veins. Note that the lateral para-arterial vein merges with the medial one proximally. (B) Cross section of the penis in middle pendulous portion. There are a total of seven veins, not just one, as was traditionally believed, between the tunica albuginea and Buck's fascia. Note that the number of independent veins becomes four at the level of the penile hilum because each pair of the nomenclature veins merges. Erection-related veins are arrayed in an imaginary arc on the dorsal aspect of the tunica albuginea with connecting network. This is a blueprint for penile venous stripping, and ligation sites (cross) are performed closest to the tunical level.

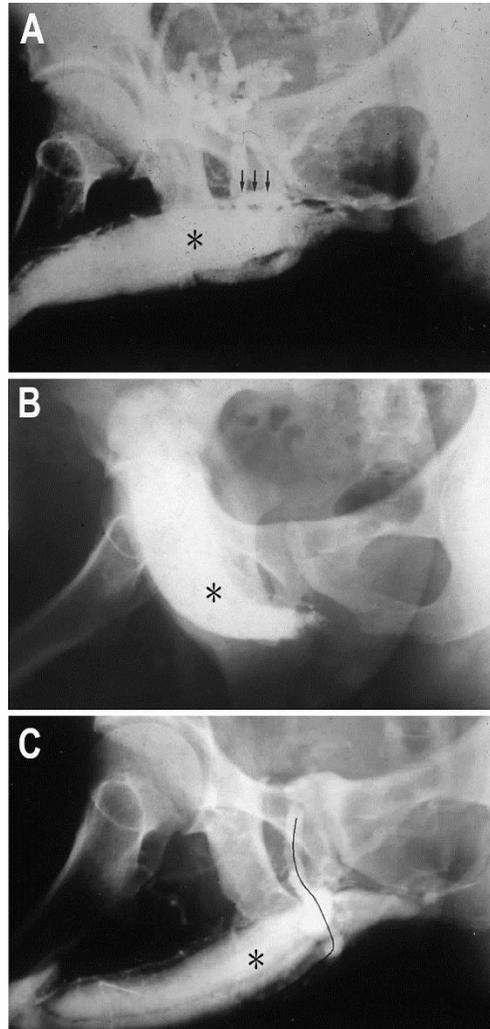


Figure 6. Cavernosograms in a 57-year-old patient whom underwent a salvaging venous stripping after unsuccessful penile venous surgery elsewhere. Erectile dysfunction had been improved for only 2 months despite two instances of penile venous ligation surgeries elsewhere in 1985. (A) A cavernosogram in our Institute disclosed conspicuous veins (arrows) after a standard dynamic infusion cavernosometry and cavernosography (DICCC) in 1986 failed to detect any vascular abnormality. Those offensive veins were subsequently stripped the following week. (B) This film was one of the serial pharmaco-cavernosograms which disclosed no veno-occlusive dysfunction in 1986. (C) A pilot cavernosogram was performed per physician request, showing a successful salvaging penile venous stripping in 2003. Not only are the offensive veins no longer visible, the penile morphology also looks like an ideal penile morphology. Note that the bulbourethral vein (dark line) becomes the exclusive route of blood return. The penile crura are well distended in contrast to those in panel A. Surgical Technique for Refined Penile Venous Stripping (PVS) Surgery

In selection of patients with suspected venogenic ED, multidisciplinary diagnostic approaches were employed. Objective vascular testing was used for diagnosis of CVOD based on PDDU and our dual pharmaco-cavernosography (Figure 7). Those with an untreated chronic systemic disease (e.g., diabetes mellitus, chronic liver disease, renal failure, hormonal

insufficiency, or psychoneurotic disorders) or other obvious etiologies, such as prostate surgery, major pelvic surgery and trauma, were excluded.

