International Surgery Journal
Rajeev TP et al. Int Surg J. 2017 Aug;4(8):2460-2469
http://www.ijsurgery.com
pISSN 2349-3305 | eISSN 2349-2902

DOI: http://dx.doi.org/10.18203/2349-2902.isj20173103

Original Research Article

Single center experience of urinary bladder malignancy: a 10-year retrospective analysis of hospital data

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Received: 24 June 2017
Accepted: 28 June 2017

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ABSTRACT

Background: Albeit the EAU, NCCN and AUA guidelines provide an excellent evidence-based protocol for the management of MIBC and NMIBC, these guidelines differ with respect to critical issues such as risk level definitions and management strategies. The NE part of the country has always bore the brunt of heavy oncological catastrophe like urinary bladder carcinoma related to extensive tobacco and pesticide usage. MIBC treatment usually encompasses RC with AC/NAC (Level I evidence for NAC use in MIBC exist) but the majority of patients seen at our center have already progressed to advanced stage at presentation and could not undertake full treatment.
Methods: Cancer registry of the last 10 yrs at Dept. of Urology and Renal Transplant Gauhati Medical College Hospital was searched for demographic, clinical, pathological and prognostic data and results summarized using statistical parameters of univariate analysis.
Results: There were a total of 168 patients in the NMIBC group with a majority in the 60-70-year age group. The most common grade was G2 and all DM type 2 and CKD were significantly associated in all the patients analyzed. Chemical exposure in the form of pesticide and smoking was a constant phenomenon in all patients of NMIBC and MIBC (n=66) population. CKD was significantly associated in the MIBC population along with positive urine cytology.
Conclusions: Despite a paucity of high level evidence regarding the majority of management topics in Urinary Bladder cancer in NE part of the country, there was general agreement among the various guideline panels and management guidelines at our institution. Identification of the upfront clinical parameters suggesting severity of disease and time to progression are the two most important domains which will decide the future of UB carcinoma treatment in this part of the world. Categories of evidence synthesized and grades of recommendations will have to be constantly gazed upon to modify and enhance treatment strategies.

Keywords: Irritative voiding, Neoadjuvant chemotherapy, Radical cystectomy, Transurethral resection of bladder tumor

INTRODUCTION

Albeit the EAU, NCCN and AUA guidelines provide an excellent evidence-based protocol for the management of MIBC and NMIBC, these guidelines differ with respect to critical issues such as risk level definitions and management strategies. Implication of the aforementioned treatment policy in a vast subcontinent like ours has always been a challenge. The NE part of the country has always bore the brunt of heavy Oncological catastrophe like urinary bladder carcinoma related to extensive tobacco and pesticide usage. MIBC treatment usually encompasses radical cystectomy (RC) with adjuvant chemotherapy (AC)/ neo-adjuvant

chemotherapy (NAC) (level I evidence for NAC use in MIBC exist) but the majority of patients seen at our center have already progressed to advanced stage at presentation and could not undertake full treatment.[1] Non-muscle-invasive bladder cancer (NMIBC) is characterized by a high risk of recurrence after transurethral resection of an initial tumor; the 1-yr recurrence rate is 15-61%, and the 5-years recurrence rate is 31-78%. These figures represent the heterogeneous character of NMIBC.[2]

Approximately 20% to 25% of patients have muscle-invasive bladder cancer (MIBC), which has a high rate of disease progression, because 50% harbor micro metastatic disease not detected by radiological imaging.[3] Initial management for MIBC consists of localized therapy, including surgery and radiotherapy but the risk of recurrence after localized therapy exceeds 50% and the 5 year mortality rate ranges from 33% to 73%.[4,5] Therefore, although patients undergo radical cystectomy, half of the patients relapse and die of metastasis. MIBC is potentially curable, but often fatal without effective treatment strategies. Optimal management of MIBC mandates a multidisciplinary approach with coordination between urologists, medical oncologists and in some cases radiation oncologists for staging, multimodality treatment, and follow-up.

The objective of this study was to most patients have NMIBC at presentation which has the propensity to rapidly progress to MIBC or even metastatic stage, so efforts must be put in to improve the early diagnosis and expeditious treatment of this disease. The major goals in treating patients with MIBC/NMIBC are to prevent the high number of recurrences and to prevent metastatic progression. Authors contemplate to evaluate and assess the risk categories in NE population and analyze upfront treatment designs based on retrospective analysis of last 10 years record for future course correction.

