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Characteristics of Patients Undergoing Open Radical Cystectomy for Management of Muscle Invasive Bladder Cancer in A Tertiary Centre in Egypt

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Authors' contributions

This work was carried out in collaboration among all authors. Author ML designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Authors MR and AH managed the analyses of the study. Author ME revised and edited the final version of the manuscript. All authors read and approved the final manuscript.

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Original Research Article

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ABSTRACT

Aims: To represent the demographic and functional data of a cohort of patients with invasive bladder cancer managed with Open Radical Cystectomy (ORC) in the Urology Department of Tanta University Hospital between January 2019 and January 2021.
Methodology: A retrospective analysis was performed on the records of ORC for the period between January 2019 and January 2021. This cross-sectional study was done in the Urology Department, Tanta University Hospital in Egypt.
Results: Data of 47 patients were collected. Most of the patients in were males (34 patients (72.3%), with male to female ratio of 3:1. Most of the patients were either smokers or ex-smokers, while only 18 patients (38.3%) never smoked before. Visible hematuria was the most common symptom at presentation (35 patients) 74.5%. The main radiological imaging used for staging was CT Urography. Most of the tumors were urothelial in 66% of patients. Squamous differentiation was the most common non urothelial variant with 8 patients. The presence of other non-urothelial variant histology was present in 6 patients.

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Conclusion: This study revealed that in the tertiary hospital of Tanta University, the mean age of patients presented with bladder cancer and undergoing ORC, was 63.5 years. Visible haematuria was the most common complaint reported. The use of MRI is valuable in staging of locally advanced bladder cancer. Most of the tumours were urothelial (66%) with significant reduction in the incidence of squamous cell bladder cancer than the previously reported data. Neoadjuvant chemotherapy has become an integral part of the treatment protocol in cases of muscle invasive bladder cancer.

Keywords: Radical cystectomy; urinary bladder; bladder cancer; characteristics.

1. INTRODUCTION

Bladder cancer (BC) is the most common urological malignancy in Egypt as it comes as the second most common cancer in males of all ages after liver cell cancer. In addition, it represents a staggering healthcare problem being the second most common urological cancer worldwide [1,2].

Open radical cystectomy (ORC) remains the gold standard of care for patients with muscle invasive bladder cancer and for those with high-risk and recurrent non-muscle-invasive disease, providing efficacy regarding local control and long-term disease-free survival [3,4]. However, ORC is associated with high perioperative complications, including significant intraoperative blood loss even when performed by the experienced surgeons [5]. Additionally, ORC involves longer incisions, prolonged abdominal wall retraction both leading to higher post-operative pain and increased wound complications. Exposure of the peritoneal surface during the procedure leads excessive fluid losses. Manual dissection in the boundaries of the narrow pelvis is challenging particularly in the retro vesical area [6,7].

The results of radical cystectomy widely vary between different centres all over the world. Therefore, we represent the demographic and functional data of a cohort of patients with invasive bladder cancer managed with ORC in the Urology Department of Tanta University Hospital between January 2019 and January 2021.

2. MATERIALS AND METHODS

2.1 Study Design

This is a cross sectional study with a retrospective analysis of performed on the records of ORC for the period between January 2019 and January 2021.

2.2 Study Population

All patients scheduled on the ORC list in the relevant period were included in the study.

2.3 Outcome Measurements

Clinical variables included baseline patients' characteristics including age, body mass index (BMI), Charlton Comorbidity Index (CCI) [8] and full laboratory investigations were gathered. The WHO performance status was documented [9], and the American Society Association ASA score [10,11]. Surgical Technique is a standard ORC performed by expert surgeons (MA, AH, MR) in Tanta University Hospital.

2.4 Statistics

All statistical analysis was performed using SPSS version 26 software (IBM SPSS Statistics, IBM Corp., Armonk, NY).

3. RESULTS

3.1 Patients' Characteristics

Baseline demographic and functional data are summarized in (Table 1). Most of the patients in were males (34 patients (72.3%), with male to female ratio of 3:1 in total of the study population. The mean age was 63.5 ± 6.68 years. The minimum age was 48 years, and the maximum age was 78 years. The majority of the patients were either smokers or ex-smokers, while only 18 patients (38.3%) never smoked before. The mean BMI was 27.7 ± 5.5 kg/m^2. For standardization of the description of the patients' comorbidities and functional state, three widely acceptable measures were used.

