Original article

Investigating the risk factors and pathological profile of penile cancer at a south african referral centre: a case-control study

Investigación de los factores de riesgo y el perfil patológico del cáncer de pene en un centro de referencia sudafricano: un estudio de casos y controles

Stephan Kruger,[1] Giovanni Drocchi,[2*] Heidi van Deventer,[1] Chantelle Scott,[1] Cecelia de Klerk,[1] Andre van der Merwe,[1] Danelo Estienne du Plessis du Plessis.[1]

Abstract

Background: Penile cancer is rare in developed countries but prevalent in developing regions. Known risk factors include phimosis, inflammation, and smoking. This study aims to determine the prevalence of these factors and explore potential novel ones in South Africa.

Methods: A case-control study was performed with 23 cases diagnosed with penile cancer from January 2008 to October 2023, and 46 age-matched controls with benign prostatic hyperplasia (BPH) or lower urinary tract symptoms (LUTS). Participants were interviewed using a standardized questionnaire. Pathological profiles and stage presentations were also documented.

Results: The most common risk factors were phimosis (OR 34.2, 95 % CI 7.9 to 244.5), inflammation (OR 14.1, 95 % CI 3.2 to 100.4), and smoking (OR 3.3, 95 % CI 1.1 to 12.9). Phimosis remained a significant risk factor even after adjusting for smoking, low income, and inflammation (OR 22.7, 95 % CI 3.9 to 210.6). Smoking and inflammation lost significance after adjusting for phimosis. The pathological profile was consistent with international data, but our patients presented with more advanced disease.

Conclusions: Phimosis was identified as the most important risk factor for penile cancer in this South African cohort, followed by smoking and preputial inflammation. The pathological profile was similar to international cohorts, though our patients presented at more advanced stages.

Keywords:
Penile cancer, risk factors, case-control, epidemiology

Citation: Kruger S., Drocchi D., van Deventer H., Scott C., de Klerk C., van der Merwe A, *et al. Investigating the risk factors and pathological profile of penile cancer at a south african referral centre: a case-control study. Rev Mex Urol. 2024;85(3)* 1-14

***Corresponding author:**
Giovanni Drocchi.
Address: Via Albaro 17/10
16145, Genova, Italy. Email:
g.drocchi@hotmail.it

[1.] Stellenbosch University, Cape Town, South Africa.
[2.] Università degli Studi di Genova, Genova, Italy.

Accepted: July 31, 2025
Received: April 2, 2025

Resumen

Antecedentes: El cáncer de pene es poco frecuente en los países desarrollados, pero prevalente en las regiones en desarrollo. Los factores de riesgo conocidos incluyen la fimosis, la inflamación y el tabaquismo. Este estudio busca determinar la prevalencia de estos factores y explorar otros potencialmente novedosos en Sudáfrica.

Métodos: Se realizó un estudio de casos y controles con 23 casos diagnosticados con cáncer de pene entre enero de 2008 y octubre de 2023, y 46 controles de la misma edad con hiperplasia prostática benigna (HPB) o síntomas del tracto urinario inferior (STUI). Los participantes fueron entrevistados mediante un cuestionario estandarizado. También se documentaron los perfiles patológicos y la presentación en estadio.

Resultados: Los factores de riesgo más comunes fueron la fimosis (OR: 34,2; IC del 95 %: 7,9 a 244,5), la inflamación (OR: 14,1; IC del 95 %: 3,2 a 100,4) y el tabaquismo (OR: 3,3; IC del 95 %: 1,1 a 12,9). La fimosis se mantuvo como un factor de riesgo significativo incluso después de ajustar por tabaquismo, bajos ingresos e inflamación (OR: 22,7; IC del 95 %: 3,9 a 210,6). El tabaquismo y la inflamación perdieron significancia tras ajustar por fimosis. El perfil patológico concordó con los datos internacionales, pero nuestros pacientes presentaron una enfermedad más avanzada.

Conclusiones: La fimosis se identificó como el factor de riesgo más importante para el cáncer de pene en esta cohorte sudafricana, seguida del tabaquismo y la inflamación prepucial. El perfil patológico fue similar al de las cohortes internacionales, aunque nuestros pacientes presentaron estadios más avanzados.

