

# Current status of management and outcomes of muscle-invasive bladder cancer in Yemen: A retrospective observational study

Khaled Al-Kohlany<sup>1</sup>, Amal Al-Maleki<sup>2</sup>, Majdi Al-Shami<sup>3</sup>, Hani Hussein<sup>4</sup>, Faisal Ahmed<sup>5</sup>

<sup>1</sup> Department of Urology, General Military Hospital, Sana'a, Yemen;

<sup>2</sup> Department of Obstetrics and Gynecology, Palestine Hospital for Motherhood and Childhood, Sana'a, Yemen;

<sup>3</sup> Department of Urology, General Military Hospital, Sana'a, Yemen;

<sup>4</sup> Department of Urology, 22 MAY Typical Specialized Surgical Center, Sana'a, Yemen;

<sup>5</sup> Department of Urology, School of Medicine, Ibb University, Ibb, Yemen.

**Summary** *Background: The lack of a cohesive diagnostic and therapeutic framework for muscle-invasive bladder cancer (MIBC) in Yemen has resulted in significant variability in patient care. This study evaluates oncological outcomes and survival rates after radical cystectomy (RC) for MIBC patients in Yemen.*

*Methods: We conducted a retrospective analysis of 300 MIBC patients who underwent RC between 2006 and 2020.*

*Demographics, histopathological findings, and survival data were meticulously collected. Kaplan-Meier survival analysis estimated survival probabilities, while prognostic factors were evaluated using the log-rank test.*

*Results: The median patient age was 67 years (IQR 65-70), with a male predominance (n = 184, 61.3%). Ileal loop reconstruction was the primary method of urinary diversion (n = 234, 78.0%). Urothelial carcinoma was the predominant diagnosis (n = 246, 82.0%), followed by squamous cell carcinoma (n = 42, 14.0%). Postoperative complications occurred in 93 patients (31.0%), primarily Grade I (n = 61, 20.3%). Overall survival was 71.7% (n = 215), with 28.3% mortality due to non-cancer-related (n = 43, 14.3%) and bladder cancer-related causes (n = 35, 11.7%). The median overall survival was 191 months, with 1-year, 3-year, 5-year, and 10-year survival rates of 99%, 93%, 88%, and 82%, respectively. In the multivariate analysis, non-ileal conduit diversion (Hazard Ratio [HR] 5.21, 95% Confidence Interval [CI]: 1.80-15.00, p = 0.003), Stage IV disease (HR 2.76, 95% CI: 1.01-7.61, p = 0.050), lymph node positivity (HR 2.92, 95% CI: 1.15-7.42, p = 0.022), and squamous cell carcinoma (HR 3.09, 95% CI: 1.25-7.63, p = 0.022) were identified as predictors of mortality.*

*Conclusions: This study highlights the urgent need for improved bladder cancer care in Yemen. Late-stage diagnosis and suboptimal surgical methods critically affect survival. Addressing these issues requires prioritizing early detection and standardized surgical techniques to develop effective care pathways for MIBC patients.*

**KEY WORDS:** Muscle-invasive bladder cancer; Cystectomy; Yemen; Disease-free survival; Mortality; Oncological outcomes.

Submitted 20 February 2025; Accepted 24 February 2025

## INTRODUCTION

Bladder cancer posed a significant epidemiological concern in the Arab world, as evidenced by the 2019 Global Burden of Disease Data. In Yemen, the *age-standardized incidence rate* (ASIR) was recorded at 4.374 per 100,000, amounting to a total of 535.947 cases. Gender-specific analysis revealed ASIRs of 7.003 for males and 4.584 for females, with corresponding *age-standardized death rates* (ASDR) of 1.863 for males and 1.433 for females. The *Age-Standardized Disability-Adjusted Life Years* (ASDALYs) attributed to bladder cancer in Yemen reached approximately 7,400.041, resulting in 57.819 deaths and a *mortality-incidence ratio* (MIR) of 2.95 (1). In 2020, the incidence of bladder cancer among males was estimated at 4.0 per 100,000, with a mortality rate of 1.6 per 100,000, underscoring the public health challenge presented by this disease in the region (2).

