

# An Update on Organ Sparing Surgeries for Cancer Penis: A Review Article

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## Abstract:

Penile cancer is less frequently occurring cancer, but one with a higher incidence rate in India. Various risk factors leading to cancer development have been identified. Organ preserving surgeries for cancer penis are gaining much grounds. For the management of PeIN (Penile Intraepithelial Neoplasia) and carcinoma in situ, topical agents like 5FU (5-flourouracil) and Imiquimod are being successfully used. Use of lasers is being advocated in all lesion still T1, while radiation therapy has been found effective up to T2 lesions. Among the surgical techniques; Moh's surgery, circumcision and glans resurfacing can be performed for lesions till T1, while Glansectomy can be used even for T2 lesions. Partial penectomy can be performed in lesions till T3 stage.

**Keywords:** Glansectomy, Glans resurfacing, Moh's surgery, Partial Penectomy, Penile cancer, Topical agents.

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## I. Introduction:

In comparison to other cancers; penile cancer is relatively a rare entity. Unfortunately, the incidence in India is 1.4 /100,000 person years, compared to 0.8 worldwide. Moreover, penile cancers are more prevalent in countries where substantial population is poor compared to countries with plentiful rich people.<sup>1</sup> This malignancy is usually seen in the 5<sup>th</sup> – 7<sup>th</sup> decade of life. A majority (48%) of lesions are present over the glans, 21% of lesions involve the prepuce, 9% of lesions involve both glans and prepuce, and only 6% involve the coronal sulcus. Rarely the lesions occur over the shaft of penis (<2%). Squamous cell carcinoma accounts for 95% of the penile cancer.<sup>2</sup>

Various risk factors have been identified for development of penile cancer:

1. HPV (Human Papilloma Virus) is highly associated with penile cancer. In a study on Squamous Cell Carcinoma (SCC) of penis, 47.2% of the patients were found infected with HPV. The most common isolated serotypes were HPV16 (28.5%), followed by HPV18(2.3%) and HPV6(2.4%). Histologically, HPV was most prevalent in basaloid SCC (85.5%) and least prevalent in papillary type (16.7%).<sup>3</sup>
2. Practice of circumcision in childhood is protective against penile cancer (OR 0.33%).<sup>4</sup> The collection of smegma, development of phimosis and balanoposthitis in uncircumcised men can attribute to development of penile cancer.<sup>5</sup>
3. In adult men, who were circumcised for any medical condition, there is a strong association with development of penile cancer (OR: 14.87).<sup>4</sup>
4. Balanoposthitis can increase the risk of penile cancer by 3.82 times, while the development of phimosis subsequent to that increases the risk of cancer penis by 12 times.<sup>6</sup>
5. The risk of cancer development is 2.4 times higher in smokers and 3 times more with current smokers, than with non-smokers.<sup>7</sup>

TNM Staging of penile cancer. <sup>8</sup>

Location of the tumour (T)	
Category	Criteria
T <sub>x</sub>	Assessment of tumour could not be done
T0	Tumour is absent
T <sub>is</sub>	Pre malignant lesion (Penile intraepithelial neoplasia)
Ta	Squamous cell carcinoma with only local invasion
T1	<ul style="list-style-type: none"> <li>• Tumours of glans penis which involve up to the layer of lamina propria</li> <li>• Foreskin tumours invading either the dermis, lamina propria or the dartos fascia</li> <li>• Tumours of the penile shaft that invade any layer before the corpora</li> </ul>
T1a	The tumour cells have not invaded into any blood vessels, lymphatics or nerves.
T1b	Invasion of tumour cells is seen into blood vessels, lymphatics or nerves or a poorly differentiated tumour
T2	Corpus spongiosum is infiltrated with tumour
T3	Corpus cavernosum is infiltrated with tumour
T4	Structures in close approximation like scrotum, prostate and pubic bone are involved with tumour.
Spread into Regional Lymph Nodes (N)	
Clinical staging of lymph nodes	
cNx	Assessment of nodes was not done
cN0	No visible lymph nodes present or impalpable lymph nodes
cN1	Solitary, mobile inguinal lymph node palpable on one side
cN2	Two or more, mobile inguinal lymph nodes are palpable on one side or mobile lymph nodes are palpable on both sides.
cN3	Pelvic lymph nodes are palpable or fixed/immobile inguinal lymph nodes are palpated on either side or both sides.
Metastasis (M)	
M0	Metastasis absent elsewhere
M1	Presence of metastasis elsewhere in the body