Palabras clave:
Cáncer de pene, factores de riesgo, casos y controles, epidemiología

Background

Penile cancer is a rare malignancy in developed countries (incidence < 1/100 000), but it represents up to 10 % of male cancers in certain regions of Africa, Asia, and South America.[1] While most commonly diagnosed in older men, its presence in individuals under 40 is not uncommon. Although the global burden remains low, recent GLOBOCAN data estimate approximately 36,000 new cases and 13,000 deaths from penile cancer worldwide in 2022, with the highest incidence rates observed in Eastern and Southern Africa.[2–4] In South Africa, penile cancer constitutes 0.49 % of all male cancers, with a lifetime risk of 1 in 1 080.[5]

The disease carries high morbidity due to disfiguring treatments and a five-year survival rate of only 50 % for all squamous cell carcinoma (SCC) subtypes.[6] Known risk factors include phimosis, poor hygiene, smoking, HPV infection, PUVA therapy, trauma, and high sexual activity.[7–12] Although HPV plays a well-established role in cervical cancer, it is found

in only one-third of penile SCC cases and most cases of penile intraepithelial neoplasia (PeIN).[13–15] Other contributing factors include psoralen exposure, complicated circumcisions, and penile injuries.[9,16–18]

Premalignant lesions such as PKMB, cutaneous horn, and lichen sclerosis also increase risk, with LS being linked to up to 30 % of SCC cases.[7,19–21] More than 95 % of penile cancers are SCC,[22] which can be classified into HPV-related and unrelated subtypes.[23] HIV infection may further increase HPV-related cancer risk, particularly in regions like South Africa.[24] While the general role of HPV has been studied, the specific pathological and risk factor profile in South Africa—especially the Western Cape—remains underexplored.[25]

The aim of this study was to assess the prevalence of known penile cancer risk factors in a South African cohort, identify potential unique regional contributors, and evaluate which factors may carry greater significance.

Methods

A case-control study was conducted at Tygerberg Hospital. Patients diagnosed with penile cancer from January 2008 to October 2023 and known to the urology oncology division were recruited as cases. Histological confirmation of squamous cell carcinoma (SCC) was required for inclusion. Controls were selected from men attending general urology clinics for non-malignant conditions such as lower urinary tract symptoms (LUTS) or benign prostatic hyperplasia (BPH), with no history or clinical suspicion of penile pathology. Controls were individually matched to cases by age (±5 years) at a ratio of 2:1 to enhance statistical power.

To minimize selection bias, controls were recruited from the same institution and within the same timeframe as cases, ensuring comparable healthcare access and referral context. All control participants were screened by clinical history and examination to confirm the absence of penile lesions or relevant pathology.

Sample size calculation was based on detecting an odds ratio of 2.5 for key exposures such as smoking and phimosis, assuming a 30 % prevalence in the control population, 80 % power, and a two-sided alpha of 0.05. This yielded a minimum requirement of 20 cases and 40 controls. Allowing for incomplete data and dropouts, a total of 23 cases and 46 controls were ultimately included. All participants were 18 years or older and provided written informed consent. A standardized questionnaire (Appendix 1) was administered in person or telephonically, capturing demographic data (age, ethnicity, income), behavioral risk factors (smoking history including pack years, condom use, number of sexual partners, age at sexual debut), clinical history (phimosis, penile trauma, inflammatory genital conditions, STI history), and HIV status. An open-ended question explored patients' beliefs about potential causes of their condition to identify novel or underreported risk factors. Pathological evaluation included histological subtyping of SCC according to WHO guidelines, distinguishing HPV-related (e.g. basaloid, warty, warty-basaloid) from non-HPV-related types (e.g. usual, verrucous, cuniculatum). Subtype distributions are reported in Table 4 and Table 5. T-stage at presentation was also recorded per AJCC criteria allowing assessment of disease extent at diagnosis. Statistical analysis was performed using R® (Vienna, Austria). Categorical variables were

summarized as frequencies and percentages; continuous variables as means ± standard deviation or medians with interquartile ranges. Associations with penile cancer were explored using univariate logistic regression. Variables with $p < 0.20$ or clinical relevance were included in multivariable logistic regression. Adjusted odds ratios and 95 % confidence intervals were reported. Model performance was assessed using McFadden's pseudo R^2.

