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RESEARCH ARTICLE

Clinicoepidemiological study of locally advanced bladder cancer: single institution experience

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ABSTRACT

Background: Bladder cancer is the ninth most prevalent disease worldwide, ranking 13th in cancer mortality. Despite aggressive surgical treatments and systemic chemotherapy, patients with locally advanced bladder cancer (LABC) show poor prognosis. In patients with muscle-invasive bladder cancer (MIBC), perioperative chemotherapy adds just a small but significant absolute survival benefit to surgery alone. **Aim:** This study aims to assess the clinical-epidemiological characteristics of LABC and to assess the progression-free survival (PFS) and overall survival (OAS) of these patients upon different treatment plans. **Material and Methods:** This is a retrospective study that includes 135 patients presented with LABC to the Clinical Oncology and Nuclear Medicine Department at Mansoura university hospitals from January 2010 to November 2016. Our patient's ages ranged from 47 to 75 years old. The data on demographics and clinical outcomes were collected from the patients' medical records for descriptive studies. **Results:** The most common diagnoses stage in our patients were N0 (55.6%), followed by N2 (23.7%). As regards treatment modalities in our study, five groups of treatment approaches were scheduled to include 135 patients either treated by radical surgery (8.9 %), chemotherapy only (14.1%), radiotherapy (17.8%), concomitant chemoradiotherapy (11.1%), or downstaging chemotherapy followed by concomitant chemoradiotherapy (48.1%). Complete response (CR) was observed in 31.1% of the studied patients and the disease progression was documented in 11.1%. **Conclusion:** MIBC accounts for about 75% of bladder malignancies. However, radical cystectomy is the gold standard for achieving high OAS rates. Another option is to adopt tri-modality therapy to preserve the native bladder and achieve satisfactory OAS and PFS data.

Keywords: bladder cancer, treatment, chemotherapy, radiotherapy, survival

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INTRODUCTION

Bladder cancer is the ninth most frequent cancer globally, with around 430,000 new cases diagnosed yearly (Cumberbatch et al., 2018). About 75% of the newly detected cases are non-invasive and can be treated with local therapy. The other 25% are muscle-invasive bladder cancer, requiring severe treatment such as surgery, radiation, or systemic therapy (Schmid et al., 2020).

Bladder cancer in Egypt is the second most frequent malignancy, with males having a higher prevalence of invasive tumors. The epidemiology of urinary bladder cancer in Egypt has changed dramatically, with an increase in the prevalence of transitional cell carcinoma (TCC) and a decrease in the incidence of squamous cell carcinoma (SCC) due to the suppression of endemic *Schistosoma crematorium* infection (Nagy et al., 2018).

The current standard of care for muscle-invasive bladder cancer (MIBC) is radical cystectomy with pelvic lymphadenectomy. According to German and European guidelines, individuals with MIBC who are candidates for platinum-based chemotherapy should receive neoadjuvant chemotherapy (Alfred et al., 2017).

Locally advanced bladder cancer (LABC) should be treated with more than one modality to

achieve local control, increase progression-free survival, and maintain quality of life. Neoadjuvant cisplatin-based chemotherapy could be given to more than half of patients, with more than 90% completing more than three cycles, with the benefit of tumor downstaging and a 16-33 percent reduction in death risk (Hermans et al., 2016).

Treatment-related adverse effects include bowel problems after radical cystectomy and urinary reconstruction, sexual dysfunction and impaired body image, proctitis and cystitis after pelvic radiotherapy and even in follow-up, repeated cystoscopy surveillance is a painful and anxiety-inducing procedure (Perlis et al., 2018).

Therefore, this study aims to assess the clinical-epidemiological characteristics of locally advanced bladder cancer patients as well as to assess progression-free survival and overall survival of locally advanced bladder cancer patients with different treatment plans.

