

Sexual and Functional Outcomes after Penile cancer treatment-perspective from a tertiary cancer care hospital in Nepal.

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Abstract

Background

The mainstay of treatment for penile cancer is Penectomy with inguinal lymph node dissection following risk stratification followed by chemo-radiotherapy. Despite satisfactory oncological result, penile surgery has significant impact on patient's functional and sexual quality of life. This retrospective analysis is to evaluate sexual and functional outcome of patient after curative treatment and its possible associations with clinic-pathological characteristics.

Methods

This is a retrospective study conducted at Bhaktapur Cancer Hospital from January 2011 to December 2015 of histologically confirmed cases of carcinoma penis. Clinical and pathological characteristic data included age, history of smoking, clinical presentation, anatomical site, presence of lymph nodes or distant metastasis, primary tumor size (pT) and TNM staging, surgery involved, length of remaining penile shaft, histopathological type, chemotherapy and radiotherapy patient received and follow ups time. International Index of Erectile Function (IIEF-5) questionnaire was used to assess sexual function which encompasses five questions and addresses the relevant domains of male sexual function respectively erectile function, orgasmic function, sexual desire, intercourse satisfaction and overall satisfaction and Urinary function were noted during follow up .

Result

Among the cases, 64 cases were pathologically proven for penile cancer. The age of patient entering the study group included from 22 years to 88 years with mean age of 58.75±12.30 years.

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All patients except one were married and sexually active prior to treatment. Vast majority of the patients 63 (98.4%) were not circumcised and majority of cases 42 (65.64%) were smoker. The mean size of the tumor was 3.25 ± 1.208 cm. Majority of patients 54(84.4%) underwent partial amputation of penis while 2(3.1%) patients had undergone total amputation of penis. The multivariate analysis of different factors showed that T staging $\geq T2$ and penile shaft(cm) < 3 cm were independent risk factors for sexual dysfunctions (odds ratio = 13.64; 95% confidence interval = 1.02-181.005), and (odds ratio = 0.03; 95% confidence interval = 00-0.05) respectively. Out of 56 cases, 33(58.9%) had different grades of sexual dysfunction where 15(26.8%) cases were severe, 5(8.9%) cases were moderate, 8(14.3%) cases were mild to moderate and 5(8.9%) cases were mild. 23 (41.1%) cases who did not have any form of sexual dysfunction. One (1.8%) case had urethral stricture, 3(5.4%) cases had meatal stenosis, 2(3.6%) cases had penile edema and 4 (7.1%) cases had penile discoloration.

Conclusions

Amputation of penis with inguinal lymph node dissection which is necessary for curative intent of the disease is disfiguring and has a profound and lasting sexual dysfunction, voiding problems, penile appearance and cosmetic problems, all of which may adversely affect the patient's quality of life. Emphasis on preventive aspects and early detection should be emphasized to get rid of this disease.

Key words: Carcinoma of Penis, Surgical treatment, Quality of Life, sexual function

Background

Carcinoma of Penis an uncommon disease in the developed countries with the incidence of less than 1 % in men while in developing countries like Africa and South America, the incidence is approximately 10–20% among all male malignancies.^{1,2,3} The mainstay of treatment for penile cancer is either Partial amputation of Penis (PAP) or total amputation of penis (TAP) as necessary with inguinal lymph node dissection following risk stratification.^{4,5} Neoadjuvant cisplatin-based combination chemotherapy is used for high-risk and locally advanced disease and adjuvant chemotherapy for node positive advanced diseases. Despite satisfactory

oncological result, penile surgery has significant impact on patient's functional and sexual quality of life^{6,7}. Recent advances in management of penile cancer with lymph node metastasis aims in penile preservation, morbidity minimization as well as sexual and functional outcomes preservation, without compromising oncological outcomes.^{8,9} The goal of this retrospective analysis is to evaluate sexual and functional outcome of penile cancer patients after curative treatment and its possible associations with clinic-pathological characteristics.

Methods

Study design and Enrollment

This is a retrospective study conducted at Bhaktapur Cancer Hospital from January 2011 to December 2015. Clinical notes of Histologically confirmed cases of cancer of penis were analyzed. The study was approved by the Ethics Review Board of the Hospital. Informed consents were taken from the study subjects.