Ethical approval was granted by the Health Research Ethics Committee of Stellenbosch University (reference S21/01/016).

Results

The study included 23 cases and 46 controls. The mean age at diagnosis was 59.8 years (SD=12.0). The ethnic background of the cases was as follows: 1 African (4.35 %), 14 admixture (60.87 %), and 8 Caucasians (34.78 %). The control group comprised of 7 African (15.22 %), 31 admixture (67.39 %), and 8 Caucasians (17.39 %).

A smoking history was noted in 19 cases (82.61 %) with a median of 17 pack years (IQR=8.0 to 27.7). 27 (58.70 %) of the controls had a smoking history with a median of 20 pack years (IQR=10.0 to 30.0). The use of recreational drugs was similar between the two groups, with 6 (26.09 %) of the cases and 14 (30.43 %) of the controls reporting use of illicit substances. Amongst the cases, 15 (65.22 %) hailed from an urban setting, while 8 (34.78 %) patients were from a rural setting. In the control group, 31 (67.39 %) were from an urban area and 15 (32.61 %) from a rural area.

A history of phimosis was present in 14 (60.87 %) cases, and in 2 (4.35 %) controls. 6 (26.09 %) of the cases, and 18 (39.13 %) of the controls were circumcised. A history of an inflammatory condition of the foreskin or penis was noted in 9 (39.13 %) of the cases and in 2 (4.35 %) of the controls. A penile trauma history was reported in 3 (13.04 %) of the cases and in 10 (21.74 %) of the controls.

The age of sexual debut was at a median of 18.0 years in both groups, with the IQR=16.5 to 19.0 amongst cases and IQR=16.0 to 20.0 in the control group. The cases were found to have a median of 4.0 (IQR=2.0 to 7.0) sexual partners, and the controls had a median of 3.0 (IQR=2.0 to 5.75). There was a history of previous STI in 6 (26.09 %) and 7 (15.22 %) of the cases and controls respectively (Table 1).

Table 1. Demographics & baseline characteristics

	Case		Control	
Variable	Number / Median	% / Std deviation / IQR	Number / Median	% / Std deviation / IQR
Total patients (n)	23		46	
Age at diagnosis	59.8	12.0		
Ethnicity				
African	1	4.35 %	7	15.22 %
Admixture	14	60.87 %	31	67.39 %
Caucasian	8	34.78 %	8	17.39 %
Smoker	19	82.61 %	27	58.7 %
Pack years	17 (median)	8.0 to 27.7 (IQR)	20 (median)	10 to 30 (IQR)
Socioeconomics				
Urban	15	65.22 %	31	67.39 %
Rural	8	34.78 %	15	32.61 %
Income < R5000 ($260)	16	69.57 %	23	50 %
Income R5k to R10k ($260 to $520)	3	13.04 %	11	23.91 %
Income R10k to R20k ($520 to $1040)	3	13.04 %	5	10.87 %
Income > R20000 ($1040)	1	4.34 %	7	15.22 %
Relationship status				
Married	14	60.87 %	36	78.26 %
Long-term committed	5	21.74 %	0	
Divorced	2	8.7 %	4	8.7 %
Single	2	8.7 %	6	13.04 %
Sexual debut age (years)	18.0 (median)	16.5 to 19.0 (IQR)	18.0 (median)	16.0 to 20.0 (IQR)
Number of partners	4.0 (median)	2.0 to 7.0 (IQR)	3.0 (median)	2.0 to 5.75 (IQR)
Phimosis	14	60.87 %	2	4.35 %
Circumcised	6	26.09 %	18	39.13 %
Inflammation	9	39.13 %	2	4.35 %
Condom use				
Almost always	3	13.04 %	6	13.04 %
>50 % of times	1	4.35 %	5	10.87 %
50 % of times	3	13.04 %	4	8.70 %
<50 % of times	2	8.70 %	12	26.09 %
Never	14	60.87 %	19	41.3 %
HIV Status				
Negative	16	69.57 %	39	84.78 %
Positive	4	17.39 %	2	4.35 %
Unknown	3	13.04 %	32	69.57 %
HPV Status				

continue...