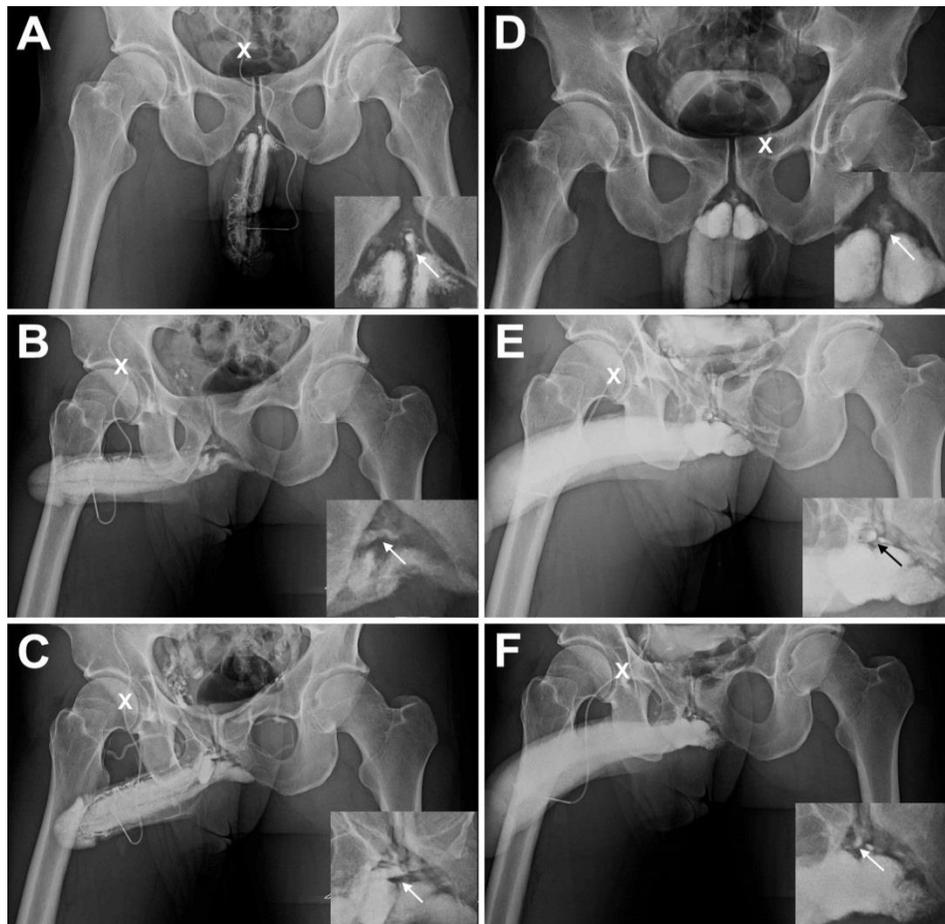


Figure 7. Dual pharmaco-cavernosography of a 45-year-old patient who underwent prior penile venous ligation (PVL) elsewhere internationally. (A) The first cavernosogram (anterior-posterior (AP) view) was obtained while a 10-ml diluted iohexol solution was intracavernously injected, resulting in the immediate opacification of the preprostatic plexus (arrow). Note the volcano-like eruption of emissary veins. (B) A 30° oblique-view cavernosogram was obtained after further injection of the 10-ml solution, while the drainage veins were not remarkable at the penile hilum (arrow). (C) This cavernosogram shows the ligation site (arrow) of the prior PVL after another 10-ml solution was perfused. (D) A second set of cavernosograms was obtained 20-30 minutes after intracavernous injection of 20 μ g of prostaglandin E1 (test). The bulking of drainage veins is relatively small in this AP view compared with that in panel A, implying that leakage veins could be relatively compressed. The veins were opacified; nevertheless, a rigid erection was attained. (E) This cavernosogram was obtained under the same condition as that in panel B; again, the offensive veins are smaller. (F) This cavernosogram provides consistent evidence of smaller veins. Overall, this can explain why PVL was misinterpreted as an improvement.

The patient was positioned supine on the operating table. Once the patient had been prepared and draped, local anesthesia was used for the procedure [119]. One dose of

intravenous broad-spectrum prophylactic antibiotic had been administered prior to the operation.

In accordance with the revolutionary penile venous anatomy as a blueprint, the penile venous stripping surgery was carried out in sequence (Figure 8). A circumcision (Figure 8A) was first made to identify the DDV (Figure 8B) which was freed 2-3 cm proximal to retrocoronal sulcus (Figure 8C), then was thoroughly stripped distally to the level of the glans penis, where several dozen branched veins may reside (Figure 8D). Care was taken to avoid injury to the paired dorsal arteries and nerves. A step-by-step pull-through maneuver of the DDV system was carried out proximal to the penile hilum, with the trunk of the DDV serving as a guide, passing through the openings made on the Buck's fascia at the exits of the emissary veins in order to minimize tissue damage (Figure 8E). In each lateral aspect of penile shaft there are 5-8 circumflex venous plexus which required ligation closest to the corpus spongiosum. A 4-0 silk tag suture is made at the 5 o'clock position for fixation during further dissection and management (Figure 8F).

