

# A retrospective chart review of the management and outcomes of penile cancer patients who underwent penectomy over a five-year period at St. Aidan's Hospital, Durban

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**Background:** Penile cancer is a physically and psychologically debilitating disease with high morbidity and mortality, and is more common in sub-Saharan regions compared to the West. Its management involves penectomy and inguinal lymph node dissection in most cases. This study aims to describe the management and outcomes thereof in our sociodemographic environment and identify potential avenues for improving outcomes.

**Methods:** A retrospective chart review of cases from 2016 to 2020 at St. Aidan's Hospital of squamous cell carcinoma of the penis who underwent penectomy and inguinal lymph node dissection, was performed. Clinical, surgical, pathological and morbidity data related to the management thereof were recorded and analysed.

**Results:** In total, 73 patients were enrolled. The median age was 47 years and 78.1% of the participants were HIV positive. Pathological T1a (39.7%) and T3 (34.2%) were more common after penectomy. The most common stage of presentation was with cN2 disease with pathological findings of pN2 of 43.4% positivity on inguinal lymph node dissection. The wound complication rate seemed to be comparable to international reports with a wound sepsis rate of 21.9%. Time from initial patient referral to our institution to the day of definitive surgery was a median duration of 17.6 weeks (range 11–29.3 weeks).

**Conclusion:** Penile cancer tends to present with advanced disease at younger ages in our region. This study highlights the need for local protocol and guideline development to allow detection and management earlier in the disease process, ultimately minimising morbidity, mortality and psychosocial effects on patients.

**Keywords:** penectomy, penis, squamous, inguinal, SCC, cancer, Durban, nodes

## Introduction

Penile cancer is an uncommon malignancy in industrialised nations, affecting between one and nine per million men.<sup>1</sup> However, there is a three- to four-fold higher prevalence in low- or middle-income countries such as Uganda, Brazil, Jamaica, Mexico and Haiti, where penile cancer represents 10–12% of all urogenital malignancies.<sup>2</sup> Its prevalence in South Africa is reported to be 1.99 per 100 000.<sup>3</sup>

Squamous cell carcinoma (SCC) of the penis is the most common type of penile malignancy.<sup>2</sup> Metastasis, which typically occurs with this type of carcinoma, is usually lethal, likely due to delayed and advanced presentation in our setting. Living in rural areas, heavy alcohol drinking and non-specific initial symptoms are significant risk factors resulting in delays in the presentation of penile cancer.<sup>4</sup> Delays of more than three months will lead to a significantly higher risk of having a large lesion size and advanced tumour, node, metastases (TNM) classification.<sup>4</sup>

Penile cancer is a disease with high morbidity and mortality, and is both physically and psychologically debilitating to both patients suffering from the condition as well as their families. It is a relatively rare malignancy occurring predominantly in elderly men,<sup>5</sup> with limited published literature from developed countries. The disease appears to be more common in sub-Saharan Africa, presenting

at younger ages in South Africa.<sup>2</sup> The management involves penectomy in most cases. Delays in presentation, diagnosis and subsequent management compound the impact on the lives of those suffering from this disease.

Much of the information available and management guideline recommendations used at our institution are based on international literature. However, institutional, infrastructure and social challenges make international guideline implementation challenging. Limited direct and regular access to healthcare has a negative impact on the management of these patients.

From local experience, following delayed initial presentation to local clinics, patients are often treated for presumed infection which further delays referral for biopsy and definitive diagnosis. Many patients do not present early enough to allow for penile-preserving surgery.

Once the patient is finally seen at the appropriate referral institution, a date for a penile biopsy is usually given. Following a penile biopsy, the reporting of the histology often takes weeks to complete. Once the histological diagnosis of cancer is made, there may be further delays in being allocated theatre time, despite prioritising malignancy patients for surgery. Added delays encountered in the management pathway include radiological staging and adjuvant

therapy options after surgery. Adjuvant therapy is typically offered via referral to a multidisciplinary team at another centre.

## Materials and methods

### Objectives

This retrospective chart review study aims to describe the management and outcomes of patients with penile cancer who underwent penectomy and inguinal lymphadenectomy over a five-year period at Saint Aidan's Hospital, Durban, in an attempt to identify potential avenues of improving outcomes in our patients and formulate local treatment protocols more suited to our institution.