Negative	7	30,43 %	7	15,22 %
Positive	2	8,69 %	6	13,04
Unknown	14	60,86 %	33	71,74
History of STI	6	26.09 %	7	15.22 %
Genital warts	5	21.74 %	2	4.35 %
Penile Trauma	3	13.04 %	10	21.74 %
Recreational drug use	6	26.09 %	14	30.43 %

With the application of univariate logistical regression models, phimosis (OR=34.222, 95 % CI 7.887 to 244.458, p-value <0.001), smoking (OR=3.343, 95 % CI 1.054 to 12.942, p-value=0.040), and inflammation (OR=14.143, 95 % CI 3.194 to 100.391, p-value <0.001) were found to be significant risk factors (Table 2).

Table 2. Univariate analysis

Univariate Categorical			
Variable	**OR**	**95 % CI**	**p-value**
Condom use rare	1.106	0.381 to 3.395	0.854
Ethnicity:			
African	0.143	0.007 to 1.075	0.147
Admixture	0.452	0.138 to 1.457	0.147
Income < R5000 ($260)	2.286	0.813 to 6.921	0.118
Circumcised	0.549	0.171 to 1.601	0.277
Illicit substance use	0.806	0.248 to 2.415	0.706
Penile trauma	0.540	0.112 to 2.009	0.372
Phimosis	34.222	7.887 to 244.458	<0.001
Smoking history	3.343	1.054 to 12.942	0.040
STI history	1.966	0.559 to 6.809	0.285
Inflammation	14.143	3.194 to 100.391	<0.001
HIV positive	4.875	0.864 to 37.776	0.193
Univariate Continuous			
Pack years smoking	0.997	0.960 to 1.033	0.849
Age of sexual debut	0.953	0.804 to 1.092	0.511
Number of sexual partners	1.027	0.937 to 1.125	0.543

In the multivariable model, the odds ratio for phimosis was lower than in the univariate model, after adjusting for exposures known from the literature (smoking, income, inflammation). The

model explains 37.84 % of the variance in presence of penile cancer, with a statistically significant p-value (Table 3).

Table 3. Multivariate analysis

Variable	OR	95 % CI
Income < R5000 ($260)	1.248	0.280 to 5.592
Phimosis	22.707	3.892 to 210.622
Inflammation	6.000	0.694 to 68.729
HIV Positive	0.907	0.048 to 14.118
Smoking history	3.748	0.800 to 24.613
McFadden pseudo R2 p-value = 0.378		

Additionally, the odds ratios for smoking and inflammation, which were significant in univariate models, were not significant after adjusting for the other factors, including phimosis. Therefore, in this cohort, phimosis was the single most important exposure associated with penile cancer with an OR=22.707 and a 95 % CI of 3.892 to 210.622.

The pathological profile of the cases showed SCC of the usual type to be the most common (60.9 %) subtype. Basaloid and warty subtypes each comprised 3 cases (13.0 %). Cuniculatum and Verrucous subtypes were found in 1 case each (4.3 %), while in 1 case (4.3 %) the subtype was not reported. There were no PeIN, papillary, or sarcomatoid subtypes in our series (Table 4). Subtype distributions are reported in Table 5.

