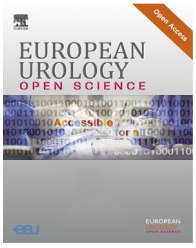
available at www.sciencedirect.com
journal homepage: www.eu-openscience.europeanurology.com



European Association of Urology

Review – Penile Cancer

What Is the Most Effective Management of the Primary Tumor in Men with Invasive Penile Cancer: A Systematic Review of the Available Treatment Options and Their Outcomes

Vasileios I. Sakalis[a,*], *Riccardo Campi*[b], *Lenka Barreto*[c], *Herney Garcia Perdomo*[d], *Isabella Greco*[e], *Łukasz Zapała*[f], *Mithun Kailavasan*[g], *Tiago Antunes-Lopes*[h], *Jack David Marcus*[i], *Kenneth Manzie*[j], *John Osborne*[j], *Benjamin Ayres*[k], *Luc M.F. Moonen*[l], *Andrea Necchi*[m], *Juanita Crook*[n], *Pedro Oliveira*[o,p,q], *Lance C. Pagliaro*[r], *Chris Protzel*[s], *Arie S. Parnham*[o], *Maarten Albersen*[t], *Curtis A. Pettaway*[u], *Philippe E. Spiess*[v], *Scott T. Tagawa*[w], *R. Bryan Rumble*[x], *Oscar R. Brouwer*[y]

[a] *Department of Urology, Agios Pavlos General Hospital, Thessaloniki, Greece;* [b] *Unit of Oncologic Minimally-Invasive Urology and Andrology, Careggi University Hospital, San Luca Nuovo, Florence, Italy;* [c] *Department of Urology, University Hospital Nitra, Nitra, Slovakia;* [d] *Division of Urology/Urooncology, Department of Surgery, School of Medicine, Universidad Del Valle, Cali, Colombia;* [e] *Department of Urological Minimally Invasive and Robotic Surgery and Kidney Transplantation, Careggi Hospital, University of Florence, Florence, Italy;* [f] *Department of Urology, Medical University of Warsaw, Warsaw, Poland;* [g] *Royal Derby Hospital, Derby, UK;* [h] *Department of Urology, Hospital de S. João, Porto, Portugal;* [i] *Multicancer Fighter Patient Advocate, Us TOO, New York, NY, USA;* [j] *Patient Advocate, ORCHID, UK;* [k] *Department of Urology, St George's University Hospitals NHS Foundation Trust, London, UK;* [l] *Department of Radiotherapy, The Netherlands Cancer Institute, Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands;* [m] *Department of Urology and Medical Oncology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy;* [n] *University of British Columbia, British Columbia Cancer Agency, Kelowna, British Columbia, Canada;* [o] *Department of Urology, The Christie NHS Foundation Trust, Manchester, UK;* [p] *Centre for the Research and Technology of Agro-Environmental and Biological Sciences (CITAB), University of Trás-os-Montes and Alto Douro, UTAD, Vila Real, Portugal;* [q] *Veterinary Sciences Department, University of Trás-os-Montes and Alto Douro, UTAD, Vila Real, Portugal;* [r] *Department of Oncology, Mayo Clinic, Rochester, MN, USA;* [s] *Helios Clinics Schwerin, Schwerin, Germany;* [t] *Department of Urology, University Hospitals Leuven, Leuven, Belgium;* [u] *The University of Texas MD Anderson Cancer Center, Houston, TX, USA;* [v] *Department of Genitourinary Oncology, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, USA;* [w] *Division of Hematology and Medical Oncology, Weill Cornell Medical College, New York, NY, USA;* [x] *American Society of Clinical Oncology, Alexandria, VA, USA;* [y] *The Netherlands Cancer Institute, Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands*

Article info

Article history:
Accepted April 6, 2022

Associate Editor:
M. Carmen Mir

Keywords:
Penile cancer
Surgery

Abstract

Context: The primary lesion in penile cancer is managed by surgery or radiation. Surgical options include penile-sparing surgery, amputative surgery, laser excision, and Moh's micrographic surgery. Radiation is applied as external beam radiotherapy (EBRT) and brachytherapy. The treatment aims to completely remove the primary lesion and preserve a sufficient functional penile stump.

Objective: To assess whether the 5-yr recurrence-free rate and other outcomes, such as sexual function, quality of life, urination, and penile preserving length, vary between various treatment options.

* Corresponding author. Department of Urology, Agios Pavlos General Hospital, Ethnikis Antistaeos 161, Kalamaria, Thessaloniki, Greece. Tel. +302313 304 545.
E-mail address: vsakkalis@hotmail.com (V.I. Sakalis).

https://doi.org/10.1016/j.euros.2022.04.002

Penile sparing
Amputation
Laser
Moh's micrographic surgery
Brachytherapy
External beam radiation
Recurrence
Quality of life
Sexual function
Psychological well-being

Evidence acquisition: The EMBASE, MEDLINE, Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials (CENTRAL; Cochrane HTA, DARE, HEED), Google Scholar, and ClinicalTrials.gov were searched for publications from 1990 through May 2021. Randomized controlled trials, nonrandomized comparative studies (NRCSs), and case series (CSs) were included.
Evidence synthesis: The systematic review included 88 studies, involving 9578 men from 16 NRCSs and 72 CSs. The cumulative mean 5-yr recurrence-free rates were 82.0% for penile-sparing surgery, 83.9% for amputative surgery, 78.6% for brachytherapy, 55.2% for EBRT, 69.4% for lasers, and 88.2% for Moh's micrographic surgery, as reported from CSs, and 76.7% for penile-sparing surgery and 93.3% for amputative surgery, as reported from NRCSs. Penile surgery affects sexual function, but amputative surgery causes more appearance concerns. After brachytherapy, 25% of patients reported sexual dysfunction. Both penile-sparing surgery and amputative surgery affect all aspects of psychosocial well-being.
Conclusions: Despite the poor quality of evidence, data suggest that penile-sparing surgery is not inferior to amputative surgery in terms of recurrence rates in selected patients. Based on the available information, however, broadly applicable recommendations cannot be made; appropriate patient selection accounts for the relative success of all the available methods.
Patient summary: We reviewed the evidence of various techniques to treat penile tumor and assessed their effectiveness in oncologic control and their functional outcomes. Penile-sparing as well as amputative surgery is an effective treatment option, but amputative surgery has a negative impact on sexual function. Penile-sparing surgery and radiotherapy are associated with a higher risk of local recurrence, but preserve sexual function and quality of life better. Laser and Moh's micrographic surgery could be used for smaller lesions.

1. Introduction

Penile cancer is a rare neoplasm representing 1% of male cancers [1]. Its peak incidence is in the 6th and 7th decades of life, and the most common histologic type is squamous cell carcinoma (SCC) [2]. A large epidemiologic study revealed that 65.4% of penile cancer cases are diagnosed as localized, 26.5% as regional, and 3.5% as distant disease [3]. Penile cancer patients should receive treatment for the primary tumor and lymph node disease burden. Most penile primary tumors are located on the glans and prepuce, and are well to moderately differentiated, rendering the disease amenable to penile-sparing techniques [2].

The aim of primary tumor treatment is complete removal, while ensuring organ and functional preservation, without compromising the oncologic outcome [4]. Partial or total penectomy is considered the standard oncologic treatment, based on the extent/size of the lesion [4]. Despite its therapeutic effectiveness, amputative surgery is a disfiguring procedure that affects patient's quality of life (QoL), sexual function, self-image, and self-esteem [5]. To improve well-being, penile-preservation techniques such as penile-sparing surgery, radiotherapy, laser excision/ablation, and Moh's micrographic surgery have been developed. Penile-sparing surgery includes the following: wide local excision, circumcision, glans resurfacing, glansectomy, and distal corporectomy. Typically, penile-sparing surgery is followed by neoglans reconstruction using grafts or vascularized flaps. Radiotherapy techniques that are used to treat primary lesion include brachytherapy and external beam radiotherapy (EBRT).

According to the European Association of Urology guidelines, penile-sparing surgery should be offered whenever possible [4]. Large retrospective series from European centers of excellence have reported local recurrence rates after penile-sparing surgery that range from 4% to 27.7% [6,7]. However, there is no consensus as to whether local recurrence influences survival outcomes [4].

We aimed to systematically review the evidence for the clinical effectiveness of the various treatment options available for the management of the primary tumor in men with penile cancer. The results will be used by the corresponding guideline development group. Consequently, the review addresses multiple research questions that have been formulated by the panel.

2. Evidence acquisition

2.1. Search strategy

The EMBASE, MEDLINE, Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials (CENTRAL; Cochrane HTA, DARE, HEED), Google Scholar, and ClinicalTrials.gov were searched up to May 30, 2021. The study protocol was published on PROSPERO (CRD42021270148). Only English-language articles

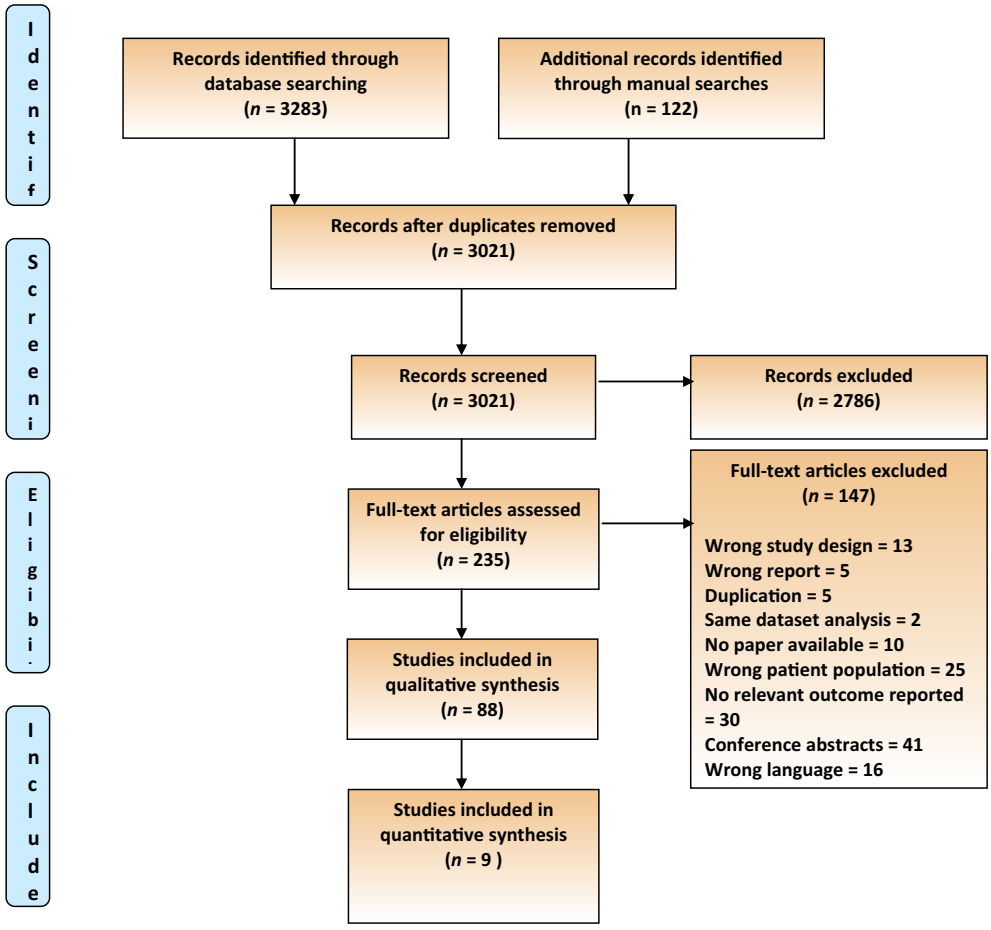


Fig. 1 – PRISMA flow diagram of the study selection process. PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-analyses.

published from 1990 were included. The detailed search strategy is provided in the Supplementary material. Additional sources were articles from reference lists of the included studies, and systematic and literature reviews. Seven reviewers (R.C., L.B., H.G., A.L., M.K., L.Z., and I.G.; Fig. 1) screened abstracts and full-text articles independently. Any potential conflicts were reviewed independently by a senior author (V.S.) who acted as an arbiter. Data extraction was performed by the same reviewers and corroborated by the senior author.

2.2. Types of study designs included

All types of peer-reviewed publications addressing the coprimary outcomes after primary tumor treatment in men with invasive penile cancer were eligible for inclusion. The minimum cohort size was 15 men. Conference abstracts, case reports, and reviews were excluded from the review, as were studies on noninvasive penile cancer or verrucous carcinoma unless those included data on eligible patients and results were reported separately.

2.3. Types of participants included

The study population included men with invasive SCC of the penis at any stage, with or without nodal involvement, who were subjected to any type of treatment with curative intent for the primary lesion. Table 1 provides an overview of the patients, interventions, comparators, and outcomes (PICO) for this review.

2.4. Types of interventions included

All treatment options for the management of primary tumor were included. Potential interventions, such as surgery, radiotherapy, laser, and Moh's micrographic surgery with any pair-wise comparisons were allowed.

2.5. Outcome measures

The primary outcome was the 5-yr recurrence-free rate. Recurrence was defined as the evidence of any histologically documented tumor relapse on the penis. Additional coprimary endpoints were post-treatment sexual function and QoL scores as measured by validated questionnaires. Secondary outcomes were 1- and 3-yr recurrence-free rate, penile-preservation rate, post-treatment urinary function, and treatment-related complications.

2.6. Assessment of risk of bias

The risk of bias (RoB) of nonrandomized controlled trial studies (NRCSs) was assessed using the Cochrane ROBINS-I tool, including additional items to assess confounding bias

Table 1 – Patients, interventions, comparators, and outcomes (PICO)

Population/participants
Inclusion criteria
Men with invasive penile cancer (pT1-T4, N+/–, M0) who underwent any type of treatment with curative intent for the primary lesion (with or without treatment of regional nodal disease)
Men with invasive penile cancer who underwent palliative treatment for the primary lesion
Men with local recurrence after organ-preserving surgery who underwent any further treatment
Exclusion criteria
Premalignancy or noninvasive (verrucous) penile cancer (PeIN, Ta)
Secondary penile cancer
Nonsquamous cell cancer (ie, sarcoma, melanoma, Paget's disease, etc.)
Urethral squamous cell carcinoma (unless outcomes reported separately)
Interventions
Patients were eligible for inclusion if they received any of these interventions
Laser (including excision, vaporization)
Photodynamic therapy
Moh's micrographic surgery
Organ-preserving penile surgery with reconstruction (total or partial glans resurfacing, total or partial glansectomy, penile shaft skin excision)
Amputating penile surgery with or without reconstruction (partial penectomy, subtotal penectomy, radical or total penectomy)
Radiotherapy, including brachytherapy (interstitial and surface mold)
Combined modality treatment for primary disease, in case data on any of the coprimary outcomes were provided
Comparator
Any of the abovementioned (included) interventions according to the disease stage
Outcomes
Coprimary endpoints
Recurrence-free rates at 5 yr. Recurrence is defined as the "evidence of any histologically-documented tumor relapse in the penis or evidence of any distant relapse"
QoL following primary lesion management as measured by validated questionnaires or validated QoL scale, or any measure of QoL, at time points defined by the trialist
Sexual function following primary lesion management as measured by validated questionnaires such as IIEF or similar questionnaires, any measure of sexual function, or at time points as defined by the trialist
Secondary endpoints
Recurrence-free rates at 1 and 3 yr (or at other time points, as defined by the trialist)
Penile-preservation rate
Complications related to primary lesion management (examples include but not limited to poor graft take, infection, and donor site problems such as infection, bleeding, meatal stenosis, soft tissue ulceration/necrosis, etc.)
Urinary function following primary lesion management measured by validated questionnaires such as IPSS or similar questionnaires, and any measure of urinary function

IIEF = International Index of Erectile Function; IPSS = International Prostate Symptom Score; PeIN = penile intraepithelial neoplasia; QoL = quality of life.

risk [8]. Five confounders were identified a priori: tumor stage, tumor grade, nodal stage, tumor margins, and previous radiotherapy or chemotherapy. For case series (CSs), a five-criterion quality appraisal checklist was used [9].

2.7. Data analysis

Owing to the lack of randomized controlled trials (RCTs), a quantitative analysis was not appropriate, so a quantitative synthesis approach was used. A subgroup analysis was planned for disease stage for outcomes at specific time points, which proved impossible due to the low data quality, and therefore a narrative synthesis of outcomes was performed.

3. Evidence synthesis

3.1. Quantity of evidence identified

Overall 3283 abstracts were screened and 235 studies were retrieved for full-text screening. Eighty-eight studies including 9758 patients were eligible for assessment: 16 NRCSs (1911 patients) [10–25] and 72 CSs (7864 patients) [6,7,26–95].

3.2. Characteristics of the studies included

The baseline characteristics of NRCSs and CSs are presented in Tables 2 and 3. All 16 NRCSs were retrospective studies, 12 comparing penile-sparing surgery with amputative surgery [11–17,20–22,24,25] and four comparing radiotherapy with penile surgery [10,18,19,23]. All 72 CSs were retrospective, with 39 studies addressing penile surgery [6,7,56–92], 20 reporting on radiotherapy [26–45], ten reporting on lasers [46–55], and three reporting on Moh's micrographic surgery [93–95].

3.3. RoB and confounding assessment for the studies included

All NRCSs were assessed to have a high RoB (summarized in Fig. 2). For most selected studies, performance, detection, and attrition biases were assessed to be high, while reporting bias was either unclear or high. All CSs had a high RoB.

