

# The Clinicopathological Profile of Bladder Cancer Undergoing Radical Cystectomy in Nepal: A Retrospective Analysis

Gyan Prasad Pokhrel<sup>1</sup>, Aditya Jalan<sup>1</sup>, Sarita Rana<sup>2</sup>, Binod Babu Gharti<sup>1</sup>, Nirmal Lamichhane<sup>1</sup>

<sup>1</sup>Urology Unit, Department of Surgical Oncology, BP. Koirala Memorial Cancer Hospital, Nepal

<sup>2</sup>Gynae-oncology, Department of Surgical Oncology, BP Koirala Memorial Cancer Hospital, Nepal

## Article History

Received: 27 Dec, 2022

Accepted: 12 Mar, 2023

Published: 18 May, 2023

**Funding sources:** None

**Conflict of Interest:** None

## Online Access



## Corresponding

Aditya Jalan  
Registrar, Urology Unit,  
Department of Surgical Oncology,  
BP. Koirala Memorial Cancer Hospital,  
Nepal  
Email: dradityajalan@gmail.com

## Introduction

Urinary bladder cancer (BC) is the tenth most prevalent malignancy and makes up roughly 3% of all cancer cases newly discovered worldwide. In Nepal, this is the 13<sup>th</sup> most common cancer, accounting for 2.3% of all cancers (GLOBOCAN data).<sup>1</sup> A hospital-based cancer registry over 4 years from different hospitals in Nepal showed BC as the fourth most common cancer in men.<sup>2</sup> Smoking, tobacco consumption and occupational exposure to various chemicals are the common risk factors.<sup>3</sup>

The spectrum of BC includes non-muscle invasive (NMIBC), muscle-invasive (MIBC), and metastatic disease. NMIBC is managed with transurethral resection of bladder tumor combined with adjuvant

## Abstract

**Introduction:** Bladder cancer is the 10th most common cancer diagnosed worldwide and the 13th most commonly diagnosed cancer in Nepal. Radical cystectomy with urinary diversion is considered the standard of care for high-risk diseases. This study aims to analyse the clinicopathological profile of bladder cancer patients that underwent radical cystectomy.

**Methods:** All patients who underwent Radical Cystectomy between January 2007 to December 2016 at BP Koirala Memorial Cancer hospital were evaluated. Their perioperative data were collected. Qualitative data were represented as mean and standard deviation whereas categorical variables were expressed as frequencies and percentages of an appropriate denominator.

**Result:** Among 142 cases that met the inclusion criteria, the median age was 60 years. Most were male (83.8%) and had a past history of smoking. Urinary diversion after cystectomy with ileal conduit was done in 83% of patients and orthotrophic neobladder reconstruction was done in 17% of patients. Mean blood loss was 925.16 ± 568 ml and operation duration was 327.11 ± 86.13 min. Most cases had Urothelial Carcinoma (88.2%). About two-third of the cases (66.2%) had NO stage and less than half of the cases (44.4%) had the T2 stage.

**Conclusion:** Bladder cancer is more prevalent among elderly men who consumed tobacco. Urothelial Carcinoma is the most common histological type.

**Keywords:** Radical cystectomy, Urinary bladder, Urothelial Carcinoma

intravesical therapy (BCG/ Mitomycin) in low-risk and intermediate-risk cases. However, in high risk cases with extensive bladder involvement when complete resection is not possible, BCG Refractory cases, BCG unresponsive, BCG relapsing cases, radical cystectomy is indicated. Similarly, a majority of BC patients will have a NMIBC, while about 25% of patients will have a MIBC at presentation. MIBC will develop in 45% of NMIBC cases after 5 years.<sup>4</sup> Presently, the standard surgical treatment for MIBC and high-grade illnesses is radical cystectomy (RC) with pelvic lymphadenectomy.<sup>5</sup> There are limited studies from Nepal on BC and those studies were conducted only on fewer patients. This study aims to retrospectively analyze the clinicopathological profile of BC patients who underwent RC.

