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REVIEW ARTICLE

Organ Preservation Surgery for Carcinoma Penis

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Abstract Carcinoma of the penis is not uncommon in India. A sizeable number of patients do not report to the doctors in fear of mutilation to the organ and hence subsequently end up with advanced disease. Many patients with T1 or T2 disease when carefully selected are amenable to organ-preserving penile procedures including surgery, topical therapy, laser, and radiation therapy. Identification of appropriate patients and institution of these treatments has been noted to produce oncologically comparable results to extirpative surgeries. In this article, we review the criteria to identify patients qualifying for organ-preserving treatments and also review outcomes with a variety of penile-preserving procedures.

Keywords Penis · Carcinoma · Organ preservation

Introduction

Carcinoma of penis is not uncommon in India, although it is rare in Western countries [1]. Wollina U et al. highlights that the prevalence of cancer of penis is linked to racial, cultural, and socioeconomic factors [2]. Irrespective of its incidence and prevalence, its management can have significant anatomical, functional, and psychological effects on patients.

Upon hearing the diagnosis, the patients are worried about their erectile function, especially sexually active men and also about their body image. These patients are reluctant to undergo a procedure which is mutilating to not only their body but also to their self-confidence. This has prompted newer penis-preserving techniques to come into light which provides both physical and psychological solution to these people. These options have brought about a major shift from "mutilation" to "conservation." Many authors in literature have expressed similar views [3–5].

This review focuses only on the penile-preserving surgeries which would help to understand the options available if one opts for a penile conservation surgery.

The goals of organ preservation surgery are to maintain cosmesis in terms of penile shaft length and function in terms of penile/glans sensation without compromising the oncological outcome.

Indications for Penile Preservation Surgeries and Options Available

Primary tumor	Penile-preserving therapy
Tis	Topical therapy
	Laser ablation using Nd:YAG laser
	Glans resurfacing
Ta, T1a (G1, G2)	Wide local excision
	Laser ablation
	Glans resurfacing
	Glansectomy with reconstructive surgery
	Radiotherapy (EBRT ± BT)
T1b (G3) and T2 confined to glans	Wide excision ± reconstructive surgery

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Laser ablation

Glansectomy with reconstructive
surgery

Radiotherapy (EBRT ± BT)

Penile preservation strategies include medical and surgical approaches. Medical treatment consists of Moh's micrographic surgery, topical applications, laser treatments, radiotherapy, and cryotherapy. Surgical options include partial and complete glansectomy, partial penectomy, wide local excision, etc.

Topical Agents

5-Flurouracil (5-FU) and immune response modifiers such as imiquimod 5% and interferona-2a cream are indicated for superficial and/or premalignant penile lesions [6, 7]. The cream is applied directly onto the lesion for 4–6 weeks with variable success.

Laser Ablation or Excision

The carbon dioxide laser and neodymium YAG laser are the most commonly used in current practice [8, 9]. Since the energy is completely absorbed at impact by the water component of the cell, the carbon dioxide laser vaporizes tissue with minimal penetration of energy into the deeper layers (only 0.1 mm) and therefore it is unsuitable for most tumors with recurrence rates of up to 50% [9]. The neodymium YAG laser penetrates tissue and causes coagulation to a depth of at least 3 to 4 mm [9]. CO2 laser has a very low penetration power (only 0.1 mm) and is, therefore, unsuitable for most tumors, resulting in recurrence rates of up to 50% [10]. Boris Schlenker et al. [11] analyzed 54 patients using organ-preserving neodymium-yttrium-aluminum-garnet laser therapy for penile carcinoma and found that there was local recurrence in 16 patients (42%); the mean (range) time to local recurrence was 53 (9–132) months. They further caution that even though organ-preserving laser therapy showed a relatively high recurrence rate in patients with a long-term follow up, the oncological outcome and survival were not compromised by local recurrence. Therefore, laser therapy appears to be appropriate for treating premalignant lesions and early stages of penile carcinoma. Contraindication to laser therapy includes a depth of > 6 mm and T2 lesion. Good cosmetic and functional outcome are obtained using laser. Francisco E et al. [12] in their review mention that though laser has significant anatomical, cosmetic, and functional advantages over traditional amputation, a close surveillance is mandatory for early detection of local recurrence, which is higher. Hence, patient selection is extremely important. Because in laser surgery the depth of tumor invasion is crucial, only those invading less than 6 mm into tissues are suitable for this treatment modality.