MATERIAL AND METHODS

This study included 135 patients presented with locally advanced bladder tumor, aged between 18 to 75 years old, both sex with adequate renal function and pathologically proved (TCC, SCC, and adenocarcinoma) treated in Clinical Oncology and Nuclear Medicine Department – Mansoura University in the period from January 2010 to November 2016. In this study, we excluded patients aged above 75 years old with non-muscle invasive and metastatic disease.

All cases were reviewed, and collected the data regards; Age, sex, performance status, history of smoking, date of first symptoms, duration of symptoms before presentation, pathological type, radiological investigation, date and site of local recurrence if occurred, and date and site of distant metastasis if occurred were collected. Patients were divided into five groups according to the treatment they received.

Group 1: Twelve patients underwent radical cystectomy; they received either neoadjuvant chemotherapy (NACT) (3 patients received three cycles of Gemzar 1000 mg/m2 D1, 8/cisplatin 80 mg/m2 D1 every 21 days) or adjuvant chemotherapy (4 patients received six cycles of Gemzar 1000 mg/m2 D1, 8/cisplatin 80 mg/m2 D1 every 21 days) or radiotherapy (3 patients received PORT 50 GY/25 fractions) or neither chemotherapy nor radiotherapy (2 patients). **Group 2:** Twenty-four patients were treated mainly by radiotherapy with either radical dose 64 GY/32 daily fractions given in 6½ weeks or palliative dose 6 GY once weekly for six weeks. **Group 3:** Fifteen patients treated with concomitant chemoradiotherapy 64 GY/32 daily fractions given in 6½ weeks (3DCRT) with cisplatin 40 mg/m2 weekly. **Group 4:** Sixty –five patients treated with three cycles of chemotherapy before the radical dose of radiotherapy aiming for downstaging of the tumor (Gemzar 1000 mg/m2 D1, 8/cisplatin 80 mg/m2 D1 every 21 days), cisplatin replaced by carboplatin (AUC 5) in a patient with renal disease then followed by concomitant chemoradiotherapy 64 GY/32 daily fractions given in 6½ weeks (3DCRT) with cisplatin 40 mg/m2 weekly.

Group 5: Nineteen patients were treated with chemotherapy with an average of 6 cycles of Gemzar 1000 mg/m2 D1,8 /cisplatin 80 mg/m2 D1 every 21 days, cisplatin replaced by carboplatin (AUC 5) in a patient with renal disease. Five patients received taxol 80 mg/m2 D1, 8/carboplatine (AUC5) D1 every 21 days.

Radiotherapy was planned by CT planning with contrast with slices each 3-5 mm using 3D Precise Treatment Planning System version 2.12. Three-Dimensional CRT was delivered by a high-energy linear accelerator (Elekta, Precise Treatment System), Version 5. The 3 or 4 fields' beams are arranged to the pelvic lymph nodes and bladder in 2 phases with 6 or 15 MeV photon energy in radical treatment patients with a dose of 64 GY/32 fractions over 6.5 weeks and localized field to the bladder in palliative radiotherapy treatment cases with dose 36 GY/6 fractions with one fraction weekly. In the adjuvant setting, the planning involved tumor bed and pelvic lymph nodes with a dose of 50 GY/25 fractions over five weeks. The response will be assessed according to RECIST criteria (Eisenhauer, 2009).

Statistical Analysis

IBM's SPSS Statistics (Statistical Package for the Social Sciences) for Windows (version 25, 2017) was used to analyze the acquired data. The Shapiro-Wilk test was done to ensure that the data distribution was normal. ANOVA test was used if data were normally distributed, whereas Chi-square was used if data were not normally distributed. All tests were carried out using a 95% confidence interval. Quantitative variables were expressed as mean and standard deviation, median, interquartile range, minimum and maximum, and frequency and percentage, if appropriate. Categorical variables were expressed as frequency and % as suitable. The median survival duration in the treated individuals was assessed using a Kaplan-Meier graph in a survival study and log-rank test for comparing survival curves. Regression: univariate and Multivariate Cox proportional hazards modeling was additionally used to identify variables associated with OAS and PFS in the entire cohort. Patients included in the multivariate analysis were those found to be statistically significant on the univariate analysis. Statistical significance was defined as a P value of less than 0.05.

