Review

Advances in penile-sparing surgical approaches

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Abstract

Objective: Penile cancer (PeCa) is a rare disease with a global incidence of 36,068 new cases in 2020. This accounts for 0.4% of all male malignancies. The surgical management of PeCa depends on the location of the tumour and depth of invasion. Here, we review the oncological and functional outcomes of penile-preserving surgery (PPS).

Methods: A PubMed search until July 2021 on PPS for PeCa was conducted; a narrative review on different penile-sparing approaches and outcomes was performed.

Results: PPS is now the standard of care in specialist centres for distal tumours not involving the corpus cavernosa. Laser therapy, glans resurfacing, and wide local excision are options for superficial lesions, whilst glansectomy is required for lesions invading into the corpus spongiosum.

Conclusion: PPS aims to preserve urinary and sexual function without compromising oncological outcomes.

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1. Introduction

Penile cancer (PeCa) is a rare disease that predominantly arises from the preputial skin and glans penis. PeCa mostly affects men of advanced age with a peak in incidence in the 6th to 7th decade [1]. Being diagnosed with PeCa and undergoing treatment may result in significant physical and psychosexual side effects.
2. Treatment of PeCa

The extent of invasion will determine the surgical treatment option. Although oncological control with tumour removal and clear margins is the goal of cancer surgery, PeCa treatment also requires preservation of function including the ability to have penetrative sexual intercourse and void standing up. PeCa tends to arise in the distal penis (e.g., the glans and prepuce) and spreads proximally. Therefore, penile-preserving procedures performed on distal part of the penis can provide oncological control and preserve urinary and sexual function. This has been the mainstay of treatment for the past three decades.

The treatment options of premalignant disease or penile intraepithelial neoplasia (PeIN) include topical chemotherapy (5-fluorouracil) or immunotherapy (imiquimod). Where these options fail, laser ablation (carbon dioxide [CO2], neodymium-doped yttrium aluminium garnet [Nd:YAG] laser) or glans resurfacing can be offered. pTa and pT1a (no lymphovascular invasion) disease can be managed with WLE, laser ablation, or glans resurfacing [5,6]. pT1b (lymphovascular invasion) and pT2 disease can be managed with WLE, or for more extensive lesions, a glansectomy is required. However, when the disease invades the corpus cavernosum (pT3) with or without involvement of the urethra, PP with reconstruction of a neoglans is required. Radiotherapy and/or brachytherapy for lesions <4 cm in diameter are also options for localised disease [5]. In more extensive pT3 disease with proximal extension of disease where preserving the penis is not possible, a total penectomy (TP) combined with a perineal urethrostomy is necessary to ensure clear margins [5,6]. Pre-operative imaging can also detect proximal lesions in the crura in which case a radical penectomy is indicated.

3. PPS technique

PPS includes laser treatments, Mohs micrographic surgery, WLE, glans resurfacing, and glansectomy [6,7]. The aim of PPS is not only to treat the disease, but also to maintain penile length and preserve urinary and sexual function. PPS is offered to those with distal disease up to pT2, adequate post resection penile length (>3 cm) and more importantly, those who will perform self-examination and adhere to a regular follow-up programme.

Historically a 2-cm excision margin was recommended; however, much smaller margins do not affect oncological outcomes [8]. The European Association of Urology guidelines [5] suggest that 3–5 mm can be considered a safe margin. An analysis of 179 men with invasive PeCa treated with PPS at a single tertiary centre demonstrated a 5-year local recurrence-free rate of 86.3%. The authors concluded that PPS is oncologically safe and a surgical excision margin of <5 mm is sufficient [9]. The shift towards smaller margins has improved both functional and cosmetic outcomes without affecting oncological outcomes [4,5,8,9].

3.1. Laser treatment

Laser ablation is indicated for PeIN and Grades 1–2, Ta-T1a penile lesions [5]. The two commonly used lasers are CO2 and Nd:YAG. Laser is used for excision or ablation of lesions. Laser dissection is commonly performed with CO2, which provides little thermal damage to surrounding tissue. Nd:YAG provides a deeper tissue penetration for ablation and can be used in conjunction with CO2 laser. Table 1

| CO2 | Nd:YAG |
|-----|--------|
| n | n |
| Z | Z |

| n | n |
|-----|-----|
| 16 | 25 |

The recurrence rate is between 6.3% [16] and 65.9% [15] with meatal stenosis occurring in 38.6% of men in the study by Lont et al. [13]. A more contemporary international, multicentre study of 161 men reported an overall recurrence rate of 43% at a median (interquartile range) follow-up of 58 (28–900) months. The 5-year recurrence-free survival was 46% with no differences observed amongst stages (p=0.98). On multivariable analysis, tumour grade was associated with an increased risk of recurrence (hazard ratio: 1.6; 95% confidence interval: 0.9–2.7, p=0.05) [19].

A recent systematic review on treatment for PeIN reported response rates for laser therapies to be 52%–100%, with recurrences in 7%–48% of cases, and a change in penile sensitivity in 50% of cases [26]. The high recurrence rates mean that laser therapy for invasive lesions is avoided.