Table 1. Patients' demographic data

Demographic data	(n = 47)	
	No.	%
Sex		
Male	34	72.3
Female	13	27.7
Age (years)		
Min. – Max.	48.0 – 78.0	
Mean ± SD.	63.51 ± 6.68	
Median (IQR)	64.0 (60.0 – 69.0)	
Smoking status		
Non-smoker	18	38.3
Smoker	11	23.4
Ex-smoker	18	38.3
Height (m)		
Min. – Max.	1.56 – 1.96	
Mean ± SD.	1.72 ± 0.09	
Median (IQR)	1.73 (1.67 – 1.77)	
Weight (kgs)		
Min. – Max.	54.0 – 124.20	
Mean ± SD.	80.67 ± 13.56	
Median (IQR)	80.0 (72.15 – 89.60)	
BMI (kg/m^2)		
Min. – Max.	18.01 – 52.30	
Mean ± SD.	27.70 ± 5.55	
Median (IQR)	28.0 (24.67 – 29.72)	
ASA score		
1	13	27.7
2	23	48.9
3	11	23.4
Calculated charlson comorbidity index		
Min. – Max.	2.0 – 10.0	
Mean ± SD.	5.09 ± 1.79	
Median (IQR)	5.0 (4.0 – 6.0)	
Performance status		
0	39	83.0
1	8	17.0

3.2 Presentation and Staging

Visible hematuria was the most common symptom at presentation (35 patients) 74.5%. This was followed by presence of significant lower urinary tract symptoms mainly storage type in the second order with (9 patients) 19.1%. Table 2 illustrates the common presentations among the included patients.

The main radiological imaging used for staging was CT Urography. For more details about local disease progression or when there is a lack of clarity about clinical staging, MRI of the bladder and the pelvis was used in total of 8 patients. The use of PET CT was limited to only one patient with suspected metastatic disease due to abnormal LNs in imaging. Four patients had significant hydronephrosis in the imaging results (all unilateral) as shown in (Table 3).

All patients underwent a formal cystoscopic TURBT and the specimen was sent for histopathological examination. The results of the histopathology and the provisional clinical staging are demonstrated in (Table4). The results showed that most of the tumors were urothelial in 66% of patients. Squamous differentiation was the most common non urothelial variant with 8 patients. The presence of other non-urothelial variant histology was present in 6 patients, one patient had undifferentiated carcinoma. The majority of the patients were clinically staged T2 disease (22 patients). Three

patients (6.4%) were staged T3 (locally advanced disease). It was noted that all patients who were categorized with locally advanced disease, had non urothelial variants in their TURBT histology. One patient had suspicious pathologic lymph nodes in imaging. Four patients staged as Ta were operated due to BCG failure.

Ten patients had a history of previous BCG intravesical therapy for either recurrent or HR-NMIBC.The presence of CIS in the TURBT histology was present in 28 patients. The presence of lymph-vascular invasion was detected in 5 patients. Nine patients were given neoadjuvant chemotherapy with the aim of local disease control and downstaging or due to non-urothelial variant histology (Table 5).

3.3 Preoperative Variables

Anemia that mandated preoperative blood transfusion for optimization of homeostasis was present in only one patient. Finally, the minimum hemoglobin blood level taken direct preoperatively was 9.3 gm/dl. Preoperatively, three patients received IV infusion of iron. The median creatinine level was 81 mmol/L (Interquartile range(IQR) 68 – 90) (Table 6).

Table 2. The main presentations

Main complaint	(n = 47)	
	No.	%
Visible (macroscopic) hematuria	35	74.5
Lower Urinary Tract Symptoms (LUTs)	9	19.1
Non-visible (microscopic) hematuria	2	4.3
Resistant UTI	1	2.1

Table 3. Different radiological imaging modalities used

Modality Used	(n = 47)	
	No.	%
MRI	8	17.0
Presence of hydronephrosis in the imaging (CTU)		
No	43	91.5
Unilateral	4	8.5
Bilateral	0	0.0
PET CT	1	2.12

Table 4. Clinical staging of the patients

	(n = 47)	
	No.	%
Clinical T Stage		
Ta	4	8.5
Tis	1	2.1
T1	17	36.2
T2	22	46.8
T3	3	6.4
Histologic variants		
Urothelial	31	66.0
Squamous	8	17.0
Glandular	3	6.4
Sarcomatoid	3	6.4
Micropapillary	1	2.1
Undifferentiated	1	2.1
Clinical N Stage		
N0	46	97.9
N1	1	2.1
Clinical M Stage		
M0	47	100.0