RESULTS

One hundred thirty-five patients with locally advanced urinary bladder cancer were included in this analysis. Characteristics of the patients and tumors are summarized in Table 1. As regards treatment modalities in our study, five main groups of treatment approaches were scheduled to include 135 patients either treated by radical surgery (12 patients), chemotherapy only (19 patients), radiotherapy (24 patients), concomitant chemoradiotherapy (15 patients), or downstaging chemotherapy followed by concomitant chemoradiotherapy (65 patients) as demonstrated in Table 2. Twelve patients underwent radical surgery, and three patients underwent radical cystectomy. Three patients received neoadjuvant chemotherapy and then underwent radical cystectomy. Seven patients received adjuvant treatment, either adjuvant chemotherapy (4 patients) or adjuvant radiotherapy (3 patients), as illustrated in Table 2. Also, twenty-four patients received radiotherapy, 18 of them with definitive dose and 6 cases received palliative radiotherapy only. In the study, 31.1 percent of patients had a complete response, 34.1 percent had a partial response, 23.7 percent had a stationary illness, and 11.1 percent had disease progression, as illustrated in Table 3. The most common cause of treatment failure was distant metastasis, which was identified in 31.1 percent of patients, followed by bone metastasis in 17%, lung metastasis in 7.4%, liver, and peritoneum in 6.7%, locoregional failure in 20%, and both local and distant failure in 9.6%. In 53 patients, there was no evidence of therapy failure, which is represented in Table 4.

The PFS and OAS according to the different treatment planes were represented in Tables 5 and 6, and Figure 1 with p values equal 0.013 and 0.007, respectively. Patients' characteristics that have a significant difference in univariate analysis for predictors of progression-free survival were found to be sex, DM, and bilharziasis with p values (0.001, 0.046, and < 0.001, respectively). Regarding pathological subtypes, grading, and lymph node staging, adenocarcinoma, TCC, grade 1, grade 2, N0 and N1 were found to have a significant difference in univariate analysis with p values (<0.001, 0.021, 0.004, 0.048, 0.001 and 0.033 respectively). Also, the cycles of treatment were statically significant with a P value equals 0.039, as illustrated in Table7.In addition, in multivariate analysis, there was a statistically significant difference in lymph node staging and cycles of treatment with p values (<0.001, 0.010, and 0.018, respectively) as shown in Table 8. In a Univariate analysis of predictors of overall free survival, it was detected that sex and Bilharziasis had statistically significant differences (p values of 0.023, and 0.001 respectively), as well as N0, N1, TCC adenocarcinoma and grade 1 (p values of 0.002, 0.015, 0.012, < 0.001 and 0.020, respectively). In addition, as shown in Table 8, there was a statistically significant difference in multivariate analysis for bilharziasis, N0, and adenocarcinoma.

Table 1. Demographic characteristics, medical history, and particular habits of the studied patients with locally advanced bladder cancer

	Mean±& SD	All patients (n= 135)
*Age/years		(64.06 ± 6.905)
Gender	**Male**	103 (76.3%)
	Female	32 (23.7%)
*Comorbidities 71 (52.6%)	**DM**	25 (18.5%)
	Hypertension	30 (22.2%)
	IHD	6 (4.4%)
	Hepatic disease	18 (13.3%)
	Renal disease	6 (4.4%)
	DVT	4 (3%)
Bilharziasis		18 (13.3%)
Smoking		50 (37%)
Patients Symptoms	**Dysuria**	62 (45.9%)
	Hematuria	82 (60.7%)
	Retention	4 (3.0%)
	Drippling	5 (3.7%)
	Urgency	4 (3.0%)
	Oliguria	3 (2.2%)
	Pain	2 (1.5%)
ECOG	**0**	27 (20%)
	1	64 (47.4%)
	2	28 (20.7%)
	3	16 (11.9%)
Tumor (T)	**2b**	10 (7.4%)
	3a	33 (24.4%)
	3b	53 (39.3%)
	4a	29 (21.5%)
	4b	10 (7.4%)
Lymph Node (LN)	**0**	75 (55.6%)
	1	28 (20.7%)
	2	32 (23.7%)
Metastasis (M)	**0**	135 (100%)
Pathology	**TCC**	102 (75.6%)
	SqCC	19 (14.1%)
	Adenocarcinoma	14 (10.3%)
Grade	**I**	23 (17%)
	II	44 (32.6%)
	III	68 (50.4%)

