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Surgical Intervention in Patients with Penile Neoplasm at a University Hospital before and after the COVID-19 Pandemic

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Abstract: Objective: Penile cancer (PC) is a rare disease associated with a lack of hygiene, phimosis, low sociocultural level and the human papillomavirus. In urology, its treatment is part of oncological surgeries that cannot be postponed for a given period of time without affecting patient's survival. Considering this, the aim of this study is to investigate surgical interventions in patients with PC at a university hospital before and after a period characterized by a tendency to postpone elective surgeries, the COVID-19 pandemic. **Methods**: This retrospective study was performed with penile cancer patients at the urology clinic of a university hospital. Data were collected from the electronic records of patients sent for hospital treatment. Descriptive statistics were conducted to compare surgical or not surgical interventions before and after the pandemic. **Results**: A total of 32 patients were analyzed, 18 and 14 were diagnosed prior and after the COVID-19 pandemic, respectively. Comparisons of the frequency of surgeries realized before and after revealed to have a nonsignificant difference ($p = 0.4651$). When the patients were stratified by age group, significant difference was found regarding the number of surgeries performed previously the pandemic ($p = 0.0366$) – a finding that was not confirmed following its onset ($p = 0.3508$). **Conclusion**: At the university hospital analyzed, COVID-19 pandemic did not have a significant impact on the frequency of surgeries for PC. Either, after its beginning, age no longer exerted an influence on the treatment decision.

Keywords: Penile Neoplasm, Penile Cancer, COVID-19

Introduction

Penile cancer (PC) is a rare disease, the incidence of which is higher among men older than 50 years of age. In Europe and North America, the incidence is approximately one new case for each 100,000 residents (1). In Brazil, PC accounts for 2% of all cancers that affect men and is more prevalent in the North and Northeast regions of the country (2). This condition constitutes a serious public health problem in some developing countries. The incidence is significantly high in Central America, South America, parts of Asia and Africa. In Brazil, the incidence is six to eight new cases for each 100,000 residents (3).

PC mainly affects non-circumcised individuals with a low sociocultural level and poor hygiene habits. It is often associated with human papillomavirus (HPV) infection and smoking and the main risk factor is phimosis. HPV is related to neoplasms of the cervix in women. As an infrequent disease, few studies explain the direct association between HPV infection and PC. However, a positive history of infection is a known risk factor for the development of PC, especially in cases of the involvement of the high-risk oncogenic viral types 16 and 18 (4).

The two most common histological types of PC are squamous cell carcinoma (SSC) and carcinoma *in situ*. SSC is the predominant type and the prognosis depends on the stage of the tumor. HPV is related to the development of SSC, especially the oncogenic viral types 16, 18, 31 and 33. In many men, HPV causes condyloma acuminatum, but many are completely asymptomatic and propagators of the virus (4). These tumors normally present as a painless, palpable, visible lesion on the penis.

The coronavirus 19 (COVID-19) pandemic exerted a considerable impact on health care, including the field of urology, as most urological cancers depend on surgery as priority treatment. The results of a review conducted by Katims et al. revealed the most urological oncological surgeries can be postponed without affecting overall patient survival. The treatment of prostate cancer of intermediate or high risk can likely be postponed three to six months without affecting the outcome. In contrast, the treatment of muscle invasive bladder cancer, high-

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grade urothelial cells of the upper tract, large renal masses, testicular cancer and PC cannot be postponed (5).

Despite the limited data, the primary treatment of PC should not be postponed and surgery is the first line of treatment due to the aggressive nature of this form of cancer. Moreover, the postponement of the early or late dissection of inguinal lymph nodes likely leads to a reduction in patient survival. Indeed, studies have demonstrated that prophylactic inguinal lymph node dissection provides significant survival benefits in comparison to delayed or therapeutic inguinal lymph node dissection (5).

According to Casco et al., some entities state that the treatment of PC with a low risk of progression (non-invasive superficial disease) could be postponed in the scenario of the COVID-19 pandemic, but other options should be considered, such as topical treatment or laser therapy. In cases of an intermediate risk of progression (T1-2; < 4 cm in diameter), surgical treatment could be postponed up to three months, with radiotherapy and brachytherapy considered effective organ-preserving approaches that achieve good results. Moreover, follow-up by telemonitoring was also considered important (6,7).

The aim of the present study was to investigate surgical interventions in patients with penile cancer at a university hospital before and after the COVID-19 pandemic.

Methods

Study population

A retrospective analysis was performed with all patients with PC at the urology clinic of a university hospital that is a reference center for 102 municipalities, located in the state of São Paulo (Brazil) in the years 2019 (prior to pandemic) and 2020 (year of pandemic).

Clinical follow-up consultations for treatments prior to the year considered in the study could reduce the percentage of surgeries performed in the interest period considered. In this sense, approaches prior to 2019 were used as an exclusion criteria.

This study was conducted in accordance with the principles outlined in the Declaration of Helsinki and approved by the local Human Research Ethics Committee of São José do Rio Preto Medical School (certificate number - 47051021.6.00005415). The need for individual informed consent was waived, as this study was a observational and retrospective analysis of collected data used for routine care.

Data collection

Data were collected from the electronic records of patients sent for hospital treatment. The variables age, male sex and the treatment (surgical or not) instituted for penile cancer were considered.