3.4. Narrative synthesis of the results

3.4.1. Primary outcomes

3.4.1.1. Five-year recurrence-free rate.

3.4.1.1.1. Surgery. The outcomes of 7841 men who underwent any type of surgery for their primary tumor are reported herein [6,7,11–25,56–92]. The overall 5-yr recurrence-free rates ranged between 33.3% and 98.2%. The studies reporting poor recurrence-free rates involve cohorts with advanced disease who received penile-sparing surgery, while those that report higher recurrence-free rates involve cohorts who were submitted to amputative surgery due to less advanced disease.

Table 2 – Baseline characteristics and primary and secondary outcome scores for nonrandomized comparative studies

Study ID Author (year) [Ref.]	Study design	Patients (*n*)	Intervention (*n*)	RFR at 5 yr, % (*n*)	RFR at 1 and 3 yr, % (*n*)	QoL score (tool name, score)	Sexual function score (tool name, score)	Urinary function score	Complications (CD classification based on grade)	PPR	RoB
Garisto et al. (202) [10]	Retrosp. comparative	51 T1: 8/51 (15.7%) T2: 8/51 (15.7%) Tx: 35/51 (68.63%) N+: 3/51 (5.9%)	BT (*n* = 35) vs PP (*n* = 16)	NR	At 3 yr: PP: 100.0% (16/16) BT: 80.0% (28/35)	NR	NR	NR	7/35 Urethral stenosis (BT group 7/35: 20%, PP group 1/16: 6.25%) Glans necrosis (BT group 4/35: 11.43%; treated with PP Infection (BT group 1/35: 2.9%)	NR	Assessed
Brkovic et al. (1997) [11]	Retrosp. comparative	51 PSS: T1: 10/15 (66.7%) T2: 3/15 (20.0%) T3: 2/15 (13.3%) AS: T1: 11/36 (30.5%) T2: 21/36 (58.3%) T3: 2/36 (5.5%) T4: 2/36 (5.5%)	PSS (Cx, Gx, laser, EBRT; *n* = 15) vs AS (PP and TP; *n* = 36)	PSS: 33.3% (5/15) T1: 45% (5/11) T2: 0/2 (0%) T3: 0/2(0%) AS: 88.9% (33/36) T1: 100% (11/11) T2: 85.7% (18/21) T3: 100% (3/3)	NR	NR	NR	NR	NR	29.40%	Assessed
Sosnowski et al. (2017) [12]	Retrosp. comparative	55 Tx: 4 (7.3%) T1–4: 51 (92.7%)	PSS: 13/51 (25.5%; circumcision, WLE) AS: 38/51 (74.51%; PP 27/38, TP 11/38)	NR	NR	EORTC QLQ-C30 v3.0 Social functioning (PSS 82, AS 75–85) Cognitive functioning (PSS 85, AS 75–82) Emotional functioning (PSS 78, AS 66–69) Role functioning (PSS 78, AS 75–83) Physical functioning (PSS 83, AS 67–81) Global health status (PSS 63, AS 50–56)	NR	NR	NR	NR	Assessed
Sosnowski et al. (2019) [13]	Retrosp. comparative	56 Tx or Tis: 16 (28.6%) T1–4: 40 (71.4%)	PSS: 13/40 (32.5%; circumcision, WLE) AS: 27/40 (67.5%; PP 27/27)	NR	NR	SES PSS: mean score 28.81 PP: mean score 29.62 CMNI-22 PSS: mean score 28.26 PP: mean score 25.31	Post-op IIEF-5 PSS: mean score 13.59 PP: mean score 16.77 (p = 0.218) Self Esteem Scale: PSS: 28.81 ± 3.99	NR	NR	NR	Assessed

Table 2 (**continued**)

Study ID Author (year) [Ref.]	Study design	Patients (*n*)	Intervention (*n*)	RFR at 5 yr, % (*n*)	RFR at 1 and 3 yr, % (*n*)	QoL score (tool name, score)	Sexual function score (tool name, score)	Urinary function score	Complications (CD classification based on grade)	PPR	RoB
							PP: 29.62 ± 3.78 (p = 0.460)				
Veeratterapillay et al. (2015) [14]	Retrosp. comparative	203 Tx/Tis: 46/203(22.66%) T1: 59/157 (37.58%) T2: 73/157 (46.50%) T3: 22/157 (14.01%) T4: 3/157 (1.9%) N+: 31/203 (15.27%)	PSS: 99/196 (50.51%; WLE, glansectomy, distal corporectomy) AS: 97/196 (49.49%; PP or TP)	PSS: 89% (88/99) AS: 96% (93/97)	NR	NR	NR	NR	NR	Penile preserving rate: 85/99 (85.86%)	Assessed
Wan et al. (2018) [15]	Retrosp. comparative	15 Tis: 3 (20%) T1–3: 12 (80%)	PSS: 7/15 (46.67%; WLE) AS: 8/15 (53.33%; PP)	NR	1 yr: 100%	EORTC-QLQ-C30 social functioning: 85.94 Post-treatment values only EORTC-QLQ-C30 Social functioning (post-WLE 87.5 [10.21], post-PP 85.94 [8.01], p = 0.745) Cognitive functioning (post-WLE 85.71 [8.63], post-PP 84.38 [5.79], p = 0.726) Emotional functioning (post-WLE 77.68 [10.11], post-PP 76.56 [12.39], p = 0.853) Role functioning (post-WLE 83.93 [9.44], post-PP 82.81 [6.47], p = 0.791) Physical functioning NR Global health status (post-WLE 70.41 [6.42], post-PP 69.65 [5.05], p = 0.8)	IIEF-15 erectile function (22.43); SEAR 1–8 (80.36); EDITS patient (80.52) Erectile function: preop score p = 0.18, postop score p = 0.128 WLE: preop 13.29 ± 2.36, postop 22.43 ± 2.64 (p < 0.05), MD 9.14 (2.51) PP: preop 11.75 ± 1.83, postop 20.38 ± 2.26 (p < 0.05), MD 8.63 (2.08) Orgasmic function: preop score p = 0.663, postop score p = 0.033 WLE preop 2.29 ± 0.76, postop 5.71 ± 1.38 (p < 0.05), MD 3.42 (1.2) PP: preop 2.13 ± 0.64, postop 3.75 ± 1.75 (p = 0.027), MD 1.62 (1.53) Sexual desire: preop score p = 0.084, postop score p = 0.838 WLE: preop 3.71 ± 1.1,	Q_{max} WLE: 19.5 ml/s PP: 20.8 ml/s	NR	NR	Assessed

(*continued on next page*)

Table 2 (**continued**)

Study ID Author (year) [Ref.]	Study design	Patients (*n*)	Intervention (*n*)	RFR at 5 yr, % (*n*)	RFR at 1 and 3 yr, % (*n*)	QoL score (tool name, score)	Sexual function score (tool name, score)	Urinary function score	Complications (CD classification based on grade)	PPR	RoB
							postop 5.86 ± 1.35 ($p < 0.05$), MD 2.15 (1.25) PP: preop 2.75 ± 0.89, postop 6.00 ± 1.31 ($p < 0.05$), MD 3.25 (1.16) Intercourse satisfaction: preop score $p = 0.094$, postop score $p = 0.75$ WLE: preop 3.43 ± 0.98, postop 5.71 ± 1.1 ($p < 0.05$), MD 2.28 (1.04) PP: preop 2.63 ± 0.74, postop 5.5 ± 1.41 ($p < 0.05$), MD 2.87 (1.22) Overall satisfaction: preop $p = 0.057$, postop $p = 0.9$ WLE: preop 3.00 ± 0.82, postop 6.86 ± 1.46 ($p < 0.05$), MD 3.86 (1.27) PP: preop 2.63 ± 0.74, postop 6.75 ± 1.67 ($p < 0.05$), MD 4.12 (1.45) Significant decrease in sexual function and satisfaction occurred in 55.6% Significant decrease in sexual function and satisfaction occurred in 55.6%				
Sedigh et al. (2015) [16]	Retrosp. comparative	41 T1: 20 (49%) T2: 21 (51%)	PSS: 35/41 (85.37%) WLE: 12/35 (34.29%) Glansectomy: 23/35 (65.71%) AS: 6/41 (14.63%) PP: 6/6 (100%)	PSS: 34/35(97.1%) AS: 6/6 (100%)		NR	IIEF-15 score: Group A (preop: erectile function 17.2 ± 1.75, postop 16.5 ± 2.0, $p = 0.3$) Orgasmic function: preop 6.0 ± 1.5, postop 5.3 ± 1.25 ($p = 0.25$) Sexual desire: preop	NR	Soft tissue necrosis 1/6 (PP) Meatal stenosis: 3/35 (8.6%; glansectomy)		Assessed

Table 2 (**continued**)

Study ID Author (year) [Ref.]	Study design	Patients (*n*)	Intervention (*n*)	RFR at 5 yr, % (*n*)	RFR at 1 and 3 yr, % (*n*)	QoL score (tool name, score)	Sexual function score (tool name, score)	Urinary function score	Complications (CD classification based on grade)	PPR	RoB
							7.2 ± 1.0, postop 6.4 ± 1.0 (p = 0.15) Intercourse satisfaction: preop 9.3 ± 1.5, postop 8.2 ± 1.5 (p = 0.09) Overall satisfaction: preop 6.0 ± 1.0, postop 4.5 ± 1.0 (p = 0.25) Total: 45.7, 40.9 (p = 0.08) Group B (Gx) Erectile function: preop 19.0 ± 2.25, postop 15.7 ± 1.5 (p = 0.012) Orgasmic function: preop 6.0 ± 1.25, postop 4.8 ± 1.25 (p = 0.04) Sexual desire: preop 7.2 ± 1.0, postop 6.0 ± 1.25 (p = 0.8) Intercourse satisfaction: preop 9.0 ± 2.0, postop 7.0 ± 1.75 (p = 0.12) Overall satisfaction: preop 7.3 ± 1.25, postop 3.6 ± 0.75 (p = 0.01) Total: 48.5, 37.1 (p = 0.003) SEP, genitalia sensitivity, and ejaculatory Index SEP-2 positive answer: A preop = 75% A postop = 75% (p > 0.05) B preop = 86.4% B postop = 59.1% (p = 0.006) SEP-3 positive answer: A preop = 75% A postop = 62.5% (p = 0.09) B preop = 71% B postop = 31.8%				

(*continued on next page*)

Table 2 (continued)

Study ID Author (year) [Ref.]	Study design	Patients (*n*)	Intervention (*n*)	RFR at 5 yr, % (*n*)	RFR at 1 and 3 yr, % (*n*)	QoL score (tool name, score)	Sexual function score (tool name, score)	Urinary function score	Complications (CD classification based on grade)	PPR	RoB
							($p < 0.004$) Genital sensitivity: A preop = 75% A postop = 62.5% ($p = 0.09$) B preop = 71% B postop = 31.8% ($p = 0.004$) Preserved ejaculatory reflex: A preop = 100% A postop = 100% ($p > 0.05$) B preop = 100% B postop = 31.8%, 59.1% reduced, 9.1% absent ($p = 0.003$)				
Yang et al. (2014) [17]	Retrosp. comparative	105 Tis/Ta: 43/105 (40.95%) T1: 58/62 (93.5%) T2: 4/62 (6.5%)	PSS Primary closure group 59/105 Tis/Ta: 25/59, T1: 31/59, T2: 3/59 Preputial flap reconstruction 46/105 Tis/Ta: 18/46, T1: 27/46, T2: 1/46	Total 94.26% (99/105) Primary closure 57/59 (96.6%) Preputial flap 42/46 (91.3%)	NR	NR	IIEF-15 score at 6 mo for primary closure: Erectile function: preop 20.5 (3.5), postop 22.2 (3.2) Orgasmic function: preop 6.7 (2.1), postop 7.5 (1.5) Sexual desire: preop 6.4(1.5), postop 7 (1.3) Intercourse satisfaction: preop 8 (3.7), postop 9.4 (2.0) Satisfaction: preop 5.5 (1.8), postop 6.3 (2.1) IIEF-15 score at 6 mo for preputial flap closure: Erectile function: preop 21.0 (3.6), postop 23.1 (3.0) Orgasmic function: preop 6.5 (2.5), postop 8.1 (1.3) Sexual desire: preop 6.2(1.7), postop 7.2 (1.3) Intercourse satisfaction: preop 7.6 (3.8), postop 10.4 (2.6) Overall satisfaction: preop 5.2 (1.7), postop	NR	Persistent hydrophallus (>14 d): 7/105 (6.7%) Skin flap necrosis: 2/105 (1.9%) Subcutaneous hematoma: 2/105 (1.9%) Painful erections: 2/105 (1.9%) Wound infection: 4/105 (3.8%) Urethral stenosis: 1/105 (0.9%) Active bleeding: 2/105 (1.9%)	100% (105/105)	Assessed

Table 2 (**continued**)

Study ID Author (year) [Ref.]	Study design	Patients (*n*)	Intervention (*n*)	RFR at 5 yr, % (*n*)	RFR at 1 and 3 yr, % (*n*)	QoL score (tool name, score)	Sexual function score (tool name, score)	Urinary function score	Complications (CD classification based on grade)	PPR	RoB
							7.0 (1.6) Rigi scan: primary closure Tip rigidity: pre-op 68 (14.3), postop 65.1 (10.5) Base rigidity: preop 72.4 (8.5), postop 74.0 (9.2) Duration (min): preop 17.5 (6.5), postop 16.9 (6.6) Preputial flap Tip rigidity: preop 64.7 (11.8), postop 64.0 (12.4) Base rigidity: preop 71.7 (7.8), postop 74.5 (9.6) Duration (min): preop 16.8 (6.7), postop 16.1 (7.5)				
Mistry et al. (2007) [18]	Retrosp. comparative	58 (61) Tx/Tis/Ta: 18/61 (29.5%) T1: 29/50 (58%) T2: 13/50 (26%) T3: 1/50 (2%) N+: 8/61 (13.1%) M+: 1/61 (1.7%)	PPS vs RT vs AS RT: 10/50 (20%; 50–55 Gy) PSS: 13/50 (26%) WLE: 10, Gx: 3 AS: 20/50 (40%; PP 14, TP 6) Unclear data: 7/50 (14%)	RT: 60% (6/10) PSS: 76.9% (10/13) AS: 85% (17/20)	RT: 1 yr: 100% (10/10) 3 yr: 90% (9/10) PSS: 1 yr: 100% (13/13) 3 yr: 85% (11/13) AS: 1 yr: 95% (19/20) 3 yr: 65% (13/20)	NR	NR	NR	RT Necrosis: 2/10 (20%) Urethral stricture: 1/10 (10%) ED: 1/10 (10%) Penectomy Wound infection: 1/20 (5%) Meatal stenosis: 1/20 (5%)	NR	Assessed
Ozsahin et al. (2006) [19]	Retrosp. comparative	60 Tx: 1/60 (2%) T1: 22/60 (37%) T2: 32/60 (53%) T3: 5/60 (8%) N+: 18/60 (30%)	AS: 27/60 (45%) vs RT: 25/60 (41.67%) at 52 Gy (26–74.5 Gy) or BT 8/60 (13.4%)	NR	1 yr: 27% AS: 88.89% (24/27) RT: 42.42% (14/33)	NR	NR	NR	NR	51.5% (17/33)	Assessed

(*continued on next page*)

Table 2 (**continued**)

Study ID Author (year) [Ref.]	Study design	Patients (*n*)	Intervention (*n*)	RFR at 5 yr, % (*n*)	RFR at 1 and 3 yr, % (*n*)	QoL score (tool name, score)	Sexual function score (tool name, score)	Urinary function score	Complications (CD classification based on grade)	PPR	RoB
Perez et al. (2020) [20]	Retrosp, comparative	44 (57) Tx/Tis/Ta: 21/57 (36.8%) T1: 14/44 (31.8%) T2: 18/44 (40.9%) T3: 12/44 (27.27%) N+: 8/57 (14%)	PSS Glans resurfacing: 20/57 (35.1%) Glansectomy: 14/57 (24.56%) vs PP: 23/57 (40.36%)	98.25% PSS: 97.00% (33/34) AS: 69.56% (16/23)		Only 32 patients replied EuroQol 5D-3L, EQ-VAS tool: Mean global health score of 82.5%, 81% had no problems with mobility, 94% had no problems with self-care, 87.5% were able to do their usual activities, 72% had no pain or discomfort, 28% reported moderate pain on daily activities, 94% did not consider themselves anxious or depressed	SHIM/IIEF-5, median score was 19 (IQR 10.75–25) TGR: 17.5 (5–24) Gx: 18 (11–23) PP: 19 (5–25)	ICIQ-MLUTS questionnaire Median VS was 4 (IQR 1–15) and median impact on QoL was 2 (IQR 0–36)	PSS Meatal stenosis: 3/44 (6.82%) Graft loss: 2/44 (4.54%) AS Meatal stenosis: 1/44 (2.3%)	NR	Assessed
Djajadiningrat et al. (2014) [21]	Retrosp. comparative	859 T1 = 320/859 (37.25%) T2 = 477/859 (55.53%) T3 = 55/859 (6.4%) T4 = 7/859 (1%) N+ = 285/859 (33.18%)	PSS = 451/859 (52.5%) AS = 408/859 (47.5%)	PSS: 73% (329/451) vs AS 96.2% (393/408)	NR	NR	NR	NR	NR	81% after 10 yr of FU (43/53)	Assessed
Lont et al. (2006) [22]	Retrosp. comparative	257 T1: 72/257 (28%) T2: 185/257 (72%)	PSS Local excision: 24/157 (15.29%) RT: 17/157 (10.83%) Local surgery + RTX: 12/157 (7.64%) Excision/ND:YAG: 60/157 (38.22%) Excision/CO_2: 44/157 (28.03%) AS PP: 96/100 (96.00%) Unknown: 4/100 (4.0%)	PSS: 63% (99/157) AS: 88% (88/100)	NR	NR	NR	NR	Urethral stenosis: 20/157 (12.74%) Infection: 10/157 (6.4%) Bleeding: 1/104 (1%) after laser	NR	Assessed
Gotsadze et al. (2020) [23]	Retrosp. comparative	223 T1: 77/223 (34.53%) T2: 120/223 (53.8%) T3: 26/223 (11.66%)	Circumcision and RT: 155/223 (69.5%) vs circumcision and chemo: 33/223 (14.8%) vs circumcision and radiochemotherapy: 35/223 (15.7%)	Circumcision and RT: 90.32% (140/155) vs circumcision and chemo: 90.9% (30/33) vs circumcision and radiochemotherapy: 62.86% (22/35)	NR	NR	NR	NR	Urethral stenosis: 6/155 (3.87%)	Circumcision and RT group (100/155, 64.5%)	Assessed