3.2. Mohs micrographic surgery

Mohs micrographic surgery is a historical procedure described in 1985 which involves the removal of the penile lesion in layers with microscopic examination and analysis of frozen sections (Table 2). The aim was to preserve maximal amounts of normal tissue and normal functions. In a series of 29 consecutive cases of penile SCC, the 5-year cure rate was 68% [27]. Another series of 33 patients
| Laser | Author | Country | Design | Patient, n | Follow-up, month | Histology, n (%) | Oncology outcome | Complication | Functional outcome/QoL |
|-------|--------|---------|--------|------------|-----------------|-----------------|----------------|-------------|------------------------|
| CO2   | Zreik et al., 2017 [10] | UK      | Retro  | 47         | Mean (range): 29 (1–76) | PeIN: 47 (100) | Rec: 8 (17.0%); TTR: 19.4 months; OS: 98.0%; DSS: 100.0% | 0           | -NR                    |
|       | Colecchia et al., 2009 [11] | Italy   | Retro  | 56         | Median: 66 | pT1: 56 (100) | Rec: 13 (23.2%); TTR: NR; OS: 94.6%; DSS: 100.0% | -NR         | -NR                    |
|       | Bandieramonte et al., 2008 [12] | Italy   | Retro  | 224        | Median (IQR): 28.6 (22.7 –46.3) | pTis: 106 (47.3); pT1: 118 (52.7) | Rec: 32 (14.4%); TTR: NR; OS: NR; DSS: NR | -0 with significant complications | -NR |
| Nd:YAG | Schlenker et al., 2010 [14] | Belgium | Retro  | 54         | Mean (range): 105 (18–262) | pTis: 11 (20.4); pT1: 39 (72.2); pT2: 4 (7.4) | Rec: 16 (42%); TTR: 53.0 months; OS: 85.2%; DSS: 98.2% | -NR | -NR                    |
|       | Meijer et al., 2007 [15] | The Netherlands | Retro  | 44         | Range: 3–192 | pTis: 6 (13.6); pT1: 21 (47.7); pT2: 17 (38.6) | Rec: 29 (65.9%); TTR: 2.3–118.0 months; OS: NR; DSS: 90.9% | -NR | -NR                    |
|       | Tewari et al., 2007 [16] | India   | Retro  | 32         | Median (range): 70 (6–120) | pT1: 25 (78.1); pT2: 7 (21.9) | Rec: 2 (6.3%); TTR: 48.0–60.0 months; OS: 100%; DSS: 100% | -NR | Normal sexual function: 23 (72.2%); Satisfied with cosmesis: 32 (100%) |
|       | Lont et al., 2006 [13] | The Netherlands | Retro  | 60         | NR | pT1: 24 (40.0); pT2: 36 (60.0) | Rec: 22 (36.7%); TTR: NR; OS: NR; DSS: NR | Meatal stenosis: 3 (6.8%) | -NR |
|       | Frimberger et al., 2002 [17] | Germany | Retro  | 29         | Mean: 46.7 | pTis: 17 (58.6); pT1: 10 (34.5); pT2: 2 (6.9) | Rec: 2 (6.9%); TTR: NR; OS: 100%; DSS: 100% | -NR | Satisfied: 29 (100%) |

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| Laser Combinations | Author | Country | Design | Patient, n | Follow-up, month | Histology, n (%) | Oncology outcome | Complication | Functional outcome/QoL |
|---------------------|--------|---------|--------|------------|-----------------|-----------------|----------------|-------------|------------------------|
| Nd:YAG, CO₂, KTP    | Kokorovic et al., 2021 [18] | USA | Pros | 8 | -Whole cohort median: 28 | NR | -Rec: 2 (25.0%); TTR: NR; OS: NR; DSS: NR | -NR | -NR |
|                     | Tang et al., 2018 [19] (Nd:YAG or CO₂) | USA, Germany, the Netherlands, UK, and China | Retro | 161 | -Median (IQR): 58 (28–900) | pTa/Tis: 59 (37.1); pT1a: 62 (39.0); pT1b: 17 (10.7); pT2:18 (11.3); pT3: 3 (1.9) | -Rec: 69 (42.9%); TTR: NR; OS: NR; DSS: NR | -NR | -NR |
|                     | Baumgarten et al., 2018 [20] (Nd:YAG or CO₂ +/− WLE) | USA, Germany, the Netherlands, UK, and China | Laser only: 149 | -NR | pTa/Tis: 57 (26.1); pT1: 77 (13.4); pT2: 15 (3.8); pTa/is: 11 (5); pT1: 48 (8.3); pT2: 32 (8.1); | -Rec for pT2: 20 | Laser +/− WLE | -NR | -NR |
|                     | Chipollini et al., 2018 [21] (Nd:YAG or CO₂ +/− WLE) | USA, Germany, the Netherlands, UK, and China | Laser only: 58 | -Median (IQR): 63.8 (20.9–95.2) | pTis: 58 (100) | -Rec: 28 (48.3%); TTR: NR; OS 5-year: 100%; DSS: NR | -NR | -NR |
|                     | Windahl and Andersson, 2003 [22] (Nd:YAG and CO₂) | Sweden | Pros | 67 | -Median (range): 42 (12–186) | pTis: 21 (31.3); pTa: 2 (3.0); pT1: 23 (34.3); pT2: 19 (28.4); pT3: 2 (3.0); pTis: 19 (100) | -Rec: 13 (19.4%); TTR: NR; OS: 88.1%; DSS: 97.0% | -Postop bleeding: 5 (7.5%); Unaltered EF: 72%; satisfied with cosmesis: 78% | 0 |
|                     | van Bezooijen et al., 2001 [23] (Nd:YAG or CO₂) | The Netherlands | Retro | 19 | -Mean (range): 32 (1–96) | -Rec: 5 (26.3%); TTR: 25 months; OS: NR; DSS: NR | -NR | -NR |
|                     | Tietjen and Malek, 1998 [24] (Nd:YAG or CO₂ or KTP) | USA | Retro | 52 (44 with follow-up) | -Mean (range): 58 (12–117) | -Rec: 5 (11.4%); TTR: 3–12 months; OS: 97.7%; DSS: 97.7% | -Pain/infection: 1 (2.3%); Preputial lymphoedema: 1 (2.3%) | -NR | -NR |