### Patients

This was a retrospective chart review of histologically-confirmed SCC of the penis after penectomy. St Aidan's Hospital is a regional hospital in Durban, to which most of the urological cases in the eThekweni region are referred. It is the largest dedicated urology centre in the province of KwaZulu-Natal (KZN).<sup>6</sup> Relevant files were obtained from a dedicated, on-site record room where all patient records are stored. Files of patients having undergone penectomy for penile cancer during the interval of January 2016 to December 2020 were reviewed.

### Statistical analysis

The recorded variables included patient age and race, HIV status, biopsy date, stage of cancer, and whether or not lymph node dissection was performed. The malignancy was staged according to the American Joint Committee on Cancer TNM classification.<sup>7</sup> For the demographic profiling of the sample, a five-number summary was used for the descriptive analyses. Regression analysis was used to determine the risk factors of the study sample relative to their pathological outcome. A sensitivity analysis was done to determine the association between the initial clinical stage and the final pathological stage following surgery. A chi-squared test was used to analyse the time delay from presentation to surgical intervention.

## Results

In total, 89 files were reviewed for the determined study period of patients having penectomy for a penile tumour. Of these, 82% ( $n = 73$ ) were included in this study as these were confirmed histologically as SCC of the penis and met the criteria of being post-penectomy with complete files and having accessible information. Among the excluded cases, 7.83% ( $n = 7$ ) were benign conditions, and the other 10.1% ( $n = 9$ ) had incomplete records or documentation.

### Demographics

The age of patients at diagnosis ranged from 29 to 72 years, with a median age of 47 years. However, 68.4% ( $n = 50$ ) of the patients were younger than 50 years old (Figure 1). The majority of the patients were African (94.5%,  $n = 69$ ). Patients were referred from various regions within the province. Of the 73 cases included, 78.1% ( $n = 57$ ) were documented as HIV positive, and all of these patients were on antiretroviral therapy at the time of penectomy. The median CD4 count was 340, ranging from 35 to 700. The average age of

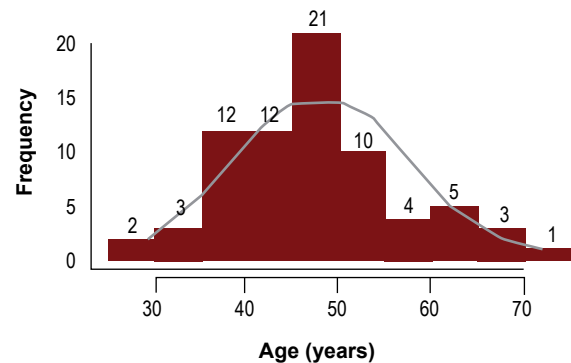


Figure 1: Age distribution of patients

HIV-positive patients was 46.7 years, compared to 51.3 years in HIV-negative patients. Only 12.9% ( $n = 11$ ) were documented as smokers, without details of pack-year. One patient had a risk factor of ultraviolet radiation for psoriasis treatment. This is detailed further in Table I.

Table I: Annual distribution of patients, comorbidities and social demographics

|                         | <i>n</i>  | %     |
|-------------------------|-----------|-------|
| <b>Annual frequency</b> |           |       |
| 2016                    | 10        | 13.7% |
| 2017                    | 11        | 15.1% |
| 2018                    | 10        | 13.7% |
| 2019                    | 23        | 31.5% |
| 2020                    | 19        | 26%   |
| <b>Smoking</b>          |           |       |
| Yes                     | 11        | 15.1% |
| <b>HIV status</b>       |           |       |
| Positive                | 57        | 78.1% |
| Negative                | 16        | 21.9% |
| <b>Comorbidities</b>    |           |       |
| Hypertension            | 10        | 13.7% |
| Diabetes                | 3         | 4%    |
| Grave's disease         | 1         | 1.4%  |
| Psoriasis               | 1         | 1.4%  |
| <b>Ethnicity</b>        |           |       |
| African                 | 69        | 94.5% |
| Other                   | 4         | 5.5%  |
| <b>Total</b>            | <b>73</b> |       |

### Clinical findings

On presentation to St. Aidan's Hospital, 60% ( $n = 44$ ) were clinically assessed as cT2 tumours. Of note is that no patient was assessed as cT1 on examination. Twenty-two (30.1%) were clinically assessed as cT3 and 9.6% ( $n = 7$ ) as cT4. Examination of patients included palpation of the inguinal region to assess for nodal status, of which 91.7% ( $n = 67$ ) had documented palpable inguinal lymphadenopathy. Of these patients, 12.3% ( $n = 9$ ) were assessed as cN1, 71.2% ( $n = 52$ ) as cN2 and 8.2% ( $n = 6$ ) as cN3. Two patients (8%) had no recording of their nodal findings. CT staging reported distant metastases were noted in 16.4% ( $n = 12$ ).