Radiotherapy

Radiation treatment of the primary tumor is an alternative organ-preserving approach with good results in selected patients with T1-2 lesions <4 cm in diameter [13–18]. External radiotherapy is given with a minimum dose of 60 Gy combined with a brachytherapy boost or brachytherapy on its own [14, 16]. Radiotherapy results are best with penile brachytherapy with local control rates ranging from 70 to 90% [14, 16]. There are two common BT techniques described in the literature: (i) a radioactive mold is placed over the penis and is worn by the patient for 12 h/day for 7 days. This delivers approximately 0.6 Gy to the tumor and 0.5 Gy dose to the urethra. (ii) Implantation of a radioactive iridium (Ir 192) seed into the penis which is removed when the predetermined dose has been delivered. Circumcision is a must before radiotherapy with glans tumor to reduce radiation-induced complications [17]. BT offers good success rates particularly for low-stage disease and in general is more successful than EBRT. The 5-year rate of penile preservation after BT ranges from 70 to 88%, which is higher than the corresponding 36–66% rates for EBRT [18–20]. The American Brachytherapy Society and the Groupe Européen de Curiethérapie-European Society of Therapeutic Radiation Oncology (ABS-GEC-ESTRO) consensus statement for penile brachytherapy reported good tumor control rates, acceptable morbidity, and functional organ preservation for penile brachytherapy for T1 and T2 penile cancers [21]. Kamsu-Kom L et al. suggested that the efficacy/toxicity results of PDR brachytherapy for the treatment of penile carcinoma are comparable with those obtained with LDR brachytherapy in historical cohorts [22]. Sharma DN et al. in their results have demonstrated excellent local control rate and acceptable toxicity with HDR-IBT in patients with T1-T2-stage penile carcinoma [23]. Azrif M et al. in their study have concluded that the rates of local recurrence after radiotherapy are higher than after partial penectomy. With local failure after radiotherapy, salvage surgery can achieve local control [24]. Patients with lesions >4 cm are not candidates for brachytherapy. Zouhair A et al. cite common complications with radiotherapy as urethral stenosis (20–35%), glans necrosis (10–20%), and late fibrosis of the corpora cavernosa [25]. With brachytherapy, meatal stenosis occurs in >40% of cases.

Cryotherapy

In this modality, liquid nitrogen is used to achieve temperatures of −20 to −50 °C to cause tissue damage by cellular

membrane disruption and subsequent cell death. Shabbir et al. in their study compared cryotherapy and topical 5-FU in the treatment of Bowen's disease and found that the risk of recurrence after cryotherapy (13.4%) was greater than after 5-FU treatment (9%) [26]. Hansen et al. studied a group of 299 patients with Bowen's disease and compared treatment with 5-FU with Cryotherapy. They found that there was a greater risk of recurrence after cryotherapy (13.4%) compared with 5-FU (9%) and surgical excision (5.5%) [27].

Moh's Surgery

An alternative surgical approach is excision using Moh's micrographic surgery. This involves removal of the entire lesion in thin sections, with concurrent histological examination to ensure clear margins microscopically [26]. The indications for performing penile Moh's surgery are carcinoma in situ or verrucous carcinoma, lesions of the distal penis or glans penis, otherwise amenable to partial penectomy and a desire for penile-preserving surgery [28]. Shindel AW et al. in their study found that Moh's micrographic surgery for low-stage penile cancer results in a relatively high local recurrence rate. The 5-year survival rate has been reported at >85% of cases [29].

In Moh's series, 79% (23/29) were cured at 5 years [30]. In the other series, 68% (17/25) were recurrence-free after a median of 37 months and 8% (2/25) had inguinal nodal recurrence and died of the disease [29]. One cancer-specific death was reported in each series, with the local recurrence rate that was 32% (8/25) in one series [29].

The advantages of adopting Moh's technique include proper and near accurate tumor mapping and excision with no positive margins and also preservation of uninvolved penile tissue with improved cosmetic or functional outcome. The disadvantage of the Moh's technique is poorer local control as evidenced by the high rates of local recurrence.

Circumcision

Uncircumcised penis is a harbinger of malignant change occasionally. Being the most common surgical procedure in the management of penile carcinoma, it is indicated for symptomatic treatment of painful or hemorrhagic tumors as well as for acquired phimosis secondary to preputial tumors. Also, it is always recommended before radiotherapy as it allows better exposure, targeting, and definition of the tumor (12). Bissada et al. mentions that circumcision alone is a sufficient primary curative treatment for small low-stage (Tis, Ta, and T1) and low-grade (grades 1 and 2) disease limited to the distal prepuce [31]. A. S. Narayana et al. in their analysis of 219 cases found that if the tumor is more proximal and close to the coronal sulcus, the circumcision margin will need to be extended proximally to the penile shaft to ensure adequate oncological resection, as recurrence rates may be as high as 50% [32]. Therefore, careful case selection is critical.

Glansectomy

About 80% of the penile carcinomas arise distally, which render them potential candidates for penile-preserving surgery (12). Glansectomy can be done either partially or totally for dealing with local excision of distal tumors on the glans and prepuce (32–35). This is followed by frozen sections from the cavernosal bed and urethral bed to confirm negative margins followed by an end-shaft urethrostomy.