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showed a recurrence rate of 32.0% and two deaths (92.0% overall survival [OS]) at a mean follow-up of 58.0 months [28]. A more contemporary report on a 30-year experience involving 42 patients showed one recurrence of the 19 primary SCCs in-situ (cure rate of 94.7%) and no recurrences amongst the 10 primary invasive SCCs at a mean follow-up of 97.4 months. Urethral stricture occurred in 9.5% of men [29].

Some of the pitfalls and disadvantages with Mohs micrographic surgery include frozen section quality, interpretation of the frozen sections, tissue orientation problems, too narrow or wide margins, transection of the tumour, and problems with multi-focal tumour. In addition, it can be a tedious and time-consuming procedure.

### 3.3. Circumcision and WLE

Lesions confined to the foreskin can be treated with circumcision alone and often any extension onto the corona can be excised at the same time. Adjuvant treatment using topical 5-fluorouracil can be used if there is adjacent PeIN. Small lesions on the distal penile skin or glans can be treated by WLE and primary closure of the defect, or covered using an outer preputial advancement flap. We identified seven studies on circumcision and/or WLE which reported a recurrence rate between 0% and 33.3% [13,18,20,21,30-32] (Table 2). Complications are minimal, and one study reported wound dehiscence in 6.2% of patients [31].

### 3.4. Glans resurfacing

Glans resurfacing involves excision of the epithelium and sub-epithelium of the glans in quadrants, with coverage of the denuded glans using a split thickness skin graft harvested from the thigh [33]. This can be offered as a primary treatment for superficial disease such as refractory lichen sclerosis or PeIN (Fig. 1), as well as Ta/T1 tumours confined to the glans. Graft take rates are high and cosmetic outcomes are good. We identified eight studies on glans resurfacing which reported recurrence rates between 0% and 20.0%, and the graft failure rates were between 0% and 5.3% (Table 2) [20,21,33-38]. A more contemporary series on 26 cases reported a recurrence rate of 11.5% at a median follow-up of 38 months. Wound infection occurred in one (3.8%) case [35]. The outcomes of a modified coronal-sparing technique to preserve the coronal ridge, maintaining erogenous sensation have recently been reported. Overall, 10 patients with PeIN or superficial SCC were treated, and at a median follow-up of 29 months, two recurrences occurred. The graft rate was 100%; no patients developed meatal stenosis; the median visual analogue scale score for cosmetic satisfaction was 4; and the median (interquartile range) International Index of Erectile Function score was 20 (17-23) [34].

### 3.5. Glansectomy

PeCa invading the spongiosum of the glans requires glansectomy. This can be a partial or complete glansectomy depending on the size and location of the tumour.
| PPS | Author | Country | Design | Patient, n | Follow-up, month | Histology, n (%) | Oncology outcome | Complication | Functional outcome/QoL |
|-----|--------|---------|--------|-------------|-----------------|----------------|----------------|--------------|-----------------------|
| Mohs | Machan et al., 2016 [29] | USA | Retro | 42 with 44 tumours (19 primary tumours with follow-up) | Mean: 97.4 | pTis: 24 (54.5); invasive: 10 (45.5) | -Rec: 1 (3.4%); TTR: 9 months; OS: 67.7%; DSS: 100.0% | Urethral stricture: 4 (9.5%) | Preserved: 42 (100%) |
|     | Shindel et al., 2007 [28] | USA | Retro | 33 (25 with follow-up) | Mean (range): 58.0 (0.5–214.0) | pTis: 26 (63.4); pT1: 4 (9.8); pT2: 7 (17.1); pT3: 4 (9.8) | -Rec: 8 (32.0%); TTR: 36 months; OS: 92.0%; DSS: 96.0% | Aborted due to: positive margins: 5 (15.2%); wound dehiscence: 1 (3.0%); meatal stenosis: 2 (6.1%); | |
|     | Mohs et al., 1985 [27] | USA | Case series | 29 - >60 | Jackson stage: 1: 18 (62.1); 2: 9 (31.0); 3: 2 (6.9) | -Rec: (92.0%); TTR: NR; OS: 89.7%; DSS: 100% | -Rec: 2 (5.6%); TTR: NR; OS: NR; DSS: NR | -NR | |
| WLE and/or Circ | Kokorovic et al., 2021 [18] (WLE) | USA | Pros | 36 - Whole cohort median: 28 | -Whole cohort median (IQR): 43.0 (27.9–60.4) | pTa/pTis: 68 (31.2); pT1: 183 (38.1); pT2: 87 (22.1) | -Rec for pT2: 29 (33.3%); TTR: NR; OS: NR; DSS: NR | -NR | -NR |
|     | Baumgarten et al., 2018 [20] (WLE) | USA, Germany, the Netherlands, UK, and China | Retro | 338 | -Whole cohort median (IQR): 43.0 (27.9–60.4) | pTa/pTis: 45 (20.6); pT1: 87 (15.1); pT2: 5 (1.3) | -Rec: 0; TTR: NR; OS: NR; DSS: NR | -NR | -NR |
|     | Baumgarten et al., 2018 [20] (Circ) | USA, Germany, the Netherlands, UK, and China | Retro | 362 | -Median (IQR): 43.0 (27.9–60.4) | pTis: 61 (100) | -Rec: 15 (24.6%); TTR: NR; OS 5-year: 100%; DSS: NR | -NR | -NR |
|     | Chipollini et al., 2018 [21] (WLE) | USA, Germany, the Netherlands, UK, and China | Retro | 44 | -Median (IQR): 40.0 (33.3–55.2) | pTis: 44 (100) | -Rec: 0; TTR: NR; OS 5-year: 100%; DSS: NR | -NR | -NR |
|     | Chipollini et al., 2018 [21] (Circ) | USA, Germany, the Netherlands, UK, and China | Retro | 44 | -Median (IQR): 35.0 (19.7–56.0) | pTis: 61 (100) | -Rec: 15 (24.6%); TTR: NR; OS 5-year: 100%; DSS: NR | -NR | -NR |