Table 4. Pathological profile

Histology	Number	Percentage
Usual	14	60.9
Basaloid	3	13.0
Warty	3	13.0
PeIN	0	0
Papillary	0	0
Cuniculatum	1	4.3
Sarcomatoid	0	0
Verrucous	1	4.3
Subtype unknown	1	4.3

Table 5. Subtypes of penile SCC

Non-HPV Related	HPV Related
SCC usual type (48-65 %)	Basaloid SCC (4-10 %)
Pseudohyperplastic carcinoma (<1 %)	Papillary basaloid carcinoma
Pseudoglandular carcinoma (<1 %)	Warty carcinoma (7-10 %)
Verrucous carcinoma (3-8 %)	Warty-basaloid carcinoma (9-14 %)
Carcinoma cuniculatum (<1 %)	Clear-cell carcinoma (1-2 %)
Papillary carcinoma (5-15 %)	Lymphoepithelioma-like carcinoma
Adenosquamous carcinoma (<1 %)	
Sarcomatoid carcinoma (1-3 %)	

Most of the patients in this study (47.8 %) presented with stage T3 disease, 7 (30.0 %) had T1a disease, and 4 (17.4 %) had T2 disease. There were no cases with PeIN, T1b, or T4 disease in this series and in one case the T-stage was not known (Table 6).

Table 6. T-Stage at presentation

T-Stage	Number	Percentage
PeIN	0	0
T1a	7	30.0
T1b	0	0
T2	4	17.4
T3	11	47.8
T4	0	0
Unknown	1	4.3

Discussion

This study aimed to determine the prevalence of known risk factors for penis cancer in a unique South African population. Furthermore, the objective was to describe the demographics, pathological profile, and stage at presentation of these patients. The mean age for patients in this population to be diagnosed with penile cancer was 59.8 years, which is similar to that from other reports.[26] In this study, phimosis was found to be the single most significant risk factor for developing penile cancer. This correlates with internationally published data, but with an even higher odds ratio (OR=22.707, 95 % CI 3.892 to 210.622) than that reported by Hung-Fu Tseng *et al*. in their 2001 case-control study.[9] The treatment of phimosis is fairly simple by means of a topical steroid ointment or circumcision.[27]

Smoking and inflammatory conditions of the foreskin were also found to be important risk factors in our population, in keeping with published data. However, these factors were not found to be significant in multivariate analysis. This may be due to the smaller sample size of the study, and the relatively high incidence of smoking in the control group (58.7 %), as both these factors are risk factors in multiple publications.[7–9,11–13]

Early age of sexual debut and a higher number of sexual partners were not shown to be etiological factors in the studied population. This differs from the findings of other case-control studies for penile cancer, where these factors are presumed to be associated

with a higher incidence of HPV infection.[7–9,11] In further contrast to reported risk factors, it also did not play a role whether our patients hailed from a rural or urban background, and what their socioeconomic status was.

The pathological profile of penile cancer in this population correlates with internationally published data. Squamous cell carcinoma of the usual type was the most common subtype (60.9 %), followed by basaloid and warty subtypes at 13.0 % each. No patients had the papillary subtype, which is reported as being present in 5-15 % of cases in Europe, but this is most likely a reflection of the limited number of cases.[23] Nearly half of the patients (47.8 %) presented with T3 disease. This represents a more advanced stage of disease at presentation than that reported out of the United States, where most patients had either T1 or T2 disease.[28] This could be due to a delay in presenting to healthcare services, as it is well known that patients with penile cancer are often embarrassed or ignorant of the seriousness of their condition.[29] Penile cancer is not often encountered in clinical practice and there might also be delays caused by physicians in referring these cases, as they are often first treated as STI's or genital warts.

There were certain limitations to the study, most notably the small sample size. As penile cancer is a rare condition, purposeful sampling was used to include as many patients as possible. However, many patients did not have working telephone numbers and stopped following up at our facility. A further limitation was the fact that patients' memories may not have been reliable when completing the questionnaire. Lastly, the study was conducted in a single centre, and therefore it cannot be taken as a representation of the whole of South Africa, nor the rest of Africa.

Conclusions

The single most important risk factor for the development of penile cancer in a South African cohort is the presence of phimosis. Smoking and inflammatory conditions of the prepuce were also identified as risk factors, but were not significant when controlling for other factors. Socioeconomic status, rural setting, number of sexual partners and age of sexual debut were not found to be risk factors in the studied population. The pathological profile of penile cancer in this cohort is similar to internationally published data, however patients presented with more advanced disease.

Conflict of interests

The authors declare that they have no conflicts of interest.

Funding

The authors declare that no source of funding was used for this work.