Table 5. Different preoperative pathological parameters

Pathological finding	(n = 47)	
	No.	%
Presence of Cis in TURBT histology		
No	19	40.4
Yes	28	59.6
Presence of LVI in TURBT histology		
No	42	89.4
Yes	5	10.6
Previous BCG intravesical therapy		
No	37	78.7
Yes	10	21.3
Neoadjuvant chemotherapy		
No	38	80.9
Yes	9	19.1

Table 6. Preoperative laboratory parameters

Preoperative parameters	(n = 47)	
	No.	%
Pre-operative blood transfusion		
No	46	97.9
Yes	1	2.1
Pre-operative iron transfusion		
No	44	93.6
Yes	3	6.4
E-GFR (ml/min/BSA)		
Min. – Max.	44.0 – 220.0	
Mean ± SD.	80.26 ± 25.63	
Median (IQR)	78.0(70.0 – 85.50)	
Creatinine (mmol/L)		
Min. – Max.	35.0 – 135.0	
Mean ± SD.	80.51 ± 17.44	
Median (IQR)	81.0(68.50 – 90.0)	
Hb		
Min. – Max.	9.30 – 15.80	
Mean ± SD.	12.84 ± 1.77	
Median (IQR)	12.80(11.35–14.45)	

4. DISCUSSION

Open radical cystectomy is still the cornerstone treatment for muscle invasive bladder cancer disease and recommended by the guidelines in indicated cases of high risk non muscle invasive bladder cancer. This surgery has stood the test of time; however, with multiple modifications and improvements aiming for decreasing the associated complications, enhancing the oncological outcomes and provision of better quality of life after surgery.

Most of the patients were males, with male to female ratio of 3:1. This is in concordance with the well documented ratio worldwide of three to fourfold higher incidence of BC in men than women [12,13]. Numerous potential contributing factors may explain these demographic trends, including gender differences in exposures, metabolic enzyme activity, and disparities in the intensity of diagnostic evaluation [14,15].

The mean age was 63.5 years. In an analysis of the incidence of bladder cancer in the Nile Delta region in Egypt, the average age of males (60.9 ±10.1 years) was similar to that of females (60.0 ±11.8 years) [16]. The younger age at presentation is also documented by the data from Kyritsi et al who found the mean age at diagnosis of bladder cancer in Egypt was the fifth decade of life [17].

Most of the patients were either current smokers or ex-smokers. These data may highlight the correlation between smoking and bladder cancer disease. An analysis conducted in 2011 on 467, 528 men and women demonstrated that former and active smokers had two- and fourfold increases, respectively, in bladder cancer risk relative to non-smokers [18].

One study found that smoking was more strongly associated with the development of muscle invasive than with non-muscle invasive bladder cancer (NMIBC) [19]. While smoking cessation attenuates UCB risk, former smokers are still approximately twice as likely to develop the disease 20 years after quitting [20]. According to the currently available literature, smoking status and cumulative lifetime smoking exposure at diagnosis and at different times during treatment seem to affect disease recurrence, progression, and survival [21].

Visible hematuria was the most common symptom at presentation in the current study. This is in concordance with the data from the literature stating that hematuria either gross or microscopic is the most spotted presentation of bladder cancer [22-24].

The interest in MRI use comes from the limitations from the current imaging modalities in identifying metastatic disease and LN involvement preoperatively. Approximately, 25% of patients having LN metastases are missed on current preoperative staging [25].

To assess the role that MRI plays in the staging evaluation of a bladder lesion, there are a few clinical questions that need to be considered: How well does MRI differentiate ≤ T1 bladder cancer from ≥ T2 and what role can MRI play as a biomarker of aggressive disease? How well does MRI differentiate between T2 and ≥ T3 disease? How can MRI enhance the detection of small, but malignant LN? [26].

Green et al have found that **c**ontrast-enhanced MRI and diffusion weighted MR (DW-MRI) can differentiate between non-muscle invasive bladder cancer and muscle invasive cancer with accuracy of more than 80% [26]. MR imaging has been shown to allow more accurate staging of bladder carcinomas than CT because of its high soft-tissue contrast resolution, which allows clear differentiation between bladder wall layers [27].