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| Author                  | Country       | Design | Patient, n | Follow-up, month | Histology, n (%) | Oncology outcome | Complication | Functional outcome/QoL |
|-------------------------|---------------|--------|------------|------------------|------------------|------------------|--------------|------------------------|
| Lucky et al., 2015      | UK            | Retro  | 18         | Mean: 3.5        | pTis: 18 (100)   | Rec: 0; TTR: NR; OS: NR; DSS: NR | -NR         | -NR                    |
|                        |               |        | 20         | Circ alone: 18   |                  |                  |              |                        |
|                        |               |        | 20         | Circ + LE: 20    | pTis: 20 (100)   | Rec: 5 (25.0%); TTR: NR; OS: NR; DSS: NR | -NR         | -NR                    |
|                        |               |        | 19         | Circ + 5-FU: 19  | pTis: 19 (100)   | No response: 5 (26.3%); TTR: NR; OS: NR; DSS: NR | Significant inflammation: 7 (36.8%) | -NR |
| Li et al., 2011         | China         | Pros   | 8; WLE: 18; WLE + circ: 6 | Median (range): 26.5 (2.0–61.0) | pTis: 2 (6.3); pTa: 5 (15.6); pT1: 23 (71.9); pT2: 2 (6.2); pT1: 13 (54.2); pT2: 11 (45.8) | Rec: 3 (9.4%); TTR: <6 months; OS: 96.9%; DSS: 96.9%; Rec: 7 (29.2%); TTR: NR; OS: NR; DSS: NR | Wound dehiscence: 2 (6.2%); Abscess: 1 (3.1%); Urethral fistula: 1 (4.2%) | -Worsened EF: 1 (3.4%) |
| Lont et al., 2006       | The Netherlands | Retro  | 24         | NR               |                  |                  |              |                        |
| Bissada et al., 2003    | USA           | Retro  | 30         | Range: 12–360    | NR               |                  |              |                        |
| Cakir et al., 2021      | UK            | Retro  | 10         | Median (IQR): 29 (14–38) | PeIN: 2 (20); pT1: 8 (80) | Rec: 2 (20.0%); TTR: 7–29 months (range); OS: 100%; DSS: NR | Meatal stenosis/graft loss: 0 | -Median VAS score for cosmetic satisfaction: 4; IIEF-5 median (IQR): 20 (17–23). | -NR |
| Falcone et al., 2020    | Italy         | Retro  | 26         | Median (IQR): 38 (13–86) | Cis: 11 (42.3); pT1: 14 (53.8); pT2: 1 (3.8) | Rec: 3 (11.5%); TTR: 11 months; OS: 100%; DSS: NR | Wound infection: 1 (3.8%) | -NR |

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| PPS | Author | Country | Design | Patient, n | Follow-up, month | Histology, n (%) | Oncology outcome | Complication | Functional outcome/QoL |
|-----|--------|---------|--------|------------|----------------|-----------------|-----------------|-------------|------------------------|
|     | Baumgarten et al., 2018 [20] | USA, Germany, the Netherlands, UK, and China | Retro | 111 | Whole cohort median (IQR): 43.0 (27.9–60.4) | pTa/Tis: 23 (10.6); pT1: 73 (12.7); pT2: 15 (3.8) | -Rec for pT2: 1 (6.7%); TTR: NR; OS: NR; DSS: NR | -NR | -NR |
|     | Chipollini et al., 2018 [21] | USA, Germany, the Netherlands, UK, and China | Retro | 22 | Median (IQR): 40.3 (34.8–66.5) | pTis: 22 (100) | Rec: 1 (4.5%); TTR: NR; OS: 100%; DSS: NR | -NR | -NR |
|     | O’Kelly et al., 2017 [36] | UK | Pros | 19 | Median (range): 21 (7–27) | pTis: 8 (42.1); pTa/T1: 11 (57.9) | -Rec: 0; TTR: NR; OS: NR; DSS: NR | -NR individually | -Preserved sexual activity: 100% |
|     | Shabbir et al., 2011 [33] | UK | Retro | 25 | Median (range): 29 (2–120) | pTis: 25 (100) | -Rec: 1 (4.0%); TTR: 14 months; OS: NR; DSS: NR | -NR | -NR |
|     | Hadway et al., 2006 [38] | UK | Retro | 10 | Median (range): 30 (7–45) | Cis: 8 (80); Severe dysplasia: 2 (20) | -Rec: 0; TTR: NR; OS: NR; DSS: NR | 0 | -Preserved: 10 (100%) |
| Glansectomy | Falcone et al., 2021 [46] | Italy | Retro | 34 | Median (IQR): 12 (12–41) | NR | -Rec: 4 (11.8%); TTR: NR; OS: 91.2%; DSS: 91.2% | -Grade 1: 4 (11.8%); Grade 2: 3 (8.8%); Grade 3a: 3 (8.8%) | -NR |
|     | Kokorovic et al., 2021 [18] (partial or total) | USA | Pros | 35 | Whole cohort median: 28 | NR | -Rec: 3 (8.6%); TTR: NR; OS: NR; DSS: NR | -NR | -NR |
|     | Beech et al., 2020 Canada [47] | Canada | Retro | 12 | Median (range): 14 (1–59) | pT0: 2 (16.7); pTis: 2 (16.7); pT1a: 5 (41.7); pT1b: 1 (8.3); pT2: 2 (16.7) | -Rec: 2 (16.7%); TTR: NR; OS: NR; DSS: NR | -90-day Grade>2: 0 | -Preserved EF and standing voiding: 12 (100%) |