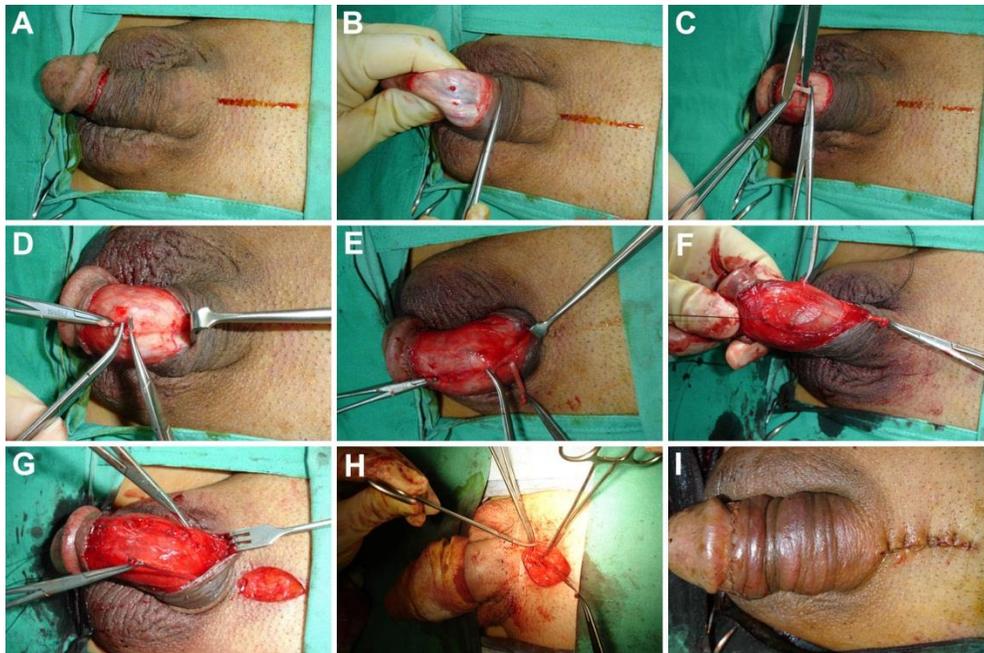


Figure 8. Photos of the progression of the penile venous stripping process. (A) A longitudinal pubic incision was marked and circumcision performed to access the offensive veins. (B) The visibility of the deep dorsal vein (DDV) was enhanced by employing a milking manipulation, mimicking a squeeze applied to a balloon, of the corpora cavernosa. (C) The DDV trunk was freed for 2 cm, firmly held by a pair of hemostats, and cut in the middle. (D) The distal stump served as a guide for stripping and ligating several dozen branches. (E) Likewise, antegrade stripping was performed in a pull-through maneuver using the proximal stump. (F) A dozen circumflex veins were identified and treated. (G) The superficial dorsal vein was spared to preserve physiological circulation. (H) A longitudinal pubic incision was performed to relay and complete the stripping procedure up to the level of the infrapubic angle, where several venous trunks are consistently encountered. (I) The wound was closed with 5-0 chromic sutures.

The CVs were similarly managed (Figure 8G). Subsequently, a longitudinal pubic incision was made to deliver the DDV and CVs trunk underneath through the wound. The

suspensory ligaments were not divided. The DDV and CV systems were respectively ligated for 7-10 and 4-9 branches (Figure 8H) proximally until the infrapubic angle was reached. Engorged circumflex veins and PAVs were attributable to rich drainage of emissary veins and resorted to simple ligation respectively. Finally, the bilateral crural veins were managed close to the bulbocavernosus muscle [120]. Excessive application of the electrocautery outside the tunica can produce tissue destruction extending far beyond the treated foci of interest [122]. With electrocautery spared, fine 6-0 nylon sutures were utilized for ligation of veins and hemostasis through the entire procedure. Upon completion of the ligation procedure and meticulous hemostasis, the penis was replaced into its anatomic position and the wound is closed (Figure 8I).

Outcome of Refined PVS Surgery

Prospects for the application of refined venous surgery appear promising. However, it is impossible to compare the outcome among series in the presence of variable criteria for selection of patients, diverse surgical techniques, different methods and durations of follow-up.

