Penile preservation surgery in penile cancer

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Abstract: Penile cancer (PC) is a rare disease in developed countries, with an estimated incidence of 1 in 100,000 men in the US and Europe. However, in certain regions, such as South America, Africa, and Asia, the incidence is higher. A common histological subtype of PC is squamous cell carcinoma (SCC), with more frequent involvement of the distal regions of the penis. Several risk factors for PC have been identified. There is a strong relationship between phimosis and SCC, likely due to chronic infections. The classical treatment for primary PC has been partial or total penectomy with perineal urethrostomy. Yet, both of these surgical procedures are mutilating and have a significant negative impact on the patient's quality of life. The then-standard 2-cm surgical margins are no longer mandatory, and today, 5-mm margins are considered to be oncologically safe. Thus, penile preservation surgery has become the standard approach. In this chapter, we discuss the current knowledge on penile preservation surgery for PC, introducing laser therapy, Mohs micrograph procedure, wide local incision, glans resurfacing, glansectomy, partial penectomy, other focal therapies, and radiotherapy. Organ-sparing surgery (OSS) should be applied in PC whenever possible, and when performed properly, conservative techniques add significant benefits to quality of life but require strict follow-up and a collaborative patient.

Keywords: Penile cancer (PC); preservation surgery; organ-sparing surgery (OSS); glansectomy

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Introduction

Background

Penile cancer (PC) is rare in developed countries, with an estimated incidence of 1 in 100,000 men in the US and Europe. However, in other regions of the world, this rate is higher. The highest incidence has been observed in South America, Africa, and Asia (2.3–8.3 cases/100,000), and in certain countries, such as Uganda, PC is the most commonly diagnosed cancer in males (1). Recently, Maranhão, Brazil recorded one of the highest incidences of PC worldwide, predominated by locally advanced disease at the diagnosis (2).

A common histological subtype of PC is squamous cell carcinoma (SCC), with more frequent involvement of the distal regions of the penis—58% of the cases occur on the glans, compared with 16% on the foreskin and 9% on both the glans and foreskin. SCC commonly develops in the sixth and seventh decades of life. But, it can also affect young patients, a Brazilian survey reported that up to 38% of men

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with SCC were aged under 55 years at diagnosis (3,4).

Several risk factors for PC have been identified. There is a strong relationship between phimosis and SCC, likely due to chronic infections, although the carcinogenic role of smegma remains unknown. Other important risk factors are low socioeconomic status, poor personal hygiene, multiple sexual partners, and human papillomavirus (HPV) infection (4). Recently, sex with animals has been reported as an independent risk factor of PC (5).

Rationale and knowledge gap

Nearly 40% of men with PC are diagnose with localized disease, which has a 5-year overall survival of ~90% (6). Historically, the classical treatment for primary PC has been partial or total penectomy with perineal urethrostomy. Both of these surgical procedures, however, are mutilating and have a significantly negative impact on the patient's quality of life, self-image, and sexual function. Although the cumulative 5-year recurrence-free rates of penile-sparing surgery are reported to be 82% in case series (CS) and 76.7% in non-randomized comparative studies (NRCSs) and the cumulative 5-year recurrence-free rates of amputative surgery are reported to be 83.9% in CS and 93.3% in NRCSs, the then-standard 2-cm surgical margins are no longer mandatory, and today, 5-mm margins are considered to be oncologically safe, rendering organ-sparing surgeries (OSSs) the standard surgical approach, whenever possible (7,8).

Objective

We aim to revisit and update the current knowledge on penile preservation surgery for PC. Ablative procedures, topical treatments, and irradiation modalities will also be addressed briefly.

Surgical techniques

Laser therapy

Laser therapy was first used for PC in the late 1960s with the ruby laser. This modality was derived from MASER (microwave amplification by stimulated emission of radiation) and was developed by Theodore Maiman (9). After decades of evolution and improvements, laser therapy is now used for small Ta, Tis, and T1 superficial tumors, yielding good aesthetic and functional results. However, local recurrence rates can reach up to 50%, occurring primarily in the first year, necessitating a restricted follow-up (10,11). Giant condylomas and papillary and warty tumors are superficially invasive neoplasms with low malignant potential that can also be treated by laser (7).