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Table 2 (continued)

| PPS | Author | Country                          | Design | Patient, n | Follow-up, month | Histology, n (%) | Oncology outcome | Complication | Functional outcome/QoL |
|-----|--------|----------------------------------|--------|------------|------------------|------------------|------------------|--------------|------------------------|
|     | Albersen et al., 2018 [49]      | UK     | Retro   | 117        | Median (range): 33.7 (1.9–151.9) | Concurrent Cis: 36.8%; pT1: 26.5%; pT2: 59.8%; pT3: 13.7% | -Rec: 15 (12.8%); TTR: NR; OS: 78.6%; DSS: 96.6% | -Graft failure: 23 (23.5%); Meatal stenosis: 4 (2.8%) | -NR |
|     | Parnham et al., 2018 [39]       | UK     | Retro   | 172        | Median (range): 41.4 (1.9–155) | NR | -Rec: 16 (9.3%); TTR: 8.7 months; OS: 83.6%; DSS: 89.7% | -Graft failure: 34 (19.8%) | -NR |
|     | Baumgarten et al., 2018 [20]    | USA, Germany, the Netherlands, UK, and China | Retro | 362        | Whole cohort median (IQR): 43 (27.9–60.4) | pTa/pTis: 14 (6.4%); pT1: 108 (18.8%); pT2: 240 (60.9%) | -Rec for pT2: 18 (7.5%); TTR: NR; OS: NR; DSS: NR | -NR | -NR |
|     | Chipollini et al., 2018 [21]    | USA, Germany, the Netherlands, UK, and China | Retro | 10         | Median (IQR): 28.6 (22.7–46.3) | pTis: 10 (100) | -Rec: 1 (10%); TTR: NR; OS 5-year: 100%; DSS: NR | -NR | -NR |
|     | Tang et al., 2017 [48]          | USA, Germany, the Netherlands, UK, and China | Retro | 410        | Median (IQR): 42 (29–56) | pTis/pTa: 14 (3.4); pT1: 108 (26.3); pT2: 240 (58.5); pT3-4: 43 (10.5) | -Rec: 31 (7.6%); TTR: NR; OS 5-year: 82.0%; DSS: NR. | -NR | -NR |
|     | Veeratterapillay et al., 2012 [37] (partial or total) | UK     | Retro   | 48         | Median (IQR): 40 (12–72) | pTis: 13 (27.1); pT1: 25 (52.1%); pT2: 10 (20.8%) | -Rec: 4 (8.5%); TTR: 15 months; OS: NR; DSS: NR. | -NR individually | -NR individually |
|     | O’Kane et al., 2011 [50]        | UK     | Retro   | 25         | Median (IQR): 28 (10–66) | pTis: 6 (24.0); pT1: 15 (60.0); pT2: 3 (12.0); pT3: 1 (4.0) | -Rec: 2 (8.0%); TTR: NR; OS: NR; DSS: 92.0%. | -Meatal stenosis: 2 (8.0%) | -Achieve erections: 81.8%; Sexually active: 54.6% | -Preserved EF: 17 (100%); reduced glans sensitivity: 15 (100%) |
|     | Morelli, 2009 [43]              | Italy   | Pros    | 15         | Median (IQR): 36 (10–67) | pTa: 2 (13.3); pT1: 7 (46.7); pT2: 4 (26.7); pT3: 2 (13.3) | -Rec: 0; TTR: NR; OS: NR; DSS: 93.3%. | -Meatal stenosis: 1 (6.7%); partial graft loss: 2 (13.3%) | -Partial graft loss: 2 (2.8%); meatal overgrowth: 1 (1.4%) | -NR |
|     | Smith et al., 2007 [44]         | UK     | Pros    | 72         | Median (range): 27 (4–68) | pT1: 35 (48.6); pT2: 37 (51.4) | -Rec: 3 (4.2%); TTR: 4–28 months (range); OS: 91.9%; DSS: 94.6% | -Partial graft loss: 2 (2.8%); meatal overgrowth: 1 (1.4%) | -NR |

