

The Discrepancy between the AUA Guidelines and Daily Practice in Management of Non-Muscle Invasive Bladder Cancer among Selected Group of Iraqi Urologists

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ABSTRACT

Background: Bladder carcinoma is the predominant malignancy among males and ranks fifth among females in Iraq. Non-muscle invasive bladder cancer management requires strict follow up and updated guidelines.

Objective: To assess the concordance between the current clinical practices & update guidelines for the diagnosis, treatment & follow up of non-muscle invasive bladder cancer among selected group of Iraqi urologists working in highly specialized teaching center.

Patients and methods: A prospective single center study conducted in Urology department of Al-ShahedGazi Al-Hariry Teaching Hospital for Surgical Subspecialties in one year duration from 1st of October, 2016 to 30th of September, 2017 on sample of 41 case of non-muscle invasive bladder cancer. Study questionnaire included daily practices in non-muscle invasive bladder cancer management among selected group of Urologists working in hospital with different level of certification.

Results: The results demonstrated that transurethral resection of bladder tumor was done for all of patients with low and high risk groups, while the Re-transurethral resection of bladder tumor was done for 40.9% of high risk group patients just. The single Mitomycin C instillation was carried out in 94.7% of low risk group and in 90.9% of high risk group, while the adjuvant Mitomycin C was carried out in 63.2% of low risk group and in 72.7% of high risk group. The intravesical Bacillus calmetteguerin and stenting were carried out only in 27.3% of high risk group patients but no patient of low risk group underwent any of these modalities of treatment.

Conclusion: There is good concordance in the daily practice of selected urologists regarding management of low risk group of non-muscle invasive bladder cancer patient with the guidelines, but poor concordance regarding high risk group.

Keywords: Non-Muscle Invasive Bladder Cancer, Management, Guidelines, AUA

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INTRODUCTION:

Nearly three quarters of all bladder cancer diagnoses are classified as non-muscle invasive (NMIBC). This type of cancer mostly affects the bladder's urothelial wall and is defined as carcinoma in situ (CIS), stage 6, or Ta.1 (1). Despite NMIBC not being acutely life-threatening, it presents considerable therapeutic difficulties due to its elevated recurrence and progression rates. Approximately 50%-70% of individuals encounter a relapse following initial therapy, and as many as 30% advances to muscle-invasive or metastatic conditions. For many years, Bacillus Calmette-Guérin (BCG) treatment following transurethral resection of bladder tumour (TURBT) has constituted the conventional approach for high-risk (HR) NMIBC, significantly diminishing recurrence and progression rates. Nonetheless, BCG treatment is ineffective for approximately 40% of patients, necessitating further procedures (2). Traditionally, radical cystectomy has been the favored intervention for these individuals, providing disease management but resulting in considerable morbidity and changes in quality of life (3).

Various genetic, environment, or molecular variables are among the many complicated reasons that contribute to the pathogenesis of bladder cancer. Mutations in tumour suppressor genes, receptors for growth factors, and genes involved in DNA repair account for the vast majority of cases. A mutation in FGFR3 is present in 70% of bladder cancer patients, while HRAS mutations occur in 30%. Cigaret consumption is regarded as the primary contributor to bladder cancer, with around 50% of bladder cancer instances in affluent nations linked to smoking (4). Additional significant risk factors include exposure to specific medications like chemotherapy, particularly cephalosporin, as well as alcohol consumption, obesity, and arsenic. Patients with persistent urinary tract infections, prolonged urinary catheterization, and bladder calculi face an elevated chance of developing bladder cancer (5). The American Joint Committee on Cancer (AJCC) TNM system is the gold standard for bladder cancer staging (6); it identifies tumors according to whether they have spread locally, to lymph nodes, or to distant sites of metastasis (M) (7).