## Hospital stays

Length of stay during penectomy admission ranged from 7 to 41 days with a median 18 days stay in the ward. Time from initial patient referral to our institution to the day of definitive surgery was a median duration of 17.6 weeks, ranging from 11 weeks to 29.3 weeks. Time from penile biopsy (either at the referral hospital or St. Aidan's Hospital) to penectomy ranged from 8 to 28 weeks with a median of 13 weeks. The length of stay of patients with lymph node dissection was 18 days and 16 days for no inguinal lymph node dissection (ILND) ( $p$ -value = 0.047).

## Complications

Postoperative complications were noted in 34% ( $n = 25$ ) of the surgeries performed, including wound sepsis in 21.9% ( $n = 16$ ) and inguinal lymphadenectomy wound dehiscence in 8.2% ( $n = 6$ ) of the patients. Also recorded were urethral stenosis in three patients and lymphoedema in one patient, thigh abscess in one patient and a patient with sloughing of his perineal urethrostomy.

Patients who underwent penectomy with bilateral inguinal lymph node dissection had more complications than those without lymph node dissection. Of the 53 patients who underwent lymph node dissection, 25% ( $n = 13$ ) developed wound sepsis during the postoperative period.

## Pathological findings

Partial penectomy was performed in 41.1% ( $n = 30$ ) of the patients and 58.9% ( $n = 43$ ) underwent total penectomy. The pathological findings varied from the clinical findings as pT1a accounted for 39.7% ( $n = 29$ ) of the penectomy histopathological reports and pT3 for 34.2% ( $n = 25$ ). Pathological T1b accounted for 4.1% ( $n = 3$ ), pathological T2 for 9.6% ( $n = 7$ ) and pT4 for 12.3% ( $n = 9$ ) of the pathological reports.

Fifty-three patients underwent ILND. Positive nodal involvement was found in 43.4% ( $n = 23$ ) of the dissections performed, whereas 56.6% ( $n = 30$ ) of the lymph node dissections were negative for malignancy. See Table II for correlation of clinical to pathological nodal stages.

Of the four documented cN0 patients, only one had lymph node dissection performed and was pathologically negative for metastases. This patient had a pT1G2 finding on histology. Of the nine patients with cN1 palpable disease, 71.4% ( $n = 5$ ) of the ILND were negative for malignancy. Of the 52 patients in the cN2 group, 55.8% ( $n = 24$ ) of the ILND were negative for nodal involvement. As cN2 is the most common presentation, clinical assessment has a

Table III: Pathological staging

|                                                                       | N  | %     |
|-----------------------------------------------------------------------|----|-------|
| <b>pT stage</b>                                                       |    |       |
| T1a                                                                   | 29 | 39.7% |
| T1b                                                                   | 3  | 4.1%  |
| T2                                                                    | 7  | 9.6%  |
| T3                                                                    | 25 | 34.2% |
| T4                                                                    | 9  | 12.3% |
| Total                                                                 | 73 |       |
| <b>pN stage</b>                                                       |    |       |
| N0                                                                    | 30 | 41.1% |
| N1                                                                    | 5  | 6.8%  |
| N2                                                                    | 13 | 17.8% |
| N3                                                                    | 5  | 6.8%  |
| Nx                                                                    | 20 | 27.4% |
| <b>M stage</b>                                                        |    |       |
| M0                                                                    | 52 | 71.2% |
| M1                                                                    | 12 | 16.4% |
| Mx                                                                    | 9  | 12.3% |
| <b>Organ confined status</b>                                          |    |       |
| Organ confined (pT <sub>1-2</sub> N <sub>0</sub> M <sub>0</sub> )     | 21 | 29%   |
| Locally advanced (pT <sub>3-4</sub> N <sub>1-3</sub> M <sub>0</sub> ) | 22 | 30%   |
| Metastatic (M1)                                                       | 12 | 16%   |
| Unspecified (Any x)                                                   | 18 | 25%   |

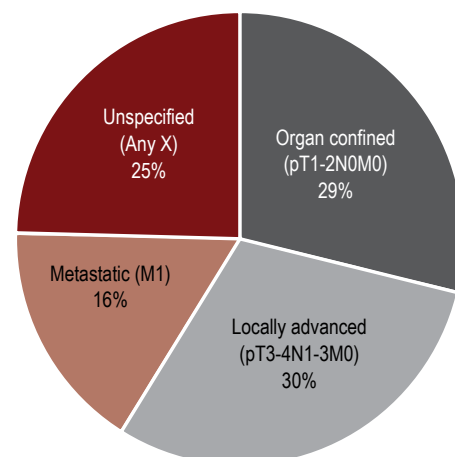


Figure 2: Pathological staging of penile cancer patients

positive predictive value of 44% for pathological involvement. Of the six patients with cN3 status, two had ILND performed and results were positive for nodal spread. Table III depicts the pathological staging.