## Methods

This study was carried out at Uro-Oncology unit of B P Koirala Memorial Cancer Hospital (BPKMCH). BPKMCH is a tertiary cancer care treatment facility located in Chitwan, a central location in Nepal for easy access for cancer patients from all over the county. Estimates of cancer cases in Nepal are nearly 21000 new cases per year. This hospital caters services to about 10,000 patients per year, which is half of this number. Ethical clearance was taken from the institutional review board of BPKMCH. All the medical records of all patients who were diagnosed with BC and underwent RC between January 2007 to December 2016 were evaluated. Records with incomplete data were excluded from the study. The study also excluded patients who underwent surgery at other hospitals and had the metastatic illness. Patient traits such as the year of diagnosis, age, marital status, and smoking status were variables. Pre-operative testing included a history check, physical exam, standard blood test, and imaging. The type of surgery, the length of the procedure, and the volume of blood loss throughout the procedure were all recorded intraoperatively. Clinical and pathological TNM stage and grade were collected in both the preoperative and postoperative stages of the disease. The margin status and the existence of lymphovascular invasion (LVI) and perineural invasion (PNI) were also assessed. The 8th edition system of the American Joint Committee on Cancer (AJCC) was used to standardize tumour and nodal staging. While categorical variables were given as frequencies and percentages of the relevant denominator, qualitative data were represented as mean and standard deviation. We transformed all continuous variables into categorical ones. The SPSS software was used to examine the data. (SPSS Inc., Chicago, IL, USA), version 16.0.

## Results

Among 142 cases that meet the inclusion criteria, the median age was 60 years ( $57.92 \pm 12.02$ ) where 83.8% ( $n=119$ ) were male, and 16.2% ( $n=23$ ) were female. During clinical staging, most patients were in the T3 stage (38.7%,  $n=55$ ) stage followed by T2 (35.2%,  $n=50$ ), T4 (16.2%,  $n=23$ ) and T1 (9.9%,  $n=14$ ) stage. Similarly,

Clinical nodal staging was done using a CT scan, 50% ( $n=71$ ) had the N0 stage, 33.8% ( $n=48$ ) had the N1 stage, 14.78% ( $n=21$ ) had the N2 stage and 1.4% ( $n=2$ ) had N3 stage. (Table 1)

Most of the patients (98.6%,  $n=140$ ) were married and were from the terai area (48.6%,  $n=69$ ) of Nepal. Out of 77 districts in Nepal we had patients from 48 districts of Nepal maximum number being from Jhapa, Chitwan, Syangja, Gulmi, Baglung, Dailekh, Rupandehi and Sunsari. Sixty-five per cent ( $n=93$ ) gave a history of smoking in past. (Table 2)

**Table 1.** The Clinical profile of the BC patients undergoing RC

Patient Characteristics	Categories	Frequency	Percentage
Age	Mean $\pm$ SD	-	$57.92 \pm 12.02$
	Median	-	years 60
	Age < 65yrs	98	69%
	Age > 65yrs	44	31%
Sex	Male	119	83.8%
	Female	23	16.2%
Marital Status	Married	140	98.6%
	Unmarried	2	1.4%
Smoking Status	Smokers	93	65.5%
	Non-smokers	49	34.5%
Clinical T Staging	T1	14	9.85%
	T2	50	35.21%
	T3	55	38.73%
	T4	23	16.19%
Clinical N Staging	N0	71	50%
	N1	21	14.78%
	N2	48	33.80%
	N3	2	1.4%

**Table 2.** District-wise distribution of patients from different districts of Nepal

.S. N	District	Frequency	Percentage	.S. N	District	Frequency	Percentage
1	Jhapa	10	7.0	25	Bardiya	2	1.4
2	Chitwan	8	5.6	26	Dang	2	1.4
3	Syangja	8	5.6	27	Gorkha	2	1.4

4	Gulmi	7	4.9	28	Kanchanpur	2	1.4
5	Baglung	5	3.5	29	Makwanpur	2	1.4
6	Dailekh	5	3.5	30	Myagdi	2	1.4
7	Rupandehi	5	3.5	31	Nawalparasi	2	1.4
8	Sunsari	5	3.5	32	Sankhuwasabha	2	1.4
9	Unknown	4	2.8	33	Sarlahi	2	1.4
10	Dhanusha	4	2.8	34	Solukhumbu	2	1.4
11	Jajarkot	4	2.8	35	Udayapur	2	1.4
12	Lamjung	4	2.8	36	Belbasi	1	0.7
13	Morang	4	2.8	37	Bhojpur	1	0.7
14	Palpa	4	2.8	38	Dadeldhura	1	0.7
15	Rautahat	4	2.8	39	Dolpa	1	0.7
16	Tanahun	4	2.8	40	Ilam	1	0.7
17	Banke	3	2.1	41	Kathmandu	1	0.7
18	Kapilbastu	3	2.1	42	Lalitpur	1	0.7
19	Kaski	3	2.1	43	Manag	1	0.7
20	Mahottari	3	2.1	44	Parbat	1	0.7
21	Parsa	3	2.1	45	Sindhuli	1	0.7
22	Saptari	3	2.1	46	Siraha	1	0.7
23	Arghakhachi	2	1.4	47	Surkhet	1	0.7
24	Bara	2	1.4	48	Tehrathun	1	0.7