References

1. **Neema S, Radhakrishnan S, Kinra P, Sandhu S.** Two Cases of Squamous Cell Carcinoma of the Penis—A Dermoscopic View. *Dermatology Practical & Conceptual*. 2021; e2020097–e2020097. https://doi.org/10.5826/dpc.1004a97.
2. **Arya M, Li R, Pegler K, Sangar V, Kelly JD, Minhas S, et al.** Long-term trends in incidence, survival and mortality of primary penile cancer in England. *Cancer Causes &*

Control. 2013;24(12): 2169–2176. https://doi.org/10.1007/s10552-013-0293-y.

3. **Baldur-Felskov B, Hannibal CG, Munk C, Kjaer SK.** Increased incidence of penile cancer and high-grade penile intraepithelial neoplasia in Denmark 1978-2008: a nationwide population-based study. *Cancer causes & control: CCC*. 2012;23(2): 273–280. https://doi.org/10.1007/s10552-011-9876-7.
4. **Graafland NM, Verhoeven RHA, Coebergh JWW, Horenblas S.** Incidence trends and survival of penile squamous cell carcinoma in the Netherlands. *International Journal of Cancer*. 2011;128(2): 426–432. https://doi.org/10.1002/ijc.25355.
5. **Cancer Association of South Africa (CANSA).** *Fact Sheet on How to Cope With a Cancer Diagnosis*. 2021.
6. **Razzaghi H, Saraiya M, Thompson TD, Henley SJ, Viens L, Wilson R.** Five-year relative survival for human papillomavirus-associated cancer sites. *Cancer*. 2018;124(1): 203–211. https://doi.org/10.1002/cncr.30947.
7. **Bleeker MCG, Heideman DAM, Snijders PJF, Horenblas S, Dillner J, Meijer CJLM.** Penile cancer: epidemiology, pathogenesis and prevention. *World Journal of Urology*. 2009;27(2): 141. https://doi.org/10.1007/s00345-008-0302-z.
8. **Dillner J, von Krogh G, Horenblas S, Meijer CJ.** Etiology of squamous cell carcinoma of the penis. *Scandinavian Journal of Urology and Nephrology. Supplementum*. 2000;(205): 189–193. https://doi.org/10.1080/00365590050509913.
9. **Tsen HF, Morgenstern H, Mack T, Peters RK.** Risk factors for penile cancer: results of a population-based case-control study in Los Angeles County (United States). *Cancer causes & control: CCC*. 2001;12(3): 267–277. https://doi.org/10.1023/a:1011266405062.
10. **Schoen EJ, Oehrli M, Colby C d, Machin G.** The highly protective effect of newborn circumcision against invasive penile cancer. *Pediatrics*. 2000;105(3): E36. https://doi.org/10.1542/peds.105.3.e36.
11. **Daling JR, Sherman KJ, Hislop TG, Maden C, Mandelson MT, Beckmann AM, et al.** Cigarette smoking and the risk of anogenital cancer. *American Journal of Epidemiology*. 1992;135(2): 180–189. https://doi.org/10.1093/oxfordjournals.aje.a116270.
12. **Hellberg D, Valentin J, Eklund T, Nilsson S.** Penile cancer: is there an epidemiological role for smoking and sexual behaviour? *BMJ*. 1987;295(6609): 1306–1308. https://doi.org/10.1136/bmj.295.6609.1306.
13. **Harish K, Ravi R.** The role of tobacco in penile carcinoma. *British Journal of Urology*. 1995;75(3): 375–377. https://doi.org/10.1111/j.1464-410x.1995.tb07352.x.
14. **Santos R da S, Hirth CG, Pinheiro DP, Bezerra MJB, Silva-Fernandes IJ de L, Paula DS de, et al.** HPV infection and 5mC/5hmC epigenetic markers in penile squamous cell carcinoma: new insights into prognostics. *Clinical Epigenetics*. 2022;14: 133. https://doi.org/10.1186/s13148-022-01360-1.
15. **Rubin MA, Kleter B, Zhou M, Ayala G, Cubilla AL, Quint WG, et al.** Detection and typing of human papillomavirus DNA in penile carcinoma: evidence for multiple independent pathways of penile carcinogenesis. *The American Journal of Pathology*. 2001;159(4): 1211–1218. https://doi.org/10.1016/S0002-9440(10)62506-0.
16. **Stern RS, null null.** Genital Tumors among Men with Psoriasis Exposed to Psoralens and Ultraviolet A Radiation (PUVA) and Ultraviolet B Radiation. *New England Journal of Medicine*. 1990;322(16): 1093–1097. https://doi.org/10.1056/NEJM199004193221601.