METHODS

Cancer registry of the last 10 years from January 2008 to January 2017 at Department of Urology and Renal Transplantation, Gauhati Medical College Hospital was searched for demographic, clinical, pathological and survival data. All the data (n=234) including the number of patients with different T stage and grades were calculated and significant relationship among variables was tested with the help of Pearson Chi Square and Fischer Exact T test (grade and stage analysis of both NMIBC and MIBC study population). Correlation analysis was based on the results of pearson R coefficient value (P value < 0.05 was considered significant for previously mentioned tests). The data analysis was centered at 5 years overall survival, 3 years disease free survival, 5 years progression free survival. The management protocol and guidelines for NMIBC/MIBC were evaluated and compared with the recent advancement of the bladder cancer treatment protocol and new strategies formulated for effective delivery of state of the art treatment.

Treatment design

(NMIBC)

Majority of the patients (69.6%, n=117, p=.0001) in the NMIBC group presented with a single mass in preliminary radiological investigation (USG/CECT Abdomen with Pelvis). Median dimensions of the UB mass lesion on USG examination was 2.5X2.2 [SD (L) - 1.14, (B)-1.49] and on CECT Abdomen with Pelvis was 3.35X3X2 [SD (L)-2.36, (B)-1.93, (H)-1.68]. All patients in the NMIBC population who were physically fit to undergo surgery with diagnostic and or curative intent were initially subjected to TUR biopsy (98.2%, n=165) and the prospective results with categorization are shown in the forthcoming tables and text. Compliance with BCG immunotherapy in authors study was at par with published data and even better in some cases. Although TURBT alone is not recommended for intermediate or high risk NMIBC, 24% of intermediate risk population and 9% of high risk patients received only TURBT with no further intra-vesical therapy as published in some recent studies.[6-8] All the patients falling in the category of high grade Ta/T1 (G2, G3) with less than equal to 3 lesions were further subjected to induction (once weekly for 6 weeks) and maintenance (once monthly for 12 months) BCG immunotherapy (69.6%, n=117). Twelve patients (7.1%) in the NMIBC population (T1, G3) underwent RC for high grade and multiple tumor masses presenting with concomitant primary CIS. Concomitant CIS was present in 35.6% (n=48, p=0.063) of the T1 sub-population and was predominant in male smokers in their sixth decade of life. Nine patients (5.4%) in the NMIBC group underwent adjuvant chemotherapy (AC) in the form of GC [Gemcitabine (1000 mg/m2 I/V on day 1, 8, 15), Cisplatin (70mg/m2 on day 2)] for a total of 4 cycles, 28 days apart. Patients (n=3) having deranged kidney function and who deteriorated post first cycle of GC were shunted for Carboplatin instead of Cisplatin. Maximum early recurrences (at 1st year of follow up) were seen with T1 (15.6%, n=21, p=.418) and G2 (17.9%, n=15, p=.269) population groups. HRQOL evaluation is crucial because these patients live constantly in fear of progression to MIBC over a long period of monitoring.[9,10] Currently there are only a few published studies regarding HRQOL in NMIBC population and the authors of the present study contemplate to evaluate this specific point in their next series.[11-18]

(MIBC)

The MIBC population presented upfront mostly with multiple tumors (72.7%, n=48, p=0.053). Median dimensions of the UB mass lesion on USG examination was 3.2X2.6 cm [SD (L) - 1.34, (B)-1.29] and on CECT Abdomen with Pelvis was 6.57X5.35X4.12 cm [SD (L)-2.57, (B)-1.79, (H)-1.59]. Only a select few patients in

the MIBC population who were fit for surgical management for either diagnostic or curative intent were subjected to TUR biopsy (50%, n=33) and the prospective results with categorization are shown in the forthcoming tables and text. Thirty patients (45.5%) further underwent RC with diversion with curative intent along with adjuvant GC chemotherapy after confirmation of muscle invasive biopsy report. Radical TURBT with intent of organ preservation along with follow up GC chemotherapy was performed in 31.8% (n=21) of the patients with maximum number of T3 category (37.5%, n=9) patients. Fifteen patients (22.72%) in the entire MIBC population mostly comprising the T4 population subcategory could only undergo cystoscopic biopsy under local anaesthesia and follow up chemotherapy. Recurrences within the first 3 years of follow up in the form of lung and liver metastasis were seen in 22.7% (n=15, p=0.001) of the MIBC population category.