*Age ranged beteewn miniumum to maximum (47-75) years old. *Some of the patients had more than comorbidity**.** DM: Diabetes Mellitus, DVT: Deep Venous Thrombosis, IHD: Ischemic Heart Disease, TCC: Transitional Cell Carcinoma, SCC: Squamous Cell Carcinoma.

Table 2. Number of cycles and type of treatment of the studied patients with locally advanced bladder cancer

*Cycles	Mean & SD	Median	Minimum	Maximum	QR
	3.52 ± 1.834	**3.00**	**1**	**11**	**2, 4.5**
Treatment	Surgery (12)	RC	2 (1.5%)		
		RC then adjuvant chemotherapy	4 (3.0%)		
		NACT followed by RC	3 (2.2%)		
		Surgery then adjuvant RT	3 (2.2%)		
	Radiotherapy (24)	Definitive radiotherapy	18 (13.3%)		
		Palliative radiotherapy	6 (4.4%)		
	Concurrent chemoradiotherapy (CCRTH)		15 (11.1%)		
	Downstaging chemotherapy followed by CCRTH		65 (48.1%)		
	Chemotherapy only		19 (14.1%)		

RC: radical cystectomy, NACT: neoadjuvant chemotherapy, RT: radiotherapy. *Minimum and maximum for cycles only.

Table 3. Treatment response in the studied patients with locally advanced bladder cancer

All patients (n= 135)	NO (%)
Complete Response	42 (31.1%)
Partial Response	46 (34.1%)
Stationary Disease	32 (23.7%)
Disease progression	15 (11.1%)

Table 4. Treatment failure in the studied patients with locally advanced bladder cancer

All patients (n= 135)		
Distant Metastasis 42 (31.1%)	Lung	10 (7.4%)
	Bone	23 (17%)
	Liver & peritoneum	9 (6.7%)
Locoregional	27 (20%)	
Both	13 (9.6%)	
No failure	53 (39.3%)	

Table 5. Progression-free survival of studied patients with locally advanced bladder cancer according to the treatment

		Median	95% CI	χ^2	P
PFS	Surgery[1]	32.000	0.000, 68.821	12.72	**0.013**
	CCRTH	23.000	7.852, 38.148		
	Downstaging chemotherapy followed by radiotherapy	16.000	11.199, 20.801		
	Chemotherapy only[2]	32.000	17.940, 46.060		
	Radiotherapy only[1,2]	12.000	9.479, 14.521		

1: significant difference between surgery and radiotherapy. 2: significant difference between Chemotherapy only and radiotherapy.

Table 6. Overall survival of studied patients with locally advanced bladder cancer according to the treatment

		Median	95% CI	χ^2	P
OAS	Surgery[1,2]	41.000	7.052, 74.948	14.1	**0.007**
	CCRTH	27.000	5.540, 48.460		
	Downstaging chemotherapy followed by radiotherapy[2,3]	26.000	20.313, 31.687		
	Chemotherapy only[3,4]	42.000	35.512, 48.488		
	Radiotherapy only [1,4]	17.000	9.794, 24.206		

1: significant difference between surgery and radiotherapy. 2: significant difference between surgery and downstaging chemotherapy followed by radiotherapy. 3: significant difference between downstaging chemotherapy followed by radiotherapy and Chemotherapy only. 4: significant difference between Chemotherapy only and radiotherapy.