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| PPS | Author Country | Design Patient, n | Follow-up, month mean | Histology, n (%) | Oncology outcome | Complication | Functional outcome/QoL |
|-----|----------------|-------------------|-----------------------|-----------------|------------------|--------------|------------------------|
| PPS combined | Pietrzak et al., 2004 [45] (partial or total and/or distal corporectomy) | UK Pros 39 | Mean: 16 | pTa: 2 (5.1); pT1: 19 (48.7); pT2: 17 (43.6); pT3: 1 (2.6) | Rec: 1 (2.6%); TTR: NR; OS: NR; DSS: NR | Partial graft loss: NR; graft overgrowth: 2 (5.1%) | - |
| | Menon et al., 2020 [57] (laser, LE, PP, and TP) | USA Retro PPS: 4407 | Whole cohort: NR | Whole cohort; cTis/Ta: 2348 (41.0); cT1: 1938 (34.0); cT2: 967 (17.0); cT3: 475 (8.0) | Rec: NR; TTR: NR; OS: 50.3 months; DSS: NR | - | -NR |
| | Lindner et al., 2020 [52] (laser, LE, glansectomy, resurfacing, PP, and TP) | Austria Retro PPS: 26 | Whole cohort mean (SD): 63.7 (11.9) | pTis: 7 (26.9); pTa: 7 (26.9); pT1a: 8 (30.8); pT1b: 1 (3.8); pT2: 3 (11.5) | Rec: 11 (42.3%); TTR: NR; OS: NR; DSS: NR | - | -NR |
| | Kamel et al., 2018 USA [53] (organ-sparing, PP, and TP) | USA Retro PPS: 1211 | Whole cohort mean (SD): 3.5 (2.7) | pTis: 1069 (90.3); pT2: 115 (9.7) | Rec: NR; TTR: NR; OS 5-year: 88%; DSS: NR | - | -NR |
| | Djadadiningrat et al., 2014 [54] (laser, WLE, glans resurfacing, and glansectomy) | The Netherlands Retro 451 | Whole cohort median (IQR): 65 (41–101) | pT1a: 191 (42.4); pT1b: 61 (13.5); pT2: 189 (41.9); pT3: 9 (2.0); pT4: 1 (0.2) | Rec: 185 (41.0%); (local only, 27); TTR: NR; OS: NR; DSS: NR | - | -NR |
| | Philippou et al., 2012 [5] (Circ, WLE, and glansectomy) | UK Retro 179 | Whole cohort median (range): 42.8 (4–107) | - | Rec: 8.9%; TTR: 26.1 months; OS: 96.1%; DSS: 98.3% | -Infection: 0.6%; necrosis: 0.6%; partial graft failure: 1.8% | -NR |
| | Feldman and McDougal, 2011 [55] (Mohs, circumcision, LE, and partial glansectomy) | USA Retro 56 | Whole cohort mean (SD): 65.6 (46.6) | Cis: 28 (50); pT1: 28 (50) | Rec: 12 (21.4%); TTR: 51 months; OS: NR; DSS: NR | -Meatal stenosis/stricture: 0 | -Maintained sexual activity: 56 (100%); standing voiding: 56 (100%); |
| | Leijte et al., 2008 The Netherlands [56] (laser, LE, and radiation) | The Netherlands Retro 415 | Median (range): 60.6 (3.0–358.0) | pTis: 95 (22.9); pTa: 9 (2.2); pT1: 168 (40.5); pT2: 111 (26.7) | Rec: 115 (27.7%); TTR: NR; OS: NR; DSS: NR | - | -NR |

(continued on next page)
Glansectomy is currently the most utilised PPS, and involves dissection over or under Buck’s fascia, depending on the proximity of suspected tumour invasion near the tunica albuginea. The shaft skin is sutured 2 cm from the tip, exposing the corporal heads. Tumours extending more proximally may require a distal corporectomy. Intraoperative frozen sections are sent to ensure negative surgical margins if there is doubt relating to the margins. A neoglans (Fig. 2) can be reconstructed using a split thickness skin graft harvested from the thigh [39]. Malone et al. [40] described a tie-over dressing for graft application technique which fixes a proflavine-soaked gauze to the skin graft allowing immediate patient mobilisation and discharge home with a catheter. Hospital stay was reduced and excellent cosmetic results were achieved with a high percentage of graft uptake. For those who are not sexually active, not too concerned with cosmetic outcomes, and who want to avoid morbidity associated with skin grafts, primary closure with the penile skin approximated to the everted urethral mucosa can be performed [41].

Table 2 (continued)

| PPS         | Design Patient, n | Follow-up, month | Histology, n (%) | Oncology outcome | Complication | Functional outcome/QoL |
|-------------|-------------------|------------------|------------------|------------------|--------------|------------------------|
| Minhas et al., 2005 [5] (WLE, glansectomy, and PP) | Retro 51 | Median (range): 26 (9–55) | pTis: 3 (5.9); pT1: 20 (39.2); pT2: 26 (51.0); pT3: 8 (1.6); pT4: 1 (0.2) | -NR | -NR | -NR |
| Minhas et al., 2005 [5] (WLE, glansectomy, and PP) | Retro 51 | Median (range): 26 (9–55) | pTis: 3 (5.9); pT1: 20 (39.2); pT2: 26 (51.0); pT3: 8 (1.6); pT4: 1 (0.2) | -NR | -NR | -NR |

Circ, circumcision; Cis, carcinoma in situ; DSS, disease-specific survival; EF, erectile function; 5-FU, 5-flurouracil; IIEF-5, International Index for Erectile Function; IQR, interquartile range; LE, local excision; NR, not reported; OS, overall survival; PP, partial penectomy; PE-in situ (PeIN) prospective study; QoL, quality of life; Rec, recurrence; Retro, retrospective study; SD, standard deviation; TTR, time to recurrence; TP, total penectomy; VAS, visual analogue scale; WLE, wide local excision.