Stages of penile cancer		
0is	Tis, N0, M0	Carcinoma in situ (PeIN)
0a	Ta, N0, M0	Non-invasive localised SCC
1	T1a, N0, M0	Low grade tumour, without any invasion of lymphatics, blood vessels and nerves.
2A	T1b or T2, N0, M0	High grade tumour, a tumour with invasion of lymphatics or blood vessels or nerves. If it invades corpus spongiosum
2B	T3, N0, M0	Invades corpus spongiosum
3A	T1-3, N1, M0	≤2 palpable mobile unilateral inguinal lymph node, no ENE.
3B	T1-3, N2, M0	≥3 palpable mobile unilateral inguinal metastases or bilateral metastases, no ENE.
4	T4, any N stage, M0 T1/T2/T3, N3, M0 Any T stage, any N stage, M1	<ul style="list-style-type: none"> <li>• Spread of tumour within structures in close proximity like scrotum, pubic bone and prostate.</li> <li>• Pelvic lymph nodes are palpable or fixed inguinal lymph nodes are palpated on either side or both sides.</li> <li>• Metastatic spread to distant organs.</li> </ul>

## Management of Penile Cancers

### A. Non -Surgical Methods

#### 1. Topical Chemotherapeutic agents

• 5-fluorouracil (5-FU) is an inhibitor of thymidylate synthase. It exerts its action by disruption of the nuclear DNA replication cycle, eventually ceasing cell replication and exerting a cytotoxic effect on cancer cells. It is used as a topical agent. Local application of 5% 5-FU cream for 4-6 weeks, at 12-hour interval is recommended. Bowen's disease, Carcinoma in situ of penis, Erythroplasia of Queyrat and (Penile Intraepithelial Neoplasia) PeIN are the conditions where its use is efficacious as a first line treatment.<sup>9,10,11,12</sup> Allaudin et al demonstrated an efficacy rate of 48-74% and a recurrence rate of 11% for 5 fluorouracil.<sup>13</sup>

• Imiquimod is an immune response modifier which activates cytokines such as tumour necrosis factor-alpha (TNF-α), interleukin-6 (IL-6) and interferon-alpha (IF-α), through toll-like receptor 7 (TLR7). It exhibits its immune response in skin by activating the Langerhans cell.<sup>14</sup> Topical application of 5% imiquimod is used for 4-6 weeks, in twice daily dose.<sup>15</sup> The efficacy of imiquimod is 40-100% and recurrence rate is 20%.<sup>13</sup>

#### 2. Laser Therapy

• Two kinds of lasers are used in penile cancer. One is the CO<sub>2</sub> laser which has a depth of penetration of 0.1mm. Another is the Neodymium doped yttrium aluminium garnet Nd:YAG laser, which has a depth of penetration of 6mm.<sup>16</sup>

• In a study on carcinoma in situ and T1 lesions of cancer penis, recurrence rate of 14-23% was seen with CO<sub>2</sub> laser and with Nd:YAG lasers it was 10-48%.<sup>17</sup>

• In another study on Cancer penis, efficacy of laser therapies was found to be 52-100%, and recurrence rate was 7-48%.<sup>13</sup>

### 3. Radiation therapy

- Radiation therapy is indicated in T1, T2 lesions and selected cases of T3 stage tumours of penile cancer.<sup>18</sup>
- EBRT (External Beam Radio-Therapy) is widely used as a treatment modality, delivering contemporary dose 60-75G homogenous radiation, using appropriate bolus to primary penile lesion with 2 cm margins.<sup>19</sup>
- In a study the efficacy of EBRT at 5 years without local recurrence ranged from 7-62% and CCS (Cancer Specific Survival) at 5 years was 66-96%.<sup>20</sup>
- In brachytherapy needles of Iridium 192 are inserted percutaneously into glans penis and they remain in-situ for 4-5 days and dose of 50-65Gy are given.<sup>19</sup>
- Local recurrence free period after brachytherapy is 88% at 90 months and 82% at five years.<sup>21,22</sup>

## B. Surgical Methods

### 1. Moh's Microscopic Surgery

- In this surgery, intraoperative frozen section of tissue is taken in real time. These tissues are examined, and it gives an idea to the surgeon about the remaining tumour. The excision is carried out until tumour free margins are encountered.<sup>23</sup>
- It is indicated in lesions of CIS, Ta and T1a disease.<sup>24</sup>
- Recurrence rates after Mohs surgery range from 0.8-4% in penile cancers.<sup>25,13</sup>