Table 7. Univariate and multivariate analysis for prediction of progression-free survival of studied patients with locally advanced bladder cancer

	Univariate				Multivariate			
	R2	B	95% CI	P	R2	B	95% CI	P
Sex (female)	2.1%	22.0	17.6, 26.4	**< 0.001**	33.1%	-	-	0.420
DM	2.3%	26.0	21.8, 30.2	**0.046**		-	-	0.504
Bilharziasis	8.0%	21.5	17.6, 25.5	**< 0.001**		25.0	12.1, 38.0	**< 0.001**
N0	7.6%	13.0	5.5, 20.4	**0.001**		14.6	3.7, 25.5	**0.010**
N1	2.7%	-10.2	-19.5, -0.85	**0.033**		-	-	0.518
Adenocarcinoma	17.6%	50.2	31.8, 68.5	**< 0.001**		-	-	0.205
TCC	3.3%	-9.1	-16.8, -1.4	**0.021**		-	-	0.094
Grade I	5.5%	15.3	5.0, 25.5	**0.004**		-	-	0.791
Grade II	2.2%	-8.3	-16.5, -0.1	**0.048**		-	-	0.471
Cycles	4.6%	3.0	0.2, 5.8	**0.039**		3.0	0.5, 5.4	**0.018**

N0: no regional lymph node, N1: regional lymph node and TCC: transitional cell carcinoma.

Table 8. Univariate and multivariate analysis for prediction of overall free survival of studied patients with locally advanced bladder cancer

		Univariate				Multivariate		
	R2	B	95% CI	P	R2	B	95% CI	P
Sex (female)	3.1%	11.5	1.6, 21.3	0.023	30.5%	-	-	0.066
Bilharziasis	8.0%	21.6	9.5, 33.6	0.001		20.5	9.8, 31.3	**< 0.001**
N0	6.4%	13.4	5.1, 21.6	0.002		9.5	0.6, 18.3	**0.037**
N1	3.7%	-12.9	-23.2, -2.6	0.015		-	-	0.702
TCC	3.9%	-10.9	-19.5, -2.4	0.012		-	-	0.392
Adenocarcinoma	14.8%	51.8	31.0, 72.6	**< 0.001**		46.8	26.8, 66.8	**< 0.001**
Grade I	3.3%	13.7	2.2, 25.3	0.020		-	-	0.140

N0: no regional lymph node, N1: regional lymph node and TCC: transitional cell carcinoma.