During this procedure, topical acetic acid, under visual magnification, can be applied to the surrounding skin to help identify satellite lesions that could be invisible to the naked eye (4).

A CO_2 or Nd:YAG laser can be used; whereas the former is limited by its superficial depth of penetration (0.02–1 mm), the latter has a deeper penetration depth of 3 mm. In certain cases, the 2 lasers can be combined—the CO_2 laser cuts better and can be used first to excise the lesion, followed by the Nd:YAG laser to coagulate the tumor bed (4).

Despite the functional advantages of laser therapy, pathological staging can be compromised due to thermal damage, rendering it difficult to determine the tumor staging precisely (9).

Schlenker *et al.* (10) retrospectively evaluated 54 patients who were treated with (Nd:YAG) laser: 11 with carcinoma in situ (Tis), 39 with T1, and 4 with T2 tumors. There was local recurrence in 16 patients (42%), but notably, there was no significant difference in recurrence rates in those with Tis or invasive penile carcinoma (11). However, for tumors stage ≥T2, the high rates of recurrences (32% to 100%) suggest that this method is unsuitable (12).

Mohs micrographic procedure

Mohs micrographic surgery (MMS) is a technique in which consecutive thin cross-sections of are lesion are resected, in association with intraoperative microscopic evaluation, until the surgical margins are negative. This approach allows one to identify subclinical lesions and effect maximum preservation of normal tissue. Some groups sharply debulk the tumor with a scalpel prior to removing the MMS layer (13,14). In the classical paper from 1985, Mohs and colleagues presented a series of 29 consecutive patients with SCC who were treated with this technique. The 5-year cure rate among the 25 determinate cases was 68% (15). In a more recent series, there was 1 recurrence among the 19 primary SCCs *in situ* that were treated with MMS, resulting in a cure rate of 94.7% (median follow-up 75 months). Of the 10 patients with primary invasive SCC, there was no recurrence (median follow-up 177 months) (13).

The success rates of MMS appear to be inversely proportional to PC lesion size. In a recent review of 43

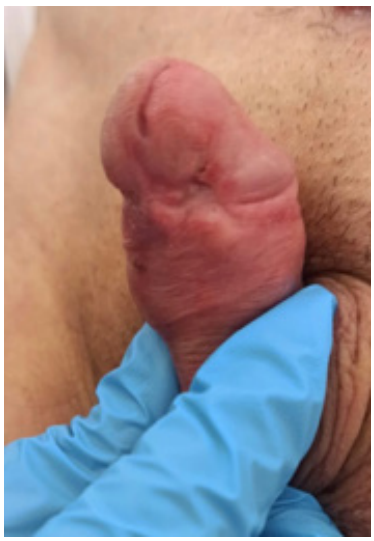

Figure 1 Wide local excision: aspect after 60 postoperative days.

patients who underwent MMS, only 1 patient experienced local recurrence at a median of 47 months of follow-up. Local recurrence rates for Ta, Tis, and T1 PCs were 0%, whereas that for T2 patients was 14% at 1 year (16).

Unfortunately, MMS is time-consuming and costly, with limited indications, and requires an experienced multidisciplinary team. Thus, this method has not been used widely in urology.

Wide local incision/circumcision

Circumcision may be appropriate for select patients with small, low-grade lesions in the distal foreskin or as an adjunct technique in other cases, providing better exposure of the glans and facilitating postoperative follow-up. In certain cases with larger lesions, there is a need to suture the foreskin directly to the glans. The estimated recurrence rate for this technique is 15% (17).

For small Ta/T1 lesions on the glans and penile shaft, wide local excision can be performed using a primary suture (*Figure 1*), foreskin flap, or extragenital split-thickness skin graft (STSG). It is important to use intraoperative frozen sections to achieve negative surgical margins.

Glans resurfacing

First described by Dr. Aivar Bracka for severe cases of lichen sclerosus of the glans, glans resurfacing can be used to excise premalignant and superficial lesions of the glans, such as *in situ* SCC that is refractory to other treatments (18,19).