*Muscle-invasive bladder cancer* (MIBC) represents a significant global health challenge, necessitating complex, multidisciplinary therapeutic approaches (3). Standard treatment protocols typically involve radical cystectomy with pelvic lymph node dissection, often integrated with neoadjuvant or *adjuvant chemotherapy* (AC) to improve oncological outcomes (3, 4). Indeed, radical cystectomy has been widely recognized as the gold standard treatment, demonstrating superior survival rates and reduced recurrence compared to less aggressive modalities (5, 6). Prognostic factors, including advanced age, non-urothelial variant histology, a reduced number of lymph nodes removed, lymph node status, tumor stage, and surgical margin status, are critical determinants of long-term survival following radical cystectomy for MIBC (7, 8).

Bladder cancer mortality remains a substantial concern, particularly in advanced disease stages, underscoring the imperative for effective interventions (9).

However, the successful implementation of these guidelines is contingent upon the availability of robust diagnostic pathways and therapeutic infrastructure (6). In resource-constrained settings such as Yemen, the management of MIBC presents considerable obstacles. These regions often face limitations in essential resources, including diagnostic imaging modalities, specialized sur-

gical equipment, and access to systemic therapies (10, 11). Moreover, limited access to trained urologic oncologists and comprehensive supportive care services can adversely affect patient outcomes. The absence of standardized protocols, compounded by these resource constraints, can lead to heterogeneous patient management and potentially compromise treatment efficacy.

Therefore, this study seeks to investigate the current status of MIBC management and the associated oncological outcomes and survival rates following radical cystectomy in Yemen, a resource-limited environment. We present a retrospective analysis of oncological outcomes and survival following radical cystectomy for MIBC performed by a single surgeon at tertiary referral centers. By characterizing the experiences of patients undergoing surgical treatment for MIBC in Yemen, this study aims to identify areas for improvement in the diagnosis, treatment, and ultimately, survival of this vulnerable patient population. This study is crucial, as it not only provides insight into existing practices but also highlights gaps in the healthcare system. These insights may be used to inform the development of evidence-based national guidelines and recommendations for bladder cancer treatment in Yemen.

## PATIENTS AND METHODS

### Study design

This retrospective observational study analyzed data from approximately 300 patients diagnosed with MIBC who underwent radical cystectomy at various governmental and private healthcare facilities in Sana'a, Yemen, between January 2006 and March 2020.

The study adhered to the principles outlined in the Declaration of Helsinki and received ethical approval from the *Ethics Research Committees of the General Military Hospital in Sana'a*. Given the retrospective nature of the study, the ethics committee waived the requirement for individual patient consent for chart review. All patient data were encrypted and anonymized to ensure confidentiality.

### Inclusion criteria

Patients diagnosed with MIBC who underwent radical cystectomy were included in the study, irrespective of tumor behavior or histology, with the exception of those diagnosed with lymphomas or small cell carcinomas.

All included patients were managed by a single urologist with over five years of experience in oncologic surgery (K. A-K.).

### Exclusion criteria

Patients were excluded from this analysis for the following reasons: failure to undergo radical cystectomy; presence of documented clinical metastatic disease or non-invasive disease; a history of multiple primary cancers; a follow-up duration of less than six months; or treatment conducted by a different urologic team.

### Treatment and follow-up

Preoperative staging comprised abdominal and pelvic *computed tomography* (CT) scans, chest X-rays, and *transurethral resection of bladder tumors* (TURBT). *Radical cystectomy* (RC)

was performed, which included either bilateral or limited *pelvic lymph node dissection* (PLND), with prostatectomy and seminal vesiculectomy conducted for male patients. Female patients also underwent hysterectomy, anterior vaginal wall resection, and bilateral salpingo-oophorectomy, as dictated by the presence of involvement in these organs. The execution and extent of lymph node dissection, along with the choice of urinary diversion, were determined based on patient preferences and the recommendations of the department's specialists.

Post-cystectomy follow-up involved clinical examination, laboratory studies, chest radiography, and abdominal/pelvic CT scans, with follow-up appointments scheduled every two months during the first year, semi-annually during the second year, and annually thereafter. Treatment failure was defined as radiological evidence of tumor relapse, categorized as either local recurrence or distant metastasis. *Neoadjuvant chemotherapy* (NAC) was administered to selected patients with clinically localized urothelial tumors. AC was offered to patients with pathological stage T3 or greater and/or node-positive disease unless medically contraindicated or declined by the patient; this regimen was initiated within three months of surgery.