The limitations of traditional MR sequence are low sensitivity for identifying small lymph node metastases, and that it does not appear to be useful for staging per T-stage even with multiparametric MRI protocols [26, 28]. Another disadvantage is that significant artifacts in bladder imaging include (lack of bladder distention, motion artifact, and chemical shift artifact) may limit the detection of small tumors and decrease sensitivity for plaque-like lesions [29]. Another factors, the cost and the availability are to be considered specially in developing countries like Egypt.

In the current study, most of the tumors were urothelial in origin. These data demonstrate the shift of the histology of bladder cancer in Egypt. This is in concordance with previous research that reported a significant decline in incidence of SCC in Egypt, although the overall bladder cancer incidence has remained steady or even increasing due to a rise in TCC over the past 40 years [30].

This is completely different from the reported data in 1980s where 22% of Egyptian BC cases were diagnosed with TCC while the majority of cases 78% were SCC [16,30]. By 2005, that ratio was nearly the opposite with 73% of bladder cancers diagnosed as TCC and 28% diagnosed as SCC [16,31]. A recent epidemiological study conducted in Tanta Urology department evaluating the characters of BC, the authors demonstrated that in 229 patients, 94% of the histopathological analysis reported TCC while SCC was present in only 5% of the cases [32].

The decrease in SCC cases has been explained by declining S. haematobium infection in the past 30 years due to construction of the Aswan Higher Dam in the 1960's, public health interventions for treatment, and changes in the Nile River system [33].

In the current study, the presence of carcinoma in situ in both TURBT and final specimen histopathology was significantly reported. Kimura and colleagues evaluated the prognostic value of concomitant carcinoma in situ in the RC specimen [34]. They have demonstrated that concomitant carcinoma in situ was reported in 39.4% of RC specimens, and it was not associated with overall mortality (pooled HR 0.92, 0.77-1.10), RFS (pooled HR 1.06, 0.99-1.13) or cancer specific mortality (pooled HR 1.00, 0.93-1.07) [34].

The presence of lymph-vascular invasion (LVI) in TURBT and final specimen pathological report gained a lot of attention. Mari et al who conducted a systematic review and meta-analysis to investigate the effect of LVI in RC specimens on disease recurrence and CSM [35]. They included 78,107 patients treated with RC. LVI was reported in 35.4% of the patients. They found that patients with LVI at RC had a 1.5-fold higher risk of developing disease recurrence (pooled HR 1.57; 95% CI: 1.45–1.70) and to dying of their disease (pooled HR 1.59; 95% CI: 1.48–1.73) compared to patients without LVI, regardless of tumor stage, nodal status, or perioperative chemotherapy [35].

Five patients were given neoadjuvant chemotherapy NAC. The selection for NAC is usually based on the clinical stage with more priority to locally advanced disease (≥T3), presence of variant histology, multifocality of the tumor, the patients' co-morbidities, the baseline renal function, the delay time during diagnosis and importantly the patient preference [36,37]. The value of neoadjuvant chemotherapy has been demonstrated, Neoadjuvant cisplatin-containing combination chemotherapy (NAC) improves overall survival (OAS) (5-8% at five years), irrespective of the type of definitive treatment used [38-41]. It is unclear if patients with variant histology will also benefit from NAC [42]. A retrospective analysis demonstrated that patients with neuroendocrine tumors had improved OAS and lower rates of non-organ-confined disease when receiving NAC. In case of micropapillary differentiation, sarcomatoid differentiation and adenocarcinoma, lower rates of non-organ confined disease were found, but no statistically significant impact on OAS. Patients with SCC did not benefit from NAC [43]. Currently, no tools are available to select patients who have a higher probability of benefitting from NAC. Response after two cycles of treatment is related to outcome [42].

There are some limitations for the present study. The analysis was done retrospectively. Moreover, the sample size included was relatively small in the relevant period because of the COVID pandemic on the regular routine scheduled lists. Additionally, this is a single center experience.

5. CONCLUSION

The mean age of bladder cancer was 63.5 years in this cohort of patients. Visible hematuria was the most common complaint reported. The use of MRI is valuable in staging of locally advanced bladder cancer. Most of the tumors were urothelial with (66%) with significant reduction in the incidence of squamous cell bladder cancer than the previously reported data. The presence of carcinoma in situ and lymphovascular invasion in the TURBT histology may be valuable pathological predictors of recurrence that need to be thoroughly studied. Neoadjuvant chemotherapy has become an integral part of the treatment protocol in cases of muscle invasive bladder cancer.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

It is not applicable.

ETHICAL APPROVAL

This study was approved after the review by the Research Ethics Committee in Tanta University.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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