

## A quality assurance review of penile cancer diagnostic delays and stage at presentation during the COVID-19 pandemic

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### ABSTRACT

**INTRODUCTION:** Penile carcinomas represent a rare malignancy associated with significant psychosocial impacts that deter afflicted individuals from seeking medical attention, thus, worsening prognosis. Following the dramatic shift in healthcare delivery to virtual platforms, it is suspected that prevalent psychosocial impacts have been further compounded by the COVID-19 pandemic, resulting in several late-stage presentations and engendering poorer outcomes.

**METHODS:** A retrospective chart review of surgically managed cases of penile cancer was conducted from January 2020 to June 2022 to identify patients that may have been unduly impacted by the COVID-19 pandemic. Included cases were analyzed in quantifying diagnostic and treatment delays, along with patient outcomes. Relevant epidemiological and pathological markers were also examined.

**RESULTS:** Ten patients met the inclusion criteria. Average time delay from first complaint of a penile lesion to surgical management was 75 days, with 60% of patients experiencing a time delay of two months or more. The average delay from first complaint to diagnosis was 62 days in 2020 and 18 days in 2021. Advanced-stage disease was present in six (60%) individuals at presentation, while four (40%) patients perished during the study period.

**CONCLUSIONS:** In cases of concern for penile malignancy, virtual care cannot replace the necessity of physical exams in preventing diagnostic and treatment delays. The present study further highlights the necessity of initial physical examination of penile abnormalities in preventing fatal outcomes for those afflicted. Such consideration warrants urgent examination of referred males with genital abnormalities to prevent further exacerbation of delays.

### INTRODUCTION

Penile cancer represents a rare subset of neoplasms with a permanent, progressive course and poor prognosis in the absence of treatment.<sup>1,2</sup> Incidence rates of penile malignancies are highest in less developed parts of the world, while rarely seen in North America or other industrialized nations.<sup>3,4</sup> Despite the overall infrequent occurrence, these malignancies cause significant psychosocial impacts and the subsequent therapeutic disfigurement can deter those afflicted from seeking medical attention.<sup>5-7</sup>

Due to the tendency for early lymphatic spread, timely diagnosis and staging of disease are imperative, as regional nodal involvement is the most powerful predictor of prognosis. As such, diagnostic delays engender late-stage presentation, which results in catastrophic consequences, including permanent post-treatment functional impairments and increased mortality.<sup>2,8-10</sup> Presentations of early-stage disease, specifically those that are carcinoma in situ, are highly treatable with organ preservation strategies, which include both medical and surgical approaches. Conversely, the depth of invasion in later presentations of disease often make organ-sparing procedures an impossibility, necessitating surgical resection via partial or radical penectomy.<sup>11-14</sup> Individuals who received treatment via conservative management have consistently reported greater preservation of sexual function, as well

## KEY MESSAGES

- Penile cancer is a devastating malignancy associated with significant psychosocial impacts that often delay diagnosis and treatment.
- The COVID-19 pandemic, and subsequent shift to virtual care, has undoubtedly exacerbated extant diagnostic and treatment delays for penile malignancies.
- The necessity of physical examination cannot be overstated in individuals presenting with penile abnormalities in reducing patient morbidity and mortality.
- Referred males with genital abnormalities should be seen urgently to prevent prolonged delays in diagnosis and treatment.

as better overall quality of life (QoL) when compared to surgical cases.<sup>11</sup> The exclusive applicability of these organ-sparing therapies in early-stage presentations of disease stresses the importance of mandatory initial evaluation of the patient by way of physical examination, especially during and following the rise of telemedicine during the COVID-19 era.<sup>15</sup>

Systematic interest in the delivery of medical care via virtual platforms existed long before the COVID-19 crisis; however, utilization of these methods has increased exponentially over the past two years.<sup>16-18</sup> In the early stages of the pandemic, the shift to entirely virtual care was viewed as a necessity to reduce individual contact and potential viral transmissions, while allowing provision of continued care to patients during uncertain times.<sup>18-20</sup> Importantly, virtual care may be inappropriately distant for some patient presentations, particularly when lack of a feasible physical exam may hinder adequate cancer diagnoses and management.<sup>21</sup> Wang and Zhang have contested that the major risk factor for cancer patients during the COVID-19 pandemic has been the inability to access the appropriate medical support required for their diagnosis.<sup>22</sup> The medical management of oncological malignancies should ideally not be subject to prolonged delays in diagnosis, as such delays will ultimately worsen outcomes.