RESULTS

(NMIBC)

Demographic data

There was a total of 168 patients in the NMIBC group with a majority of 39.3% (n=66) patients in the 60-69 years age group. There were 81.5% (n=137) male patients along with 18.5% (n=31) female patients in the NMIBC study population (p=0001).

Median age of the patient at surgery in the NMIBC population category was 62.3 years. The maximum number of patients amongst different grades of G1 and G2 following TURBT fell in the 60-69 years age group which was a total of 35.7% (n=15) and 46.4% (n=39) patients in the G1 and G2 grade category respectively (Grade, 1973 WHO definition). The second most common age group in terms of number of patients was 70-79 years harboring 35.7% (n=15) patients of G3 grade category there which was maximum as compared with any other age category. The maximum number of patients that we encountered in our study of NMIBC population (grade wise) were in G2 category (50%, n=84). The distribution of patients according to the WHO TNM stage was based on the individual tumor T stage following surgery (TURBT) and histopathological typing. There were 19.6% (n=33) patients in the Ta stage category along with 80.4% (n=135) patients in the T1 stage category respectively. The maximum number of patients in the Ta stage category (36.4%, n=12) were in 60-69 years age group while the same for T1 (40%, n=54) stage were in the same age category (60-69 years) as well.

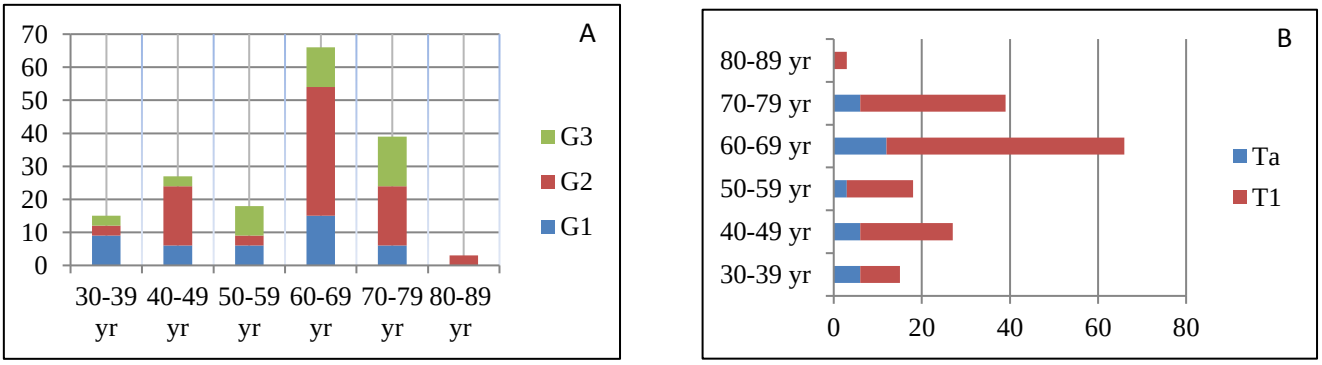

Figure 1 (A), (B): Grade and T stage distribution following surgery among various age categories in NMIBC population.

The distribution in the gender category was 81.5% (n=137) male patients along with 18.5% (n=31) female patients. The maximum number of male patients were seen in the G2 category with 53.28% (n=73) of the patients in that category. The maximum number of female patients were in G1 with 54.83% (n= 17) of the patients in the respective category. Likewise, the maximum number of male patients (83.9%, n=115) were in the T1 stage category while the maximum number of female patients (67.7%, n=20) were also present in the same T1 stage category as well.

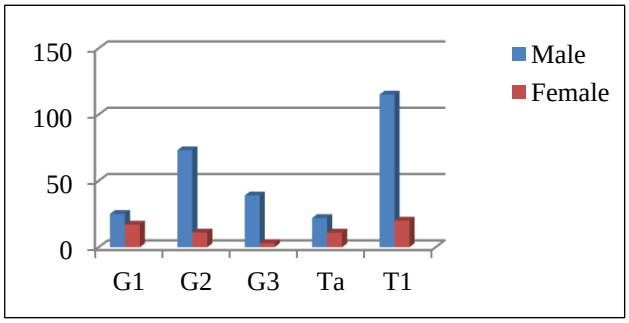

Figure 2: Grade and T stage distribution following surgery among gender categories in NMIBC population.