Study Population

The study population included the entire group of patients that presented to the Bhaktapur Cancer Hospital who were histologically confirmed case cancer of penis. Patients who were sexually inactive pre-operatively and had distant metastatic disease were excluded in the final analysis. All the records regarding the patients were extracted from the patient's files stored in the records department. The patients were followed up at outpatient department every 3 months for 2 years and every 6 months for next 3 years after penile cancer surgery. Clinical and pathological data included age, smoking history, clinical presentation, anatomical site, presence of lymph nodes or distant metastasis, surgery involved, length of penile shaft, histopathological type, primary tumor size (pT) and TNM staging, chemotherapy and radiotherapy used in treatment and follow ups. Staging was performed according to the 7th edition of tumor-node-metastasis (TNM) classification¹⁰ and Jackson's clinical stage.¹¹ Remaining penile shaft length is measured by rigid ruler from the pubic bone to the end of the shaft taken on the dorsal side in a flaccid state.

Nepali language translated version of International Index of Erectile Function (IIEF-5)¹² questionnaire was used to assess sexual function which encompasses 5 questions and addresses the relevant domains of male sexual function: erectile function, orgasmic function, sexual desire, intercourse satisfaction and overall satisfaction. The IIEF score is scaled from 5 to 25 with the score of 1-5 is given for each 5 questions. Sexual functional grade then determined by additional of all scores and categorized as follows: 5–7 severe dysfunction, 8–11 moderate, 12–16 mild to moderate, 17–21 mild and greater than 21 no dysfunction. The IIEF-5 questionnaire was verbally asked pre-operatively and during follow periods after treatment. Urinary function such as urethral stricture, meatal stenosis, penile edema were subsequently evaluated during follow up period.

Data analysis & Results

The Socio-demographic information and clinical data was collected in an excel database and the data was subsequently transferred to SPSS 18.0 (SPSS Inc., Chicago, IL) for statistical analysis. Data are presented as mean \pm standard deviation. The chi-square test was used to compare differences in sexual dysfunction and functional outcomes with different clinic-pathological factors. The Mann-Whitney U test was used to compare various parameters between different sexual dysfunction categories. Univariate and multivariate logistic regression analysis was used to investigate clinico-pathological risk

factors for sexual dysfunction in penile cancer after treatment. All p values <0.05 were considered statistically significant.

Results

Out of 4,409 malignancies registered in Bhaktapur Cancer Hospital during the period of 5 years, 64 cases were pathologically proven for penile cancer. The age of patient entering the study group included from 22 years to 88 years with mean age of 58.75 ± 12.30 years. All patients except one were married and sexually active prior to treatment. Vast majority of the patients 63 (98.4%) were not circumcised and majority of cases 42 (65.64%) were smoker. The mean size of the tumor was 3.25 ± 1.208 cm. Majority of patients 54 (84.4%) underwent partial amputation of penis while 2 (3.1%) patients had undergone total amputation of penis. Eight cases of Jackson's stage IV who had distant metastasis did not undergo any surgery and treated with palliative chemotherapy. The mean length of remaining penile shaft after surgery is 2.83 ± 1.69 cm. During the presentation of the symptoms 45 patients (70.3%) already had inguinal lymph nodal metastasis. Anatomical site, Jackson's stage, histopathological type and metastasis are depicted in the table 1. Squamous cell carcinoma was the most common histopathological type representing 62 cases (96.87) and the rest 2 (3.13%) was verrucous carcinoma.

Fig 1 and 2. Advance stage penile cancer during presentation and post total penectomy .



Table 2 shows sexual dysfunction of 56 Cases of Penile Cancer who underwent surgical, chemoradiation treatment in cross comparison with age, tumor size, surgery type, remaining penile shaft, lymph node metastasis, pathological T stage, and

Jackson's clinical staging. Tumor size >2cm 27(48.2%) cases, penile shaft < 3 cm 30(53.6%) cases, lymph node metastasis 27(48.2%) cases, Jackson's clinical stage III 26(46.4%) cases had statistically significant sexual dysfunction. In Table 3 the multivariate analysis of these factors showed that T staging \geq T2 and penile shaft(cm) <3cm were independent risk factors for sexual dysfunctions (odds ratio = 13.64; 95% confidence interval = 1.02-181.005), and (odds ratio = 0.03; 95% confidence interval = 0.00-0.05) respectively. Total of 44 cases received further management with either Chemotherapy or Radiotherapy, among which 21 cases received Radiotherapy (32.81%) and 23 case received Chemotherapy (35.93%). 13 cases received both Radiotherapy and Chemotherapy during the course of treatment.