Table II: Correlation of clinical findings to pathological findings

|       | pN0        | pN positive | pNX        | Total |                  |
|-------|------------|-------------|------------|-------|------------------|
| cN0   | 1 (25%)    | 0 (0%)      | 3 (75%)    | 4     | $p$ -value 0.007 |
| cN1   | 5 (55.6%)  | 2 (22.2%)   | 2 (22.2%)  | 9     |                  |
| cN2   | 24 (46.2%) | 19 (36.5%)  | 9 (17.3%)  | 52    |                  |
| cN3   | 0 (0%)     | 2 (33.3%)   | 4 (66.7%)  | 6     |                  |
| cNX   | 0 (0%)     | 0 (0%)      | 2 (100%)   | 2     |                  |
| Total | 30 (41.1%) | 23 (31.5%)  | 20 (27.4%) | 73    |                  |

For the other 20 patients without LND, there was no clear documentation or reason why it was not performed. Figure 2 illustrates a classification of the penile cancer pathological stages of the patients.

## Discussion

Penile cancer is reported as relatively rare in developed countries, occurring predominantly in elderly men. The mean age at diagnosis of patients with penile cancer is 60 years, with age-related incidence rising to its highest level at 70 years.<sup>5</sup> The current study demonstrates a relatively younger demographic of penile cancer patients, with most being in their 5th decade. This figure is in keeping with that reported by Chalya et al.<sup>8</sup> in a large study in Tanzania in which they also described a young population with median age of 47 years. Disease incidence varies among different populations, with developing countries seeing a higher rate of the disease as described in the systematic review and meta-analysis by Montes Cordona and García-Perdomo.<sup>9</sup> Our institution does not have a cancer tracking registry and therefore does not enable the tracking of the incidence of penile cancer.

Of note is the significant annual increase of penile cancer patients being managed at the institution from 2019 which could be attributed to an adjustment of referral patterns. The institution had more specialists from that time and there was a diversion of urology services from northern KZN province following their lack of specialist care at the centre, all of which resulted in an increased overall number of urology patients at St Aidan's Hospital during this time period.

A large proportion of the patients that present to the local facility are African men, which is consistent with the ethnic distribution in the study sample. African men tend to present late to healthcare facilities, possibly due to various cultural perceptions and views on manhood, particularly when related to conditions of the urogenital system.<sup>10</sup> Further factors are the lack of both education and men's awareness of their own health, thus facilitating their underutilisation of healthcare facilities and services.<sup>11</sup> This delay in health-seeking behaviour of men may contribute to the late presentation with a more destructive lesion. The younger ages of penile cancer presentation in this population contribute to the delayed health-seeking behaviour. In a study done by Nyalela et al.<sup>12</sup> in Durban, South Africa, younger men were found to only seek medical help when signs and symptoms of sexually transmitted infections were perceived to be severe.

Phimosis is another identifiable risk factor for penile cancer. It invariably leads to retention of the normally desquamated epidermal cells and urinary products (smegma), which results in chronic irritation and inflammation of the prepuce and glans. The destructive lesion at presentation in all our patients makes the presence of phimosis challenging to ascertain on examination. However, it has been shown that penile cancer is far more common in uncircumcised men than those who were circumcised much earlier in life.<sup>15</sup> Cultural factors affect the state of circumcision in South Africa. The majority of the people in the region where the study took place do not practice neonatal or ritual childhood

circumcision. According to a social science study done by Phili and Karim,<sup>13</sup> some communities believe that circumcision should be delayed until adolescence so that traditional rites can be observed after any circumcision procedure.