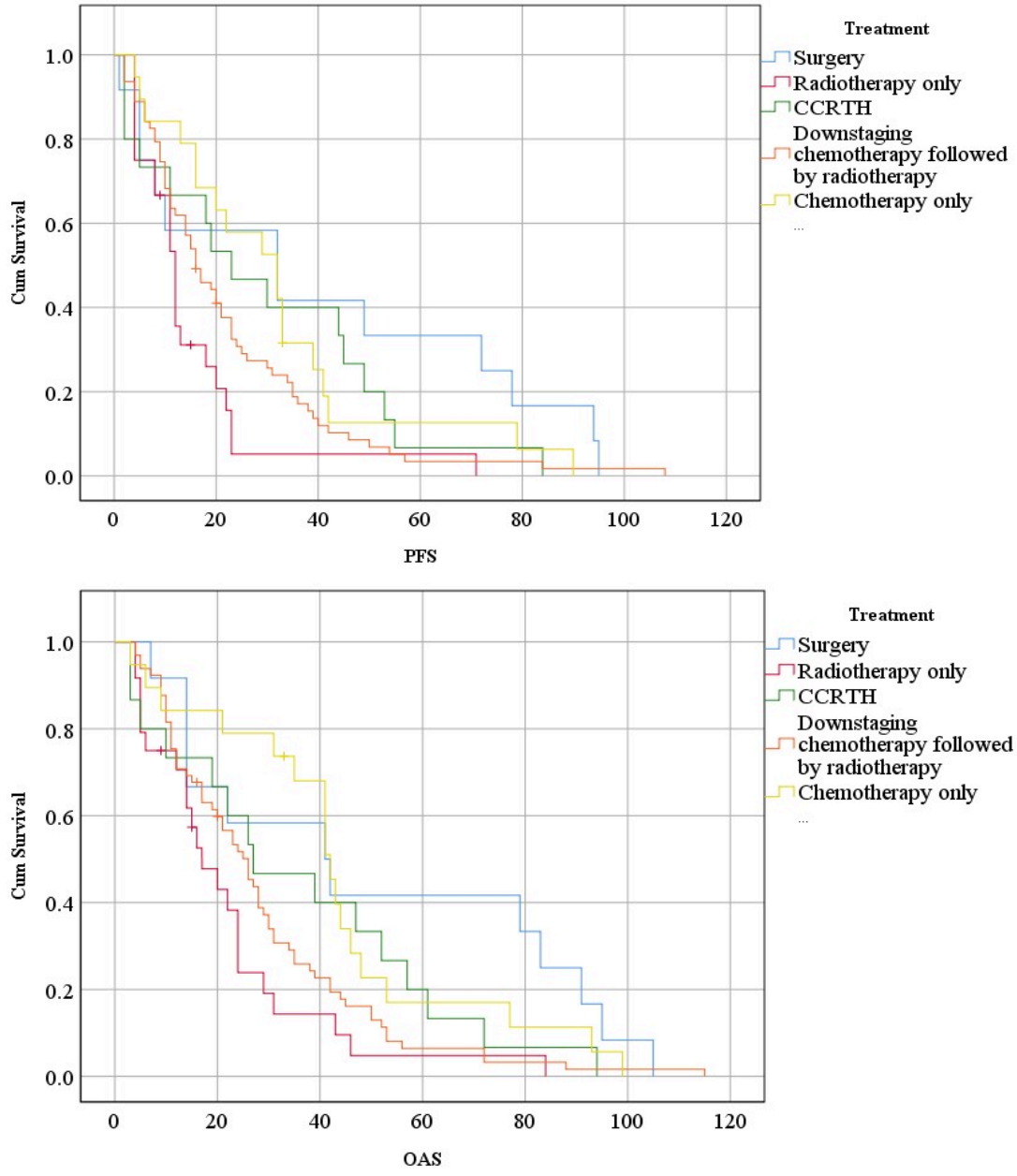

Figure 1. Kaplan Meir curves compare Progression-free survival (top) and overall survival (bottom) of studied patients with locally advanced bladder cancer according to the treatment.

DISCUSSION

With about 430,000 new cases diagnosed yearly, bladder cancer ranks the ninth among all cancers in the world. About 25% of the patients have a muscle-invasive condition at the time of diagnosis (Schmid et al., 2020). The objective of this study was to examine the clinical-epidemiological characteristics of a group of patients with locally advanced bladder cancer. Furthermore, the overall survival and disease-free survival of patients with localized advanced disease underwent assessment.

The study included a total of 135 cases of locally advanced bladder cancer. The cases were 64.06 years old on average (range: 47 to 75). The included cases ranged in age from 30 to 91, with an average age of 58.3 years (Amin et al., 2013). As a result, the chance of having this cancer is inversely correlated with age (Soria et al., 2018). 76.3 percent of the cases in the current study involved men, with the remaining cases involving women. Several earlier types of research support the predominance of men (Amin et al., 2013; Gouda et al., 2007). In terms of risk factors for bladder cancer, smoking accounted for 37% of the cases (50 instances), whereas 18 had a history of bilharziasis (13.3 percent). Another study discovered that smoking was responsible for 47.4% of cases of bilharziasis, which was present in 26.8% of cases (Amin et al., 2013; Yang et al., 2005).