Urinary Diversion after cystectomy was performed with ileal conduit (IC) in 83% (n= 118) of patients and Orthotopic Neobladder reconstruction (ONB) in 16.9% (n= 24). Intra-operatively, the mean volume of blood loss was  $925.16 \pm 568$  ml and the mean Operation duration was  $327.92 \pm 84.48$  min. (Table 3)

**Table 3.**The intraoperative characteristics of BC patients undergoing RC

Patient Characteristics	Categories	Frequency	Percentage
Surgical Procedure	RC + IC	118	83.1%
	RC + ONB	24	16.9%
OT duration	Mean $\pm$ SD	-	$327.92 \pm 84.48$ min
Intraoperative blood loss	Mean $\pm$ SD	-	$925.16 \pm 568$ ml

However, in pathological staging most cases were found

in T2 stage (44.36%, n=63) followed by T3 stage (30.98%, n= 44), T1 stage (14.78%, n= 21) and T4 stage ( 9.85%, n= 14). Similarly, Pathological nodal staging was 66.19 % (n=94) in the N0 stage, 21.1% (n=30) in the N1 stage and 12.67% (n=18) in the N2 stage. Similarly, PNI was present in 11.3% (n=16) of patients and LVI was seen in 9.9 % of patients. Post Radical cystectomy surgical margins were found positive in 5.6% (n=8) patients. (Table 4)

Most cases in this study had Urothelial Carcinoma (UC) as the most common histological type seen in 88.1% (n=125) of cases, followed by UC with squamous differentiation seen in 4.9% (n=7), purely squamous cell carcinoma in 2.8% (n=4) of patients, Adenocarcinoma in 2.1% (n=3) and sarcomatoid subtype in 2.1% (n=3) of patients. Out of 132 patients, who had urothelial carcinoma as the predominant histological type, high-grade UC was seen in 88.6% (n=117) of patients. (Table 4)

**Table 4.** The pathological characteristics of the BC patients undergoing RC

Patient Characteristics	Categories	Frequency	Percentage
Pathological T Staging	T1	21	14.78%
	T2	63	44.36%
	T3	44	30.98%
	T4	14	9.85%
Pathological N Staging	N0	94	66.19%
	N1	30	21.12%
	N2	18	12.67%
	N3	0	0
Histopathology	Urothelial carcinoma	125	88.1%
	Urothelial carcinoma with Squamous differentiation	7	4.9%
	Pure SCC	4	2.8%
	Adenocarcinoma	3	2.1%
	Sarcomatoid subtype	3	2.1%
(Grade (out of 132 UC	High-Grade UC	117	88.63%
	Low-Grade UC	15	11.36%
LVI	Present	14	9.9%
	Absent	128	90.1%
PNI	Present	126	88.7%
	Absent	16	11.3%
Surgical Margins	Free	134	94.4%
	Ppositive	8	5.6%

## Discussion

Bladder cancer is the disease of the elderly population especially those over the age of 64, with a median age of 69 years and 70 to 80% of patients being male. In this study, the median age was 60 years, and 83% of the participants were men.<sup>6-8</sup> The male-to-female ratio was 5.17. This finding is higher than the study conducted in Nepal.<sup>3</sup> The worldwide incidence rate is 4 times higher in men than in women.<sup>9,10</sup> Tobacco consumption in any form is a well-established risk factor for bladder cancer and this accounts for approximately 65% of disease risk in men and 20% to 30% in women. Tobacco contains a variety of chemicals such as 2-naphthylamine, 4-aminobiphenyl and other arylamines are known bladder carcinogens.<sup>8,11,12</sup>

Preoperative imaging with a CT or MRI scan plays a crucial role in the clinical staging (tumour, nodes and

metastasis) of BC.<sup>13</sup> The role of preoperative lymph node evaluation with imaging in detecting malignant lymph nodes is limited.<sup>14,15</sup> On preoperative evaluation, the majority of our patients (38.7%) had the T3 tumour stage and 50% had N0 nodal stage.