It is well understood that patient attitudes regarding penile malignancies have resulted in delays in diagnosis, a situation that has undoubtedly worsened following

the onset of the COVID-19 pandemic.<sup>23,24</sup> It is suspected that prevalent psychosocial impacts of penile lesions have been further compounded by pandemic-induced delays, leading to several late-stage presentations, engendering poorer outcomes. The present study sought to assess how virtual care delivered during the COVID-19 pandemic has impacted the diagnoses and treatment of penile cancer in our province. It was hypothesized that the COVID-19 pandemic resulted in poorer outcomes for patients diagnosed with penile cancer during the study timeframe, secondary to delayed diagnosis and prolonged wait times for surgical intervention.

## METHODS

Ethics approval for this project was granted by the provincial health research ethics board at Memorial University (St. Johns, Newfoundland and Labrador, Canada). The present study conducted a retrospective chart analysis of all surgically managed cases of penile cancer during the timeframe of the pandemic from January 2020 to June 2022. We aimed to identify those subjected to pandemic-induced delays in diagnosis and treatment while describing relevant outcomes.

All provincial diagnoses of penile cancer are managed in the Department of Urology at the Health Sciences Centre, St. John's, Newfoundland. Patients diagnosed with and treated for penile cancer during the study timeframe were identified via the nurse educator using operating room codes for partial and radical penectomy. While all provincial diagnoses of malignancy are recorded in a centralized database, reporting is typically delayed approximately three years. Given the low global incidence of penile cancer and the high rate of surgically managed cases, it was felt that our employed methodology gave an accurate representation of penile cancer cases diagnosed at our centre.

Extracted data from each eligible chart included time delay from first complaint to diagnosis, diagnostic tests, and treatment delays, defined as  $\geq 2$  months from time of first documented complaint to surgical intervention. Further, relevant epidemiological and pathological markers were examined for each patient.

All statistical analyses were conducted using SPSS version 27.0 (IBM Corporation, Armonk, NY, U.S.). Descriptive analysis of the study cohort was summarized as percentages and absolute counts for categorical variables, while means and standard deviations were used to report continuous variables. A Kaplan-Meier survival curve was generated to show cumulative survival over time, with patients categorized by vital status as

those alive at study endpoint and those who were deceased.

### RESULTS

During the COVID-19 pandemic (January 2020 – June 2022), 11 patients received surgical management for penile cancer at our institution. One of these patients underwent revision radical penectomy following recurrence of disease initially diagnosed outside the study timeframe and was subsequently excluded from the data analysis. Of the 10 analyzed patients, all presented with penile lesions clinically suspicious for malignancy and received a diagnostic biopsy, as well as imaging via computed topography (CT) assessing for disseminated disease. Two of these patients did not have access to a general practitioner. The average patient age was 62.9 years (range 51–79). Phimosis was present in four (40%) cases and only one patient had a previous circumcision, while a further four (40%) had Balanitis Xerotica Obliterans (BXO) at diagnosis. The mean body mass index (BMI) of the cohort was 33.6, with eight (80%) individuals being considered obese. There were three (30%) individuals that indicated they were previous smokers, while four (40%) indicated they actively smoked. Of these 10 patients, four were P16 positive on immunohistochemical staining, indicating HPV-associated disease. The observed incidence of surgically managed penile cancer diagnoses in 2020, during the height of the

pandemic, was 1.53/100 000, calculated from the total Newfoundland and Labrador population.

Secondary to virtual care appointments, three patients were unable to receive an initial physical exam, which delayed primary care referral and subsequent diagnosis. One additional patient had a physical exam delayed six months while receiving virtual care. The average delay from first complaint to diagnosis in 2020 was approximately 62 days compared to 18 days in 2021. Full details regarding the delays experienced by each patient and their outcomes are described in Table 1.

Partial penectomy was undertaken in nine (90%) cases, while one patient had an initial radical penectomy. Two of the patients having undergone initial partial procedures had recurrent disease requiring revision radical penectomy at two and three months, respectively. All but one of the patients underwent subsequent inguinal lymphadenectomy and two of these had additional negative pelvic nodal dissection. Full details regarding the clinical and pathological characteristics for each diagnosis are provided in Table 2.