This technique involves placing a tourniquet at the base of the penis and making circular incisions in the perimeatal area and coronal sulcus. Next, the glans is divided into 4 quadrants, and the epithelium and subepithelium are removed completely from the underlying corpus spongiosum, from the meatus to the coronal sulcus for each quadrant. Biopsies of the underlying tissue are necessary. The STSG is removed from the thigh region or another glabrous skin area with a dermatome and fixed in the exposed area of the glans with 5.0 absorbable sutures and separate stitches. A Foley catheter is placed for 5 days, and the patient is on strict bedrest for 2–5 days to prevent shearing of the skin graft, it is noteworthy that a variation of this technique, called tie-over dressing for graft application (TODGA), eliminates the necessity to maintain the patient in bedrest. Partial glans resurfacing can also be performed by adding a frozen biopsy to the edges of the resection (20-23).

This procedure is associated with rapid recovery, quick return to sensation of the glans, and good preservation of penile function (24). The oncological results should be analyzed with caution, considering that studies have included small samples; nevertheless, the technique has proven to be safe for well-selected cases. Shabbir *et al.* evaluated 25 patients with *in situ* SCC, reporting an overall local recurrence rate of 4% and no cases of progression (22).

The glans resurfacing technique usually results in cosmetic changes, due the difference in skin tone between the penile shaft and grafted area (18).

Glansectomy and reconstruction techniques

Glansectomy is indicated for T1 and T2 tumors that are confined to the glans. The procedure begins with a subcoronal circumferential incision in the shaft skin, down to the level of Buck's fascia, after which the dorsal neurovascular structures are ligated. The surgical plane under the Buck's fascia is developed; the glans is then dissected off the corporal distal extremities, and the urethra is divided, completing the excision. Frozen sections are obtained from the dorsal surface of the corporal bodies and urethra (25,26).

The simplest approach for reconstruction after glansectomy is urethral spatulation, followed by suturing of the penile skin at the midline and around the neomeatus. However, this technique does not yield the appearance of a neoglans (27). To obtain a better aesthetic result, other

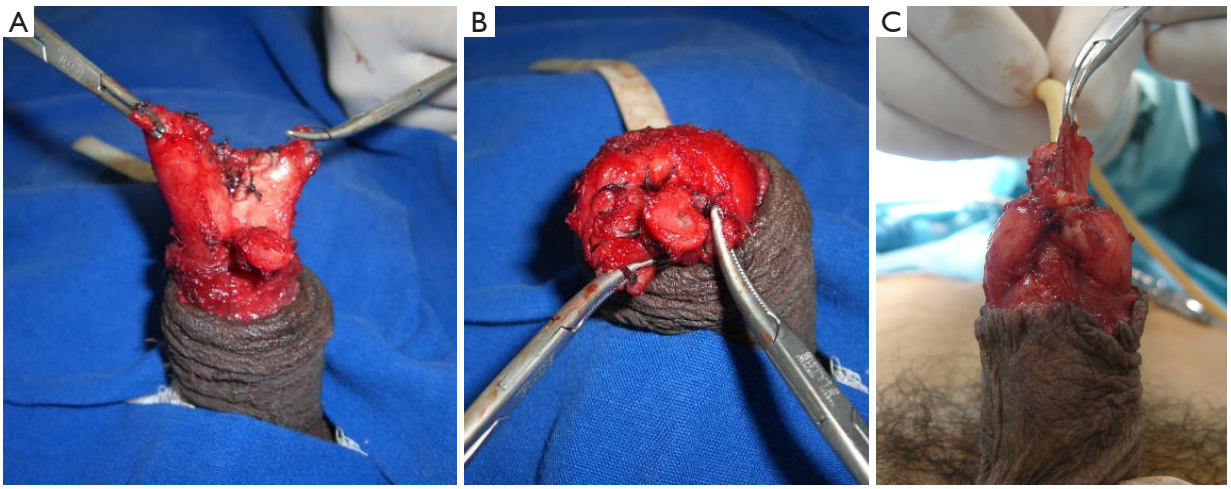

Figure 2 Neoglans with cavernous rotation. (A) The tips of the corpora cavernosa separated from each other and from the urethral stump. (B) Ventral rotation of the corpora cavernosa. (C) Corpora cavernosa sutured under the urethra.

techniques can be added to reconstruct a neoglans.