Table 2 (**continued**)

Study ID Author (year) [Ref.]	Study design	Patients (*n*)	Intervention (*n*)	RFR at 5 yr, % (*n*)	RFR at 1 and 3 yr, % (*n*)	QoL score (tool name, score)	Sexual function score (tool name, score)	Urinary function score	Complications (CD classification based on grade)	PPR	RoB
Kieffer et al. (2014) [24]	Retrosp. comparative	90	PPS (54) vs PP (36)	NR	NR	SF-36 Physical component Mental component Physical function (0–100) PSS: mean 48.59; SD 9.42 PP: mean 49.56; SD 9.59 Role physical (0–100) PSS: mean 53.34; SD 8.78 PP: mean 53.70; SD 8.93 Bodily pain (0–100) PSS: mean 81.52; SD 21.94 PP: mean 91.14; SD 22.28 General health (0–100) PSS: mean 68.37; SD 22.93 PP: mean 67.06; SD 23.29 Vitality (0–100) PSS: mean 69.66; SD 18.92 PP: mean 69.35; SD 19.21 Social functioning (0–100) PSS: mean 86.12; SD 19.34 PP: mean 88.2; SD 19.64 Role emotional (0–100) PSS: mean 82.58; SD 31.77 PP: mean 86.83; SD 32.25 Mental health (0–100) PSS: mean 79.52; SD 16.88 PP: mean 80.81; SD 17.16 IOCv2 Positive impact scale PSS: mean 49.10; SD 11.10 PP: mean 47.99; SD 11.27 Negative impact scale PSS: mean 42.08; SD 13.54 PP: mean 45.50; SD 13.76 Altruism and empathy PSS: mean 12.18; SD 3.14 PP: mean 12.14; SD 3.19	IIEF-15 Erectile function PSS: mean 14.34; SD 9.07 PP: mean 11.3; SD 9.32 Orgasmic function PSS: mean 5.48; SD 3.21 PP: mean 3.76; SD 3.29 Sexual desire PSS: mean 5.93; SD 2.2 PP: mean 3.63; SD 4.8 Intercourse satisfaction PSS: mean 5.37; SD 4.67 PP: mean 11.3; SD 9.32 Overall satisfaction PSS: mean 5.35; SD 2.62 PP: mean 4.54; SD 2.69	Urine spraying 43% of men after PSS 83% of men after AS	NR	NR	Assessed

(*continued on next page*)

Table 2 (continued)

Study ID Author (year) [Ref.]	Study design	Patients (*n*)	Intervention (*n*)	RFR at 5 yr, % (*n*)	RFR at 1 and 3 yr, % (*n*)	QoL score (tool name, score)	Sexual function score (tool name, score)	Urinary function score	Complications (CD classification based on grade)	PPR	RoB
						Health awareness PSS: mean 12.42; SD 3.72 PP: mean 11.59; SD 3.78 Meaning of cancer PSS: mean 79.52; SD 16.88 PP: mean 80.81; SD 17.16 Positive self-evaluation PSS: mean 11.89; SD 3.68 PP: mean 12.22; SD 3.74 Appearance concerns PSS: mean 5.65; SD 2.79 PP: mean 7.35; SD 2.83 Body change concerns PSS: mean 6.38; SD 2.62 PP: mean 6.66; SD 2.66 Life Interference PSS: mean 13.02; SD 4.52 PP: mean 15.24; SD 4.59 Worry PSS: mean 17.03; SD 6.1 PP: mean 16.25; SD 6.21				
Lindner et al. (2020) [25]	Retrosp. comparative	39 (55) Tis/Ta: 16/55 (29.1%) T1: 13/39 (33.34%) T2: 16/39 (41.02%) T3: 10/39 (25.64%) N–: 16/55 (29.1%)	PSS: 26/55 (47.28%) vs PP or TP: 29/55 (52.73%)	PSS: 52.9% (14/26) vs AS: 79.31% (23/29)	NR	NR	NR	NR	NR	NR	Assessed

AS = amputative surgery; BT = brachytherapy; CD = Clavien-Dindo; CES = CMNI-22 = Conformity to masculinity Norms Inventory; EBRT = external beam radiotherapy; ED = erectile dysfunction; EORTC-QLQ-C30 = European Organization for Research and Treatment of Cancer quality of life questionnaire; EQ-5D-3L = EuroQol 5D-3 questionnaire; EQ-VAS = EuroQol visual analogue scale; FU = follow-up; ICIQ-MLUTS = International Consultation on Incontinence Questionnaire Male Lower Urinary Tract Symptoms Module; IIEF = International Index of Erectile Function; IQR = interquartile range; MD = median; *n* = number; ND:YAG = neodymium-doped yttrium aluminum garnet laser; NR = not reported; PP = partial penectomy; PPR = penile-preservation rate; PSS = penile-sparing surgery; preop = preoperatively; postop = postoperatively; QoL = quality of life; Retrosp. = retrospective; RFR = recurrence-free rate; RoB = risk of bias; RT = radiotherapy; RTX = definitive radiotherapy; SD = standard deviation; SEP (2/3) = sex encounter profile; SES = self-esteem scale; SF-36 = 36-item Short Form survey; SHIM = Sexual Health Inventory for Men; TP = total penectomy; WLE = wide local excision.

Table 3 – Baseline characteristics and primary and secondary outcome scores for case series

Study ID Author (year) [Ref.]	Study design	Patients (*n*)	Intervention (*n*)	RFR at 5 yr, % (*n*)	RFR at 1 and 3 yr, % (*n*)	QoL score (tool name/score)	Sexual function score (tool name/score)	Urinary function score	Complications (CD classification based on grade)	PPR	RoB assessment
Radiotherapy											
Akimoto et al. (1997) [26]	Retrosp. case series	15 T1: 8/15 (53.3%) T2: 5/15 (30.0%) T3: 2/15 (13.3%) N+: 4/15 (26.67%)	BT using silicon mold (32–74 Gy administered in 1–3 fractions)	80% (12/15) T1: 8/8 (100%) T2: 4/5 (80%) T3: 0/2(0%)	NR	NR	NR	NR	Glans edema and erythema (15/15; GR1) Focal mucocutaneous ulceration (1/14; GR 2)	73% (11/15)	High risk
Azrif et al. (2006) [27]	Retrosp. case series	41 T1: 37/41 (90.2%) T2: 4/41 (9.8%) N+: 1/41 (2.4%)	EBRT 50–52.5 Gy administered in 16 fractions (22 d)	58.5% (24/41) T1: 12/37 (32.4%) T2: 2/4 (50%)	NR	NR	NR	NR	Penile ulceration 8% (4/41; GR 1) Urethral stenosis 29% (12/41; GR 1)	62% (25/41)	High risk
Chaudhary et al. (1999) [28]	Retrosp. case series	23 T1: 7/23 (30.4%) T2: 7/23 (30.4%) T3: 9/23 (39.1%)	BT Radical radiation therapy using Ir-192 temporary interstitial implant The median dose of implant was 50 Gy (range 40–60 Gy), using the LDR after loading system and the Paris system of implant rules for dosimetry	73.9% (17/23) T1: 4/7 (57.1%) T2: 4/7 (57.1%)	NR	NR	NR	NR	2 (8.6%) meatal stenosis	82.60%	High risk
Cordoba et al. (2016) [29]	Retrosp. case series	73 Tis: 6 (8.2%) T1–4: 67 (91.8%) N+: 13/73 (17.8%)	Low dose of interstitial BT with iridium-192	65.8% (48/73) NR results per disease stage	1 yr: 86.2%	NR	NR	NR	CTCAE-NCI 4.0 score Late toxicity: 15 (20.5%) Late dermatitis: 9 (12.3%) Dysuria: 4 (5.5%) Meatal stricture: 5 (6.8%) Sexual pain: 2 (2.1%)	72.6% (53/73)	High risk
Crook et al. (2005) [30] The dataset is similar to that of Leijte et al. [6] but provides evidence on sexual function	Retrosp. case series	49 Tis: 2/49 (4%) Tx: 2/49 (4%) T1: 25/45 (55.5%) T2: 16/45 (35.5%) T3: 4/45 (9%)	Primary interstitial BT Pulsed dose rate (PDR) at doses 50–61.2 cGy/h BT (n = 23), iridium wire (n = 22), or seeds (n = 4)	64.4% (32/49) NR results per disease stage	NR	NR	81.5% able to have intercourse (27 men reported normal potency before BT, 22 still experience satisfactory erections)	NR	Soft tissue necrosis: 8/49 (16%) Urethral stenosis rate: 6/49 12%	86.5% (42/49)	Low risk

(*continued on next page*)

Table 3 (**continued**)

Study ID Author (year) [Ref.]	Study design	Patients (*n*)	Intervention (*n*)	RFR at 5 yr, % (*n*)	RFR at 1 and 3 yr, % (*n*)	QoL score (tool name/score)	Sexual function score (tool name/score)	Urinary function score	Complications (CD classification based on grade)	PPR	RoB assessment
Crook et al. (2009) [31]	Retrosp. case series	67 Tx: 2 (3%) T1: 37/67 (56%) T2: 22/67 (33%) T3: 6/67 (8%)	Primary interstitial BT PDR (60 Gy, range 55–65Gy) at a rate of 50–65 cGy/h BT (*n* = 41), iridium wire (*n* = 26)	71.0% (48/67) NR results per disease stage	At 10 yr: 58.8% (39/67)	NR	NR	NR	Soft tissue necrosis: 8/67 (12%) Urethral stenosis rate: 6/67 (9%)	88% (59/67)	Low risk
Pimenta et al. (2015) [32]	Retrosp. case series	25 T1–2: 25/25 (100%)	BT LDR BT and 65 Gy delivered via manually loaded 192 Ir wires, PDR BT 16 Gy/d, HDR BT 10 fractions/5 d	92% (23/25) NR results per disease stage	NR	NR	NR	NR	Telangiectasia: 11/25 (44%) Urethral stenosis: 10/25 (40%) Necrosis: 1/25 (4%) Fibrosis: 2/25(8%) Glans/penile atrophy: 4/25 (16%) Urinary incontinence: 2/25 (8%)	88.0% (22/25)	High risk
McLean et al. (1993) [33]	Retrosp. case series	26 (37) T1: 19/26 (73.1%) T2: 4/26 (15.4%) T3: 2/26 (7.7%) T4: 1/26 (3.8%) N+: 7/26 (26.9%)	EBRT 25–60 Gy (50 Gy in 20 fractions over 4 wk was mostly used)	50.0% (13/26) T1: 12/19 (63.2%) T2: 2/4 (50.0%) T3: 1/2 (50%)	At 1 yr: 61.54% (16/26) At 3 yr:. 57.7% (15/26)	NR	NR	NR	Meatal stricture: 7/26 (26.9%) Telangiectasia/ulceration: 7/26 (26.9%)	69.23% (18/26)	High risk
De Crevoisier et al. (2009) [34]	Retrosp. case series	144 (100% were stage I Jackson criteria, no subdivision of T disease)	Interstitial low-dose BT (65 Gy, range 37–75)	88.19% (127/144; calculated from data [20% recurrence after 8 yr])	NR	NR	NR	NR	Painful ulcerations: 25/144 (17.36) Urethral stenosis: 26/144 (18.05%)	Overall: 126/144 (87.5%)	High risk
Delannes et al. (1992) [35]	Retrosp. case series	51 Tis: 3/51 (5.9%) T1: 14/51 (27.45%) T2: 28/51 (54.91%) T3: 6/51 (11.76%) N+: 8/51 (15.7%)	BT iridium-192 interstitial therapy (50–65 Gy, mean 60 Gy)	86.27% (44/51; unknown time of recurrence) T1–2: 38/42 (90.5%) T3: 1/6 (16.7%)	NR	NR	NR	NR	Erythema, edema: 51/51 (100%) Urethral stenosis: 17/51 (33.34%) Foreskin sclerosis: 3/51 (5.89%) ED: 1/51 (2.0%) Delayed local necrosis: 9/51 (17.65%)	75% (38/51)	High risk

Table 3 (**continued**)

Study ID Author (year) [Ref.]	Study design	Patients (*n*)	Intervention (*n*)	RFR at 5 yr, % (*n*)	RFR at 1 and 3 yr, % (*n*)	QoL score (tool name/score)	Sexual function score (tool name/score)	Urinary function score	Complications (CD classification based on grade)	PPR	RoB assessment
Delaunay et al. (2014) [36]	Retrosp. case series	47 T1: 33/47 (70.2%) T2: 5/47 (10.6%) Tx: 9/47 (19.2%)	BT with low-dose-rate iridium-192 Mean dose: 60 Gy (42–70) Mean dose rate: 80 cGy/h (35–161)	59.6% (28/47; data at 80 mo, NR results per disease stage)		NR	IIEF Before treatment, 89.5% sexually active, 78.9% reported no ED. After treatment, 58.8% (10/17) remained sexually active, 36.8% (7/10) reported no erectile function 78.9% had nocturnal erections 52.6% observed modifications at glans sensitivity IIEF post-treatment only IIED 26–30 = 36.8% IIED 22–25 = 5.3% IIED 17–21 = 5.3% IIED 11–16 = 0% IIED 01–10 = 52.6%	NR	Ulcerations: 8/47 (17.02%) Urethral stenosis: 8/47 (17.02%) Bleeding: 7/47 (14.9%) Pain: 10/47 (21.28%)	66% (31/47)	High risk
Escande et al. (2017) [37]	Retrosp. case series	201 N+: 9.95%	BT Either LDR BT or pulse-dose rate BT (60 Gy)	70.15% (160/201) NR results per disease stage	NR	NR	NR	NR	Acute local toxicity (mucositis/urethritis): 100% (201/201) Late painful ulceration: 43% (87/201) Meatal stenosis: 25.9% (52/201) Stenosis more frequent in radiation doses >60 Gy (10.3% vs 37.2%, $p = 0.037$) Painful ulceration: higher risk when dose rate >0.43 Gy/h (6.5% vs 30.7%, $p = 0.021$)	85% (95% CI 79–91) 32 patients required surgery for relapse (11 pGx, 14 Gx, 7 total penectomy)	High risk
Makarewicz et al. (2010) [38]	Retrosp. case series	33 T1: 23/33 (69.7%) T2: 7/33 (21.2%) T3: 3/33 (9.1%) N0: 100%	HDR BT mean dose 51 Gy (48–54 Gy) given twice daily using HDR remote or 60 Gy applied for 6 consecutive days using PDR	78.8% (26/33) NR results per disease stage	NR	NR	Erectile function is not affected after treatment (descriptive)	NR	Acute reactions limited to implant site: 33/33 (100%) Sterile distal urethritis: 10/33 (30.3%) Telangiectasia: 5/33 (15.15%)	84.85% (28/33)	High risk

(*continued on next page*)

Table 3 (**continued**)