Etiological and clinical profile

NMIBC

Chronic smoking (> 20 pack years) along with common chemical exposure (Nitrate -N chemicals, DDT, endosulfan, dicofol, ethion, cypermethrin) for more than a period of 20 years was a dominating factor present in majority of these patients while analyzing patient's characteristics retrospectively. We found out that smoking was present in 78.6% (n=132) of the NMIBC population. The maximum number of patients who were affected by smoking were in G2 (85.7%, n=72) and G3 (85.7%, n=36) grades (p =0.00048). Tea plantation is a perennial crop grown extensively in areas of Assam and other NE states. This crop is mainly raised in a constant type of homogeneous environment which accounts for extensive pest growth. Recently there has been major dependency on pesticide use (7.35-16.75 kgha(-1)) with little emphasis on safety mechanism19. Chronic chemical exposure in form of occupational hazards was also recorded from the previous records and its duration determined. Our study found out that chronic chemical exposure (in any form) was present in 37.5% (n=63) of the NMIBC population. The maximum number of patients who were affected by smoking were in G3 (64.3%, n=27) and G2 (35.7%, n=30) grades (p =0.00001). Both characteristics (smoking and chemical exposure) significantly affected the G3 group patients (57.1%, n=24, p =0.00001).

Table 1: Grade distribution (NMIBC) with etiological characteristics.

Variable	G1	G2	G3	Total
Smoking	57.1% (n=24)	85.7% (n=72)	85.7% (n=36)	78.6% (n=132)
Pesticide	14.3% (n=6)	35.7% (n=30)	64.3% (n=27)	37.5% (n=63)
Smoking and pesticide	7.1% (n=3)	25% (21)	57.1% (n=24)	28.6% (n=48)
Hemorrhage	85.7% (n=36)	96.4% (n=81)	100% (n=42)	94.6% (n=159)
Irritative voiding	14.3% (n=6)	67.9% (n=57)	78.6% (n=33)	57.1% (n=96)
Hemorrhage and Irritative voiding	7.1% (n=3)	64.3% (n=54)	71.4% (n=30)	51.8% (n=87)
DM	28.6% (n=12)	42.9% (n=36)	57.1% (n=24)	42.9% (n=72)
CKD	14.3% (n=6)	25% (n=21)	35.7% (n=15)	25% (n=42)
DM+CKD	7.1% (n=3)	10.7% (n=9)	28.6% (n=12)	14.3% (n=24)
Urine cytology	14.3% (n=6)	53.6% (n=45)	92.9% (n=39)	53.6% (n=90)
No. of tumors				
Single	92.9% (n=39)	67.9% (n=57)	50% (n=21)	69.6% (n=117)
Multiple	7.1% (n=3)	32.1% (n=27)	50% (n=21)	30.4% (n=51)
Chronic analgesic use	21.4% (n=9)	28.6% (n=24)	50% (n=21)	32.1% (n=54)
Diet (Non-veg)	50% (n=21)	50% (n=42)	50% (n=21)	50% (84)

Table 2: T stage (NMIBC) distribution with etiological characteristics.

Variable	Ta	T1	Total
Smoking	63.6% (n=21)	82.2% (n=111)	78.6% (132/168)
Pesticide	27.3% (n=9)	40% (n=54)	37.5% (63/168)
Smoking and pesticide	18.2% (n=6)	31.1% (n=42)	28.6% (48/168)
Hemorrhage	90.9% (n=30)	95.6% (n=129)	94.6% (159/168)
Irritative voiding	36.4% (n=12)	62.2% (n=84)	57.1% (96)
Hemorrhage and irritative voiding	27.3% (n=9)	57.8% (n=78)	51.8% (n=87)
DM	36.4% (n=12)	44.4% (n=60)	42.9% (n=72)
CKD	18.2% (n=6)	26.7% (n=36)	25% (n=42)
DM+CKD	9.1% (n=3)	15.6% (n=21)	14.3% (n=24)
Urine Cytology	9.1% (n=3)	64.4% (n=87)	53.6% (n=90)
No. of tumors			
Single	90.9% (n=30)	64.4% (n=87)	69.6% (n=117)
Multiple	9.1% (n=3)	35.6% (n=48)	30.4% (n=51)
Chronic analgesic use	27.3% (n=9)	33.3% (n=45)	32.1% (n=54)
Diet (Non-veg)	45.5% (n=15)	51.1% (n=69)	50.0% (n=84)

While analyzing the incidence of smoking and chemical exposure of T stage in NMIBC population it was found that T1 group was maximally effected (Smoking: 82.2%, n=111, p = 0.031), (chemical exposure: 40%, n=54, p=0.023). The incidence of both characteristics in T1 category was 31.1% (n=42, p=0.020).