STSG reconstruction

The STSG is a frequently used option. This technique begins with suturing of the skin 2 cm from the tip, leaving the corporal heads exposed, after which an STSG is taken from the lateral thigh to cover the corporal heads. The graft is secured with absorbable sutures, and a Foley catheter is left in place for 5 days. Care must be taken with the frozen section—if the tips of the corpora cavernosa are compromised, they should be resected (25). Beech *et al.* evaluated 12 patients after reconstruction with STSG, reporting a disease-free survival rate of 91.7% (11/12) at a median follow-up of 14 months. Standing voiding, erectile function, and satisfied cosmesis were preserved in all patients, and no graft-related complications occurred (28).

Autologous testicular tunica vaginalis graft

In 2018, an Austrian group published a case report, using an autologous testicular tunica vaginalis graft to recover the glans. This tool appears to be a more reproducible technique for urologists, considering that it does not require dermatomes to remove the thigh graft. However, more studies should be performed (29).

Reconstruction of neoglans with cavernous rotation

This interesting technique is used to create the shape of the glans. After glansectomy, the tips of the corpora cavernosa are separated from each other and from the urethral stump, after which they are rotated ventrally and sutured under the urethra, resulting in the appearance of a balanopreputial sulcus (*Figure 2A-2C*). A skin graft is sutured over the corpora and stapled urethral stump (30).

Distal urethral advance

This technique has been described to preserve penile sensitivity. After glansectomy, the penile urethra is separated completely from the corpora cavernosa to obtain a urethral stump that is at least 3 cm longer than the tips of the corpora. The urethra is then sectioned 3 cm ventrally and shaped to cover the cavernous apexes, everting the mucosa over the dorsal side of the penile albuginea. The urethral borders are fixed to the corpora cavernosa with absorbable sutures, and the skin of the penis is sutured 5 mm away from the neoglans. In 2007, Gulino *et al.* published a series of 14 patients who underwent glans reconstruction with urethral advance—8 after glansectomy and 6 after distal amputation. The tactile and thermal sensitivity of the neoglans was preserved in all patients, and no local disease recurrence was reported after a mean follow-up of 13 months (31).

In small tumors on the glans, it is possible to perform a partial glansectomy and use a foreskin flap to cover the defect (*Figure 3A-3C*). It is important that the tumor be sufficiently far from the urethral meatus, to avoid deviation of micturition (30).

Oncological results after glansectomy

Albersen *et al.* retrospectively evaluated 117 patients after glansectomy. After a mean follow-up of 33 months, 12.8% of patients experienced local recurrence. Perineural