Figure 1 Glans resurfacing. (A) Refractory PeIN and lichen sclerosis before glans resurfacing; (B) STSG being used to cover the denuded glans; (C) Appearance following glans resurfacing. PeIN, penile intraepithelial neoplasia; STSG, split thickness skin graft. Intraoperative pictures taken from Institute of Andrology, University College London Hospital, Courtesy of Mr Asif Muneer.

Figure 2 Glansectomy and neoglans formation. (A) Glans dissected off corporal heads; (B) Neoglans reconstruction following glansectomy. Pictures taken from Institute of Urology, University College London Hospital, Courtesy of Mr. Asif Muneer.
however, the final cosmetic result may be inferior to that of split thickness skin graft [42]. We identified 13 studies on partial or total glansectomy and the recurrence rates were 2.6%–16.7% (Table 2) [18,20,21,37,39,43–50]. Graft failure rates were 2.6%–23.5% and the meatal stenosis rate is 2.8%–8.0%. Tang et al. [48] reported the largest multi-centre series on 410 patients undergoing glansectomy. At a median follow-up of 42 months, the local recurrence rate was 7.6% and the 1-, 2-, and 5-year recurrence-free survival rates were 98%, 94%, and 78%, respectively. In addition, there were no differences in OS when stratified by stage.

Albersen et al. [49] investigated predictive factors for local recurrence following glansectomy using pathological data from 117 men. On univariate analysis, PeIN, high grade disease, perineural invasion, and positive margin were predictive of local recurrence. Patients could be stratified into low-, intermediate-, and high-risk groups depending on the number of predictive factors. This may be used to tailor follow-up.

Sedigh et al. [51] evaluated sexual function following WLE (n = 12) or glansectomy with urethral granuloplasty (n = 23). A decrease in the postoperative IIEF score was noted in both groups, but was statistically significant only with glansectomy (p = 0.003). With regards to sex encounter profile, no significant changes were recorded post-operatively with WLE, but a decrease was reported with glansectomy, with a decrease in the possibility of achieving penetrative intercourse (p = 0.006) and in the perceived satisfaction during sexual activity (p = 0.004) [51].

3.6. Combined PPS

Several studies have reported outcomes of PPS as a whole although differentiating between the procedures is difficult. Kokorovic et al. [18] analysed 129 patients who had a WLE (n = 36), partial or total glansectomy (n = 35), laser therapy (n = 8), or PPS with laser (n = 50) for pTis-pT2 disease. At a median follow-up of 28 months, the local recurrence rate was 13.2% with a median time to local recurrence of 20.9 months. The 5- and 10-year local recurrence-free survival rates were 76% and 73%, respectively. The 5- and 10-year OS rates were 83% and 62%, respectively, and were not influenced by recurrence. Outcomes from individual PPS approach are shown in Table 2. Tumour stage and the use of laser were associated with an increased risk of recurrence on univariate analysis [18].

Lindner et al. [52] compared the outcomes of organ-sparing surgery (OSS: laser, WLE, and glansectomy, n = 26) with PP/TP (n = 29), and found a higher local recurrence in the OSS group (42.3% vs. 10.3% with penectomy, p = 0.007). However, there was no statistical significance between the two groups with regards to OS and metastasis-free survival.

Baumgarten et al. [20] reported an international multi-centre series on PPS for PeCa. A total of 1188 men were included for analysis and procedures performed included circumcision (n = 137), glansectomy (n = 362), WLE (n = 338), laser with local excision (n = 91), laser alone (n = 149), and glans resurfacing (n = 111). At a median follow-up of 43 months, there were 252 (21.2%) local recurrences (median time to recurrence, 16.3 months). The 5-year local recurrence-free survival rates were not statistically different according to stages (pT1a/Tis, 75.0%; pT1, 71.4%; and pT2, 75.9%). Only margin status was significantly associated with local recurrence on multivariate analysis [20]. The same international collaborative group analysed PPS for PeIN alone using the same techniques and at a median follow-up of 40 months, the local recurrence rate was 23.4%. The median time to recurrence was 15.9 months, and the 1-, 2-, and 5-year recurrence-free survival were 88.4%, 85.6%, and 75.0%, respectively. Overall, 58.3% recurrences were managed with repeat organ-sparing treatment, and the PP rate was 10.0% [21].

Kamel et al. [53] analysed the outcome from OSS (n = 1211), PP (n = 2360), and TP (n = 584) for pT1-2 PeCa. The 5-year OS rates for OSS, PP, and TP were 88%, 85%, and 79%, respectively, and the 10-year OS rates for OSS, PP, and TP were 74%, 72%, and 63%, respectively (p < 0.001). In a multivariable regression analysis, predictors of poor OS were advancing age, higher grade, positive lymph nodes, positive surgical margins, and higher Charlson comorbidity score. OSS did not predict poor OS. From this national study, OSS in early stage PeCa provided comparable outcomes compared to PP and TP. In addition, OSS was not associated with any significant reduction in OS in early stage PeCa [53].