Almost all patients in NMIBC category presented with hematuria as evident from the Table 1, 2 and 3. Hematuria marked the trigger point for majority of the patients for hospital visit and indoor admission. The total incidence of hematuria in T1 and G3 population was 95.6% (n=159, p= 0.031) and 96.4% (n=81, p=0.009) respectively. Irritative voiding was present in 78.6% (n=33, p=0.0001) of G3 population and 62.2% (n=84, p= 0.01) of T1 population. Both the characteristics of hematuria and irritative voiding were maximally seen in the G3 (71.4%, n=30, p=0.0001) and T1 (57.8%, n=78, p=0.002).

DM type II and CKD were also remarkably noted in the NMIBC population spectrum with significant proportion of DM II mainly affecting the G3 (57.1%, n=24, p=0.03) and the T1 (44.4%, n=60, p=0.438) population categories. Noteworthy presence of CKD was also seen in G3 (35.7%, n=15, p=0.076) and T1 (26.7%, n=36, p=0.376) population categories. Simultaneous presence of both chronic diseases were maximally seen in G3 (28.6%, n= 12, p=0.008) and T1 (15.6%, n= 21, p=0.418) population.

Urine cytology was consistently performed in all the indoor patients at the time of admission. Positive urine cytology was significantly present in 92.9% (n=39, p=0.0001) of G3 population and 64.4% (n=87, p=0.0003) of the T1 population. The incidence of positive urine cytology was only 14.3% (n=6) in G1 category and a meager 9.1% (n=3) in Ta population group. Chronic analgesic consumption was present in 50% (n=21, p=0.012) of the G3 population and 33.3% (n= 45, p=0.541) of T1 population category. Non-vegetarian diet was present in almost 50 % cases of each subgroup (Grade) of NMIBC and 45.5% (n=15) of Ta and 51.1% of (n=69) T1 population (stage) (p=0.695).

MIBC

Demographic data

There was a total of 66 patients in the MIBC group with a majority of 31.8 % (n=21) patients in the 50-59 years age group. A peculiar inference was obtained while analyzing age group data in the MIBC group in which we observed that the mean age of the male population was 56.6 years and the mean age of the female population was 54.4 years. There was a clear early age migration towards the MIBC study group in our analysis. In the study population of MIBC patients 45.45% (n=30) of patients were diagnosed to have T2 stage while the percentage of T3 and T4 stage in the same population was 36.36% (n=24) and 18.18% (n=12) respectively. Non-organ confined cases at the time of diagnosis were 54.54% (n=36).

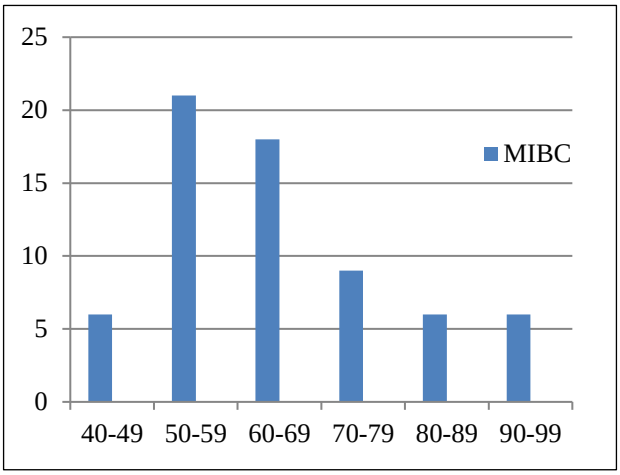

Figure 3: Age group distributions in MIBC groups.

Etiological and clinical profile

Smoking was rampant in the MIBC study population with 95.5% (n=63, p=0.034) of the study population being affected by the menace. Chronic chemical exposure was present in 72.7% (n=48, p=0.028) of the MIBC population. Both characteristics (smoking and chemical exposure) significantly affected the T2 sub group patients (80%, n=24, p =0.017).