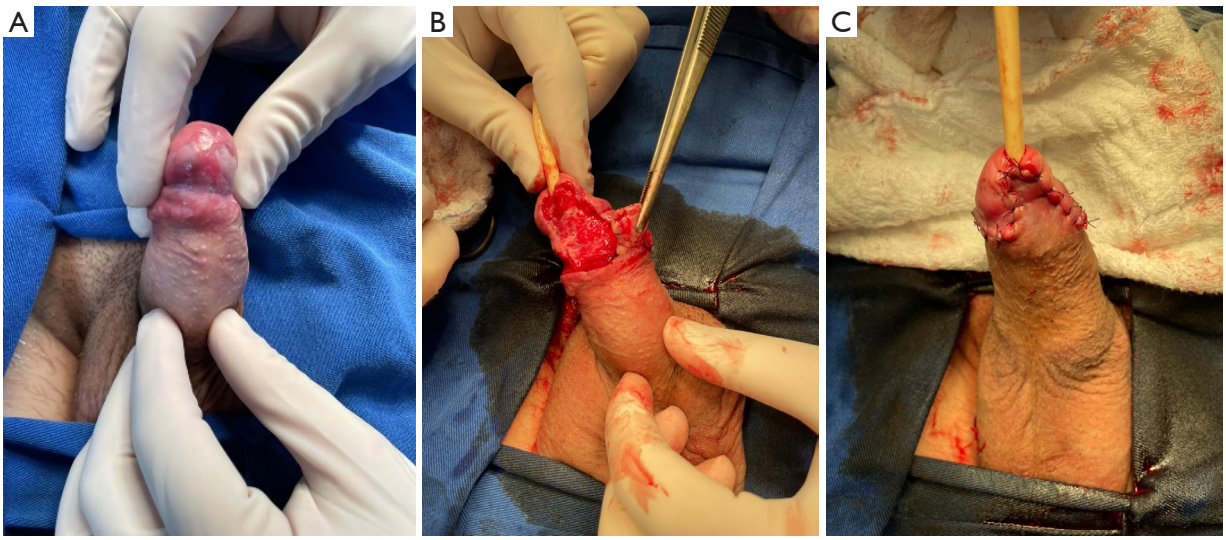

Figure 3 Foreskin Flap at partial glansectomy (Courtesy of Dr. Pedro H. Mota, Instituto do Câncer do Ceará, Brazil). (A) T1 lesion on glands. (B) Partial glansectomy. (C) Foreskin flap.

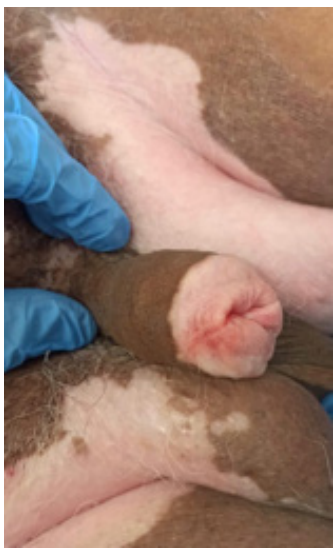

Figure 4 Classical partial penectomy.

invasion, carcinoma *in situ*, positive definitive margins, and the presence of high-grade SCC were predictive factors of recurrence (32).

A retrospective study that involved several international centers evaluated 410 patients who were treated with glansectomies. Only 31 patients experienced local recurrence, representing 7.6% of the study population. Fourteen patients (3.4%) developed regional recurrence, and 9 patients (2.2%) had distant recurrence. The authors concluded that glansectomy is a safe technique for SCC of the glans in appropriately selected invasive tumors (33).

The European Society of Urology considers glansectomy with reconstruction an option for distal pTa, pT1, and pT2 tumors (34).

Partial penectomy and procedures to enhance penile length

Classically, partial penectomy (*Figure 4*) is indicated when there is involvement of the corpora cavernosa. Additional goals of the procedure are to preserve the ability to void in a standing position and maintain sexual function. The surgery is similar to glansectomy, but the distal areas of the corpora cavernosa and urethra are resected together. Ideally, the urethral stump should be 1.5 cm longer than the corpora cavernosa. The corpora are closed transversally, and the penile skin is closed at the midline over the corporeal ends. The urethrostomy is performed by approximating the urethral stump to the adjacent penile skin with separate sutures (35).

Korkes *et al.* proposed a simple modification to the classical partial penectomy method to obtain better cosmetic and functional results: the parachute technique. In the updated version, the urethra is spatulated ventrally, and an inverted "V" skin flap with 0.5 cm of extension is sectioned ventrally. The suture is performed with Vicryl 4-0 in a "parachute" fashion, beginning from the ventral section of the urethra and the "V" flap, followed by "V" flap angles

and then the dorsal portion of the penis. As a result, when the penis is flaccid and the skin is not retracted, the aspect is similar to the prepuce of an uncircumcised man (36).

In 2021, an Indian group developed a revised version of the "parachute technique" of Korkes *et al.*, in which no V-shaped skin flap is created. After ventral urethral spatulation, the first skin suture is made on the apex of spatulation, followed by the lateral sides and finally on the dorsal side. Three patients were treated with this technique; at a mean follow-up of 8 months, all achieved good cosmesis and satisfactory functional preservation (37).