Partial glansectomy is indicated in localized tumors of corona or central glans with no surrounding carcinoma in situ or obvious erectile tissue involvement on MRI. In partial glansectomy, a portion of the glans affected by the tumor is removed leaving behind remaining glanular epithelium with malignant potential, and in total glansectomy, all the glans tissue is removed. Glansectomy leaves a defect which may be a simple one or a larger and more complex one. In a simple defect, a primary closure would be amenable but if the defect is larger precluding a primary closure, then other techniques would be needed to cover the defect. Other techniques include glans reconstruction using full or slit-thickness grafting, lateral prepucial, or scrotal skin flap etc. [33–36]. C. T. Brown et al. describes procedure of subtotal glans excision without grafting as a simple and cosmetically attractive alternative to other forms of conservative surgery for penile carcinoma [33]. Mc Dougal et al. performed partial glansectomy in five patients preserving the meatus. In two patients, a full thickness graft was used and in one, a split thickness graft was used [39]. Brown C. T. et al. in their study of five men with squamous cell carcinoma of glans penis performed subtotal resection of glans and showed that with preservation of distal urethra, spraying of urine observed with total glansectomy can be reduced. At a mean follow-up of 12 months, no recurrence was noted with good cosmetic and functional outcome [34].

Total glansectomy first described by Austoni in 1996 [40] is indicated in lesions which are localized but are not amenable to partial glansectomy or are T2 lesions. If the tumor invades tunica albuginea and/or corpora cavernosa, then total glansectomy was performed followed by either split-thickness skin graft reconstruction or reconstruction of cavernosal tips and grafting, if a distal corporectomy was required. In some cases, a penile-lengthening procedure was added to the reconstruction to maintain as much cavernosal tissue as possible [29].

Pietrzak et al. in a prospective study of 49 patients performed organ preservation surgery in 39 patients. Of the 78 patients referred, 49 required surgeries, with penile-preserving

procedures in 39 of them. At a mean follow-up of 16 months, one patient who had glans preserving surgery developed recurrence whereas none of the patient who had undergone total glansectomy recurred. They conclude that with careful patient selection and meticulous follow-up, most patients with invasive penile carcinoma can be offered penile-preserving surgery. New studies conducted by Philippou P et al. have shown that a margin of 0.5 cm is oncologically safe [37].

The disadvantages of this procedure include potential cancer recurrence in the remaining glans, risk of loss or contraction of graft, or graft overgrowth over the external urethral meatus, decreased penile sensitivity and a loss of penile length is a common complaint [32, 35, 36, 38].

Wide Local Excision

Wide local excision (WLE) is considered as one of the gold standard for T1, T2 and selected T3 tumors [39]. WLE may be performed in conjunction with primary closure or split-skin grafting. For low-risk tumors a 10 mm clearance is adequate for grade 1 and 2 lesions, and 15 mm for grade 2 tumors in contrary to the 2-cm surgical margin traditionally proposed [10]. Philippou and colleagues also concluded that penile conserving surgery is oncologically safe and a surgical excision margin of less than 5 mm is adequate [37]. WLE can be performed for pre-cancerous lesions, discrete lesions, extensive preputial disease where circumcision alone is not curative and T1, low-grade tumors of the shaft [17]. Lont AP et al. looked into the 5-year local recurrence-free estimate after penis preservation for T1 and T2 tumors. They found it to be similar and concluded that the incidence of local recurrence increases with penis preservation but can be treated accurately in most cases.

Contraindications to wide local excision include tumor very close to the urethra, meatal involvement or lesions extending more than 50% of glans penis. To avoid complications such as deformity or deviation, it may be combined with split-skin grafting.

Omid Sedigh et al. looked into the sexual function after surgical treatment for penile cancer and found that wide local excision lead to better sexual outcomes and less postoperative complications as compared to glansectomy with urethral glanduloplasty hence when feasible; wide local excision could represent the best conservative approach to treat localized primary penile cancer [40].

Partial Penectomy

Partial penectomy remains the standard care for men with distal penile cancer especially if there is disease extension into the urethra or corporal bodies and/or local recurrence of disease after previous more conservative attempts at treatment

[41, 42]. Leijte JA et al., in their retrospective study, analyzed 700 patients from two referral centers for penile carcinoma for recurrences and compared laser therapy, WLE, and radiotherapy to partial or total penectomy. They concluded that local disease recurrence rates were lower with the latter treatment (5.3 vs. 27.7%) but there was no significant difference in overall disease survival [43]. Also, patients undergoing penile-preserving therapy (pN+), and those undergoing a wait-and-see policy for the nodal status are at high risk of developing a recurrence [44–48].

Conclusion

Earlier, the treatment of penile cancer was limited to penectomy and radiotherapy. But now, with the progress in science and availability of newer technology, penis-sparing strategies are available. These avoid the mental and physical trauma the patient undergoes due to the mutilating procedures. These procedures do not compromise any oncological principle as well. But one should be aware that these newer surgical techniques are stage dependant and hence proper patient selection is essential.

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