Discussion

Penile cancer treatment is associated with sexual and functional dysfunction like urine voiding, penile disfiguring and ultimately causes physiological, psychological effects on long term quality survival¹². Even though there has been a paradigm shift in penile cancer treatment directing more towards organ preservation,¹³ the mainstay of treatment in developing countries is still either total or partial amputation of penis with inguinal lymph node dissection due to delay presentation. Our study has well illustrated that there is sexual and functional dysfunction in 33(58.9%) patients with penile cancer who underwent surgery followed by chemo-radiation therapy.

Table 1. Baseline Clinicopathological Characteristics of 64 Penile Cancer patients.

Parameters		Frequency(percent)
Age(years)Mean		58.75±12.30(22-85)
Smoker	Yes	42(65.64%)
	No	22(34.36%)
Circumcision	Yes	1(1.60%)
	No	63(98.4%)
Tumor Size (cm) mean		3.25±1.208
Surgery Type	TAP	2(3.1%)
	PAP	54(84.4%)
	No	8(12.5%)
	Surgery	
Penile Shaft(cm)		2.83±1.696
Lymph Nodes metastasis	Yes	45(70.3%)
	No	19(29.7%)
Pathological T Stage	< T2	12(18.8%)
	\geq T2	52(81.3%)
Jackson's stage	I	15(23.4%)
	II	5(7.8%)
	III	36(56.3%)
	IV	8(12.5%)
Histopathological type	Squamous cell carcinoma	62(96.87)
	Verrucous carcinoma	2(3.13%)

Anatomical Site	Glans penis	11(17.18%)
	Glans penis + Shaft	36(56.25%)
	Shaft	6(9.37%)
	Whole penis	7(10.93%)

This finding is in accordance to study done by D’Ancona, C. A. et al who presented 64% decrement in overall sexual function¹³. Similarly, our study showed that 23(41.1%) patients who had PAP surgery were still sexually satisfied especially when penile shaft is >3cm (21(37.5%).Several studies have reported that vaginal intercourse is still feasible with remaining erect penis stump.¹⁴

Table 2. Sexual Dysfunction of 56 Cases of Penile Cancer who underwent surgical treatment.

Clinico-pathological Variables		Sexual Dysfunction		P value
		No	Yes	
Age(years) Mean	≥40	23(41.1%)	30(53.6%)	0.26
	<40	0(0.0%)	3(5.4%)	
Tumor Size (cm)	<2 cm	11(19.6%)	6(10.7%)	0.037
	≥2 cm	12(21.4%)	27(48.2%)	
Surgery Type	TAP	0(0.0%)	2 (3.6%)	

	PAP	23(41.1%)	31(55.4%)	0.50
Penile Shaft(cm)	<3cm	2(3.6%)	30(53.6%)	0.00
	≥3cm	21(37.5%)	3(5.4%)	
Lymph Nodes metastasis	Yes	10(17.9%)	27(48.2%)	0.004
	NO	13(23.2%)	6(10.7%)	
T Stage	<T2	9(16.1%)	3(5.4%)	0.018
	≥T2	14(25.0%)	30(53.6%)	
Jackson’s stage	I	11(19.6%)	4 (7.1%)	0.011
	II	2(3.6%)	3(5.4%)	
	III	10(17.9%)	26(46.4%)	

Table 3: Multivariate analysis of risk factors for Sexual Dysfunctions

	Multivariate analysis		
	OR	(95 % CI)	p
Tumor Size (cm) ≥2 cm	4.53	0.409	50.254
L y m p h N o d e s metastasis	0.11	0.06-2.23	1.53

T Staging $\geq T2$	13.6 4	1.02-181. 005	0.04
Penile Shaft(cm) ≥ 3 cm	0.03	00-0.05	<0.0 01

Although total penectomy with perineal urethrostomy by nature would have distressing level sexual function and harsh effect on self-image and self-esteem they had less functional urinary voiding complications such as meatal and urethral stricture .