Several maneuvers have been described to enhance the length of the penile stump. Dividing the dorsal penile ligament and mobilizing the bodies proximally out of the pubic arch can lengthen the shaft by up to 2 cm; however, this technique can alter the angulation of the penile shaft during an erection (38). Ventral V-Y phalloplasty, which excises a segment of skin and the dartos of the penile/scrotal region, can help relieve tethering and create a new penoscrotal angle, lengthening the penis (7,39). Lipoaspiration of prepubic or penoscrotal fat has also been proposed (7).

Topical therapies and photodynamic therapy (PDT)

For all noninvasive PCs (e.g., carcinomas *in situ* and such eponymous tumors as Queyrat and Bowen disease), in 2016, the World Heal Organization recommended a single umbrella denomination: penile intraepithelial neoplasia (PeIN).

For the nonsurgical treatment of PeINs, beyond the laser (described above), several topical treatments have been historically applied, including 5-fluorouracil (5-FU), imiquimod (IQ), and PDT. The literature, varying widely and limited to small series, has generally reported a complete response rate of 40% to 50%, significant expenses for several weeks of therapy, and out-of-pocket expenses for drugs; local dermatological side effects and irritation can also develop, which are usually clinically manageable (40,41).

PDT has emerged recently as an effective treatment for PeINs; however, it is associated with postoperative pain and local erosions after application (41). Usually, PDT entails approximately 5 visits but is unavailable for urologists, being more commonly used by dedicated dermatological centers.

In 2020, Gao *et al.* reported 100% local control rates in China in 3 patients who underwent PDT with circumcision. The authors considered PDT to be controversial, but in this setting, they recommended it in conjunction with circumcision (42). It is unknown whether this combination is significantly superior to the exclusive postectomy, used in the last decades. In a large series of 315 patients who were treated by multidisciplinary urological and dermatological teams from several London hospitals, a group found that only 14.4% was treated successfully solely by cryotherapy or other topical treatments. The results on the use of topical treatment for PeIN remain "disappointing", and 85.5% requires surgical procedures, with satisfactory results (43).

Radiotherapy

External beam radiotherapy (EBRT) has been used classically in PC to treat localized disease for patients who desire preservation of the phallus, but it has inferior local control rates compared with surgical treatment. When local recurrence occurs (20% to 40% of cases), salvage surgeries are effectives in most cases (44,45).

Penile tumors can be treated with interstitial brachytherapy (IB), surface mold plesiotherapy, and EBRT. Since the 1990s, EBRT has been replaced gradually by IB as the preferred irradiation modality for phallus preservation, given that its 5-year local control and cancer-specific survival rates (70% to 85% and 72% to 90%, respectively) are superior to those for EBRT for T1–T2 tumors (41% to 65% and 66% to 85%, respectively) (45,46).

The results of all radiotherapy modalities are volume-dependent and stage-dependent, beyond the inherent tissue radioresistance and radiosensitivity. Better oncological results and lower complication rates are achieved with IB for PC only for small lesions and for limited tumor radioactive lengths (<18 cm), tumor diameters (<4.0 cm), and tumoral volumes (<22 cc) (47).

It is important to emphasize that in addition to the previously described promising results involving radiation therapy, some recent series in brachytherapy as described by Pohanková and collaborators and Martz and collaborators demonstrate even better results in local control with rates close to or greater than 80% of penile preservation at 5 years in localized disease (T1–T2). Therefore, this well-established treatment modality is an excellent option when available (48,49).

Margins status, follow-up, and salvage procedures

As in other organ-sparing treatments in urological oncology, when OSS protocols are applied for PC patients, fundamental principles must be strictly followed to

minimize and obtain secure intraoperative surgical margins, necessitating the use of frozen section biopsies. After such surgeries, patients must be monitored through rigorous long-term follow-up that promotes highly proactive and clinical suspicion of early detection of local recurrences. If necessary, salvage treatments must be as oncologically safe as primary radical procedures, without compromising survival rates (6,34).

Conclusions

OSS should be uses in PC whenever possible. Compared with classical penile amputations, OSSs are associated with a higher local recurrence rate (8). However, most of these recurrences can be treated with another OSS or amputation; thus, overall survival does not appear to be affected (50). In conclusion, when used properly, conservative techniques add significant benefits to quality of life but require strict follow-up and a collaborative patient.

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Footnote

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