Therefore, smoking appears to be linked to a higher incidence of bladder cancer than schistosomal infection, which may be due to the nearly complete elimination of schistosomal infection in Egypt (Yang et al., 2005). In this study, T2b (7.4 percent), T3a (24.4 percent), T3b (39.3 percent), T4a (21.5 percent), and T4b (7.4 percent) were the TNM stages encountered in the research cases. Furthermore, N1 and N2 classes were observed in 20.7% and 23.7% of patients, respectively, while 55.6% of cases had no lymph node infiltration. In a study of locally advanced bladder cancer patients conducted by Zaghloul et al., respectively, in the chemoradiation and radiotherapy groups, T2, T3, and T4a disease were found in 8, 81.3, and 10.7% of cases. In the radiation group, the same stages were discovered in 11, 64.4, and 24.4 percent of cases. In the same study, patients in the chemoradiation and chemotherapy groups, respectively, had positive lymph nodes identified in 46.7 and 37.8 percent of patients (Zaghloul et al., 2018). Another study by Amin et al. indicated that stages I, II, III, and IV were present in 8.2, 18.6, and 67.7% of the sample.

Transitional cell carcinoma (75.6%) was the most commonly encountered pathological type in our investigation, followed by squamous cell carcinoma (14.1%) and adenocarcinoma (10.3%). Separate research in Upper Egypt revealed that transitional cell carcinoma (60.8%) was the most common pathology, followed by squamous cell carcinoma (26.8%) and adenocarcinoma (6.2 percent). In addition, 6.2 percent of cases had transitional cell carcinoma with squamous differentiation (Amin et al., 2013); these findings were consistent with our study.

In our research, many therapeutic methods were used. In 8.9% of cases, surgical resection was performed, while radiotherapy was used in 17.8% of cases. Furthermore, only 14.1% of patients received chemotherapy, while 11.1% received chemoradiation, and 48.1% of patients received neoadjuvant chemotherapy followed by radiotherapy. Treatment for muscle-invasive bladder cancer, which accounts for roughly two-thirds of all cases in Egypt, is still challenging. The treatment seeks to control local disease, eradicate micrometastases, and preserve a high quality of life while minimizing the risk of death (Galsky et al., 2016).

In our study, a complete response was reached in 31.1 percent of cases, whereas 34.1 percent of cases resulted in a partial response. Additionally, stable and progressive illness categories were present in 23.7 and 11.1 percent of cases, respectively. According to another study, complete responses were achieved in 49.4% of cases, while partial responses were seen in 28.6% of patients. p progressive and stable disease was discovered in 15.6 and 6.5 percent of cases (Amin et al. 2013), respectively; this really is slightly better than our results.

Additionally, PFS had a mean value of 24.51 months (range, 1–108 months), while OAS had a mean of 32.03 months (range, 3–115 months). In our analysis, patients who underwent radical

cystectomy followed by adjuvant radiation, chemotherapy, or both had the best mean progression-free survival, which was 32 months, respectively. This is based on the fact that radical cystectomy is the gold standard of treatment in almost all cases of muscle-invasive bladder cancer worldwide. It has been associated with a 30–50% 5-year disease-free survival rate (Kiss et al., 2016). Also, there are significant differences between surgery, chemotherapy alone, and radiotherapy, supporting the idea that a tri-modality treatment is preferable for control and organ preservation. Radiation therapy was added to radical surgery for patients with locally advanced bladder cancer. This led to a statistically meaningful increase in pelvic control with a 27% absolute improvement in 2-year local, regional free survival (96 percent vs. 69 percent,). The two-year OAS was improved by the addition of chemotherapy to radiotherapy, but the difference (71 percent versus 60 percent) was not statistically significant (Zaghloul et al., 2018), which is close to this finding because surgery is statistically more significant than either chemotherapy or radiotherapy.