17. **Bissada NK, Morcos RR, el-Senoussi M.** Post-circumcision carcinoma of the penis. I. Clinical aspects. *The Journal of Urology*. 1986;135(2): 283–285. https://doi.org/10.1016/s0022-5347(17)45614-x.
18. **Morris BJ, Gray RH, Castellsague X, Bosch FX, Halperin DT, Waskett JH, et al.** The Strong Protective Effect of Circumcision against Cancer of the Penis. *Advances in Urology*. 2011;2011: 812368. https://doi.org/10.1155/2011/812368.
19. **Solivan GA, Smith KJ, James WD.** Cutaneous horn of the penis: its association with squamous cell carcinoma and HPV-16 infection. *Journal of the American Academy of Dermatology*. 1990;23(5 Pt 2): 969–972. https://doi.org/10.1016/0190-9622(90)70315-9.
20. **Perry D, Lynch PJ, Fazel N.** Pseudoepitheliomatous, keratotic, and micaceous balanitis: case report and review of the literature. *Dermatology Nursing*. 2008;20(2): 117–120.
21. **Nasca MR, Innocenzi D, Micali G.** Penile cancer among patients with genital lichen sclerosus. *Journal of the American Academy of Dermatology*. 1999;41(6): 911–914. https://doi.org/10.1016/s0190-9622(99)70245-8.
22. **Ornellas AA, Alves G, Schwindt AB dos S.** Pathology and Genetics. In: Culkin DJ (ed.) *Management of Penile Cancer*. New York, NY: Springer; 2014. p. 47–76. https://doi.org/10.1007/978-1-4939-0461-7_4.
23. **Brouwer O R, Tagawa ST, Albersen M, Ayres B, Crook J, van der Heijden MS, et al.** *EAU-ASCO Collaborative Guidelines*. 2023.
24. **Wentzel S, Vermeulen L, Beukes C, Thiart J, Joubert G, Goedhals J.** Human immunodeficiency virus (HIV) infection in men with penile carcinoma is associated with increased prevalence of human papilloma virus infection and younger age at presentation. *South African Journal of Surgery*. 2018;56(3): 47–50. https://doi.org/10.17159/2078-5151/2018/v56n3a2075.
25. **Lebelo RL, Boulet G, Nkosi CM, Bida MN, Bogers J, Mphahlele MJ.** Diversity of HPV types in cancerous and pre-cancerous penile lesions of South African men: Implications for future HPV vaccination strategies. *Journal of Medical Virology*. 2014;86(2): 257–265. https://doi.org/10.1002/jmv.23730.
26. **Chaux A, Netto GJ, Rodríguez IM, Barreto JE, Oertell J, Ocampos S, et al.** Epidemiologic profile, sexual history, pathologic features, and human papillomavirus status of 103 patients with penile carcinoma. *World Journal of Urology*. 2013;31(4): 861–867. https://doi.org/10.1007/s00345-011-0802-0.
27. **Moreno G, Corbalán J, Peñaloza B, Pantoja T.** Topical corticosteroids for treating phimosis in boys. Cochrane Urology Group (ed.) *Cochrane Database of Systematic Reviews*. 2014;2024(1). https://doi.org/10.1002/14651858.CD008973.pub2.
28. **Tobert C, Guidos JP, Erickson B, Nepple K.** Improving access to care and guideline compliance in a veterans affairs cystoscopy clinic: mp92-13. *Journal of Urology*. 2017;197(4): e1232.
29. **Gursel EO, Georgountzos C, Uson AC, Melicow MM, Veenema RJ.** Penile cancer Clinicopathologic study of 64 cases. *Urology*. 1973;1(6): 569–578. https://doi.org/10.1016/0090-4295(73)90517-7.