Study ID Author (year) [Ref.]	Study design	Patients (*n*)	Intervention (*n*)	RFR at 5 yr, % (*n*)	RFR at 1 and 3 yr, % (*n*)	QoL score (tool name/score)	Sexual function score (tool name/score)	Urinary function score	Complications (CD classification based on grade)	PPR	RoB assessment
Martz et al. (2021) [39]	Retrosp. case series	28(29) Tx: 1/29 (3.45%) T1: 22/29 (75.9%) T2: 6/29 (20.7%) N0: 26/29 (89.7%)	Multicatheter HDR BT 35 or 39 Gy	82.76% (24/29) NR results per disease stage	NR	NR	14/29 (54%) were sexually active before BT 14/14 reported no change after surgery	25/29 (86%) reported mild LUTS before therapy No change reported after therapy	Acute local toxicity (mucositis/urethritis): 100% (29/29) Telangiectasia: 17% (5/29) Necrosis: 10.3% (3/29) Urethral meatus stenosis: 2/29 (6.7%)	28/29 (96.55%)	High risk
Gambachidze et al. (2017) [40]	Retrosp. case series	23 T1: 23/23 (100%) N+: 3/23 (13.1%)	BT (BT was delivered using iridium-192 wires for continuous LDR irradiation or using a PDR remote after loader (delivering continuous hourly pulses of 0.42 Gy per pulse]) Median BT dose: 65 (IQR 60–65)	NR	NR	Median QoL score (0–100): 80 (IQR 65–90)	Index of Male Genitalia Image score: median 21 (IQR 16–22) IIEF-5 score: 20 (IQR 13–24) 16/23 (70%) maintained sexual activity	Median LUTS score: 6 (IQR 2–10)	Glans ulceration: 6/23 (26%) Urethral meatus stenosis: 7/23 (30%)	NR	High risk
Kamsu-Kom et al. (2015) [41]	Retrosp. case series	27 T1: 1/27 (4%) T2: 26/27 (96%)	Circumcision and pulse dose rate interstitial BT (60 Gy, range 60–70)	NR	At 3 yr: 77.78% (21/27)	NR	NR	NR	Acute local toxicity (mucositis, urethritis): 22/27 (81%) such as glans ulceration: 2/27 (7.4%) Meatal stenosis: 5/27(18.5%) Meatal stenosis and ulcerations were reported in 60% of patients with treated volume >25 cm^3 vs 17% of patients with treated volume <25 cm^3 ($p < 0.05$)	85.19% (23/27)	High risk
Kellas-Sleczka et al. (2019) [42]	Retrosp. case series	67 (76) Tis: 9/76 (11.8%) Tx: 9/76 (11.8%) T1: 35/67 (52.24%) T2: 16/67 (23.89%) T3: 7/67 (10.45%)	Superficial high-dose-rate BT ($n = 6$): median total dose 25 Gy Interstitial high-dose-rate BT ($n = 70$): median dose 42.8 Gy (21–54)	82.1% (55/67; whole group 65.6% [50/76]) T1: 94.3% (33/35) T2: 56.3% (9/16) T3: 57.1% (4/7)	1 yr: 85.1% (95% CI 76.9–93.2) 3 yr: 72.2% (95% CI 61.5–83.0)	NR	NR	NR	Moderate penile edema: 38/76 (50%) Patchy mucositis: 35/76 (46%) Pain: 32/76 (42.1%) Pigmentation changes: 27/76 (35.5%) Telangiectasia: 16/76 (21%) Patchy atrophy: 4/76 (5.3%) Atrophy: 3/76 (3.9%) Glans ulceration: 2/76 (2.6%) Urethral stenosis: 1/	53/76 (69.5%, 95% CI: 57.9–81.0%)	High risk

Table 3 (**continued**)

Study ID Author (year) [Ref.]	Study design	Patients (*n*)	Intervention (*n*)	RFR at 5 yr, % (*n*)	RFR at 1 and 3 yr, % (*n*)	QoL score (tool name/score)	Sexual function score (tool name/score)	Urinary function score	Complications (CD classification based on grade)	PPR	RoB assessment
									76 (1.3%)		
Kiltie et al. (2000) [43]	Retrosp. case series	31	BT iridium-191 Median dose 63.5 Gy (range: 60–66.5 Gy)	80.6% (25/31)	NR	NR	NR	NR	Urethral stricture: 11/31 (35.5%) Glans ulcerations: 9/31 (29.03%) Telangiectasia: 8/31 (25.8%) Necrosis: 1/31 (3.22%) Fibrosis: 1/31 (3.22%) 12 treated with <63 Gy, 5 needed (41.7%) dilatations 13 treated by >63 Gy, 7 needed (53.8%) dilatation or developed necrosis requiring penectomy (p = 0.68)	74.2% (23/31, 95% CI 56.8–92.7)	High risk
Rozan et al. (1995) [44] Results only for the BT arm	Retrosp. case series	259 Tx/Tis: 41/259 (15.8%) T1: 96/218 (44.04%) T2: 97/218 (44.49%) T3: 25/218 (11.47%) N+: 22/259 (8.5%)	Any surgery plus BT (n = 56) BT (iridium wire; n = 259) RT (n = 26) BT (iridium wire; n = 218, mean dose 59 Gy, range: 10–87)	83.94% (183/218) T1: 85/96 (88.54%) T2: 81/97 (83.5%) T3: 20/25 (80.0%)	At 3 yr: 187/218 (85.78%)	NR	NR	NR	NR	86.24% (188/218)	High risk
Zouhair et al. (2011) [45] Data only on 23 patients who had BT	Retrosp. case series	41 T1: 12/41 (29.0%) T2: 24/41 (59.0%) T3: 4/41 (10.0%) Tx: 1/41 (2%) N+: 12/41 (29.0%)	BT in 23 patients (data presented) Range of dose: 45–74Gy The rest of the cohort received surgery plus RT	39.1% (9/23)	NR	NR	NR	NR	Meatal stenosis: 2/23 (9%)	36% (8/23)	High risk
Laser											
Musi et al. (2018) [46]	Retrosp. case series	12(23) Tx/Ta/Tis: 11/23 (47.8%) T1: 7/12 (58.33%) T2: 3/12 (25%) T3: 2/12 (16.67%)	Laser therapy Thulium-yttrium-aluminum garnet	Not reached	83.3% (10/12; median FU 24 [15–30] mo)	NR	56.5% of patients felt that laser had impact on their sexual life	NR	Preputial edema: 12/12 (100%) Dysuria: 12/12 (100%)	100%	High risk

(*continued on next page*)

Table 3 (**continued**)

Study ID Author (year) [Ref.]	Study design	Patients (*n*)	Intervention (*n*)	RFR at 5 yr, % (*n*)	RFR at 1 and 3 yr, % (*n*)	QoL score (tool name/score)	Sexual function score (tool name/score)	Urinary function score	Complications (CD classification based on grade)	PPR	RoB assessment
Meijer et al. (2007) [47]	Retrosp. case series	38 (44) Tis: 6/44 (13.63%) T1: 21/38 (55.26%) T2: 17/38 (44.73%) N+: 2/38 (5.3%)	Laser treatment (Nd:YAG)	34.2% (13/38) T1: 9/21 (42.86%) T2: 4/17 (23.53%)	NR	NR	NR	NR	NR	50% (19/38)	High risk
Schlenker et al. (2010) [48]	Retrosp. case series	54 Tis: 11/54 (20%) T1: 39/43 (90.7%) T2: 4/43 (8.3%)	Laser therapy (yttrium-aluminum garnet [Nd:YAG]) combined with radical circumcision	69.77% (30/43)	NR	NR	NR	NR	NR	86.05% (37/43)	High risk
Windahl and Andersson (2003) [49]	Retrosp. case series	67 Tis/Ta: 23/67 (34.33%) T1: 23/44 (53.3%) T2: 19/44 (44.2%) T3: 2/44 (4.5%)	Laser treatment (CO_2/Nd:YAG laser; CO_2 laser; Nd:YAG laser)	77.27% (34/44) T1: 17/23 (73.9%) T2: 16/19 (84.2%) T3: 1/2 (50%)	NR	NR	NR	NR	Minor postop bleeding: 3/44 (7%)	95.46% (42/44)	High risk
Windahl et al. (2004) [50] Same population as for Lindner et al. [25] but provides data on sexual outcomes	Retrosp. case series	46 (67)	Laser treatment (CO_2/Nd:YAG laser;CO_2 laser; Nd:YAG laser)	80% (37/46)	NR	NA	PROM34 men have been sexually active; 27 (80%) resumed sexual life; 10 patients report decrease in erectile function (22%); 33 (72%) men report no change in erections; 3 (6%) men report improvement; Sexual dysfunction: 50% (23/46) report satisfied or very satisfied by sex, 72% or 33/36 report sexual life as they wanted	NA	NR	100% (46/46)	High risk
Tang et al. (2018) [51]	Retrosp. case series	161 Tx/Ta/Tis: 64 (39.8%) T1: 79/97 (81.44%) T2: 18/97 (18.56%)	Laser treatment (Nd:YAG or CO_2 laser)	52.58% (51/97) T1: 50.63% (40/79) T2: 66.67% (12/18)	At 1 yr T1: 63.3% (50/79) T2: 72.2% (13/18)	NR	NR	NR	NR	91.9% (148/161)	High risk

Table 3 (**continued**)

Study ID Author (year) [Ref.]	Study design	Patients (*n*)	Intervention (*n*)	RFR at 5 yr, % (*n*)	RFR at 1 and 3 yr, % (*n*)	QoL score (tool name/score)	Sexual function score (tool name/score)	Urinary function score	Complications (CD classification based on grade)	PPR	RoB assessment
Tewari et al. (2007) [52]	Retrosp. case series	106 Tx/Ta/Tis: 74 (69.8%) T1: 25/32 (78.13%) T2: 7/32 (21.87%)	Laser treatment Nd: YAG 100 W	94% (30/32) Local recurrence: 1/32 (3%) Distant recurrence: 1/32 (3%)	NR	NR	NR	NR	NR	96.8% (31/32)	High risk
Tietjen and Malek (1998) [53]	Retrosp. case series	17 (52) Tx/Tis/Tis: 35 (67.2%) T1–2: 17 (32.8%)	Laser treatment Nd: YAG, KTP/532, or CO_2 laser	82.35% (14/17)	NR	NR	NR	NR	NR	Overall: 88.26% (15/17)	High risk
Skeppner et al. (2008) [54]	Retrosp. case series	46 Tis: 13 (28.2%) T1–2: 33 (71.74%)	Laser treatment	NR	NR	LiSat-11-life as whole: 35/46 satisfied pts (76%)	Life satisfaction-11-sexual life: 23/43 (54%) satisfied pts 29/30 had intercourse 13 men were sexually inactive	NR	NR	NR	High risk
Bandieramonte et al. (2008) [55]	Retrosp. case series	118 (224) Tis: 106/224 (47.3%) T1: 118/224 (52.7%)	Excisional laser biopsy: 64 Partial surface laser excision: 47 Total surface laser excision: 113	83.05% (98/118)	NR	NR	NR	NR	Postop bleeding: 0.9% (2/224) Urethral stenosis: 7.4% (2/27 patients submitted to resection of the meatal region) From chemotherapy: 0.9% (2/224)	94% (111/118)	High risk
Surgery											
Baumgarten et al. (2018) [56]	Retrosp. case series	1188 Ta: 16 Tis: 202 T1: 576 T2: 394	Penile-sparing surgery Circumcision: 137 (11.5) Glansectomy: 362 (30.5) WLE: 338 (28.5) Laser with local excision: 91 (7.7) Laser monotherapy: 149 (12.5) Glans resurfacing: 111 (9.3)	73.6% (874/1188) T1: 71.4% (411/576) T2: 75.9% (299/394)	At 1 yr: 90.7%	NR	NR	NR	NR	pT1: 55.2% pT2: 60.9%	Low risk
Bissada et al. (2003) [57]	Retrosp. case series	30 N+: 12/30	PSS	70% (21/30) NR results per disease stage	NR	NR	NR	NR	NR	80% (24/30)	High risk
Carver et al. (2002) [58]	Retrosp. case series	36 (45) Tis: 9/45 (20%) T1–4: 36/45 (80%) N+: 11/36 (30.5%)	Any type of surgery including PSS (Cx, Gx, laser, EBRT; *n* = 13) Amputative (partial and total penectomy; *n* = 32)	NR	22 mo PSS: 69.23% (9/13) Amputative: 31/32 (96.87%)	NR	2/25 (8%) with PP were able to have satisfactory sexual intercourse NR for other treatment modalities	All patients with PP had satisfactory voiding and continence	Partial or total penectomy: 3 meatal stenosis, 1 wound infection	(71.1%) 32/45 refers to the whole sample Men who had OSS: 100% (13/13)	High risk

(*continued on next page*)

Table 3 (**continued**)

Study ID Author (year) [Ref.]	Study design	Patients (*n*)	Intervention (*n*)	RFR at 5 yr, % (*n*)	RFR at 1 and 3 yr, % (*n*)	QoL score (tool name/score)	Sexual function score (tool name/score)	Urinary function score	Complications (CD classification based on grade)	PPR	RoB assessment
Philippou et al. (2012) [59]	Retrosp. case series	179 T1: 88/179 (49.1%) T2: 68/179 (38.0) T3: 23/179 (12.8%)	PSS Circumcision: 13 (7.3%) WLE ± grafting: 29 (16.2%) Glansectomy: 87 (48.6%) Glansectomy and distal corporectomy: 50 (27.9%)	86.3% (154/179) T1: 93.2% (82/88) T2: 89.7% (61/68) T3: 87.0% (20/23)	NR	NR	NR	NR	Wound infection: 1/179 (0.6%) Neoglans necrosis: 1/179 (0.6%) Graft loss: 3/179 (1.8%)	87.7% (157/179)	High risk
Chalya et al. (2015) [60] Results only for 23% of the dataset	Retrosp. case series	236 N+: 154/236 (65.3%)	Any type of surgery including PSS (Cx, Gx, WLE; *n* = 22) Amputative (partial and total penectomy; *n* = 214)	77.78% (42/54). 5-yr data available for only 54 men	NR	NR	NR	NR	58 postop complications in 52 patients: SSI: 26 (44.8) DVT: 9 (15.5) Chronic pain: 8 (13.8) Scrotal edema: 6 (10.3) Wound dehiscence: 4 (6.9) Fournier's gangrene: 3 (5.2) Urethral stricture: 2 (3.4)	26.10%	Low risk
Chen et al. (2004) [61]	Retrosp. case series	44 Ta: 5(11%) T1–4: 39 (89%) N+: 18/40 (45%)	PP: 34 Total penectomy: 5 Conservative: 5	89.74% (35/39)	NR	NR	NR	NR	1: urethra stenosis 2: wound infection	13.6% (6/44)	High risk
Croghan et al. (2021) [62]	Retrosp. case series	35 Tis: 3 (8.6%) T1–3: 32 (91.4%)	PSS Partial glansectomy: 15 Radical glansectomy: 18 Partial penectomy: 2	NR	91.43% (32/35) at 3 yr	EORTC QLQ-C30 Question 29 mean QoL over past week on 7-point EORTC QLQ-C30 scale was: partial glansectomy 5.88, radical glansectomy: 5.7, PP: 6.0	Mean IIEF-5 scores Partial glansectomy 14.9 (5–25) and 15.8 radical glansectomy 15.8 (5–25) Satisfaction rates after glansectomy 60–82.4%	High satisfaction with postop urinary function was reported 85.3% (29/34) could void from a standing position, and 79.4% (27/34) reported little or no spraying of urine	NR	94.3% (33/35)	High risk
Smith et al. (2007) [63]	Prospective case series	72 T1: 35/72 (49%) T2: 37/72 (51%) N+: 1	Glansectomy with split-thickness skin graft reconstruction	95.8% (69/72)	NR	NR	NR	NR	Partial graft loss: 2/72 (3%) Graft overgrowth over the external urethral meatus: 1/72 (1%)	100% (72/72)	High risk

Table 3 (**continued**)

Study ID Author (year) [Ref.]	Study design	Patients (*n*)	Intervention (*n*)	RFR at 5 yr, % (*n*)	RFR at 1 and 3 yr, % (*n*)	QoL score (tool name/score)	Sexual function score (tool name/score)	Urinary function score	Complications (CD classification based on grade)	PPR	RoB assessment
Sri et al. (2018) [7]	Prospective cohort	332 (374) Tx/Tis: 42/374 (11.23%) T1: 163/332 (49.0%) T2: 135/332 (40.7%) T3: 34/332 (10.2%)	PSS Glansectomy: 151/332 (45.5%) Radical circumcision: 73/332 (22%) WLE: 48/332 (14.5%) Glans resurfacing: 30/332 (9%) Glansectomy with distal corporectomy: 30/332 (9%)	95.78% (318/332) T1: 159/163 (98%) T2: 127/135 (94%) T3: 32/34 (94%)	NR	NR	NR	NR	NR	NR	Low risk
Szeto et al. (2016) [64]	Retrosp. case series	30 20 men radical Rx Tx/Tis: 5/30 (16.7%) T1: 7/25 (28%) T2: 8/25 (32%) T3: 9/25 (36%) T4: 1/25 (4%) N+: 11/30 (36.6%) M+: 1/30 (3.3%)	Circumcision: 1/20 (5%) Partial/total penectomy: 7/20 (35%) Penectomy plus LND: 10/20 (50%) RT: 2/20 (10%)	44.4% (9/20)	NR	NR	NR	NR	NR	NR	High risk
Tang et al. (2017) [65]	Retrosp. case series	410 T1: 108/410 (26.3%) T2: 240/410 (58.5%) T3-T4: 43/410 (10.4%)	Glansectomy with split-thickness skin graft reconstruction	78% (320/410) Local recurrence: 7.6% (31/410) Regional recurrence: 3.4% (14/410) Distant recurrence 2.2% (9/410)	At 1 yr: 98% (402/410)	NR	NR	NR	NR	98.8% (405/410)	High risk
Veeratterapillay et al. (2012) [66]	Retrosp. case series	65 Tx/Tis: 15 (23.08%) T1: 31/50 (62%) T2: 19/50 (38%)	PSS Glansectomy and glanuloplasty: 34/50 (68%) Partial glansectomy and reconstruction: 1/50 (2%) Glansectomy and distal corporectomy and reconstruction: 15/50 (30%)	NR	At 3 yr: overall: 94% (4/50)	NR	NR	NR	Graft loss: 1/50 (2%) Graft contractures: 3/50 (6%) Meatal stenosis: 5/50 (10%)	Overall: 98.4% (62/63)	High risk

(*continued on next page*)

Table 3 (**continued**)