Precise staging of bladder cancer is crucial for determining the optimal treatment strategy. To assess the efficacy of the treatment and the likelihood of a positive outcome, the pathologic stage (pTNM) is the gold standard. Among the most reliable predictors of bladder cancer

prognosis, this staging system is still in use today (8). Three out of ten patients show signs of muscle-invasive disease (T2-4), which carry a significant risk of metastases to distant regions, whereas around 70% of patients present with superficial tumors (Ta, T1, carcinoma in situ) (9). Furthermore, the recurrence rate of superficial tumors ranges from 50% to 70%, with an approximate 10–20% likelihood of advancing to muscle-invasive illness. Consistent monitoring of non-muscle-invasive bladder cancer (NMIBC) with routine cystoscopy and, where necessary, upper tract imaging is crucial (10).

In Iraq, studies discussing compliance of Urologists with updated guidelines for the management of NMIBC remain scarce to date, and further studies are still required in this field. Therefore, this study aimed to assess the concordance between the current clinical practices & updated guidelines for the diagnosis, treatment & follow up of NMIBC among selected group of Iraqi urologist working at highly specialized teaching center.

PATIENTS AND METHODS:

A prospective single center study conducted in Urology department of Al-ShahedGazi Al-Hariry Teaching Hospital for Surgical Subspecialties in one year duration from 1st of October, 2016 to 30th of September, 2017, on sample of 41 patients with NMIBC.

Inclusion criteria:

Adults Iraqi patients with proved diagnosed NMIBC

Exclusion criteria:

1. Patients with muscle invasive Bladder Cancer.
2. Tumor in bladder diverticulum.
3. Patients who were unfit for surgery and incomplete resection.

Ethical considerations:

The study was conducted after approval from Ethics Committee of the Iraqi Board of Medical Specialities. Informed consent was obtained from each patient and all patients were assured that their information would be kept confidential and would be used for research purposes only.

Data collection and statistical analysis:

The collected patients' Data of included sociodemographic characteristics (age, gender, family history and occupation), diagnostic modalities (cytology, abdominal ultrasound, abdominal CT-scan, flexible cystoscopy and cystoscopy), treatment types (TURBT, RETURBT, single MMC instillation, BCG and stenting) and risk status of NMIBC (low risk or high risk). All patient diagnosed to have NMIBC as a result of detailed history, complete physical examination which reveal non palpable tumor before and after TURBT, urine cytology was done for 6 patient, imaging which include abdominal US was done for all of the patient and CT scan was done for 31 patient for evaluation of bladder tumor and upper tract regarding concomitant tumor or hydronephrosis. The study statistics was accomplished through using statistical package of social sciences, version 26 and apply of chi-square or fissures exact tests for categorical variables. Level of significance was 0.05 or less.

RESULTS:

The mean age of the studied group was 61.5 ± 11.7 years. Our patients were grouped into two subgroups according to risk; the high risk group which consisted of 22 patients (including T1 & CIS) & the low risk group which consisted of 19 patients (Ta). The findings showed that 51.2% were male, 17.1% had positive family history of disease and 78% of them were unemployed. However, no significant association between status of risk of NMIBC and each of the; gender, family history of the disease and occupation (P. value>0.05) (**Table 1**).

To confirm the diagnosis for patients in low and high risk groups, white light rigid cystoscopy and abdominal ultrasound were used in all patients of both low and high risk groups. The abdominal CT scanning used in 73.7% of low risk group and 77.3% of high risk group, flexible cystoscopy in 57.9% of low risk and 36.4% of high risk group and cytology done for 15.8% of low risk group and 13.6% of high risk group, in total, Cystoscopy and Abdominal U/S were done for all of the 41 (100.0%) patients while Abdominal CT scan in 31 (75.6%) patients, Flexible cystoscopy in 19 (46.3%) and Cytology in only 6 (14.6%) patients, however, no significant association was found between risk status and the used diagnostic modalities, (P. value >0.05), (**Table 2**).