Not surprisingly all patients of MIBC category presented with hematuria as evident from the table. The maximal incidence of irritative voiding was present in 80% (n=24, p=0.003) of T2 sub population. Both the characteristics of hematuria and irritative voiding were maximally seen in the T2 sub population as well (n=24, p=0.003). DM type II and CKD were also explicitly noted in the MIBC population spectrum with significant proportion of DM II mainly affecting the T3 and the T4 sub population categories (p=228). Significant presence of CKD was also seen in T3 and T4 (p=0.005) population categories. Simultaneous presence of both chronic diseases was maximally seen in T4 (75%, n= 9, p=0.302). Positive urine cytology was significantly present in all patients of T3 sub population and 75% (n=9, p=0.014) of the T4 sub-population. Chronic analgesic consumption was present in 50% (n=12, p=0.054) of the T3 population.

Follow up data and survival statistics

A total number 78 patient who had completed 5 years regular follow up and who were admitted and treated at Department of Urology and Renal Transplantation, Gauhati Medical College Hospital from a period of January 2008 to January 2012 were recently analyzed for survival characteristics. The 5 years OS (overall survival), DFS (disease free survival), PFS (progression free survival) were estimated. Here we would like to state that we have excluded all those patients who have been

out of follow up for more than 3 months in the first 2 years and yearly thereafter till 5 years.

Table 3: T Stage (MIBC) distribution with etiological characteristics.

Variable	T2	T3	T4	Total
Smoking	90% (n=27)	100% (n=24)	100% (n=12)	95.5% (n=63)
Pesticide	80% (n=24)	62.5% (n=15)	75% (n=9)	72.7% (n=48)
Smoking and pesticide	80% (n=24)	62.5% (n=15)	75% (n=9)	72.7% (n=48)
Hemorrhage	100% (n=30)	100% (n=24)	100% (n=12)	100% (n=66)
Irritative voiding	80% (n=24)	50% (n=12)	100% (n=12)	72.7% (n=48)
Hemorrhage and irritative voiding	80% (n=24)	50% (n=12)	100% (n=12)	72.7% (n=48)
DM	80% (n=24)	87% (n=21)	100% (n=12)	62.4% (n=57)
CKD	50% (n=15)	75% (n=18)	100% (n=12)	68.2% (n=45)
DM+CKD	50% (n=15)	62.5% (n=15)	75% (n=9)	59.1% (n=39)
Urine cytology	70% (n=30)	100% (n=24)	75% (n=9)	81.8% (n=54)
No. of tumors				
Single	30% (n=9)	12.5% (n=3)	50% (n=6)	27.3% (n=18)
Multiple	70% (n=21)	87.5% (n=21)	50% (n=6)	72.7% (n=66)
Chronic analgesic use	20% (n=6)	50% (n=12)	25% (n=3)	31.8% (n=21)

Table 4: Survival statistics for NMIBC population.

Stage/grade	5 years OS (overall survival)	3 years DFS (disease free survival)	5 years PFS (progression free survival)
pTa	81.81% (n=9)	72.72% (n=8)	72.72% (n=8)
pT1	74.44% (n=32)	62.7% (n=27)	65.11% (n=28)
Grade 2	76.19% (n=16)	66.67% (n=14)	71.40% (n=15)
Grade 3	64.23% (n=9)	57.14% (n=8)	64.30% (n=9)

Table 5: Survival statistics for MIBC population.

Stage/grade	5 year OS (overall survival)	3 year DFS (disease free survival)	5 year PFS (progression free survival)
pT2	70% (n=7)	60% (n=6)	60% (n=6)
pT3	62.5% (n=5)	50% (n=4)	62.5% (n=5)

Recurrence pattern (NMIBC+MIBC)

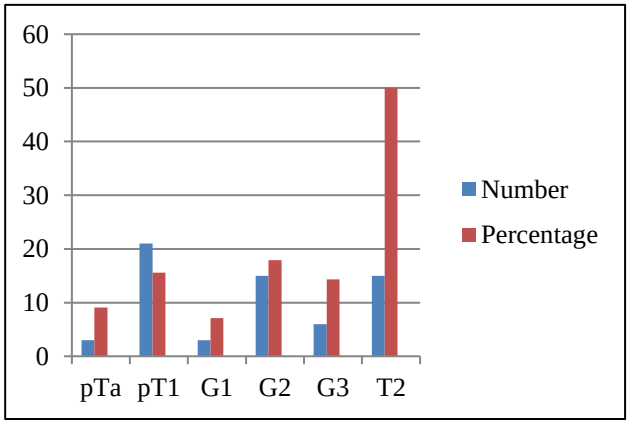

Figure 4: Recurrence data for (NMIBC+MIBC) study population (grade + stage).