### 2. Circumcision and Wide local Excision

- About 15.2% of penile cancers are confined to the prepuce.<sup>26</sup>
- Lesions of CIS and Ta, T1 group on prepuce skin can be managed with radical circumcision and lesions on shaft and glans can be managed with wide local excision.<sup>27</sup>
- The efficacy of this technique was found to be 90.6% in a follow-up of 2 years 7 months.<sup>27</sup>
- In another study, local recurrence with circumcision in PeIN of prepuce was 0% and 25% recurrence were found with wide excision of lesion.<sup>13</sup>

### 3. Glans Resurfacing

- This technique was pioneered by Depasquale *et al* for lichen sclerosus of glans penis.<sup>28</sup>
- Here there is application of split thickness skin graft, after removal of epithelial and sub-epithelial layers of glans penis.<sup>29</sup>
- Indications for this technique are CIS and Ta, T1a lesions of glans penis.<sup>30</sup>
- At the base of the penis, a tourniquet is tied and skin marking of gland is done from meatus up to coronal sulcus. Using sharp dissection, epithelial and sub-epithelial layer are removed from a plane between glans and corpus spongiosum. Multiple biopsies are taken to ensure negative margin.
- Harvested skin graft is fenestrated to cover the defect, Tourniquet is released and dressing change is done on 3<sup>rd</sup> and on 7<sup>th</sup> day after the surgery.<sup>28,29</sup>
- Within a follow-up period of 38 months no recurrence was encountered for superficial or T1 lesions.<sup>31</sup>
- In 22 patients who underwent glans resurfacing, recurrence was found in 4.5% (1/22).<sup>32</sup>

### 4. Glansectomy

- It is indicated for stages Ta, T1 and T2.<sup>30</sup>
- In Glansectomy, a tourniquet is tied at the base of penis and incision is made in sub-coronal region, which extends upto Buck's fascia.
- Cap of glans and corporal bodies are dissected with sharp dissection.
- Dorsal neurovascular bundle is tied.
- Then at the level of corporal head, urethra is transacted.
- Suturing of the penile skin to the corporal head is done, leaving an opening; which functions as pseudo glans penis.
- Donor skin graft is harvested from thigh, fenestrated and placed over neo-glans and transfixed with vicryl suture.<sup>33</sup>
- Incidence of recurrence was 2.6-16.7%, after recurrence 1.2-8.3% underwent salvage penectomy.
- Disease specific survival rate was 89-96.6%
- Good cosmetic outcomes (95-100%) and normal erections (50-100%) were reported and meatal stenosis was reported in 2.8-14.3% after glansectomy.<sup>34</sup>
- In another study, local recurrence was reported in 9.3%.<sup>35</sup>

**5. Partial Penectomy**

- The success of partial penectomy depends upon the length of the shaft which remains back and the ability of the patient to achieve sexual functions and voiding in standing positions.



**Fig.1.a:** Stage 1 penile cancer



**Fig. 1.b:** Picture post Partial Penectomy



**Figure 2.a**



**Figure 2.b**



**Figure 2.c**

**Figure 2.a:** Peri-operative photo of Cancer Penis.

**Figure 2.b:** After partial penectomy

**Figure 2.c:** Excised specimen of Cancer Penis

- It is useful for T2 or T3 lesions of cancer penis.
- The base of penis is ligated with tourniquet and skin marking is done, ensuring adequate healthy margin. A glove is used to cover the tumour to avoid spillage and contamination. A circumferential incision is made. This incision is developed down until the tunica albuginea around the corporal bodies is reached. Ligation and cutting of the surrounding neurovascular bundle are done. Next step is the mobilisation of the urethra over the corporal bodies. About 2.5cm distal to the marked margin, urethra is detached from corporal bodies. Urethral spatulation is done to cover the corporal head. With continuous suturing using 3/0 braided absorbable sutures, corporal stump closure is done. Neo-glans is created by suturing of the urethra to underlying corpora. Finally using 5-0 Vicryl, suturing of neo-glans and neo-meatus to the penile skin is done.<sup>36</sup>
- After partial penectomy 8.6% patients developed recurrence and 62% cases had erectile dysfunction.<sup>37</sup>

## II. Conclusion:

The use of organ sparing surgeries, improves the functional outcome, decreases the hospital stay and provides better cosmesis and psychological satisfaction for the patient in carcinoma in situ, T0 and T1 lesions. Every effort should be made to preserve the penis before resorting to drastic and radical therapy like total penectomy.

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