Among the 41 participant patients, all underwent TURBT while 22% underwent Re-TURBT, 92.7% had a single instillation MMC, 68.3% adjuvant MMC, 14.6% received intravesical BCG & 14.6% of patients got ureteric stenting. No significant difference in using the TURBT according to risk status where it was done for all patients of low and high risk groups, while the RETURBT was done for 40.9% of high risk group patients but no patient of low risk group and this difference was statistically significant (P. value=0.002). The single MMC instillation was carried out in 94.7% of low risk group and in 90.9% of high risk group as well as the adjuvant MMC was carried out in 63.2% of low risk group and in 72.7% of high risk group, however no significant difference reported with these treatment modalities, (P. value >0.05). Each of intravesical BCG and stenting were carried out in 27.3% of high risk group patients but none of low risk group with a statistically significant difference (P. value <0.05), (**Table 3**).

Table 1. Distribution and comparison of sociodemographic characteristics of the risk groups

Variable		Groups				Total		P. value
		Low risk (Ta)		High risk (T1, CIS)				
		No.	%	No.	%	No.	%	
Gender	Male	10	47.6	11	52.4	21	51.2	0.884
	Female	9	45	11	55	20	48.8	
Family history	Positive	2	28.6	5	71.4	7	17.1	0.535
	Negative	17	50	17	50	34	82.9	
Occupation	Employed	3	33.3	6	66.7	9	22.0	0.612
	Unemployed	16	50	16	50	32	78.0	
Total		19	46.3	22	53.7	41	100.0	

Table 2. Association between diagnostic modality and risk status

Diagnostic modality		Groups				Total		P. value
		Low risk		High risk				
		No.	%	No.	%	No.	%	
Cystoscopy	Yes	19	100	22	100	41	100.0	-
	No	0	-	0	-	0	0.0	
Abdominal U/S	Yes	19	100	22	100	41	100.0	-
	No	0	-	0	-	0	0.0	
Abdominal CT scan	Yes	14	73.7	17	77.3	31	75.6	0.922
	No	5	26.3	5	22.7	10	24.4	
Flexible cystoscopy	Yes	11	57.9	8	36.4	19	46.3	0.217
	No	8	42.1	14	63.6	22	53.7	
Cytology	Yes	3	15.8	3	13.6	6	14.6	0.803
	No	16	84.2	19	86.4	35	85.4	

Table 3. Association between type of treatment and risk status

Type of treatment		Groups				Total		P. value
		Low risk		High risk				
		No.	%	No.	%	No.	%	
TURBT	Yes	19	100.0	22	100.0	41	100.0	-
	No	0	0.0	0	0.0	0	0.0	
RETURBT	Yes	0	0.0	9	40.9	9	22.0	0.002*
	No	19	100.0	13	59.1	32	78.0	
Single MMC	Yes	18	94.7	20	90.9	38	92.7	0.894
	No	1	5.3	2	9.1	3	7.3	
Adjuvant MMC	Yes	12	63.2	16	72.7	28	68.3	0.748
	No	7	36.8	6	27.3	13	31.7	
Intravesical BCG	Yes	0	0.0	6	27.3	6	14.6	0.021*
	No	19	100.0	16	72.7	35	85.4	
Stenting	Yes	0	0.0	6	27.3	6	14.6	0.021*
	No	19	100.0	16	72.7	35	85.4	

DISCUSSION:

The guidelines are important component of medical practice for certain disease in which the level of evidence is not so high to avoid question, so it is reasonable to expect a great level of concordance between the guidelines and medical practice (11). However in this study we found some discrepancy between the guidelines and current practice regarding NMIBC diagnosis and treatment.