The gold standard treatment for muscle-invasive urothelial and high-risk recurrent cancer is radical cystectomy with pelvic lymph node dissection, which provides the best survival benefit. RC involves the removal of the bladder, adjacent organs, and regional lymph nodes. In males, it includes the removal of the prostate and the seminal vesicles whereas, in females, the reproductive organs (ovaries, fallopian tubes, uterus and anterior vagina) may also be removed.<sup>16</sup>

The primary goals in choosing IC and ONB as a urinary diversion are to offer the patient the best local cancer control and quality of life while still enabling the patient

to successfully finish chemotherapy and therapeutic goals on time.<sup>17</sup> The choice of diversion type is also influenced by the patient's comorbidities, surgical appropriateness, capacity to manage diversion care following surgery, and personal preference.<sup>18</sup> In our scenario, most of the patients had IC as a major form of urinary diversion.

Similarly, on average a patient loses approximately 120 mL to 2700 mL of blood during RC, with an average OT duration of 170-900 minutes, indicating that this type of surgery results in significant blood loss and lengthy operative duration.<sup>19</sup>

UC is the most common BC histology (~90%), followed by squamous (2-5%) and adenocarcinoma (2%). Sarcomatoid Subtype is seen in less than one percent of BC.<sup>20</sup> The exact correlation between clinical and pathological staging is debatable. Pathological staging revealed that the majority of tumours had T2 (44.4%) and N0 (66.2%) stages. This pathological finding is similar to a study conducted by Supit et al in 2014, among 150 patients, in which 50% were in the T2 stage, 24.2% were in the T3 stage and 21.5% were in the T4 stage.<sup>21</sup> Also, Haque et al. from an analysis of data between 2004 to 2014 found that the majority of cases are at the T2 stage (86%), followed by the T3 stage (9.8%), and T4 stage (5.5%) at presentation.<sup>22,23</sup> Also, LVI and PNI are an important part of the pathological evaluation. LVI is seen in 7-8% and PNI seen in 13.6% of patients is itself an independent predictor of prognosis for those undergone radical cystectomy.<sup>6, 24</sup> Positive surgical margin frequency after radical cystectomy ranges from 4-15%. The positive surgical margins is considered a poor prognostic factor-affecting outcome after RC for BC.<sup>25</sup>

## Limitations

This study also has some limitations, postoperative complications (both early and late), and outcomes and survival analysis are not evaluated. Some of the findings in our study may not be directly reflected in the findings of other studies.

## Conclusion

Bladder cancer is more prevalent among elderly men who consumed tobacco. Urothelial Carcinoma is the most common histological type.

## References

1. Saginala K, Barsouk A, Aluru JS, Rawla P, Padala SA, Barsouk A. Epidemiology of Bladder Cancer. *Medical sciences (Basel, Switzerland)*. 2020;8(1).
2. Poudel KK, Huang Z, Neupane PR, Steel R, Poudel JK. Hospital-Based Cancer Incidence in Nepal from 2010 to 2013. *Nepal journal of epidemiology*. 2017;7(1):659-65.
3. Parajuli P, Luitel BR, Pradhan MM, Chapagain S, Poudyal S, Chudal S, et al. Clinicopathological patterns of bladder carcinoma over 1 year: experience from University Hospital of Nepal. *International Urology and Nephrology*. 2021;53(11):2289-94.
4. Golombos DM, O'Malley P, Lewicki P, Nguyen DP, Stone BV, Al Hussein Al Awamlh B, et al. The impact of socioeconomic status on perioperative complications and oncologic outcomes in patients undergoing radical cystectomy. *World J Urol*. 2017;35(7):1063-71.
5. Kaufman DS, Shipley WU, Feldman AS. Bladder cancer. *Lancet*. 2009;374(9685):239-49.
6. Sefik E, Celik S, Basmaci I, Yarimoglu S, Bozkurt IH, Yonguc T, et al. Effect of variant histology presence and squamous differentiation on oncological results and patient's survival after radical cystectomy. *Arch Ital Urol Androl*. 2018;90(3):172-5.
7. Sathianathen NJ, Weight CJ, Jarosek SL, Konety BR. Increased Surgical Complications in Smokers Undergoing Radical Cystectomy. *Bladder Cancer*. 2018;4(4):403-9.
8. Nik Ab Kadir MN, Mohd Hairon S, Yaacob NM, Ab Manan A, Ali N. Survival and Characteristics of Bladder Cancer: Analysis of the Malaysian National Cancer Registry. *Int J Environ Res Public Health*. 2021;18(10).
9. Cancer Facts & Figures (2023) American Cancer Society [Internet]. Cancer.org. 2023 Available from: <https://www.cancer.org/research/cancer-facts-statistics/all-cancer-facts-figures/2023-cancer-facts-figures.html>
10. Dobruch J, Daneshmand S, Fisch M, Lotan Y, Noon AP, Resnick MJ, et al. Gender and Bladder Cancer: A Collaborative Review of Etiology, Biology, and Outcomes. *European Urology*. 2016;69(2):300-10.
11. Cumberbatch MGK, Noon AP. Epidemiology, aetiology and screening of bladder cancer. *Transl Androl Urol*. 2019;8(1):5-11.
12. Li Y, Tindle HA, Hendryx MS, Xun P, He K, Liang X, et al. Smoking Cessation and the Risk of Bladder Cancer among Postmenopausal Women. *Cancer Prevention Research*. 2019;12(5):305-14.
13. McKibben MJ, Woods ME. Preoperative imaging for staging bladder cancer. *Curr Urol Rep*. 2015;16(4):22.
14. Starmans MPA, Ho LS, Smits F, Beije N, de Kruijff I, de Jong JJ, et al. Optimization of Preoperative Lymph Node Staging in Patients with Muscle-Invasive Bladder Cancer Using Radiomics on Computed Tomography. *J Pers Med*.