NMIBC population

In the NMIBC study population 9.1% (n=3) patients with stage Ta and 15.6% (n=21) patients with stage T1 had tumor recurrence at 6 month which were treated with re - TURBT (p=0.258). Nearly 7.1% (n=3) patients with Grade 1 and 17.9% (n=15) of the patients with grade 2 had recurrent growth during first year of follow up and were treated with Re-TURBT. Grade 3 population were also affected with recurrence during the first 6 months post initial TURBT (14.3%, n=6) (p=0.269). In the MIBC study population the T2 study population had 50% recurrence rate (n=15) at 24 months which included patients treated upfront with radical TURBT (n=6) and radical cystectomy (n=9) (p=0.001).

DISCUSSION

This retrospective analysis showed that the population of urinary bladder cancer patients treated in our institute was highly heterogeneous. The characteristic of urinary bladder cancer patients included in our analysis were similar to those of the patients enrolled in many clinical trials. The single-institutional study showed that bladder cancer management at our setup encompasses a well-defined and robust diagnostic and therapeutic protocol along with timely intervention to decrease the risk of progression of NMIBC cases to MIBC and MIBC to metastatic cases. All the mentioned categorical variables in the Table 6 were significantly related to the corresponding grade in the NMIBC study population. Smoking, chemical exposure, irritative voiding were significantly correlated with both grade and stage of NMIBC population. Chronic kidney disease was also significantly correlated with the MIBC study population in addition to the previously mentioned factors.

Table 6: Correlation analysis according to Grade (NMIBC).

Variable	Pearson Chi square	P value (2 tailed)	Significance	Correlation (Pearson's R)	P-value	Significant correlation
Smoking	15.273	0.00048	Significant	0.246	0.001	Significant
Pesticide	22.629	0.00001	Significant	0.365	0.001	Significant
Smoking and pesticide	26.775	0.00001	Significant	0.391	0.001	Significant
Hemorrhage	9.509	0.009	Significant	0.224	0.003	Significant
Irritative voiding	43.313	0.0001	Significant	0.459	0.001	Significant
Hemorrhage and irritative voiding	45.272	0.0001	Significant	0.455	0.001	Significant
DM	7.0	0.030	Significant	0.204	0.008	Significant
CKD	5.143	0.076	Not-significant	0.175	0.023	Significant
DM+CKD	9.625	0.008	Significant	0.217	0.005	Significant
Urine cytology	52.129	0.0001	Significant	0.557	0.001	Significant
Chronic analgesic use	8.842	0.012	Significant	0.216	0.005	Significant

(P value < 0.05 - Significant)

Table 7: Correlation analysis according to T stage (NMIBC).

Variable	P value (2 sided)	Significant/NS	Correlation (Pearson's R)	P-value	Significant correlation
Smoking	0.031	Significant	0.180	0.020	Significant
Pesticide	0.023	Significant	0.104	0.178	NS
Smoking and pesticide	0.020	Significant	0.114	0.142	NS
Hemorrhage	0.031	Significant	0.082	0.291	NS
Irritative voiding	0.010	Significant	0.208	0.007	Significant
Hemorrhage and irritative voiding	0.002	Significant	0.243	0.002	Significant
DM	0.438	NS	0.065	0.403	NS
CKD	0.376	NS	0.078	0.316	NS
DM+CKD	0.418	NS	0.073	0.344	NS
Urine cytology	0.0003	Significant	0.058	0.001	Significant
Analgesic use	0.541	NS	0.052	0.507	NS
Diet (Non-veg)	0.695	NS	0.045	0.563	NS

(P value < 0.05 - Significant).

The main objectives of the analysis were to calculate the disease-free survival (DFS) for patients with completely resected tumors and to determine the progression free survival (PFS) for patients with post-operative residual disease and patients who did not receive a surgical treatment upfront. Our 60 months follow up of the 78 patients with 54 patients in the NMIBC group and 24 patients in the MIBC study population showed encouraging result. We are aware of numerous drawbacks in our series including, apart from the fact it was a single center study, low number of patients in the follow up series (n=78) completing 5 years observation period and retrospective character.

Table 8: Correlation analysis according to T stage (MIBC).