Study ID Author (year) [Ref.]	Study design	Patients (*n*)	Intervention (*n*)	RFR at 5 yr, % (*n*)	RFR at 1 and 3 yr, % (*n*)	QoL score (tool name/score)	Sexual function score (tool name/score)	Urinary function score	Complications (CD classification based on grade)	PPR	RoB assessment
Romero et al. (2005) [67]	Retrosp. case series	18 T1: 12/18 (66%) T2: 2/18 (11%) T3: 4/18 (23%)	PP (modified LND, *n* = 12)	NR	NR	NR	Portuguese version of the IIEF (before and after penectomy) Erectile function: preop 29.56 ± 1.4, postop 19.36 ± 12.44 (p = 0.012) Orgasmic function: preop 9.94 ± 0.24, postop 7.67 ± 3.9 (p = 0.027) Sexual desire: preop 8.89 ± 0.76, postop 7.61 ± 1.94 (p = 0.018) Intercourse satisfaction: preop 12.67 ± 1.46, postop 6.89 ± 5.57 (p = 0.002) Overall satisfaction: preop 8.61 ± 1.58, postop 6.11 ± 2.65 (p = 0.001) Significant decrease in sexual function and satisfaction occurred in 55.6%	NR	Meatal stricture and excessive penile shaft skin: *n* = 2/18 (11.1%)	NR	High risk
Sakai et al. (2010) [68]	Retrosp. case series	62 T1: 28 (45.16%) T2: 22 (35.48%) T3: 9 (14.5%) T4: 3 (4.8%) N+: 43/62 (69.36%)	AS: 59/62 PP: 43/59 Total penectomy: 13/59 Emasculation: 3/59 Local excision: 3/62	75.8% (47/62)	At 1 yr: 80.6% (52/62) At 3 yr: 75.8% (47/62)	NR	NR	NR	NR	NR	High risk
Sansalone et al. (2017) [69]	Retrosp. case series	25 T1: 11/25 (44%) T2: 14/25 (56%) N+: 11/25 (44%)	PP and reconstruction	NR	NR	NR	EDITS: Score: EDITS patient 74.97, EDITS patient 74.97 IIEF: Erectile function: preop 28.68 ± 1.04, postop 21.28 ± 3.07 (p < 0.001) Orgasmic function: preop 9.86 ± 0.59, postop 7.92 ± 0.86 (p = 0.03) Sexual desire: preop 8.75 ± 1.67, postop 7.16 ± 0.94 (p < 0.001) Intercourse satisfaction: preop 12.5 ± 1.75, postop	NR	NR		Low risk

Table 3 (**continued**)

Study ID Author (year) [Ref.]	Study design	Patients (*n*)	Intervention (*n*)	RFR at 5 yr, % (*n*)	RFR at 1 and 3 yr, % (*n*)	QoL score (tool name/score)	Sexual function score (tool name/score)	Urinary function score	Complications (CD classification based on grade)	PPR	RoB assessment
							7.32 ± 2.65 ($p < 0.001$) Overall satisfaction: preop 9.01 ± 1.58, postop 6.52 ± 1.84 ($p < 0.001$) QEQ: Quality of Erection Questionnaire score: 77.46 SEAR: SEAR items 1–8 Total score: 68.06 SEAR items 9–12 Total score: 73.25 SEAR items 13–14 Total score: 74.5				
Schlenker et al. (2011) [70]	Retrosp. case series	38 T1G2: 38/38 (100%)	PP: 11/38 (28.9%) Tumor excision: 5/38 (13.16%) Laser therapy (Nd:YAG laser): 22/38 (57.9%)	PP: 9/11 (81.82%) Circumcision: 4/5 (80%) Laser: 13/22 (59.09%)	NR	NR	NR	NR	NR	16/22 (72.73%; laser only)	High risk
Yu et al. (2016) [71]	Prospective case series	43 T status NR	PP ± lap bilateral or unilateral LND PP alone: 8/43 (18.6%) PP plus LND: 35/43 (81.4%)	95.35% (41/43)	NR	NR	IIEF-15 score at regular FU postop: the results is for the whole group Erectile function: preop 26.0 (3.07), postop 17.8 (10.66), $p < 0.01$ Orgasmic function: preop 8.44 (1.16), postop 5.81 (3.35), $p < 0.01$ Sexual desire: preop 8.33 (1.27), postop 6.28 (2.16), $p < 0.01$ Intercourse satisfaction: preop 12.3 (2.21), postop 7.07 (4.56), $p < 0.01$ Overall satisfaction: preop 8.0 (1.19), postop 5.91 (2.01) SAS score: preop 46.3 (8.73), postop 54.72 (11.74), $p = 0.01$ SDS score: preop 43.6 (8.32), postop 51.26 (10.7), $p = 0.04$	NR		NR	High risk

(*continued on next page*)

Table 3 (**continued**)

Study ID Author (year) [Ref.]	Study design	Patients (*n*)	Intervention (*n*)	RFR at 5 yr, % (*n*)	RFR at 1 and 3 yr, % (*n*)	QoL score (tool name/score)	Sexual function score (tool name/score)	Urinary function score	Complications (CD classification based on grade)	PPR	RoB assessment
Minhas et al. (2005) [72]	Retrosp. case series	48(51) Tx: 3/51 (5.9%) T1: 20/48 (41.67%) T2: 26/48 (54.17%) T3: 2/48 (4.17%)	PSS (WLE, partial or total glansectomy)	NR	At 1 yr: 95.8% (46/48) T1: 19/20 (95%) T2: 25/26 (96.16%)	NR	NR	NR	NR	95.8% (46/48) 1st year data only	Low risk
Monteiro et al. (2021) [73]	Retrosp. case series	79 (81) Tis: 2/81 (2.5%) T1: 42/79 (53.1%) T2: 35/79 (44.3%) T3: 2/79 (2.5%)	Amputative surgery: partial penectomy	92% (72/79)	NR	NR	Total IIEF score: preop 100% satisfactory erections, postop: 16.18 ± 7.08 ($p < 0.05$) Postop 61.7% had ED (9/50 [11.2%] mild ED, 17/50 [21%] mild-to-moderate ED, 9/50 [11.2%] moderate ED, and 15/50 [18.3%] severe ED)	NR	NR	NA	High risk
Morelli et al. (2009) [74]	Retrosp. case series	13 (15) Tx: 2/15 (13.3%) T1–3: 13/15 (86.7%)	PSS surgery: glansectomy	92.3% (12/13)	At 3 yr: 92.3% (12/13)	NR	All patients maintained their erectile function, orgasm, and ejaculation All patients reported reduced glans sensitivity	NR	Partial graft loss: 2/13 (15.4%) Meatal stenosis: 2/13 (15.4%).	92.3% (12/13)	Low risk
Moses et al. (2014) [75]	Retrosp. case series	94 (127) Tx/Ta/Tis: 33/127 (25.98%) T1: 34/94 (36.17%) T2: 42/94 (44.68%) T3: 17/94 (18.01%) T4: 1/94 (1%)	PSS: 42/127 (33.1%; WLE, Cx) Amputative surgery: 85/127 (66.9%; partial or total penectomy)	PSS: 92.85% (39/42) Amputative surgery: 67.06% (57/85)	NR	NR	NR	NR	NR	NR	Low risk
O'Kane et al. (2011) [76]	Retrosp. case series	19 (25) Tis: 6/25 (24%) T1: 15/19 (78.9%) T2: 3/19 (15.8%) T3: 1/19 (5.2%)	PSS: glansectomy	Not reached	At 2 yr: 84% (16/19)	NR	11 patients evaluated with regard to sexual function 81.8% (9/11) had good erectile functions to achieve erections 6/11 patients continued to be sexually active	NR	Meatal stenosis: 2/19 (10.52%)	100%	High risk
O'Kelly et al. (2017) [77]	Retrosp. case series	10 (19) Tx/Tis/Ta: 9/19 (47.37%)	PSS: total glans resurfacing	Not reached median	At 1 y:. 95% (18/19)	NR	14 patients were sexually active 14/14 resumed sexual activity within 6 mo	NR	Graft loss: 1/19 (5.3%)	100%	High risk

Table 3 (**continued**)

Study ID Author (year) [Ref.]	Study design	Patients (*n*)	Intervention (*n*)	RFR at 5 yr, % (*n*)	RFR at 1 and 3 yr, % (*n*)	QoL score (tool name/score)	Sexual function score (tool name/score)	Urinary function score	Complications (CD classification based on grade)	PPR	RoB assessment
		T1–2: 10/19 (52.63%)					postop IIEF-5 score: preop 21, postop 22 (p = 1.0)				
Opjordsmoen and Fossa (1994) [78]	Retrosp. case series	27 (30) Tx/Ta: 3/30 (10.0%) T1: 22/27 (81.5%) T2–4: 5/27 (18.5%)	Various treatments WLE: 4/27 (14.82%) RT: 11/27 (40.74%) PP: 8/27 (29.62%) Total penectomy: 4/27 (14.82%)	NR	100%	EORTC QLQ-C30 and General Health Questionnaire and Impact of Events Scale. The treatment was not related to overall well-being or social contact and activity	Those treated with amputative surgery had worst outcome in sexual outcome compared with those treated conservatively. There was no difference in domains of QoL between groups	NR	NR	NR	Unclear
Opjordsmoen et al. (1994) [79]	Retrosp. case series	27 (30) Tx/Ta: 4/30 (13.3%) T1: 22/30 (73.34%) T2–4: 4/30 (13.3%)	Various treatments WLE: 5/30 (16.67%) RT: 12/30 (40.00%) Partial penectomy: 9/30 (30.00%) Total penectomy: 4/30 (13.34%)	96.6% (29/30)	NR	NR	RT appears superior to surgery in terms of sexuality preservation	NR	NR	100%	Unclear
Ornellas et al. (2008) [80]	Retrosp. case series	688 Tx: 53/688 (7.7%) T1: 93/688 (13.5%) T2: 323/688 (46.95%) T3: 176/688 (25.58%) T4: 43/688 (6.25%)	Penile surgery WLE: 27/688 (3.92%) Circumcision: 41/688 (5.95%) PP: 522/688 (75.9%) Total penectomy: 83 (12.1%) Unclear: 15/688 (2.2%)	89.39% (615/688) 10-yr DFS 71% in patients with immediate LND In those with delayed LND, this percentage decreased to 30%		NR	NR	NR	NR	NR	High risk
Palminteri et al. (2011) [81]	Retrosp. case series	13 (21) Tx/Tis/Ta: 8/21 (38.1%) T1–2: 13/21 (61.9%)	PSS Total glans resurfacing: 3/21 (14.0%) Glansectomy: 10/21 (47.62%) PP: 4/21 (19.04%) Unclear: 4/21 (19.04%)	10/13 (76.92%; FU at 45 mo)	At 1 yr: 100%	No tool All men were satisfied	No tool 13/13 men reported having recovered sexual functioning 13/13 reported reduced penile sensitivity	NR	NR	100%	High risk
Parnham et al. (2018) [82]	Retrosp. case series	177 T1: 58/177 (33%) T2: 99/177 (56%) T3: 20/177 (11%)	PSS Glansectomy	90.69% (156/172), median FU 41 mo	95% at 1 yr 90% at 3 yr	NR	NR	NR	Complete or near-complete graft loss: 35/177 (20.34%) Meatal stenosis: 4/177 (2.3%)	100%	Low risk

(*continued on next page*)

Table 3 (**continued**)

Study ID Author (year) [Ref.]	Study design	Patients (*n*)	Intervention (*n*)	RFR at 5 yr, % (*n*)	RFR at 1 and 3 yr, % (*n*)	QoL score (tool name/score)	Sexual function score (tool name/score)	Urinary function score	Complications (CD classification based on grade)	PPR	RoB assessment
Draeger et al. (2018) [83]	Retrosp. case series	76	Total number: 76 Organ sparing: 73 Penectomy: 3	NR	NR	QLQ-C30 tool compared between postcohort results and reference data of age-matched population Global Quality of Life score: 54 (5.9) vs 60.2 ($p = 0.05$) Physical functioning: 73.0 (10.4) vs 75.7 ($p = 0.157$) Role functioning: 61.2 (9.7) vs 76.0 ($p < 0.001$) Emotional functioning: 60.6 (8.3) vs 77 ($p < 0.001$) Cognitive functioning: 69 (13.4) vs 83.6 ($p < 0.001$) Social functioning: 63.6 (5.9) vs 85.9 ($p < 0.001$)	NR				
Falcone et al. (2020) [84]	Retrosp. case series	15 (26) Tx/Tis/Ta: 11/26 (42.31%) T1–2: 15/26 (57.69%)	PSS Glans resurfacing	NR	At 1 yr: 96.1% (25/26 men may include CIS patients) At 2 yr: 88.5% (23/26) At 3 yr: 80% (12/15)	NR	NR	NR	Overall rate: 3.8% (wound complication) Wound infection: 1/26 (3.8%) Partial graft loss: 4/26 (15.3%)	100% at 2 yr	High risk
Feldman and McDougal (2011) [85]	Retrosp. case series	28 (56) Tis: 28/56 (50%) T1: 28/56 (50%)	PSS Moh's microsurgery: 1 Circumcision: 6 Local excision: 9 Partial glansectomy: 12	85.7% (24/28); calculated as 21.4% in T1 with 25% of recurrence developed after 5 yr	NR	Excellent functional outcomes	NR	NR	NR	NR	High risk
Pietrzak et al. (2004) [86]	Prospective case series	69 Tis/Ta: 2/69 (2.9%) T1: 19/69 (27.54%) T2: 17/69 (24.64%) T3: 1/69 (1.5%)	PSS: 39 Partial glansectomy: 5/39 (12.8%) Glansectomy and reconstruction: 21/39 (53.85%) Glansectomy and distal corporectomy and reconstruction: 8/39	NR	Results at 1-yr FU PSS: 97.4% (38/39) Amputative surgery: 100% (10/10)	NR	NR	NR	NR	NR	High risk

Table 3 (**continued**)

Study ID Author (year) [Ref.]	Study design	Patients (*n*)	Intervention (*n*)	RFR at 5 yr, % (*n*)	RFR at 1 and 3 yr, % (*n*)	QoL score (tool name/score)	Sexual function score (tool name/score)	Urinary function score	Complications (CD classification based on grade)	PPR	RoB assessment
		Tx: 30/69 (43.48%)	(20.52%) Amputative surgery: 10 PP: 3/10 (30.0%) Radical penectomy: 7/10 (70.0%)								
Ficarra et al. (1999) [87]	Retrosp. case series	45 (47) Tis: 2/47 (4.25%) T1: 20/45 (44.45%) T2: 21/45 (46.67%) T3: 4/47 (8.51%)	PSS: 8 Local excision: 5/8 (62.5%) Circumcision: 3/8 (37.5%) Amputative surgery: 39 PP: 30/39 (76.9%) Radical penectomy: 9/39 (23.1%)	40.4% (19/47) pTis/pT1: 10 (45.4%) pT2: 8 (38.1%) pT3: 1 (25%) Difficult to extract recurrence rates based on procedure type	NR	NR	NR	NR	NR	NR	High risk
Albersen et al. (2018) [88]	Retrosp. case series	117 T1: 31/117 (26.5%) T2: 70/117 (59.7%) T3: 16/117 (13.7%)	PSS Glansectomy and glans reconstruction (117/117)	82.4% (97/117)	At 1 yr: 105/117 (89.5%) At 3 yr: 97/117 (82.4%)	NR	NR	NR	NR	NR	High risk
Gulino et al. (2013) [89]	Retrosp. case series	42 Tis/Ta: 6/42 (14.29%) T1: 11/36 (30.56%) T2: 25/36 (69.44%)	PSS Glansectomy	NR	NR	Bigelow's questionnaire Significant improvement at 6 mo postop compared with those 2 wk preop	IIEF-15 domains No significant changes between in all domains 2 wk preop and 6 mo postop	NR	NR	NR	High risk (answer is no at the following questions: 1, 2, 4)
Roussel et al. (2021) [90]	Retrosp. case series	897 T1: 230/897 (26%) T2: 534/897 (60%) T3: 108/897 (12%) Tx: 25/897 (2.8%)	Penile-sparing surgery Glansectomy: 657/897 (73%) Glansectomy and distal corporectomy: 240/897 (27%)	86.4% (775/897)	At 1 yr: 840/897 (93.6%) At 3 yr: 799/897 (89.1%)	NR	NR	NR	NR	NR	High risk
Kokorovic et al. (2021) [91]	Retrosp. case series	84 (129) Tis/Ta: 41/129 (31.8%) T1: 66/84 (78.6%) T2: 18/84 (21.4%) N–: 25/129 (19.38%) Nx: 96/129 (74.42%)	Penile-sparing techniques Wide local excision: 36/129 (27.9%) Partial or total glansectomy: 35/129 (27.1%) Laser (KTP or CO_2): 8/129 (6.2%) PSS plus laser: 50/129 (38.8%)	84.5% (109/129) Wide local excision: 94.4% (34/36) Partial or total glansectomy: 31/35 (88.5%) Laser (KTP or CO_2): 6/8 (75.0%) PSS plus laser: 38/50 (76.0%)	NR	NR	NR	NR	NR	NR	High risk

(*continued on next page*)

Table 3 (**continued**)