In a nationwide cross-sectional survey in 2017, HIV prevalence in men over the age of 35 years in South Africa was 12.7%.<sup>14</sup> In this penile cancer study population, HIV prevalence was 78.1% which is significantly higher than the population average. This suggests an increased risk of human papillomavirus (HPV) acquisition and perhaps a direct association of HIV with penile cancer. Additionally, HIV-positive patients with penile cancer tended to be younger (mean age of 46.8 years) compared to their HIV-negative counterparts (mean age of 51.3 years). In a similar South African study by Wentzel et al.,<sup>2</sup> the mean age of the HIV-positive group was significantly lower compared to the HIV-negative group (43.7 vs 57.2 years).

An increase in the number of sexual partners predisposes a patient to sexually transmitted diseases and genital warts. HPV types 16 and 18 are involved in the pathogenesis of penile carcinoma.<sup>2,5</sup> Unfortunately, documentation of the HPV status of patients in the histopathology reports was not routinely included. The administration of an HPV vaccine is currently not routine in state practice.

Several studies have found cigarette smoking (tobacco use) to be strongly associated with penile carcinoma.<sup>5</sup> As this is a retrospective study, information could only be gathered from what was documented in the patient records; there were inconsistencies in the documentation regarding the patients' smoking status. Hence, this aspect was excluded from the study.

As St. Aidan's Hospital is a high-volume urology centre, potential patients with malignancies are prioritised for appointments, and, once the diagnosis of cancer is made, theatre is expedited. Patients occasionally have to wait several weeks before a scheduled appointment date due to long lists. On arrival, most of the patients still require biopsies to confirm the diagnosis before getting an elective date for surgical intervention. Therefore, a delay in the initial presentation, followed by multiple attempts to treat the lesion at a local clinic before eventually being referred, protract the management of penile cancer in these patients. Delays in initial presentation and referral to urology are difficult to address and require wider health promotional campaigns. Furthermore, health system access and infrastructure challenges should be addressed.

Penile cancer typically presents as a lesion that fails to heal, a subtle induration in the skin, a small excrescence, a papule, a pustule, a warty growth, a large exophytic growth, or a reddened area on the glans. Physical examination of the primary tumour is mandatory to evaluate the morphologic and physical characteristics of the lesion.<sup>15</sup> Many would have phimosis obscuring the lesions or not allowing them to grow, and in advanced cases it would have ulcerated and become fungating. The malodorous state causes most patients to finally present to the urologist. Pain is uncommon. In advanced disease, patients can become cachectic, with fatigue and generalised weakness.

Clinical staging of the primary tumour can be incorrect in as much as 26% of patients. Understaging results from histologic infiltration not being clinically evident and overstaging from oedema and infection, giving a misconception of infiltration.<sup>15</sup> Patients usually have destructive penile lesions and are clinically challenging to assess for tumour stage. However, some of the external lesions seen do not always correlate with the degree of invasiveness, as is evident by the clinical assessment of cT2 in 60.3% of the patients with the histopathological findings ending up being pT1a (39.7%).

In the literature, approximately 20% of patients have palpable inguinal lymph nodes at the time of diagnosis.<sup>16</sup> In our study population, 91.7% of the patients presented with clinically palpable inguinal lymph nodes.

The management of patients with unremarkable inguinal lymph nodes on physical examination is particularly challenging because in up to 20–25% of cases, inguinal lymphatic micro metastases are present.<sup>16</sup> If left untreated, a regional lymph node recurrence will occur within a period of 1–2 years.<sup>16</sup> Most of our patients ( $n = 67$ ) presented with palpable bilateral inguinal nodes, with 53 undergoing lymph node dissection. However, only 43.4% ( $n = 23$ ) nodes had pathological involvement following lymph node dissection. With a large percentage (56.6%) of clinically palpable nodes, in fact, being pathologically negative in this study. With the high morbidity associated with ILND, consideration to revisit the criteria and timing of lymph node dissection in this group of patients is recommended. The presence and extent of inguinal lymph node metastases are the most important prognostic factor in determining long-term survival for men with penile cancer. Management of palpable inguinal nodes affects prognosis.<sup>17</sup> Unfortunately, reasons were not documented for the 20 patients who did not have LND done; in some cases, it was due to intraoperative findings of clinically insignificant shotty lymph nodes that would be considered for lymphadenectomy after pathological tumour grade findings, while in other cases, the nodes were too advanced for resection. This area will be addressed by the chart review to improve the management outcomes of the patients, and can also be followed up in a prospective study. The extensive surgery involving ILND and management of postoperative complications contribute to the patient's length of stay. Since the study period, the department has formally implemented guidelines for performing invasive lymph node staging in patients with high-risk tumours and non-palpable lymph node disease.