Appendices

1. Data Collection Sheet

Folder Number	
Name and Surname	
Date of Birth	
Ethnicity	African Asian Coloured White Other
Relationship status	Single (never married) Casual relationship Married Long-term committed relationship Divorced
Address (Rural or urban)	
Average monthly household income	<R5000 R5000 - R10 000 R10 000 - R20 000 R20 000 - R30 000 >R30 000
Are you circumcised?	
If circumcised, what was the reason?	Unsure Medical indication (phimosis / paraphimosis / redundant foreskin) Hygiene Religious Cultural Personal preference
Did you have a tight foreskin that you could not retract (phimosis)?	
Did you have any chronic inflammation, rash, or white discolouration of the foreskin or penis?	
How old were your when you had sex for the first time?	
How many sexual partners have you had over the years?	
Do you use condoms?	Never Less than half of the time About half of the time More than half of the time Almost always

continue...

Have you ever had a Sexually Transmitted Infection (STI)?	
Have you ever had warts on your penis or genital area?	
What is your HIV status?	Unknown Negative Positive Wish to not disclose
Are you, or were you ever, a smoker?	
If you smoked, how many cigarettes did you smoke a day?	
How long have you been smoking / did you smoke?	
Have you ever smoked illegal substances (eg. Tik, dagga etc)?	
Have you ever injured your penis?	
If you have injured your penis, what type of injury did you have?	Cut Tear / Abrasion Penile fracture Bruise / contusion Bite – Human Bite – Animal Burn
Did you ever receive Psoralen and Ultraviolet light treatment for Psoriasis or other skin conditions?	
Did you ever have any other problems or abnormalities of your penis? Please describe	
Are there any factors that you feel may have played a role in getting penis cancer?	

2. UICC/AJCC 8th edition TNM clinical and pathological classification of penile cancer

Clinical classification	
T - Primary Tumour	
TX	Primary tumour cannot be assessed
T0	No evidence of primary tumour
Tis	Carcinoma *in situ* (Penile Intraepithelial Neoplasia – PeIN)
Ta	Non-invasive verrucous carcinoma*
T1	Tumour invades subepithelial connective tissue
T1a	Tumour invades subepithelial connective tissue without lymphovascular invasion or perineural invasion and is not poorly differentiated
T1b	Tumour invades subepithelial connective tissue with lymphovascular invasion or perineural invasion or is poorly differentiated
T2	Tumour invades corpus spongiosum with or without invasion of the urethra
T3	Tumour invades corpus cavernosum with or without invasion of the urethra
T4	Tumour invades other adjacent structures
N - Regional Lymph Nodes	
cNX	Regional lymph nodes cannot be assessed
cN0	No palpable or visibly enlarged inguinal lymph nodes
cN1	Palpable mobile unilateral inguinal lymph node
cN2	Palpable mobile multiple or bilateral inguinal lymph nodes
cN3	Fixed inguinal nodal mass or pelvic lymphadenopathy, unilateral or bilateral
M - Distant Metastasis	
cM0	No distant metastasis
cM1	Distant metastasis
Pathological classification	
The pT categories correspond to the clinical T categories. The pN categories are based upon biopsy or surgical excision	
pN - Regional Lymph Nodes	
pNX	Regional lymph nodes cannot be assessed
pN0	No regional lymph node metastasis
pN1	Metastasis in one or two inguinal lymph nodes
pN2	Metastasis in more than two unilateral inguinal nodes or bilateral inguinal lymph nodes
pN3	Metastasis in pelvic lymph node(s), unilateral or bilateral or extranodal extension of regional lymph node metastasis
pM - Distant Metastasis	
pM1	Distant metastasis microscopically confirmed
G - Histopathological Grading	
GX	Grade of differentiation cannot be assessed
G1	Well differentiated
G2	Moderately differentiated
G3	Poorly differentiated
G4	Undifferentiated

*Including verrucous carcinoma.