### Data collection

Comprehensive data were meticulously extracted from patient charts and compiled into a Microsoft Excel database. The collected data included demographic information (age, sex, smoking status) and key clinicopathological variables such as the date of diagnosis, tumor histology and behavior, date of last follow-up or date of death, and cause of death (whether bladder cancer-related or due to other causes). Tumors were classified pathologically using the 2002 TNM system established by the *International Union Against Cancer* and graded according to the World Health Organization system from 2004 (12, 13). Additional noteworthy factors were documented, including the *American Society of Anesthesiologists* (ASA) classification, type of urinary diversion, and any postoperative complications or mortality. Duplicate records and cases with implausible dates of diagnosis (e.g., incidence date after the date of death or less than two weeks from death for patients undergoing radiotherapy and/or chemotherapy) were excluded from analysis.

Postoperative complications occurring within 30- and 90-days following surgery were classified according to the Clavien-Dindo grading system, categorized as overall (any grade), minor (grades 1-2), and major (grades 3-5) (14). Postoperative ileus was defined as the inability to tolerate oral alimentation after cystectomy or the occurrence of nausea, emesis, and abdominal distension that necessitated gastrointestinal decompression or nutritional support at any point during the postoperative period. Furthermore, data concerning complications specifically attributable to radical cystectomy were also collected.

### Study outcomes

The primary outcome of this study was the association of bladder cancer treatment with *overall survival* (OS) and *cancer-specific survival* (CSS). *Progression-free survival* (PFS) was also assessed, defined as the interval from the index date to either the date of progression or death from

any cause, or the initiation of a new treatment regimen, with patients who were alive and did not experience progression censored at their last visit date. Median PFS (mPFS) was estimated, along with 95% confidence intervals (CIs), measured in months using the Kaplan-Meier method. CSS was defined as the duration from RC to cancer-related death, while OS was defined as the duration from RC to any cause of death. The secondary outcome involved the identification of factors associated with mortality among patients undergoing radical cystectomy.

### Statistical analysis

Data were analyzed using SPSS Statistics version 24 (IBM Corp., Armonk, NY). Descriptive statistics summarized patient characteristics and tumor features, using mean  $\pm$  standard deviation for continuous variables and frequency and percentage for categorical variables. The Chi-squared test compared categorical variables, while survival analyses were conducted using Kaplan-Meier methods and Cox proportional hazards models to assess *recurrence-free survival* (RFS), *disease-free survival* (DFS), and *overall survival* (OS). The log-rank test was applied to compare survival distributions, with a p-value of less than 0.05 considered statistically significant. Survival time was calculated from the date of diagnosis to either the date of death or the last follow-up, with patients who were alive and without clinical evidence of disease at the last follow-up censored. The proportional hazards assumption was evaluated for each covariate in the Cox regression models, with covariates selected for the final regression model based on the likelihood ratio test. Included covariates were ECOG performance status, type of urinary diversion, tumor grade, pathological stage, lymph node status, histological type, gender, smoking status, gender, and age.

## RESULTS

### Baseline patient, operative details, and tumor characteristics

The patient cohort consisted of 300 individuals, with a mean age of  $67.6 \pm 4.8$  years and a median age of 67.0 years (IQR 65.0, 70.0). The majority of patients were male ( $n = 184$ , 61.3%), and a substantial proportion reported a history of tobacco use ( $n = 186$ , 62.0%). Curative radical cystectomy was the most common surgical intervention, performed in 272 patients (90.7%), followed by palliative cystectomy in 22 (7.3%) and salvage cystectomy in 6 (2.0%). Ileal loop urinary diversion was the most frequently employed reconstruction technique, used in 234 patients (78.0%). Other reconstruction techniques included ileal W neobladder (53 patients, 17.7%), ureterosigmoidostomy (5 patients, 1.7%), cutaneous ureterostomy (3 patients, 1.0%), indwelling PCN (1 patient, 0.3%), and Studer pouch (4 patients, 1.3%). Urothelial carcinoma was the predominant pathological diagnosis, observed in 246 patients (82.0%). Squamous cell carcinoma, mixed carcinoma, and adenocarcinoma were also identified in 42 (14.0%), 7 (2.3%), and 5 (1.7%) patients, respectively. The majority of tumors were classified as high grade ( $n = 270$ , 90.0%). Stage II disease was the most frequently observed pathological stage ( $n = 131$ ,