Following surgical intervention, four (40%) went to observation, while six (60%) patients received additional treatment modalities that included radiotherapy and chemotherapy. One patient originally failed conservative treatment with imiquimod and underwent a margin-positive partial penectomy, requiring revision radical penectomy two months later before also being treated with radiotherapy and chemotherapy. An additional patient underwent a partial penectomy and was found to have scrotal cutaneous metastases four months later requiring inguinal lymphadenectomy, orchidectomy for cord involvement, plastic surgery rotational flap for skin coverage, and ultimately radiotherapy. Three of the 10 patients presented with recurrent disease within the first 12 months, two of which were at the local level, while the third had recurrent unilateral inguinal adenopathy. Four patients succumbed to their disease, three of which died within the first 12 months following diagnosis (Figure 1).

### DISCUSSION

This study aimed to identify areas of improvement for care under the pandemic conditions, including the provision of virtual care (without physical examination), along with the timeliness and urgency of reported urogenital concerns. Our results indicate that the impacts of the COVID-19 pandemic on diagnostic and therapeutic outcomes for patients with penile cancer cannot be ignored.

The average time delay observed from first complaint of a penile lesion to surgical management was 75

**Table 1. Time delays and outcomes for individuals surgically treated for penile cancer in Newfoundland and Labrador during the COVID-19 pandemic**

Case	Year of diagnosis	Time to diagnosis* (days)	Time to surgery from diagnosis (days)	Total time delay (days)	Patient vital status
1	2020	31	16	47	Alive
2	2020	43	18	61	Deceased
3	2020	17	23	40	Deceased
4	2020	0	60	60	Deceased
5	2020	41	27	68	Deceased
6	2020	75	26	101	Alive
7	2020	76	6	82	Alive
8	2020	210	13	223	Alive
9	2021	18	14	32	Alive
10	2021	19	23	32	Alive
Average	–	53	23	75	-

\*Time to diagnosis is relative to first recorded complaint in our institution's hospital-based charting system.

**Table 2. Clinical and histopathological characteristics of individuals surgically managed for penile cancer in Newfoundland and Labrador during the COVID-19 pandemic**

Case	Age	Cancer classification	Anatomical location	Grade	Inguinal lymph node involvement	LVI	pTNM staging**
1	71	Sarcomatoid SCC	Glans	G3	Negative	Pos	pT2N0MX
2	52	Invasive SCC	Glans	G3	Bilateral	Neg	pT1bN3MX
3	77	Clear Cell SCC	Glans	G3	Bilateral	Pos	pT3N3MX
4	72	Invasive SCC	Corpus	G2	Not excised*	Pos	pT2NXMX
5	79	Invasive Melanoma	Glans	G3/4	Left	Neg	pT3bN1MX
6	45	Invasive SCC	Glans	G1	Left	Neg	pT2N2MX
7	51	Invasive SCC	Glans	G1/G2	Negative	Neg	pT2N0MX
8	54	Invasive SCC	Corpus	G3	Bilateral	Pos	pT3N3MX
9	56	Invasive SCC	Glans	G2	Bilateral	Pos	pT3N3MX
10	72	Invasive SCC	Glans	G1	Negative	Neg	pT2N0MX

\*Nodal excision could not be undertaken in patient 4 due to previous bilateral inguinal vascular surgery. \*\*pTNM staging conducted according to American Joint Committee on Cancer (AJCC) 8th edition guidelines with radiological correlation for metastases. Neg: negative; Pos: positive; SCC: squamous cell carcinoma.

days, with 60% of patients experiencing a time delay of two months or more. Two of the 10 cases examined did not have access to a general practitioner, secondary to the ongoing provincial physician shortage and consistent with statistics citing 20% of the province is currently without a family doctor.<sup>25</sup> The additional high rate of inguinal adenopathy at diagnoses in our patients (60%) indicated late stage at presentation, which limited available treatment options for these individuals. Historically, penile cancer has been an uncommon pathology, accounting for a small percentage of oncological malignancies, and has likely been low-priority in access to resources during the COVID-19 pandemic. As such, the exacerbated delays in diagnosis and treatment seen in the present study likely impacted the extent of the primary lesion and development of nodal metastases, further contributing to the observed plethora of poor outcomes.<sup>2,8-10,23,24</sup>

The overall survival (OS) associated with penile cancer is contingent on multiple factors, including disease stage at diagnosis, with numerous studies indicating an average five-year OS ranging from 60–65%.<sup>26-28</sup> Poor OS was documented in the present study with 40% of patients deceased at the conclusion of the study period at 28 months. Diagnosis of penile cancer has traditionally proven difficult due to the accompanying psychosocial implications, which often delay seeking treatment by six months in 65% of patients and up to one year or longer in 50% of those afflicted.<sup>2,6,7,29,30</sup> It is possible that the rise of telemedicine during the