Radical inguinal lymphadenectomy remains the standard of care for palpable, resectable node disease, and it involves the removal of all lymphatic tissues in a quadrilateral area (anterior superior iliac spine, superior margin of the inguinal canal, a point 20 cm inferior to the anterior superior iliac spine, and a point 15 cm inferior to the pubic tubercle) circumscribing the femoral triangle.<sup>18</sup> Although inguinal lymphadenectomy is a life-saving procedure, a significant percentage of patients do not undergo this procedure. Even in specialised centres, 25% of patients are not treated according to guideline recommendations.<sup>19</sup> The associated high morbidity contributes to why ILND is not done in some cases where it is doubtful to be malignant, and we do not have facilities to do dynamic sentinel LND.

Wound dehiscence and sepsis are common postoperative complications, especially following inguinal lymph node dissection. This also leads to a prolonged hospital stay.<sup>4</sup>

To date, there is no national or provincial database of penile cancer. The spectrum of penile cancer according to severity and lymph node status has not previously been described in KwaZulu-Natal, despite the apparently high prevalence of advanced disease. This study serves to provide insight into the local disease patterns, potentially affecting the standard of care tailored to the unique disease profile of our patients, and highlights the need for urological cancer registries in South Africa.

There is extremely limited data in the literature concerning the psychological and social impact of penile cancer on patients. In the local setting, the majority proceed to have a total penectomy done, and one can imagine the effect on an individual and his family. In situations where organ preserving surgery could be performed, a better quality of life and sexual function is ensured, and this should be offered to all patients wherever feasible.<sup>20</sup>

As a treatment for advanced penile cancer, total amputation significantly debilitates the patient's quality of life and sexual function. A recent study by Sosnowski et al.<sup>21</sup> looked at patients' quality of life after total penectomy in a small sample of 11 patients using the European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ C-30), Socio Economic Status (SES), The Conformity to Masculine Norms Inventory (CMNI), and a modified International Index of Erectile Dysfunction (IIEF)-15 questionnaires. Although the study sample was small, they concluded that total amputation of the penis significantly affects one's sex life and overall quality of life.<sup>21</sup> However, this does not have negative implications in terms of partnership relations, self-assessment or masculinity evaluation.<sup>21</sup> Local patients have access to a dedicated counsellor preoperatively to prepare them psychologically for the treatment plan. It was unfortunately not documented how the patients respond to their new state after penectomy, and an area that would be beneficial for the patients in the long run is if they start getting counselling postoperatively. This is a potential area for a future social science study.

Being a retrospective chart review, this study was restricted by the amount of information that could be extracted from the patient records. The study review was done for a long time period, which means patients were seen by different practitioners and the surgical procedures were not done by one dedicated surgeon. There was also an inability to ascertain some important risk factors in the patients as not all the histopathological reports mentioned the presence or absence of HPV, and documentation on history was not standardised.

## Conclusion

Penile cancer is a disease with high morbidity and mortality. The condition is often debilitating both for the patient and for their family due to the disease itself, the management and the psychological implications. Delays in patient presentation, followed by a delay in diagnosis and subsequent management, create a significant

negative impact on the lives of those involved. This reflects an unacceptably poor standard of public healthcare in South Africa.

There are areas in which clinicians can effect improvement in service delivered to patients despite the poor resources and referral system. Optimum care using guideline approaches will improve the overall outcome of surgery and patient survival. It would be beneficial to have local protocols developed in managing these patients as we deal with a much younger population. A local registry with complete statistics would also be ideal for pursuing a better management plan. A timeous clinical assessment and diagnosis at first presentation to the local healthcare centre and an improved referral pathway to the definitive urology hospital are paramount. Having a protocol and guideline for penile lesion biopsies at referring institutions could potentially shorten the otherwise protracted management course for these patients.

### Acknowledgements

The authors would like to thank Kiran Singh for the conception of the research topic, Partson Tinarwo for his assistance in the statistical analysis and Haroun Patel for his input and contribution to the manuscript.

### Conflict of interest

There is no conflict of interest.

### Funding source

No funding was required for this study.

### Ethical approval

This study was approved by the Biomedical Research Ethics Committee of the University of KwaZulu-Natal (BREC/00001781/2020). Consent to participate was not applicable as this was a retrospective chart review. This decision to waiver was approved by the Biomedical Research Ethics Committee of the University of KwaZulu-Natal (BREC/00001781/2020).

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