Traditionally 2 cm excision margin was required¹⁵ but Philippou et al. reported that a less than 5-mm excision margin is considered adequate and safe in penile preserving procedures without compromising oncological outcome.¹⁶ Paradigm shift in penile cancer treatment towards more conservative and penile preserving surgeries have saved patients from major functional and psychological morbidities with acceptable oncological outcomes especially when combined with vigorous follow-up.¹⁷

Table 4. Sexual and Functional Outcomes in 56 Cases of Penile Cancer after treatment.

Sexual Dysfunction		33(58.9%)
Sexual Dysfunction Grading	Severe	15(26.8%)
	Moderate	5(8.9%)
	Mild to Moderate	8(14.3%)
	Mild	5(8.9%)
No Dysfunction		23(41.1%)
Functional Outcome	Urethral Stenosis	1(1.8%)

Meatal Stenosis	3(5.4%)
Penile Edema	2(3.6%)
Penile Discoloration	4(7.1%)

We used standardized and validated questionnaires tool IIEF-5 for sexual functional measurement as shown in table 6. The IIEF-5 includes 5 questionnaire relevant domains of male sexual function including erectile function, orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction. Each domain has 5 scores and total of all scores provides the grading of sexual dysfunction of severe, moderate, mild to moderate, mild and no dysfunction.

Penile cancer is considered as a disease of older men of 6th -7th decade and from developing countries especially of Africa, Asia and North America. It is a continuing challenge to both oncologist and urologist in developing country such as Nepal as 52(81.3%) cases presented in advanced stage of diseases and among them 8(12.5%) cases presented in stage IV with distant metastasis possibly due to social cultural taboos and ignorance.

The present study had several drawbacks. Firstly, it was retrospective in nature and had selection bias and unmeasured confounding variables. Secondly a small sample size due to its uncommon malignancy incidence and single institute analysis. Thirdly, this study did not include the hormonal, psychological

and quality of life which were also etiologies for sexual dysfunction.

Conclusions

Penile cancer is a rare malignancy with dismal prognosis. Amputation of penis with inguinal lymph node dissection is the surgical choice for this disease. However, this treatment is disfiguring and has a profound and lasting sexual dysfunction, voiding and cosmetic problems, penile appearance, all of which may adversely affect the patient's quality of life. A better understanding of the impact of penile cancer and its treatments on men's sexual and functional outcomes will help to identify interventions to treat sexual dysfunction and to help in decision making in surgical approach. A large randomized trial is warranted to further verify the necessity of penile preserving surgery to reduce the sexual dysfunction in penile carcinoma.

Author Contribution

PK carried out surgical procedures, conceived the study and drafted the manuscript; UMS carried out surgical procedures and follow-up; MR carried out surgical procedures and follow-up; PRN carried out surgical procedures and participated in the study coordination; PB conceived the study, participated in its design and coordination and helped in initial manuscript draft. NS helped in statistical analysis and manuscript revision. All authors have read and approved the final version of the manuscript and agree with the order of presentation of the authors.

COMPETING INTERESTS

All authors declare no competing interests

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Table 6 International Index of Erectile Function (IIEF-5)

Domains		Score	Total Score	Sexual Dysfunction Grading
Erectile function, ,	5) Very good			Severe(5-7)
	4) Good			
	3) Fair			
	2) Poor			
	1) Very poor			
Orgasmic function	5) Excellent			Moderate(8-11)
	4) Very good			
	3) Good			
	2) Fair			
	1) Poor			
Sexual desire,	1) Not at all			Mild to Moderate (12-16)
	2) A little bit			
	3) Somewhat			
	4) Quite a bit			
	5) Very			
Intercourse satisfaction	1) Not at all			Mild (17-20)
	2) A little bit			
	3) Somewhat			
	4) Quite a bit			
	5) Very			
Overall satisfaction	1) Not at all			No Dysfunction(>21)
	2) A little bit			
	3) Somewhat			
	4) Quite a bit			
	5) Very			

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