Study ID Author (year) [Ref.]	Study design	Patients (*n*)	Intervention (*n*)	RFR at 5 yr, % (*n*)	RFR at 1 and 3 yr, % (*n*)	QoL score (tool name/score)	Sexual function score (tool name/score)	Urinary function score	Complications (CD classification based on grade)	PPR	RoB assessment
Leijte et al. (2008) [6]	Retrosp. case series	580 (700) Tis/Ta: 120/700 (17.14%) T1: 207/580 (35.7%) T2: 289/580 (49.83%) T3: 45/580 (7.76%) T4: 39/580 (6.72%)	Wide local excision: 105/700 (15.0%) Laser (Nd:YAG or CO_2): 289/700 (41.28%) RT: 21/700 (3%) PP: 214/700 (30.57%) Total penectomy: 71/700 (10.14%)	70.7% (495/700)	NR	NR	NR	NR	NR	NR	High risk
Li et al. (2011) [92]	Retrosp. case series	25 (32) Tis/Ta: 7/32 (21.9%) T1: 23/25 (92%) T2: 2/25 (8%)	PSS WLE: 18/32 (56.2%) WLE and circumcision: 6/32 (18.7%) Radical circumcision: 8/32 (25%)	NR	At 3 yr: 88% (22/25)	NR	22/32 reported none to mild ED Postop 1/22 reported mild-moderate ED, while 21/22 reported same sexual function as before	NR	NR	96% (24/25)	High risk
Moh's micrographic surgery											
Shindel et al. (2007) [93]	Retrosp. case series	33 Tis: 16 (55.5%) T1–3: 15 (45.5%)	Moh's micrographic surgery	71.43% (11/15)	NR	NR	NR	NR	Meatal stenosis: 2/15 (13.3%)	NR	High risk
Lukowiak et al. (2021) [94]	Retrosp. case series	22 (119) Tx/Tis: 87/119 (73.2%) T1: 18/22 (81.8%) T2–3: 4/22 (18.2%)	Moh's microsurgery	100% (22/22)	NR	NR	Response rate: 57.5% (23/40; questionnaires) 23/23 reported no change postop	Response rate: 66% (27/41; questionnaires) 27/27 reported no change postop	NR	NR	High risk
Machan et al. (2016) [95]	Retrosp. case series	14 (44) Tx/Tis: 24/44 (58.54%) T1–3: 14/44 (31.82%) Other: 6/44 (13.64%; recurrent lesions)	Moh's microsurgery	85.7% (12/14)	NR	NR	NR	NR	NR	100% (14/14)	High risk

AS = amputative surgery; BT = brachytherapy; CI = confidence interval; CD = Clavien-Dindo; CIS = carcinoma in situ; DFS = disease-free survival; DVT = deep venous thrombosis; EBRT = external beam radiation therapy; ED = erectile dysfunction; EDITS = Erectile Dysfunction Inventory of Treatment Satisfaction score; EORTC QLQ-C30 = European Organisation for the Research and Treatment of Cancer core quality of life questionnaire; GR = group; FU = follow-up; HDR = high-dose rate; IIEF = International Index of Erectile Dysfunction; IQR = interquartile range; KTP = potassium titanyl phosphate; Lap = laparoscopy; LDR = low-dose rate; LND = lymph node dissection; LUTS = lower urinary tract symptoms; NA = not available; ND:YAG = neodymium-doped yttrium aluminum garnet laser; NR = not reported; PDR = pulse dose rate; pGx = pharmacogenomics; PP = partial penectomy; PPR = penile-preservation rate; preop = preoperative; postop = postoperative; PSS = penile-sparing surgery; pts = patients; QoL = quality of life; Retrosp. = retrospective; RFR = recurrence-free rate; RoB = risk of bias; RT = radiotherapy; SAS = Self-Rating Anxiety Scale; SDS = Self-Rating Depression Scale; SEAR = Self-Esteem and Relationship score; SSI = surgical site infection; WLE = wide local excision.

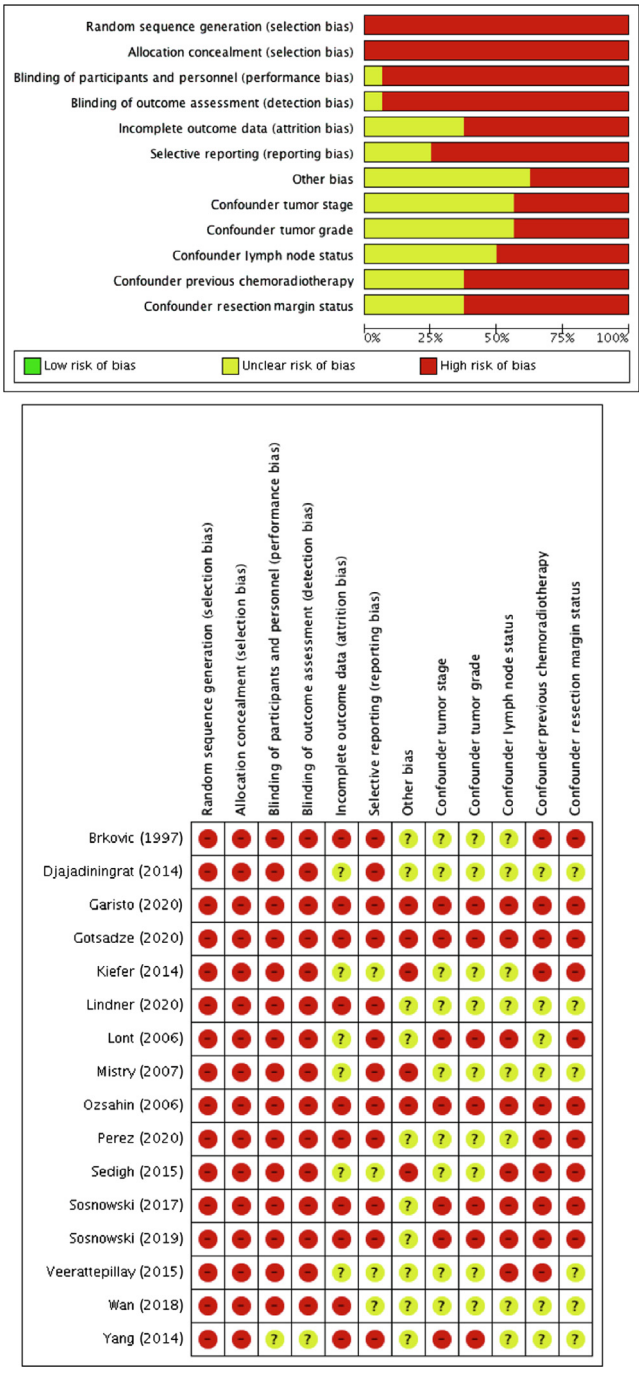


Fig. 2 – Risk of bias graph and summary of nonrandomized comparative studies using Cochrane tool ROBINS-I, including additional items to assess confounding bias risk. The five confounders were identified a priori: tumor stage, tumor grade, nodal stage, tumor margins, and previous radiotherapy or chemotherapy.

Eleven studies reported on 3438 men after penile-sparing surgery, with 42.1% of men were staged as T1, 50.1% as T2, and 7.8% as T3 [7,56,57,59,63,65,74,82,85,88,90]. The 5-yr recurrence-free rates across all cases ranged from 70% to 95.8%. The cumulative mean 5-yr recurrence-free rate was 82.0% (2820/3438). Glansectomy, with or without distal corporectomy, was reported in six studies involving 1681 men, 86.4% of whom were T1-T2 [63,65,74,82,88,90]. The 5-yr recurrence-free rates ranged from 78.0% to 95.8%.

Amputative surgery is reserved for more advanced disease. Five trials reported on 243 men; 71.6% were staged as T1-T2, who underwent partial or total penectomy [61,64,68,71,73]. The cumulative mean 5-yr recurrence-free rate was 83.9% (204/243; range 75.8–95.4%). Two CSs including T1 and T2 men reported 5-yr recurrence-free rates of 92% and 95.4% after partial penectomy [71,73].

A handful of single-center studies reported overall 5-yr recurrence-free rates from 70.7% to 96.6%, irrespective of the surgical approach or disease stage [6,60,79–81,87,91]. Three studies including men who received radiotherapy or laser were excluded to prevent contamination of data [6,79,92].

Seven NRCSs retrospectively compared 5-yr recurrence-free rates of penile-sparing surgery versus amputative surgery [11,14,16,20–22,25]. Of the men, 41.1% were staged as T1, 49.6% as T2, and 9.3% as ≥T3. Data on 785 men who received any type of penile-sparing surgery and 699 men who had amputative surgery are presented. The cumulative recurrence-free rates were 76.7% (602/785) for penile-sparing surgery and 93.3% (652/699) for amputative surgery (Fig. 3). Two NRCSs reviewed T1 and T2 cases only, and reported a 5-yr recurrence-free rate of 69.3% (133/192) after penile-sparing surgery as compared with 88.7% (94/106) after amputative surgery [16,22]. An NRCS compared 5-yr recurrence-free rates of penile-sparing surgery, amputative surgery, and radiotherapy, and reported rates of 76.9%, 85%, and 60%, respectively [18]. A small cohort study, which included men with T1G2 penile SCC, reported comparable 5-ar recurrence-free rates for circumcision and partial penectomy (80.0% vs 81.8%) [70].

3.4.1.1.2. Radiotherapy. Twenty-one studies evaluated the efficacy of radiotherapy in the management of primary tumor in men with penile cancer. A total of 1222 men had low-, pulse-, or high-dose-rate brachytherapy after circumcision [10,26,28–32,34–45]. Two studies reported the outcomes of EBRT in 67 men showing 5-yr recurrence-free rates for all cases ranging from 39.1% to 92% [27,33]. The cumulative mean 5-yr recurrence-free rates were 78.6% (861/1096) after brachytherapy and 55.2% (37/67) after EBRT. Seven studies reported recurrence-free rates per disease stage, with 5-yr recurrence-free rates ranging from 32.4% to 100% in T1, 50% to 80% in T2, and 0% to 80% in T3 disease [26–28,33,35,42,44].

3.4.1.1.3. Laser treatment. Nine studies reported the outcomes of 389 men, 81.2% (316/389) with T1 and 18.5% (71/389) with T2 disease [45–49,51–53,55]. The cumulative mean 5-yr recurrence-free rate was 69.4% (270/389; range 34.2–94%). Three studies reported 5-yr recurrence-free rates per disease stage: 42.9–73.9% for T1 and 23.5–84.2% for T2 disease [47,49,51].

3.4.1.1.4. Moh's micrographic surgery. Three studies reported 5-yr recurrence-free rates in 51 men, most diagnosed with T1 disease [93–95]. The cumulative mean 5-yr recurrence-free rate was 88.2% (45/51; range 71.4–100%).

3.4.1.2. Post-treatment sexual function. Sexual function was assessed in 27 studies involving 991 men. The five- or 15-

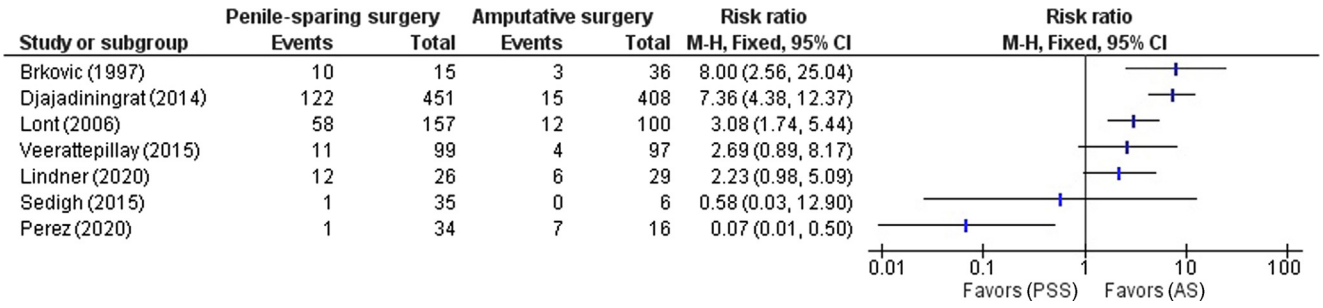


Fig. 3 – Recurrence rates at 5 yr following penile-sparing surgery (PSS) versus amputative surgery (AS). CI = confidence interval; M-H = Mantel-Haenszel test.

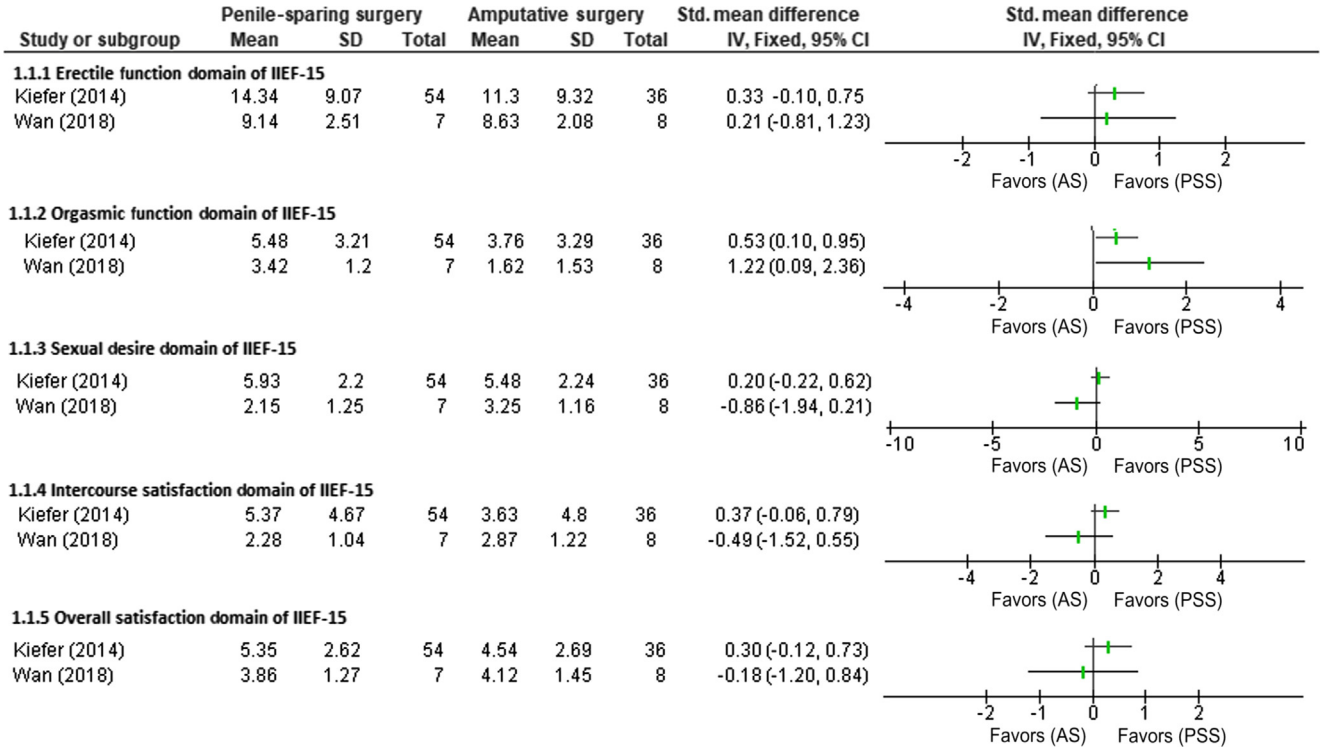


Fig. 4 – International Index of Erectile Function-15 questionnaire (IIEF-15) score, presented per questionnaire domain. AS = amputative surgery, CI = confidence interval; M-H = Mantel-Haenszel test; PSS = penile-sparing surgery; SD = standard deviation; Std. = standard.

question International Index of Erectile Function (IIEF) scores were used most often. Nearly all studies reported either post-treatment scores only or the mean difference from retrospectively collected pretreatment scores.

Three NRCSs and one CS (n = 202) compared the impact of penile-sparing surgery versus amputative surgery on sexual function [13,15,24,78]. Two studies, using the IIEF-15 questionnaire, reported significant post-treatment changes in erectile and orgasmic function domains in favor of penile-sparing surgery (p = 0.033 and p = 0.033; Fig. 4) [15,24]. Two studies, using the IIEF-5 questionnaire, reported no difference between treatments [13,20]. A study comparing the impact of penile-sparing surgery, amputative surgery, and radiotherapy reported worst sexual outcome after penectomy [78]. Three trials retrospectively compared penile-sparing surgery techniques [16,17,62]. Wide local excision was superior to glansectomy in each IIEF domain [16]. Partial glansectomy scored similar to total glansectomy [62].

Findings from CSs were similar to those from NRCSs. Five studies on patients after penile-sparing surgery and reconstruction reported that 85.0–100% of men were sexually active, but reduced glans sensitivity was consistently reported [74,76,77,81,92]. Four studies on 167 men treated by partial penectomy reported significant changes in IIEF scores [58,67,69,73]. In a single trial, 61.7% of men reported erectile dysfunction after partial penectomy [73].

Five studies assessed sexual function after brachytherapy [30,36,38–40]. Among sexually active men, 58.8–70.0% still had intercourse [36,40] and potency was maintained in 81.5–100% of men [30,36,38–40]. Altered sensitivity of the glans area is reported by 52.6% in one study [36].

Three studies assessed sexual function after laser treatment [46,50,54], with 46.0–56.5% of men reporting an

impact on their sexual life in two trials [50,54]. In the third trial (n = 46), 72% of men reported no change in erectile function, while 22% reported decreased erectile function [46].

No change in sexual function after Moh's micrographic surgery treatment was reported by 57.5% of men in one trial [94].

3.4.1.3. Post-treatment QoL. QoL was assessed in ten studies including 346 men [12,15,20,24,40,54,62,78,83,89]. The European Organisation for Research and Treatment of Cancer (EORTC) Core Quality of Life (EORTC QLQ-C30) questionnaire was used most frequently. Two studies compared QoL scores between treatments as the primary outcome [12,78]. One study reported that treatment itself was not related to the overall well-being or to social contact and activity; however, 53% patients reported mental symptoms at follow-up [78].