Statistical analysis

The data were tabulated on a spreadsheet using the Excel program. Descriptive statistics were performed with the calculation of frequencies as well as measures of central tendency and dispersion. Comparisons were made of the number of patients and respective ages submitted to surgical treatment and those treated non-surgically before and after the pandemic.

The Kolmogorov-Smirnov test was used to determine normality of the data. The Student's t-test and pair t-test were used for the comparison of quantitative variables. Frequencies were compared using Fisher's exact test. A *P-value* ≤ 0.05 was considered indicative of statistical significance. The analyses were performed with the aid of the SPSS (IBM, version 23, 2014) and GraphPad Instat (3.10, 2009) programs.

Results

All 32 patients with a diagnosis in the years considered were included in the study. In the year prior to the COVID-19 pandemic, 18 patients were diagnosed with PC, 13 of whom (72.2%) with a mean age of 63.9 years did not undergo surgery and five of whom (27.8%) with a mean age of 48.4 years were submitted to penectomy (Table 1).

Before pandemic	Patients not submitted to surgery (n= 13)	Patients submitted to surgery (n= 5)
Mean age (n [± SD])	63.92 (± 12.599)	48.4 (± 13.885)
Median age (Q1 – Q3)	63 (47 – 87)	48 (33 – 69)
Passed normality test (%)	Yes (72.2%)	Yes (27.8%)

Q1 – 25th percentile; Q3 – 74th percentile; SD – standard deviation

Table 1: Age of patients with diagnosis of PC in year prior to onset of pandemic

After the onset of the COVID-19 pandemic, 14 patients were diagnosed with PC, eight of whom

(57.1%) with a mean age of 60.5 years did not undergo surgery and six of whom (42.9%) with a mean age of 66.5 years were submitted to penectomy (Table 2).

After onset of pandemic	Patients not submitted to surgery (n= 8)	Patients submitted to surgery (n= 6)
Mean age (n [± SD])	60.5 (± 8.281)	66.5 (± 14.775)
Median age (Q1 – Q3)	58.5 (49 – 75)	70.5 (44 – 82)
Passed normality test (%)	Yes (57.1%)	Yes (42.9%)

Q1 – 25th percentile; Q3 – 74th percentile; SD – standard deviation
Table 2: Age of patients with diagnosis of PC in year after onset of pandemic

The Kolmogorov-Smirnov test demonstrated the normal distribution of ages in the four groups (with and without surgery prior to the pandemic and without and without surgery after the onset of the pandemic).

Fisher's exact text was used for comparisons of the frequency of surgeries before and after the onset of the pandemic, revealing a nonsignificant difference (p = 0.4651) (Table 3).

	Prior to pandemic (n= 18)	After onset of pandemic (n = 14)
Number of surgeries (n [%])	5 (27.78 %)	6 (42.86 %)

Table 3: Number of surgeries before and after onset of COVID-19 pandemic

A significant difference was found regarding the number of surgeries performed for PC between the group of patients with a mean age of 63.9 years and the group with a mean age of 48.4 years in the pre-pandemic period (p = 0.0366). In contrast, no significant difference in the number of surgeries was found between these same groups in the period after the onset of the pandemic (p = 0.3508).

Discussion

Penile cancer (PC) can have worse sexual or oncological outcomes with the prolonged postponement of surgery (7, 8, 9). This is an important point with regards to surgical approaches in the context of the COVID-19 pandemic, especially when considering the recent relatively increase of the proportion of patients who died of PC (mainly the squamous cell carcinoma) (10) and the potential diagnostic delay in the face of safety measures (11) , associated with some later recommendations for surgery during the period (invasive or obstructive cancers) (12). Ian Janes et al. (13) even points to the potential delay in this type of diagnosis in the face of telemedicine and the lack of physical examination during the pandemic (13).

The present findings reveal that age exerts an influence on the choice of surgery as an essential therapeutic measure in accordance with context. Prior to the pandemic, when greater stability was found in public health, younger patients opted more for surgery compared to older patients. Though, after the onset of the pandemic, a period characterized for health insecurity, the number of surgeries was similar between middle-aged and older patients. Finding that is in line with what was established in Cakir et al. (11), according to which age should not be used as a criterion to prioritize surgical treatment of young patients.

Moreover, it is important to point out the lack of studies about penile cancer. According to a review published in 2022 (14), the study of the disease has been neglected in favor of more common illnesses. In addition, although Fu et al. (15) indicates the rise of cases in developed countries, Bandini et al. (14) supports that most analyzes are not carried out where there is a higher prevalence of PC (Africa, South America, and South Asia).

This single-center, observational and retrospective study emphasizes its importance as it seeks to fill the gap in the scientific literature regarding PC in one of the countries with the highest prevalence of this type of cancer. However, some limitations are still noteworthy in this research. First, we did not perform analyzes in relations to sexual outcomes, death or worsening in the clinical tumor staging outcomes of patients who did not undergo to surgery. Secondly, analysis of local prevalenc e of the disease was not accomplished. In addition, only the first year of pandemic and the previous one were studied, without a clinical follow-up to assess the long-term impacts of proceeding or not with surgical treatment.

Conclusion

The COVID-19 pandemic did not have a significant impact on the frequency of surgeries for penial cancer at the university hospital analyzed in the present study. Moreover, when the patients were stratified by age group, this variable no longer exerted an influence on the decision to undergo surgery or not for the treatment of penile cancer after the onset of the pandemic.

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