Variable	Pearson Chi square	P-value	Significance	Correlation Pearson's R	P-value	Significant correlation
Smoking	6.771	0.034	Significant	0.572	0.028	Significant
Pesticide	7.097	0.028	Significant	-0.587	0.048	Significant
Smoking and pesticide	8.096	0.017	Significant	-0.687	0.048	Significant
Irritative voiding	11.550	0.003	Significant	0.050	0.693	NS
Hemorrhage and irritative voiding	11.550	0.003	Significant	0.050	0.693	NS
DM	2.953	0.228	NS	0.209	0.092	NS
CKD	10.886	0.005	Significant	0.402	0.001	Significant
DM+CKD	2.397	0.302	NS	0.191	0.125	NS
Urine cytology	8.525	0.014	Significant	0.143	0.252	NS
Analgesic use	5.846	0.054	NS	0.118	0.344	NS
Diet (Non-veg)	2.700	0.259	NS	-0.121	0.332	NS

(P value < 0.05 - Significant).

However, to the best of our knowledge in this part of the world, this is one of the first comprehensive analysis of 200 odd patients including both NMIBC and MIBC patient groups spanning a 10-year period. From our experience, we have learnt two essential assumptions: firstly, patients' good compliance is fundamental during the active treatment and secondly that a close and continuous collaboration between Urologists, Medical Oncologists and Radiation Oncologists is of extreme importance in order to reach an optimal multidisciplinary approach. According to a similar series of 230 patients who underwent RC with PLND and TURBT as their treatment schemes, 5 years OS was 74% for pT2 stage and 80% for pTa stage which is similar to that achieved in our series.20 The 5 year PFS in the same series for pT2 and pT3 stage patients was 57% and 55% which was comparable to our study.

We have seen while analyzing the data at our setup that the 5 years OS for grade 3 patients in NMIBC group was 64.23%. Majority of these tumors presented with multiple masses which meant that timely RC with PLND and diversion was an important aspect in their treatment as these grade 3 tumors had 50% (n=7) recurrence rate and 5 years PFS was a low 64.3% (n=90). NAC was utilized in 10% (n=3) cases of T2N0M0 and 12.5% (n=3) cases of T3N1M0 before RC and the patients were under surveillance for the last 2 years without any evidence of recurrence. Smoking in male and female population under scanner was an important aspect in authors study and there is a paucity of literature in NE India about its correct incidence. Higher incidence rates in men could also reflect occupational exposures since men are more likely than women to work in specific conditions that have been associated with bladder cancer risk, such aromatic amine-manufacturing worker, leather worker, painter, machinist, and aluminum worker.[21-24]

Comparing the current scenario of smoking and chemical exposure in this part of the world with the NIH-AARP cohort in the USA, where the prevalence of smoking is generally similar in men and women the population attributable risk (PAR) for smoking was about 50% in both sexes.[25,26] Previous studies have found PARs of 50-65% in men and 20-30% in women but were conducted in populations where the prevalence of smoking in women was considerably lower than in men.[27-31] Renal impairment was also an important issue in the timely management of the NMIBC population in this part of the world as suggested by the presented data. Up to 40% of patients with bladder cancer have renal impairment, defined as a creatinine clearance ≤60 ml/min, as calculated by the Cockroft-Gault formula.[32] Renal insufficiency may be disease related, caused by ureteral blockage, prior nephrectomy or, more often, age-related decrease in the glomerular filtration rate (GFR).[33]

Under-utilization of NAC in our study design has been a major finding in our analysis and optimal utilization of Radical TURBT and NAC is currently more desirable in our future strategy. Buoyed by the aforementioned results we would like to progress to bladder preservation protocols for our future cases on a more frequent basis.

CONCLUSION

The guidelines for MIBC/NMIBC from the EAU, AUA, NCCN provide considerable consensus regarding the management of this often-dreaded disease. Despite a paucity of high level evidence regarding the majority of management topics in urinary bladder cancer in North Eastern part of the country, there was general agreement among the various guideline panels and management guidelines at our institution. Identification of the upfront clinical parameters suggesting severity of disease and time to progression are the two most important domains which will decide the future of UB carcinoma treatment in this part of the world. Categories of evidence synthesized and grades of recommendations will have to

be constantly gazed upon to modify and enhance future treatment strategies.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Rajeev TP, Singh Y, Barua SK, Sarma D. Single center experience of urinary bladder malignancy: a 10-year retrospective analysis of hospital data. Int Surg J 2017;4:2460-9.