A retrospective study compared the EORTC QLQ-C30 scores in a cohort of men after penile-sparing surgery with those in an age-matched reference population and reported that surgery significantly impacts every domain of the questionnaire ($p < 0.05$) except physical functioning ($p = 0.157$) [83]. Another study using the Bigelow's questionnaire compared the postoperative QoL scores with those at 2 wk before surgery, and reported significant improvements in the scores relating to unpleasant feeling, sexual pleasure, and familial/partner relations ($p < 0.01$) [89].

Two NRCSs compared QoL after penile-sparing surgery and amputative surgery based on the EORTC QLQ-C30 questionnaire, with contradictory results; the first study demonstrated an inverse correlation between aggressiveness of surgery and global health status, while the second found no difference in QoL between treatments [12,15]. Two studies, using the EQ-5D and Short Form Health Survey (SF-36) tools, reported comparable QoL scores for penile-sparing surgery and amputative surgery [20,24]. However, after amputative surgery, men reported more appearance concerns ($p = 0.008$) and more life interference ($p = 0.032$) depending on the degree of disfigurement caused by the procedure.

3.4.2. Secondary outcomes

Data regarding secondary outcomes were unreported across studies. The available evidence is described below.

3.4.2.1. Recurrence-free rates at 1 and 3 yr. Recurrence-free rates at 1 and 3 yr were reported in 26 CSs [10,18,19,29,33,41,42,44,46,51,56,58,62,65,66,72,74,76,77,81,82,84,86,88,90,92]. In men who underwent penile-sparing surgery, the 1-yr mean recurrence-free rate was 95.6% (range 84–100%) and the 3-yr mean recurrence-free rate was 88.8% (range 80.0–94.0%) [15,56,65,66,72,74,76,77,81,82,84,86,88,90,92]. In men after amputative surgery, the mean 1-yr recurrence-free rate was 90.3% (range 80.6–100%) and the mean 3-yr recurrence-free rate was 88.5% (range 59.7–100%) [10,15,18,19,68,86]. The 1- and 3-yr mean recurrence-free rates after radiotherapy were 77.6% (range 61.5–86.2%) and 74.7% (range 57.7–85.8%), respectively [10,29,33,41,42,44].

3.4.2.2. Penile-preservation rate. Thirteen studies on 2166 men reported a mean penile-preservation rate after penile-sparing surgery of 79.7% (range 67.0–100%) [11,14,17,56,57,61,63,65,66,72,74,76,92]. Eighteen studies reported a mean penile-preservation rate after brachytherapy of 86.3% (range 69.5–96.5%) and a penile-preservation rate ranging from 62.0% to 69.2% after EBRT [26–39,41–44]. In ten studies of 512 men, the mean penile-preservation rate following laser therapy was 89.2% (range 50–100%) [46–55]. A study on Moh's micrographic surgery reported 100% penile-preservation rate.

3.4.2.3. Post-treatment urinary function. Urinary function has been evaluated in eight studies. Two CSs reported improved urinary function and high satisfaction after penile surgery [58,62]. Two NRCSs reported no difference in urination between penile-sparing surgery or amputative surgery. The first study reported a comparable maximum flow rate (19.5 vs 20.8 ml/s) for penile-sparing surgery and amputative surgery, and the second study found no difference in ICIQ-MLUTS scores between glans resurfacing, glansectomy, and partial penectomy [15,20]. Urine spraying was reported to be more common after partial penectomy (83% vs 43%) in one study [24]. Three CSs reported that neither brachytherapy nor Moh's micrographic surgery affected urinary function [39,40,94].

3.4.2.4. Treatment-related complications. Eighteen studies reported on surgery-related complications [16–18,20,22,23,45,58–61,63,66,67,76,77,82,84]. Graft-related problems (loss, contraction, or overgrowth) were reported in 10.5% (range 1.6–20.4%) of patients [17,20,59,63,66,74,77,82,84]. Neomeatus stenosis was reported in 6.3% (range 1–15.4%) [16,17,20,22,23,58,61,66,67,74,76,82]; wound-related complications (dehiscence or bleeding) were reported in 3.96% (range 0.6–6.9%) [17,22,59,60] and wound infection in 5.2% (range 0.6–10%) of cases [17,22,58–61,84].

Twenty studies reported on radiotherapy-related complications [10,26–43,45]. Acute reactions limited to implant site were frequent and consistently reported. Local toxicities such as mucositis and urethritis were reported in 82–100% of cases. Glans or penile ulceration incidence was reported in 24.2% (range 2.6–43%) [26,27,34,36,37,40,41–43] and meatal stenosis in 20.0% (range 1.3–40.0%) [10,27,28,30–37,39–43,45]. One study suggested a dose-depended stenosis risk (10.3% in doses >60 Gy vs 37.2% in doses <60 Gy) [37], while another described the treated area–depended risk (60% in treated area >25 cm^3 vs 17% in <25 cm^3) [41]. Pain was reported between 3.2% and 40%. Less frequent complications were bleeding, necrosis, atrophy, and fibrosis.

Three studies reported on laser-related complications, with preputial edema and dysuria occurring more frequently [46,49,55]. Meatal stenosis was reported in 7.4% and postoperative bleeding in 1–7%. Meatal stenosis was reported in 13.3% of Moh's micrographic surgery cases [93].

3.5. Discussion

Penile cancer is a rare neoplasm that in many cases, upon presentation, is confined to the prepuce or glans, and it is

well to moderately differentiated. These characteristics render the primary tumor amenable to treatment by penile conservative techniques, rather than by amputative surgery. In order to assess whether this translates to a clinically meaningful benefit, we conducted this systematic review to provide a higher level of evidence. A Cochrane protocol on the surgical management of localized penile cancer was previously submitted but withdrawn 1 yr later due to lack of progress and low prioritization [96,97].

3.5.1. *Principal findings*

This systematic review includes 88 studies and 9758 men with invasive penile cancer who underwent any type of treatment for their primary tumor. Treatment modalities included are surgery, radiotherapy, laser, and Moh's micrographic surgery. Since the bulk of the presented evidence relies on retrospective CS, results need to be interpreted with caution. However, some conclusions regarding primary and secondary outcomes of this study can be drawn.

The review includes 16 NRCSs, with an overall unclear to high RoB, while the remaining studies have a high RoB and therefore the quality of evidence is poor.

Most CSs report similar recurrence-free rates between penile-sparing surgery and amputative surgery. In a series of T1 and T2-only disease, 5-yr recurrence-free rates after amputative surgery were superior to those after penile-sparing surgery, which are in line with the findings of a recent systematic review [98]. The cumulative 5-yr recurrence-free rates of penile-sparing surgery are reported to be 82% in CS and 76.7% in NRCSs. Similarly, the cumulative 5-yr recurrence-free rates of amputative surgery are reported to be 83.9% in CS and 93.3% in NRCSs. These variations reflect the differences of study design as well as the different cohorts included in the analysis. The higher recurrence-free rates observed after amputative surgery need to be weighed against the impact on sexual function and QoL. The 5-yr recurrence-free rate after brachytherapy is superior to that after EBRT and comparable with that after penile-sparing surgery (78.6% vs 82%). Laser treatment and Moh's micrographic surgery are associated with worthy recurrence-free rates, but the majority of treated patients were T1, making a comparison with other modalities impossible.

The impact on sexual function is related to the aggressiveness of treatment. Wide local excision is superior to glansectomy, and penile-sparing surgery is superior to partial penectomy. Most men after penile-sparing surgery achieved erection, maintained sexual function, and scored better at IIEF questionnaires as compared with those after amputative surgery. Studies after partial penectomy reported significant changes in IIEF-15 scores and erectile dysfunction in 61.7% of men. Brachytherapy affects a third of sexually active men, while laser treatment and Moh's micrographic surgery do not influence erectile function, although reduced glans sensitivity was consistently reported across studies.

Surgery has a negative impact on QoL without significant difference between treatments. However, after amputative surgery, men report more appearance concerns and life interference due to disfigurement.

Data show that 1- and 3-yr recurrence-free rates were close to 5-yr recurrence-free rate, indicating that most recurrences occur within the first years after treatment. Moh's micrographic surgery is associated with a better penile-preservation rate than laser therapy (100% vs 89.2%), brachytherapy (86.3%), or penile-sparing surgery (79.7%). Urine spraying was frequently reported after partial penectomy, even though no other difference was recognized between treatments. Frequent complications include graft and wound problems after surgery, local toxicity and ulceration after brachytherapy, edema, and bleeding after laser treatment, and meatal stenosis after Moh's micrographic surgery.

3.5.2. *Implications for clinical practice*

Penile-sparing surgery should be considered, when possible, to treat primary penile lesions, aiming to preserve functional penile length, avoid disfigurement, and maintain QoL. The benefits must be weighed against the potential risk of residual disease and positive surgical margins, two factors that are correlated with an increased risk of local recurrence [98]. Evidence from CSs showed similar 5-yr cumulative recurrence-free rates between penile-sparing surgery and amputative surgery (82.0% vs 83.9%), thus strengthening the role of penile-sparing surgery in many cases. In addition, studies coming from large-volume centers present the lowest recurrence-free rates, supporting the concept of centralization of penile cancer care [7]. Evidence from NRCSs showed the superiority of amputative surgery over penile-sparing surgery in 5-yr recurrence-free rates (93.3% vs 76.7%), reflecting the different study designs. The results should be interpreted with caution since patients who underwent amputative surgery have more advanced disease than penile-sparing surgery patients (≥T3: 29.4% vs 7.8%). Two NRCSs on T1-T2 men only confirmed the superiority of amputative surgery over penile-sparing surgery (88.7% vs 69.3%), at a cost of sacrificing sexual function and psychological well-being [16,22].

Evidence from radiotherapy studies shows that compared with EBRT, brachytherapy results in better 5-yr recurrence-free rates with comparable results to penile-sparing surgery. An NRCS comparing amputative surgery, penile-sparing surgery, and radiotherapy reported that the 5-yr recurrence-free rates were 85%, 76.9%, and 60%, respectively [18]. The results are in accordance with the literature, reporting comparable 5-yr recurrence-free rates for penile-sparing surgery and brachytherapy (84% vs 79% and 85% vs 84% in T1-T2 cohorts) [99,100]. Laser treatment and Moh's micrographic surgery are effective in T1 men, but conclusions are difficult to draw. The 1- and 3-yr recurrence-free rate patterns indicate that local recurrences occur soon after treatment.

Penile cancer surgery impacts QoL and sexuality, hence the interest in penile-sparing surgery. It should be noted that patient-reported outcome measures have never been validated in penile cancer patients. Evidence from NRCSs show that penile-sparing surgery resulted in better sexual function, intercourse confidence, partner satisfaction, and IIEF-15 scores than amputative surgery [15,24,101]. In addition, penile cancer treatment affects mental well-being and

increases the risk of mental symptom development [12,71,78]. Literature reports that following penile cancer treatment, the risk of depression is 6–39% and the risk of anxiety is 31–58% [71,102]. A systematic review identified the need for standardized tools and interventional pathways to adequately assess the psychological and sexual dysfunction in penile cancer patients [5,103].

3.5.3. Implications for further research

The lack of well-designed, prospective trials highlights the need for further research. It is important to promote high-quality trials to allow comparison of different treatment options of primary tumors. Trial accrual and funding remain challenging in rare disease areas.

3.5.4. Limitations and strengths

The limitations of this systematic review relate to the weaknesses of the evidence analyzed. All studies were retrospective and of lower quality. It is therefore impossible to draw any firm conclusions, but only to observe trends and narratively report data. An additional limitation is data duplication. Data originating from high-volume centers may circulate in multiple publications, and thus influence the results to be skewed toward the means of those large centers that publish a lot and treat a high number of patients. Another limitation is the retrospective collection of data from relevant questionnaires such as sexual function or QoL, making the results open to a recall bias. Finally, we identified that all studies failed to report on censoring at 5-yr out.

The strengths of this review include adherence to Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines, an a priori written protocol, a well-designed methodology, and a systematic and transparent approach.

4. Conclusions

We systematically reviewed studies assessing the efficacy of surgery, radiotherapy, laser, and Moh's micrographic surgery in the treatment of the primary tumor in penile cancer patients, using standard methods for evidence acquisition and synthesis. The findings and clinical relevance were interpreted using an appropriate clinical context provided by the expert panel. Even though the quality of evidence is poor, there are data to support that penile-sparing surgery is not inferior to amputative surgery and should be offered whenever possible. Limitations relate to the weak evidence base, and the lack of large prospective studies and RCTs. Despite these limitations, this review provides up-to-date evidence of the predefined variables and can help provide clinical guidance.

***Author contributions*:** Vasileios I. Sakalis had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Sakalis, Brouwer, Tagawa.
Acquisition of data: Sakalis, Antunes-Lopes, Barreto, Campi, Perdomo, Greco, Kailavasan, Zapala.
Analysis and interpretation of data: Sakalis, Brouwer, Tagawa, Antunes-Lopes. Barreto, Campi, Perdomo, Greco, Kailavasan, Zapala.
Drafting of the manuscript: Sakalis.
Critical revision of the manuscript for important intellectual content: Sakalis, Brouwer, Tagawa, Albersen, Ayres, Crook, Moonen, Necchi, Oliveira, Parnham, Pagliaro, Pettaway, Protzel, Rumble, Spiess, Manzie, Marcus, Osborne.
Statistical analysis: None.
Obtaining funding: None.
Administrative, technical, or material support: None.
Supervision: Sakalis, Brouwer, Tagawa.
Other: None.

Financial disclosures: Vasileios I. Sakalis certifies that all conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript (eg, employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending), are the following: Maarten Albersen received research grants from Ipsen and Pfizer. Benjamin Ayres received speaker honorarium from Olympus KeyMed, is a company consultant for Cepheid UK Ltd, and participates is a trial by MSD. Juanita Crook received company consultancy fees for Ferring and Tersera. Arie Parnham received company speaker honorarium from Boston Scientific and participated in a trial by VELRAD. Curtis A. Pettaway received company consultant fees from Wolters Kluwer, contributing to their 'Up to date' Penile Cancer series. Philippe E. Spiess is President of the Global Society of Genitourinary Tumours, Vice-chair of the NCCN Bladder and Penile Cancer Guidelines, and Chair of the AUA Core-Curriculum Committee. Scott T. Tagawa, Oscar R. Brouwer, Pedro Oliveira, Lance C. Pagliaro, R. Bryan Rumble, Andrea Necchi, Chris Protzel, Tiago Antunes-Lopes, Lenka Barreto, Riccardo Campi, Herney Garcia Perdomo, Isabella Greco, Luc M.F. Moonen, Mithun Kailavasan, Vasileios I. Sakalis, Łukasz Zapala, Kenneth Manzie, Jack David Marcus, and John Osborne have nothing to disclose.

***Funding/Support and role of the sponsor*:** None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.euros.2022.04.002.

References

[1] Verhoeven RH, Janssen-Heijnen ML, Saum KU, et al. Population-based survival of penile cancer patients in Europe and the United States of America: no improvement since 1990. Eur J Cancer 2013;49:1414–21.
[2] Hernandez BY, Barnholtz-Sloan J, German RR, et al. Burden of invasive squamous cell carcinoma of the penis in the United States, 1998–2003. Cancer 2008;113:2883–91.
[3] Barnholtz-Sloan J, Maldonado JL, Pow-Sang J, Giuliano AR. Incidence in primary malignant penile cancer. Urol Oncol 2007;25:361–7.
[4] Hakenberg OW, Comperat E, Minhas S, Necchi A, Protzel C, Watkin N. EAU guidelines on penile cancer. Presented at EAU Annul Meeting, Barcelona, Spain, 2001.
[5] Maddineni SB, Lau MM, Sangar VK. Identifying the needs of penile cancer sufferers: a systematic review of the quality of life, psychosexual and psychosocial literature in penile cancer. BMC Urol 2009;9:1–8.
[6] Leijte JA, Kirrander P, Antonini N, Windahl T, Horenblas S. Recurrence patterns of squamous cell carcinoma of the penis: recommendations for follow-up based on a two-renter analysis of 700 patients. Eur Urol 2008;54:161–8.