Djadiningrat et al. [54] compared the outcome of PSS as a whole (n = 451) with amputation (n = 408) for the treatment of invasive SCC. PSS included lasers, WLE, glans resurfacing, and glansectomy. At a median follow-up of 65 months, the overall recurrence rate was 36% (PSS, 41% and amputation, 29%). The 5-year cumulative incidence of local recurrence as the first event with PPS was significantly higher at 27%, compared with amputation (3.8%, p < 0.0001). Out of the 451 men treated with PPS, 70 (16%) eventually underwent amputation. The OS was 67% and 5-year disease-specific survival (DSS) in the whole group was 81%. Although patients treated with PPS experienced more local recurrences, the 5-year DSS was not jeopardized. Factors associated with DSS were pT and N stages, and lymphovascular invasion on multivariate analysis [54].

Feldman and McDougal [55] looked at the outcome of WLE, circumcision, Mohs procedure, and partial glansectomy for carcinoma in situ and pT1 disease. Overall, 56 patients were analysed and the recurrence rate was 21.4% for PPS [55].

Philippou et al. [9] analysed the outcomes of circumcision (n = 13), WLE (n = 29), and glansectomy with/without distal corporectomy (n = 137) for pT1–3 disease. At a mean follow-up of 42.8 months, the local recurrence rates were 15.4%, 10.3%, 8.0% for circumcision, WLE, and glansectomy with/without distal corporectomy, respectively. The 5-year DSS after recurrence for PPS was 54.7% and the overall 5-year local recurrence-free rate was 86.3%. On multivariate analysis, tumour grade, tumour stage, and lymphovascular invasion were predictors of local recurrence. Local recurrence had no negative impact on long-term survival, and a surgical excision margin of <5 mm was adequate [9].

Veeratterapillay et al. [37] evaluated outcomes following glansectomy and granuloplasty (n = 46), partial glansectomy (n = 1), glans relining (n = 3), and glansectomy and distal corporectomy (n = 15). At a median follow-up of 40 months, four (6.2%) men had local recurrence; one (1.5%) had partial graft loss; three (4.6%) had graft
contractures; and five men (7.7%) had meatal stenosis. Overall, three men (4.6%) were deemed to have poor cosmetic outcome and 85% described good erections at 1 year following surgery.

Leijte et al. [56] analysed 415 patients treated with PPS (laser, \(n=289\); LE, \(n=105\); and radiation, \(n=21\)) and 285 who had a penectomy. At a median follow-up of 60.6 months, the local recurrence following PPS was 27.7% (vs. 5.3% with amputation) [56].

Lont et al. [13] evaluated the outcomes of PPS (laser, radiotherapy and WLE; \(n=157\)) and PT/TP (\(n=100\)) for pT1-2 PeCa. At a median follow-up of 106 months, the recurrence rate was 34% in the PSS group and 10.4% in the PP group. Local recurrence after amputation carried a poor prognosis.

Minhas et al. [8] analysed the outcomes of WLE (\(n=9\)), glansectomy (\(n=26\)), and PP (\(n=16\)), and the recurrence rate was 3.9% at a median follow-up of 51 months. This study also evaluated the surgical excision margin required for local cancer control; 49 (48%) of the 102 margins were measured within 10 mm of the tumour edge and 92 (90%) within <20 mm. The authors concluded that the traditional 2 cm excision margin is unnecessary and only a few millimetres is sufficient.

4. Trends in penile surgery

Menon et al. [57] analysed the trend of local management for preinvasive and clinical (c) T1-3 PeCa in USA between 2004 and 2013. Overall, 5728 patients were included for analysis—375 (7%) received topical or no therapy, 252 (4%) laser, 2244 (39%) local excision, 2163 (38%) PP, 588 (10%) TP, and 106 (2%) radiotherapy with or without chemotherapy. The cTis/Ta or cT1 lesions were more likely to undergo PPS, and LE (68%) was the most common procedure for cTis/Ta lesions. However, LE was associated with a higher positive surgical margin rate (20%) compared with PP (8%). No survival differences were observed between penectomy (49.3 months) and PPS (50.3 months) [57].

A systematic review has shown that centralization of care for PeCa has optimised adherence to guidelines, increased utilisation of organ-sparing treatments and invasive inguinal lymph node staging, and reportedly improved survival outcomes [58]. The recurrence rates following different PPS approaches vary, with the highest rate seen with lasers and the lowest with glans resurfacing for superficial lesions. Recurrences commonly occur within the first 5 years, and patients are followed up closely during this period [13,20]. Any significant local recurrences can be managed with repeat PPS or partial amputation. Although compared with PP, the local recurrence rate is higher, while OS is generally unaffected [39,60].

5. Penile-lengthening procedures

Men who have had a glansectomy and have loss of penile length can undergo penile-lengthening procedures. This can be achieved by releasing the suspensory ligament and dissection of the proximal corpora from the pubic arch, or treating an existing peno-scrotal web. More extensive surgery involves a neo-phalloplasty, which involves harvesting free tissue flaps from the radial forearm, antero-lateral thigh, scapula, or latissimus dorsi. In addition, local rotational grafts from the abdomen, groin, and thigh can be used [7,61].

6. Conclusion

PeCa is a rare disease but its presentation and subsequent surgical treatment may affect urinary and sexual function, as well as psychosocial well-being. For superficial disease, PPS is the mainstay of treatment. The adoption of laser treatment is not universal and is associated with the highest rate of local recurrence compared with WLE or glans resurfacing. For lesions invading the spongiosum, glansectomy offers good cancer control with good functional and cosmetic outcomes.

Author contributions

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Conflicts of interest

The authors declare no conflict of interest.

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