2022;12(5):726.

15. Grabbert M, Grimm T, Buchner A, Kretschmer A, Apfelbeck M, Schulz G, et al. Risks and benefits of pelvic lymphadenectomy in octogenarians undergoing radical cystectomy due to urothelial carcinoma of the bladder. *Int Urol Nephrol*. 2017;49(12):2137-42.
16. Aminoltejari K, Black PC. Radical cystectomy: a review of techniques, developments and controversies. *Transl Androl Urol*. 2020;9(6):3073-81.
17. Colombo R, Naspro R. Ileal Conduit as the Standard for Urinary Diversion After Radical Cystectomy for Bladder Cancer. *Eur Urol Suppl*. 2010;9(10):736-44.
18. McAlpine K, Lavallée LT, Stacey D, Moodley P, Cagiannos I, Morash C, et al. Development and Acceptability Testing of a Patient Decision Aid for Urinary Diversion with Radical Cystectomy. *J Urol*. 2019;202(5):1001-7.
19. Wayan Y, Ayu PD, Gde OAA, Wayan N, Widyadharma IPE. Pathological Profile, Early Complications, Functional and Oncological Outcome after Radical Cystectomy - Ileal Conduit for Bladder Cancer Patients in Sanglah General Hospital between January 2013 and December 2016. *Open Access Maced J Med Sci*. 2018;6(9):1647-51.
20. Hansel DE, Amin MB, Comperat E, Cote RJ, Knüchel R, Montironi R, et al. A contemporary update on pathology standards for bladder cancer: transurethral resection and radical cystectomy specimens. *Eur Urol*. 2013;63(2):321-32.
21. Supit W, Mochtar CA, Santoso RB, Umbas R. Outcomes of radical cystectomy and bladder preservation treatment for muscle-invasive urothelial carcinoma of the bladder. *Asian J Surg*. 2014;37(4):184-9.
22. Haque W, Verma V, Butler EB, Teh BS. Radical Cystectomy Versus Chemoradiation for Muscle-invasive Bladder Cancer: Impact of Treatment Facility and Sociodemographics. *Anticancer Res*. 2017;37(10):5603-8.
23. Rose TL, Deal AM, Ladoire S, Crehange G, Galsky MD, Rosenberg JE, et al. Patterns of Bladder Preservation Therapy Utilization for Muscle-Invasive Bladder Cancer. *Bladder Cancer*. 2016;2(4):405-13.
24. YukHD, JeongCW, KwakC, KimHH, KuJH. Lymphovascular invasion have a similar prognostic value as lymph node involvement in patients undergoing radical cystectomy with urothelial carcinoma. *Sci Rep*. 2018;8(1):15928.
25. Dotan ZA, Kavanagh K, Yossepowitch O, Kaag M, Olgac S, Donat M, et al. Positive surgical margins in soft tissue following radical cystectomy for bladder cancer and cancer specific survival. *J Urol*. 2007;178(6):2308-12; discussion 13.