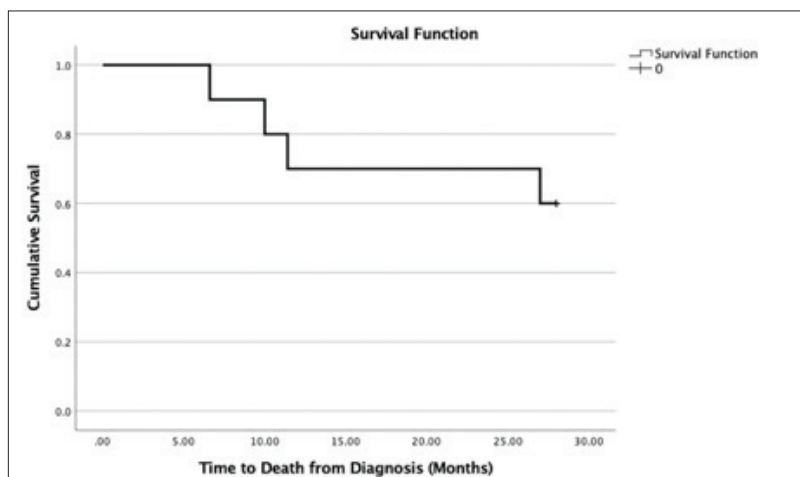
COVID-19 pandemic further delayed physical examination and prolonged the diagnostic sequelae, thus resulting in poor outcomes for several of our patients.

The average age of diagnosis in our study was 62.9, consistent with extant literature citing mean age at presentation of 60 years. Several localized risk factors have been documented for penile cancer, including BXO and the presence of the foreskin, which were observed in 40% and 90% of our cohort, respectively. Additionally, phimosis has been shown to be associated with as high as 90% of penile carcinomas and was noted in 90% of our cohort. Modifiable risk factors, such as smoking, tobacco usage, and obesity status have also been associated with the development of penile cancer.<sup>31,32</sup> Daling et reported a 4.5-fold increased incidence of invasive penile cancer in men with a history of smoking compared to those who did not.<sup>31</sup> Similarly, a significant positive correlation between incidence and obesity was

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“ NL has the highest national rate of cancer and low rates of circumcision, a protective factor for penile malignancies. This, plus the high incidence during our study, warrants a closer look at healthcare resource allocation & educational efforts. ”

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**Figure 1.** Kaplan-Meier curve depicting time to death in individuals diagnosed with penile cancer in Newfoundland and Labrador during the COVID-19 pandemic.

noted by Barnes et al, reporting a 53% increase in the risk of developing invasive penile cancer for each five-unit increase in BMI.<sup>32</sup> The combination of risk factors present, along with documented diagnostic delays, may provide some explanation for the observed development of disease and necessity of surgical intervention.

Several previous studies have examined patient-related outcomes following surgical management of penile malignancies, offering significant insight into the insults that may arise from delayed diagnoses in general. A review by Maddineni et al reported that following treatment for penile cancer, approximately half of patients developed psychiatric conditions, with 65% having a reduction in sexual function and a further 40% indicating negative effect on well-being.<sup>5</sup>

Surgical intervention is typically used with the intention of disease cure; however, management of this malignancy via partial or radical penectomy often results in disfigurement and sexual dysfunction, with subsequent psychological trauma.<sup>33,34</sup> Kieffer et al reported that men treated with partial penectomy had significantly greater sexual dysfunction compared to those treated with penile-sparing surgery.<sup>35</sup> These results are mirrored by Yu et al, who additionally indicated that more aggressive procedures, such as partial penectomy, are associated with higher rates of anxiety and depression among patients.<sup>36</sup> Evidently, several studies have reported that sexual dysfunction and its effects on the psyche can vary based on disease stage at presentation and subsequent treatment decisions, further stressing the importance of early presentation and treatment in preserving QoL and preventing mortality.<sup>11,34-36</sup>