[7] Sri D, Sujenthiran A, Lam W, et al. A study into the association between local recurrence rates and surgical resection margins in organ sparing surgery for penile squamous. BJU Int 2018;122:576–82.
[8] Sterne JA, Hernan MA, Reeves BC, et al. ROBINS-I: a tool for assessing the risk of bias in non-randomised studies of interventions. BMJ 2016;355:i4919.
[9] Knoll T, Omar MI, Maclennan S, et al. Key steps in conducting systematic reviews for underpinning clinical practice guidelines: methodology of the European Association of Urology. Eur Urol 2018;73:290–300.
[10] Garisto J, Nayan M, Fadaak K, et al. Oncological outcomes in the management of T1z–T2 cN0 penile squamous cell carcinoma. Can Urol Assoc J 2021;15:187–91.
[11] Brkovic D, Kalble T, Dorsam J, et al. Surgical treatment of invasive penile cancer—the Heidelberg experience from 1968 to 1994. Eur Urol 1997;31:339–42.
[12] Sosnowski R, Wolski JK, Kulpa M, et al. Assessment of quality of life in patients surgically treated for penile cancer: impact of aggressiveness in surgery. Eur J Oncol Nurs 2017;31:1–5.
[13] Sosnowski R, Wolski JK, Kulpa M, et al. Assessment of selected quality of life domains in patients who have undergone conservative or radical surgical treatment for penile cancer: an observational study. Sex Health 2019;16:32–8.
[14] Veeratterapillay R, Teo L, Asterling S, Greene D. Oncologic outcome of penile cancer treatment at a UK supraregional center. Urology 2015;85:1097–103.
[15] Wan X, Zheng D, Liu C, et al. A comparative study of two types of organ sparing surgeries for early stage penile cancer: wide local excision vs partial penectomy. Eur J Surg Oncol 2018;44:1425–31.
[16] Sedigh O, Falcone M, Ceruti C, et al. Sexual function after surgical treatment for penile cancer: which organ-sparing approach gives the best results? Can Urol Assoc J 2015;9:E423–7.
[17] Yang J, Chen J, Wu XF, et al. Glans reconstruction wit preputial flap is superior to primary closure for post-surgical restoration of male sexual function in glans preserving surgery. Andrology 2014;2:729–33.
[18] Mistry T, Jones RWA, Dannatt E, Prasad KK, Stockdale AD. A 10-year retrospective audit of penile cancer management in the UK. BJU Int 2007;100:1277–81.
[19] Ozsahin M, Jichlinski P, Weber DC, et al. Treatment of penile carcinoma: to cut or not to cut? Int J Radiat Oncol Biol Phys 2006;66:674–9.
[20] Perez J, Chavarriaga J, Ortiz A, et al. Oncological and functional outcomes after organ sparing plastic reconstructive surgery for penile cancer. Urology 2020;142:161–5.
[21] Djajadiningrat RS, van Werkhoven E, Meinhardt W, et al. Penile sparing surgery for penile cancer—does it affect survival? J Urol 2014;192:120–6.
[22] Lont AP, Gallee MPW, Meinhardt W, van Tinteren H, Horenblas S. Penis conserving treatment for T1 and T2 penile carcinoma: clinical implications of a local recurrence. J Urol 2006;176:575–80.
[23] Gotsadze D, Matveen B, Zak B, Mamaladze V. Is conservative organ-sparing treatment of penile carcinoma justified? Eur Urol 2000;38:306–12.
[24] Kieffer JM, Rosa S, Djajadiningrat RS, et al. Quality of life in patients treated for penile cancer. J Urol 2014;192:1105–10.
[25] Lindner AK, Schachtner G, Steiner E, et al. Organ sparing surgery of penile cancer: higher rate of local recurrence yet no impact on overall survival. World J Urol 2020;38:417–24.
[26] Akimoto T, Mitsuhashi N, Takahashi I, et al. Brachytherapy for penile cancer during silicon old. Oncology 1997;54:23–7.
[27] Azrif M, Logue JP, Swindell R, Cowan RA, Wylie JP, Livsey JE. External beam radiation in T1–2N0 penile carcinoma. Clin Oncol 2006;18:320–5.
[28] Chaudhary AJ, Ghosh S, Bhalavat RL, Kulkarni JN, Sequeira BVE. Interstitial brachytherapy in carcinoma of penis. Strahlenther Onkol 1999;175:17–20.
[29] Cordoba A, Escande A, Lopez S, et al. Low-dose brachytherapy for early stage penile cancer: a 20 year single institution study (73 patients). Radiat Oncol 2016;11:1–7.
[30] Crook JM, Jezioranski J, Math M, Grimard L, Esche B, Pond G. Penile brachytherapy: results for 49 patients. Int J Radiat Oncol Biol Phys 2005;62:460–7.
[31] Crook J, Ma C, Grimard L. Radiation therapy in the management of the primary penile tumor. World J Urol 2009;27:189–96.
[32] Pimenta A, Gutierrez C, Mosquera D, et al. Penile brachytherapy—retrospective review of a single institution. Brachytherapy 2015;14:525–30.
[33] McLean M, Akl AM, Warde P, Bissett R, Panzarella T, Gospodarowicz M. The results of primary radiation therapy in the management of squamous cell carcinoma of the penis. Int J Radiat Oncol Biol Phys 1993;25:623–8.
[34] De Crevoisier R, Slimane K, Sanfilippo N, et al. Long term results of brachytherapy for carcinoma of the penis confined to the glans (N- or Nx). Int J Radiat Oncol Biol Phys 2009;74:1150–6.
[35] Delannes M, Malavaud B, Douchez J, Bonnet J, Daly NJ. Iridium-192 interstitial therapy for squamous cell carcinoma of the penis. Int J Radiat Oncol Biol Phys 1992;24:479–83.
[36] Delaunay B, Soh PN, Delannes M, et al. Brachytherapy for penile cancer: efficacy and impact on sexual function. Brachytherapy 2014;13:380–7.
[37] Escande A, Haie-Meder C, Mazeron R, et al. Brachytherapy for conservative treatment of invasive penile carcinoma: prognostic factors and long term analysis of outcome. Int J Radiat Oncol Biol Phys 2017;99:563–70.
[38] Makarewicz R, Lebioda A, Terlikiewicz J, Kabacinska R. Interstitial brachytherapy for penile cancer. The experience of oncology centre in Bydgoszcz. J Contemp Brachyther 2010;2:157–9.
[39] Martz N, Bodokh Y, Gautier M, et al. High-dose rate brachytherapy in localised penile cancer: 5-year clinical outcome analysis. Clin Transl Radiat Oncol 2021;27:89–95.
[40] Gambachidze D, Lebacle C, Maroun P, et al. Long-term evaluation of urinary, sexual and quality of life outcomes after brachytherapy for penile carcinoma. Brachytherapy 2017;17:221–6.
[41] Kamsu-Kom L, Bidault F, Mazeron R, et al. Clinical experience with pulse dose rate brachytherapy for conservative treatment of penile carcinoma and comparison with historical data of low dose rate brachytherapy. Clin Oncol 2015;27:387–93.
[42] Kellas-Sleczka S, Bialas B, Fijalkiwski M, et al. Nineteen-year single-center experience in 76 patients with penile cancer treated with high doe rate brachytherapy. Brachytherapy 2009;18:493–502.
[43] Kiltie AE, Elwell C, Close HJ, Ash DV. Iridium-192 implantation for node-negative carcinoma of the penis: the Cookridge Hospital experience. Clin Oncol 2000;12:25–31.
[44] Rozan R, Albuisson E, Giraud B, et al. Interstitial brachytherapy for penile carcinoma: a multi centric survey (259 patients). Radiother Oncol 1995;36:83–93.
[45] Zouhair A, Coucke PA, Jeanneret W, et al. Radiation therapy alone or combined surgery and radiation therapy in squamous-cell carcinoma of the penis. Eur J Cancer 2011;37:198–203.
[46] Musi G, Russo A, Conti A, et al. Thulium-yttrium-aluminium-garnet (Tm:YAG) laser treatment of penile cancer: oncological results, functional outcomes and quality of life. World J Urol 2018;36:265–70.
[47] Meijer RP, Boon TA, Van Venrooij GEPM, Wijburg CJ. Long term follow up after laser therapy for penile carcinoma. Urology 2007;69:759–62.
[48] Schlenker B, Tilki D, Seitz M, et al. Organ-preserving neodymium-yttrium-aluminium-garnet laser therapy for penile carcinoma: a long term follow up. BJU Int 2010;106:786–90.
[49] Windahl T, Andersson SO. Combined laser treatment for penile carcinoma: results after long term follow up. J Urol 2003;169:2118–21.
[50] Windahl T, Sleppner E, Andersson SO, Fugl-Meyer KS. Sexual function and satisfaction in men after laser treatment from penile carcinoma. J Urol 2004;172:648–51.
[51] Tang DH, Yan S, Ottenhof SR, et al. Laser ablation as mono therapy for penile squamous cell carcinoma: a multicenter cohort analysis. Urol Oncol 2018;36:147–52.
[52] Tewari M, Kumar M, Shukla HS. Nd:YAG Laser treatment of early stage carcinoma of the penis preserves form and function of penis. Asian J Surg 2007;30:126–30.
[53] Tietjen DN, Malek RS. Laser therapy of squamous cell dysplasia and carcinoma of the penis. Urology 1998;52:559–65.
[54] Skeppner E, Windahl T, Andersson SO, Fulg-Meyer KS. Treatment-seeking, aspects of sexual activity and life satisfaction unman with laser-treated penile carcinoma. Eur Urol 2008;54:631–9.

[55] Bandieramonte G, Colecchia M, Mariani L, et al. Peniscopically controlled CO2 laser excision for conservative treatment of in situ and T1 penile carcinoma: report on 224 patients. Eur Urol 2008;54:875–84.
[56] Baumgarten AS, Chipollini J, Yan S, et al. Penile sparing surgery for penile cancer: a multicenter international retrospective cohorts. J Urol 2018;199:1233–7.
[57] Bissada NK, Yakout HH, Fahmy WE, et al. Multi-institutional long term experience with conservative surgery for invasive penile carcinoma. J Urol 2003;169:500–2.
[58] Carver BS, Mata JA, Venable DD, Eastham JA. Squamous cell carcinoma of the penis: a retrospective review of forty-five patients. South Med J 2002;95:822–5.
[59] Philippou P, Shabbir M, Malone P, Nigam R, Muneer A. Conservative surgery for squamous cell carcinoma of the penis: resection margins and long-term oncological control. J Urol 2012;188:803–8.
[60] Chalya PL, Rambau PF, Masalu N, Simbila S. Ten year surgical experiences with penile cancer at a tertiary care hospital in north west stern Tanzania: a retrospective study of 236 patients. World J Surg Oncol 2015;13:71.
[61] Chen MF, Chen WC, Wu CT, Chuang CK, Ng KW, Change JTC. Contemporary management of penile cancer including surgery and adjuvant radiotherapy: an experience in Taiwan. World J Urol 2004;22:60–6.
[62] Croghan SM, Compton N, Danoels AE, Fitzgibbon DPI, Cullen IM. Phallus preservation in penile cancer surgery: patient-reported aesthetic and functional outcomes. Urology 2021;152:60–6.
[63] Smith Y, Hadaway P, Biedrzycki O, Perry MJA, Corbishle C, Watkin NA. Reconstructive surgery for invasive. Eur Urol 2007;52:1179–85.
[64] Szeto OY, Cheng HC, Ng WS, Ngan KC. Squamous cell carcinoma of the penis: fourteen-year experience from a tertiary institution. Hong Kong J Radiol 2016;19:111–7.
[65] Tang DH, Yan S, Oteenhof SR, et al. Glansectomy as primary management of penile squamous cell carcinoma: an international study collaboration. Urology 2017;109:140–4.
[66] Veeratterapillay R, Sahadevan K, Aluru P, Asterling S, Rao GS, Greene D. Organ-preserving surgery for penile cancer: description of techniques and surgical outcomes. BJU Int 2012;110:1792–5.
[67] Romero FR, Romero KR, Mattos MA, Garcia CR, Fernandes Rde C, Perez MD. Sexual function after partial penectomy for penile cancer. Urology 2005;66:1292–5.
[68] Sakai I, Miyake H, Terakawa T, Mutotsugu M, Takenaka A, Fujisawa M. Oncological outcomes following surgical treatment for Japanese men with squamous cell carcinoma of the penis. Curr Urol 2010;4:125–30.
[69] Sansalone S, Silvani M, Leonardi R, Vespasiani G, Iacovelli V. Sexual outcomes after partial penectomy for penile cancer: results from a multi-institutional study. Asian J Androl 2017;19:57–61.
[70] Schlenker B, Tilki D, Gratzke C, et al. Intermediate-differentiated invasive (pT1G2) penile cancer—oncological outcome and follow-up. Urol Oncol 2011;29:782–7.
[71] Yu C, Hequn C, Longfei L, et al. Sexual function after partial penectomy: a prospectively study from China. Sci Rep 2016;6:21862.
[72] Minhas S, Kayes O, Hegarty P, Kumar P, Freeman A, Ralph D. What surgical resection margins are required to achieve oncological control in men with primary penile cancer? BJU Int 2005;96:1040–3.
[73] Monteiro LL, Skowronski R, Brimo F, et al. Erectile function after partial penectomy for penile cancer. Int Braz J Urol 2021;47:515–22.
[74] Morelli G, Pagni R, Mariani C, et al. Glansectomy with split-thickness skin graft for the treatment of penile carcinoma. Int J Impotence Res 2009;21:311–4.
[75] Moses KA, Winer A, Sfakianos JP, et al. Contemporary management of penile cancer: greater than 15-year MSKCC experience. Can J Urol 2014;21:7201–6.
[76] O'Kane HF, Ho AP, Thwaini A, Nambirajan T, Keane P. Outcome of glansectomy and skin grafting in the management of penile cancer. Adv Urol 2011;2011:240824.
[77] O'Kelly F, Lonergan P, Lundon D, et al. A prospective study of total glans resurfacing for localised penile cancer to maximise oncologic and functional outcomes in a tertiary referral network. J Urol 2017;197:1258–63.
[78] Opjordsmoen S, Fossa SD. Quality of life in patients treated for penile cancer. a follow-up study. Br J Urol 1994;74:652–7.
[79] Opjordsmoen S, Waehere H, Aass N, Fossa SD. Sexuality in patients treated for penile cancer: patient's experience and doctors' judgement. Br J Urol 1994;73:554–60.
[80] Ornellas AA, Kinchin EW, Nobrega BL, Wisnescky A, Koifman N, Quirino R. Surgical treatment of invasive squamous cell carcinoma of the penis: Brazilian National Cancer Institute long-term experience. J Surg Oncol 2008;97:487–95.
[81] Palminteri E, Fusco F, Berdondini E, Salonia A. Aesthetic neo-glans reconstruction after penis-sparing surgery for benign, premalignant or malignant penile lesions. Arab J Urol 2011;9:115–20.
[82] Parnham AS, Albersen M, Sahdev V, et al. Glansectomy and split-thickness skin graft for penile cancer. Eur Urol 2018;73:284–9.
[83] Draeger DL, Sievert KD, Hakenberg OW. Cross-sectional patient reported outcome measuring of health-related quality of life with establishment of cancer and related treatment-specific functional and symptom scales inpatients with penile cancer. Clin Genitourin Cancer 2018;16:e1215–20.
[84] Falcone M, Preto M, Oderda M, et al. Total glans resurfacing for the management of superficial penile cancer: a retrospective cohort analysis in a tertiary referral center. Urology 2020;145:281–6.
[85] Feldman AS, McDougal WS. Long-term outcome of excision organ sparing surgery for carcinoma of the penis. J Urol 2011;186:1303–7.
[86] Pietrzak P, Corbishley C, Watkin N. Organ-sparing surgery for invasive penile cancer: early follow up data. BJU Int 2004;94:1253–7.
[87] Ficarra V, D'Amico A, Cavalleri S, et al. Surgical treatment of penile carcinoma: our experience from 1976 to 1997. Urol Int 1999;62:234–7.
[88] Albersen M, Parnham A, Joniau S, et al. Predictive factors for local recurrence after glansectomy and neoglans reconstruction for penile squamous cell carcinoma. Urol Oncol 2018;36:141–6.
[89] Gulino G, Sasso F, Palermo G, et al. Sexual outcomes after organ potency-sparing surgery and glans reconstruction in patients with penile carcinoma. Indian J Urol 2013;29:119–23.
[90] Roussel E, Peeters E, Vanthoor J, et al. Predictors of local recurrence and its impact on survival after glansectomy for penile cancer: time to challenge the dogma? BJU Int 2021;127:606–13.
[91] Kokorovic A, Duplisea J, Qiao W, et al. Oncologic outcomes and subsequent treatment following organ sparing surgery for penile carcinoma: the University of Texas M.D. Anderson Cancer Center experience. Urol Oncol 2021;39:302.e19–27.
[92] Li J, Zhu Y, Zhang SL, et al. Organ-sparing surgery for penile cancer: complications and outcomes. Urology 2011;78:1121–4.
[93] Shindel AW, Mann MW, Lev RY, et al. Mohs micrographic surgery for penile cancer: management and long term follow up. J Urol 2007;178:1980–5.
[94] Lukowiak TM, Perz AM, Aizman L, et al. Mohs micrographic surgery for male genital tumors: local recurrence rates and patient-reported outcomes. J Am Acad Dermatol 2021;84:1030–6.
[95] Machan M, Brodland D, Zitelli J. Penile squamous cell carcinoma: penis-preserving treatment with Mohs micrographic surgery. Dermatol Surg 2016;42:936–44.
[96] Imamura M, MacLennan S, Lam TBL, et al. Surgical management for localised penile cancer. Cochrane Database Syst Rev 2015;3:CD011533.
[97] Dimitropoulos K, Stewart F, Imamura M, et al. Surgical management for localised penile cancer (protocol). Cochrane Database Syst Rev 2017;3:CD011533.
[98] Kamel MH, Bissada N, Warford R, Farias J, Davis R. Organ sparing surgery for penile cancer: a systematic review. J Urol 2017;198:770–9.
[99] Hasan S, Francis A, Hagenauer A, et al. The role of brachytherapy in organ preservation for penile cancer: a meta-analysis and review of the literature. Brachytherapy 2015;14:517–24.
[100] Hu X, Huang J, Wen S, Fu J, Chen M. Comparison of efficacy between brachytherapy and penectomy in patients with penile cancer: a meta-analysis. Oncotarget 2017;8:100469–77.
[101] Yang J, Chen J, Wu XF, Song NJ, Xu XY, Quan L. Glans preservation contributes to postoperative restoration of male sexual function: a multicenter clinical study of glans preserving surgery. J Urol 2014;192:1410–7.

[102] Ficarra V, Righetti R, D'Amico A, et al. General state of health and psychological well-being in patients after surgery for urological malignant neoplasms. Urol Int 2000;65:130–4.

[103] Drager DL, Milerski S, Sievert KD, Hakenberg OW. Psychosocial effects in patients with penile cancer: a systematic review. Urology A 2018;57:444–52.