In our study, chemotherapy and radiation were applied in two different ways: downstaging chemotherapy was followed by CCRTH, which had a median PFS and OS of 16 and 26 months and a median PFS and OS of 23 and 27 months, respectively. After surgery, radiotherapy was utilized at 6 Gy per fraction weekly for six weeks with a median PFS and OAS of 12 and 17 months in patients who were unable to receive systemic cytotoxic therapy and in older patients. Although James et al., 2012 detected that OAS curves started to separate at two years, with hazard ratios that were not statistically significant, a phase 3 trial that examined the addition of chemotherapy to radiotherapy led to a 33 percent reduction in locoregional recurrence risk and a 50 percent reduction in invasive recurrence risk (James et al., 2012). According to a separate study, univariate analysis using log-rank testing revealed that adjuvant chemotherapy did not improve survival.

There was no discernible difference in median overall survival between patients who received adjuvant chemotherapy and those who were kept under observation (22.6 vs. 21.1 months). Particularly in patients with N2-3 disease (17.5 vs. 14.4 months) and those who had positive surgical margins (16.7 vs. 12.2 months), adjuvant chemotherapy was related to a longer median overall survival on subset analysis (Haque et al., 2018).

The 5-year overall survival (OS) rate after radical cystectomy, according to another author, was about 60%, ranging from 32% in patients with regional lymph node involvement (N+) to 75% in those with no lymph node involvement (N0) (Yafi et al., 2011). The prognosis is worse for patients with node-positive bladder cancer, who have a 5-year recurrence-free survival (RFS) rate of 4-35 percent (Shariat et al., 2006; Tilki et al., 2013). Female patients, bilharziasis, diabetes mellitus, lymph node status, pathological subtypes, and tumor grade were all found to be clear predictors of progression-free survival in our study. The same factors, with the exception of DM and grade II, were predictors of overall survival apart from lymph node status. In a different study, univariate and multivariate analyses revealed no significant predictors of overall survival, while marginal factors such as diseased T stage could be significant. Neither the chemotherapy and radiation treatment nor the pathological T stage had any effect (Zaghloul et al., 2018).

In comparison to the chemotherapy-only group, which had a 2-year OS of 60% (95 percent CI, 52 percent-68 percent), the chemotherapy plus radiation groups had a 2-year OS of 71% (95 percent CI, 65 percent-77%) (Zaghloul et al., 2018). In another study, according to multivariate Cox proportional hazard modeling analysis, poorer OS was associated with older age, pT4 stage, positive margins after radical surgery or positive lymph node, and lower socioeconomic status (Haque et al., 2018).

In line with these findings, lymph node status is one of the most effective pathologic predictors of long-term disease-specific survival (DSS) and overall survival (OS) (Shariat et al., 2006; Stein et al., 2001).

CONCLUSION

Muscle invasive bladder cancer accounts for about 75% of newly diagnosed bladder malignancies. Although radical cystectomy is currently the gold standard for achieving high OAS rates, it significantly influences the quality of life. Another option is to adopt tri-modality therapy to preserve the native bladder and achieve satisfactory OAS and PFS data. Immunotherapy will undoubtedly make a significant difference in the future standard of care for bladder cancer. Patients' ineligible for cisplatin-based regimens because of age, comorbidities, or patient acceptance now have real hope thanks to the discovery of checkpoint inhibitors. PD-L1 inhibitors appear to be well tolerated and may be a feasible treatment option for many patients.

ETHICAL CONSIDERATIONS

This study was conducted upon approval of the Institutional Research Board (IRB) at Faculty of Medicine, Mansoura University, Egypt, with Ethical Code (MS.18.10.329).

CONFLICT OF INTEREST

No conflict of interest.

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AUTHOR CONTRIBUTIONS

All authors participated in the design of the study and performed the statistical analysis; all authors contributed to the manuscript revision; all authors approved the final manuscript.

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