The complexity of the venous drainage of the penis may be a significant problem in explaining the lack of long-term success of venous ligation procedures reported in previously published research. Employing the refined PVS surgery, Hsu et al. reported an improvement rate of 90.4% in well-selected patients with CVOD during a period of follow-up ranging from 5.1 to 8.2 years [120]. They also reported salvaging PVS surgery with fair outcomes on patients who had suffered poorer erectile capability and/or penile deformity from preceding venous surgery elsewhere [123]. Controversy exists as to whether the insufficient response to PVS surgery in an attempt to restore erectile function results from recurrent or residual veins. Hsu et al. proposed that the clinical relapse of ED was a consequence of “residual” veins rather than “recurrent” ones [124]. Furthermore, most surgeons’ training instills a preference for electrocautery usage, which may be a major cause of cavernosal fibrosis, resulting in unfavorable postoperative erectile function (Figure 9). It is of interest to note that a number of surgical failures can also be rescued with intracavernosal administration of vasoactive agents to which patients were unresponsive prior to the operation [125]. Wen et al. reported their results on the synergism of penile venous surgery and oral sildenafil in treating patients with erectile dysfunction [126]. Furthermore, in conjunction with corporoplasty and PVS, combination surgeries may offer a viable option for treatment of ED and penile morphology reconstruction [127].

Possible Complications

Compared with those reported in the literature, perioperative complications seem minor and negligible, including minor bruising, hematoma formation, and temporary edema.

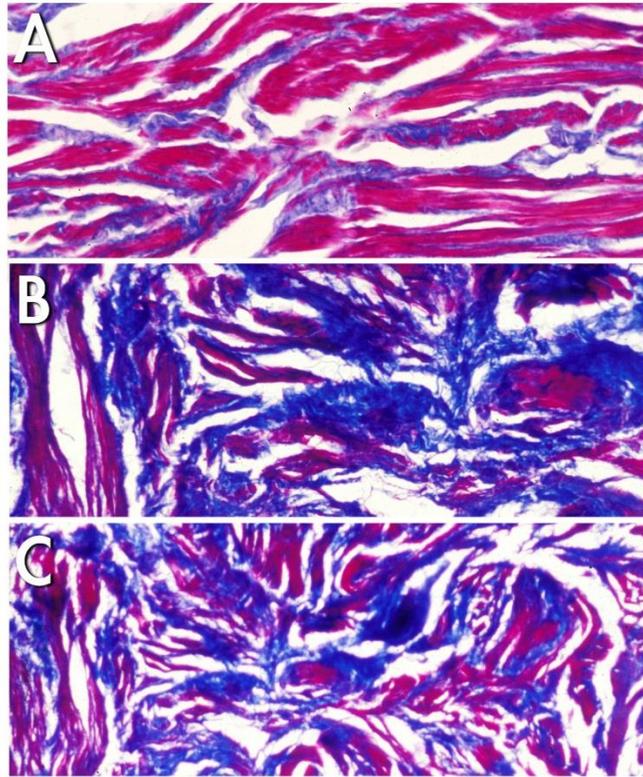


Figure 9. Histology evidence of electrocautery effect. (A) Photo of the sinusoids in a 52-year old patient who underwent total penectomy. The regular and healthy sinusoid with abundant smooth muscle (red color) is evident ($\times 400$, Masson trichrome stain). (B) and (C) Representative histology image of the corpus cavernosum taken from patients who received penile implants after our unsuccessful salvaging venous surgery for their previous PVL elsewhere in this study, disclosing extensive and significant fibrosis in which the collagen filers (blue color) are predominant ($\times 400$, Masson trichrome stain). (Reproduction from *J Androl*, 2010. 31(3) p. 250-60.).

CONCLUSION

With the current review of evidence-based analysis there are no additional outcomes data of sufficient quality or quantity to supersede the recommendations proposed by the guideline panels. The efficacy of this surgery is controversial, largely because selection and outcome criteria have not been objective, and because a variety of different surgical techniques have been used.

Despite the limited long-term benefits, penile venous surgery is an option that offers the possibility of obtaining spontaneous, unaided erections. The extensive collateral venous drainage of the penis is probably a major reason why most venous ligation procedures fail to have a consistent beneficial effect in the vast majority of patients with venogenic ED. Based on the new insight into penile venous anatomy, a definitive surgical removal of offending veins appears promising, and may bode well with better results in properly selected patients. This is intuitively attractive to both patients and surgeons. Patient consent should be provided in all cases on the basis of detailed information regarding the current uncertainties of this

procedure, alternative therapies, possible complications, the probability of secondary corrective surgery and the need for long term follow-up. There is still a need for further study with well-defined diagnostic criteria, and standardized patient and partner outcome assessment, preferably through randomized clinical surgical trials [128].

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