A review by Cakir et al found limited available evidence for delaying the management of patients with

penile malignancies, with pertinent suggestions for the reconfiguration of penile cancer treatment pathways and development of measures aimed at preventing perioperative nosocomial transmission of COVID-19.<sup>24</sup> Of note in our findings is the significant difference between diagnostic delays seen in 2020 compared with 2021. This is likely a result of the introduction of vaccination against the COVID-19 virus introduced in late 2020, which resulted in decreased hospitalization rates, which in turn allowed shorter government-mandated healthcare access limitations.<sup>37</sup>

Furthermore, as the pandemic unfolded, clinicians in general began to recognize that physical examination during the pandemic remained a high priority for certain clinical scenarios despite the risks associated with breaching distancing requirements. There have been several studies that have suggested telemonitoring may be an appropriate method of follow-up for these patients; however, utility is contingent on multiple factors, including tumor grade and lymphatic involvement.<sup>15,24</sup> Presently, it is evident that in cases suspicious for penile malignancy, virtual care cannot be employed as an effective substitute for initial physical examination.

A final interesting finding of the present study was the high incidence of surgically managed penile malignancies reported in 2020, which excludes conservatively managed diagnoses. Current age-standardized incidence rates are reported at 0.84/100 000 globally; however, this number varies relative to geographical location.<sup>3,38-41</sup> Arguably, these findings may be related to the impact of the COVID-19 pandemic on diagnostic delays; however, the province of Newfoundland and Labrador has been shown to have the highest national incidence of cancer, along with low rates of circumcision, a known protective factor for penile malignancies.<sup>42,43</sup> Such considerations, paired with the high incidence rate noted during our study may warrant greater investigation of these malignancies in the province in order to allocate healthcare resources and educational efforts effectively.

Additionally, given the provinces high incidence of cancer, further examination of pandemic-induced delays on diagnosis and treatment of other urogenital malignancies may aid in allocating surgical resources moving forward.

### Limitations

There are limitations of the present study that must be acknowledged. The first of these is the retrospective nature of the project, which by design, is predisposed to the possibility for inconsistent reporting or mis-

sing variables. While no information was missing from the collected variables, it is possible there may have been inaccuracies in the data recorded when assessing timeframes of delay. Despite these possibilities, we are confident that the results reported are indicative of an increased timeframe of delay secondary to virtual care modalities necessitated by the pandemic.

Further, time delays were calculated using the hospital-based charting system, with first point of contact being the initial urology consultation. Prior to this point, it is impossible to assess number of healthcare interactions, if physical exams were conducted virtually by primary healthcare providers, or if referral to urology was based on presentation. To this effect, it is possible that our results may have underrepresented the total diagnostic delay experienced by patients prior to receiving a diagnosis of penile cancer.

Additionally, the present study did not assess the difference in diagnostic and treatment delays relative to years prior to COVID-19, which may have provided greater clarification as to how pandemic conditions impacted individuals diagnosed with and treated for penile cancer. Contrastingly, the comparison of surgically managed cases between the years of 2020 and 2021 and the associated delays provides an adequate interpretation of the impacts of the pandemic and associated utilization of virtual care modalities on penile cancer diagnoses and outcomes.

Finally, the sole examination of penile cancer cases managed surgically during the study timeframe may have failed to provide a complete representation of diagnostic delays seen during the pandemic. All provincial diagnoses of malignancy are recorded in the Newfoundland and Labrador Cancer Care Registry (NLCCR); however, the time delay in reporting by the registry is approximately three years. Given this delay, it would be impossible to accurately detect all cases of penile cancer reported at the time of writing. The present study employed the use of operating room codes in selecting a cohort for examination. Given that surgical intervention is a mainstay in the management of penile malignancies, paired with the low reported global incidence, we are confident this cohort accurately captures the vast majority of cases during this timeframe.

Additionally, the results provided from surgically managed cases demonstrates an evident effect of pandemic conditions on delays in diagnosis and management that would undoubtedly be mirrored when assessing any conservatively managed cases.

## CONCLUSIONS

Penile cancer is a rare malignancy with longstanding difficulties in diagnosis secondary to patient attitudes that have resulted in delays in diagnosis and treatment. To date, there has been limited research examining the impact of pandemic-induced delays in the diagnosis and treatment of penile malignancies. The results of the present study indicate that in cases of concern for penile malignancy, virtual care modalities cannot replace the necessity of physical exams in preventing diagnostic and treatment delays. In response, urologists at our center have altered practices for urgent examination of referred males with genital abnormalities to prevent further exacerbation of delays.

COMPETING INTERESTS: The authors do not report any competing personal or financial interests related to this work.

This paper has been peer-reviewed.

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