Regarding low risk bladder cancer (Ta) diagnosis and treatment this study found that there was good compliance with the guidelines as most of our patients receiving intravesical MMC after TURBT either single cycle 94.7% or 6 cycles adjuvant intravesical MMC 63.2 % in comparative to study (50) who found poor concordance to the guidelines and only 7.5% of patients received intravesical MMC post TURBT. Another study showed that Intermediate-risk patients in Europe were more likely to receive a single immediate postoperative instillation of chemotherapy and 6 cycles intravesical chemotherapy 12. In this study isolated TURBT was done for 3 patients of the sample about 7.3% of patient with bladder cancer that was small papillary lesion and completely resected so this study did not offer intravesical chemotherapy as compared with other authors (12) who use TURBT monotherapy for 9% of patients. In high risk bladder tumor (T1 & CIS) there is good compliance with intravesical chemotherapy but poor compliance with immunotherapy. Another study in Spain (13) found 39.8 % received

BCG, while another Italian study (14) revealed 12.5% of patients received intravesical chemotherapy and 66% of high risk bladder cancer received BCG. The cause for lower percentage of patient receiving immunotherapy as some of current study patients were old age, immunocompromised and cannot tolerate BCG side effect and some time the drug was not available in the hospital and the patients cannot afford to buy it. Regarding Re-TURBT which was done for 22% of all NMIBC cases and when stratifying patients according to risk group, Re-TURBT was done for 40.9 % of high risk (T1 & CIS), but no patient with low risk (Ta) group underwent Re-TURBT. When compared with Italian study 14 which revealed 49.2 % of high risk patients underwent Re-TURBT and with (another study (50) showed that 67.7 % of high risk patient underwent Re-TURBT. Another study show Re-TURBT was done for 28% 13 while some authors (15) found that Re-TURBT was done for 10.4% of patients. This is because Re-TURBT is a second procedure done within 2-4 weeks after the primary procedure this make patient compliance with surgery difficult. Flexible cystoscopy was done for 46.3 % of all study patient; 57.9 % for low risk group (Ta) and 36.4% for high risk group (T1 & CIS). This modality was used for patient presented with hematuria but had no bladder mass on US (16 patients had no bladder mass of 19 patients who underwent flexible cystoscopy) about 84% so we proceed with flexible cystoscopy to decrease risk, cost & complication of rigid cystoscopy. As compared to another study (16) who found the use of Flexible cystoscopy is feasible and appears comparable with rigid white light cystoscopy. Another study show that all patients underwent flexible cystoscopy except patients with positive CT urography for bladder cancer are directly referred for rigid cystoscopy (17).

Stenting in present study was done for 14.6 % of all patients, 27.3% of high risk group (T1 & CIS), but no stenting for low risk group (Ta), and 40% of patients with lateral bladder mass according to imaging study. This was done for patient with hydronephrosis or high renal indices to improve upper tract drainage and renal function and decrease risk of subsequent stenosis after TURBT. There are two common studies that discuss the advantage and disadvantage of ureteric stenting during TURBT (18, 19). Urine cytology was done for 14.6 % of all patients, 15.8% of low risk (Ta) and 13.6 % of high risk group (T1 & CIS). This is because urine cytology is specific but has poor sensitivity especially for low risk tumor. One study showed that the role of urine cytology seems to be limited for detection of patients who would

likely develop high-grade and recurrent tumors (20). Another study showed that the sensitivity of urine cytology is too low to explain its use as screening for patient presented with hematuria and replaced by rapid diagnosis clinic using CT urography and flexible cystoscopy (17). In this study we find that most of the urologists in our hospital are compliant with the updated guidelines that may be because of the attendance of many meetings and conferences regarding the updated guideline in this highly specialized teaching center and frequent attendance of AUA and EAU annual meetings.

CONCLUSION:

This study concluded a good concordance in the daily practice of selected urologists regarding management of low risk group (Ta) NMIBC patient with the guideline, but poor concordance regarding high risk group (T1& CIS) especially regarding intravesical BCG treatment for high risk patient with NMIBC. This study recommended regular attendance for meetings and conferences regarding updated guidelines and try to apply it as much as possible.

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