**Table 1.**

*Baseline patient, operative details, and tumor characteristics in muscle-invasive bladder cancer patients undergoing radical cystectomy.*

Characteristic	N (%)
Age (years), mean $\pm$ SD	67.6 $\pm$ 4.8
Gender	
Female	116 (38.7%)
Male	184 (61.3%)
Smoking status	
No	114 (38.0%)
Yes	186 (62.0%)
ECOG performance status	
0	131 (43.7%)
1	110 (36.7%)
2	59 (19.7%)
Operative type	
Radical cystectomy	272 (90.7%)
Palliative cystectomy	22 (7.3%)
Salvage cystectomy	6 (2.0%)
Urinary diversion type	
Ileal loop	234 (78.0%)
Ileal W neobladder	53 (17.7%)
Ureterosigmoidostomy	5 (1.7%)
Cutaneous ureterostomy	3 (1.0%)
Indwelling PCN	1 (0.3%)
Studer pouch	4 (1.3%)
Pathology type	
Urothelial carcinoma	246 (82.0%)
Squamous cell carcinoma	42 (14.0%)
Mixed carcinoma	7 (2.3%)
Adenocarcinoma	5 (1.7%)
Tumor stage	
Tis	57 (19.0%)
I	37 (12.3%)
II	131 (43.7%)
III	42 (14.0%)
IV	33 (11.0%)
Tumor grade	
High	270 (90.0%)
Low	30 (10.0%)
Lymph node status	
Negative	202 (67.3%)
Positive	98 (32.7%)

43.7%). Stage III and Stage IV disease were observed in 42 (14.0%) and 33 (11.0%) patients, respectively. Lymph node involvement was documented in a significant proportion of the cohort ( $n = 98$ , 32.7%) (Table 1).

### Postoperative and survival outcomes

Postoperative complications were documented in 93 patients (31.0%). Grade I complications were the most common ( $n = 61$ , 20.3%). Grade II complications occurred in 21 patients (7.0%), while Grade III to V (major complications) were observed in 6 (2.0%) and 7 (2.3%) patients, respectively. The mean follow-up duration was 102.1 months (SD 52.0), with a range of 1.0 to 227.0 months and a median of 111 months (IQR: 62, 141).

The overall survival rate was 215 (71.7%), with 85 (28.3%) cases resulting in death. Specifically, 7 (2.3%) cases were mortality-related deaths that occurred during

**Table 2.**

*Oncological outcomes and postoperative complications in muscle-invasive bladder cancer patients undergoing radical cystectomy.*

Characteristic	N (%)
Follow-up duration (months)	
Mean ± SD	102.1 ± 52.0
Range	1.0 to 227.0
Median	111 (IQR: 62, 141)
Outcome	
Alive without disease	184 (61.3%)
Non-cancer mortality	43 (14.3%)
Cancer mortality	35 (11.7%)
Died early	7 (2.3%)
Alive with disease	31 (10.3%)
Progression-free survival (PFS)	
Median PFS, 95% CI (months)	155 (143-191)
Any complication	
No	207 (69.0%)
Yes	93 (31.0%)
Complication grade	
Grade 1	61 (20.3%)
Grade 2	21 (7.0%)
Grade 3	6 (2.0%)
Grade 4	7 (2.3%)

postoperative hospital admission within 30 days of the operation.

Significantly, a substantial fraction of the cohort experienced mortality attributed to non-cancer causes (n = 43, 14.3%) or bladder cancer-related causes (n = 35, 11.7%). At the time of data analysis, among patients who were alive, 184 (61.3%) were alive free of disease, and 31 (10.3%) were alive with disease (Table 2).

### Survival analysis

Single-arm survival analysis of 293 patients with bladder cancer demonstrated a median overall survival (mOS) of 191 months (95% CI: 116-267 months) (Figure 1). Kaplan-Meier estimates indicated 1-year, 3-year, 5-year, and 10-year survival probabilities of 99% (95% CI: 97%-100%), 93% (95% CI: 90%-96%), 88% (95% CI: 84%-92%), and 82% (95% CI: 78%-87%), respectively.

### Factors associated with mortality

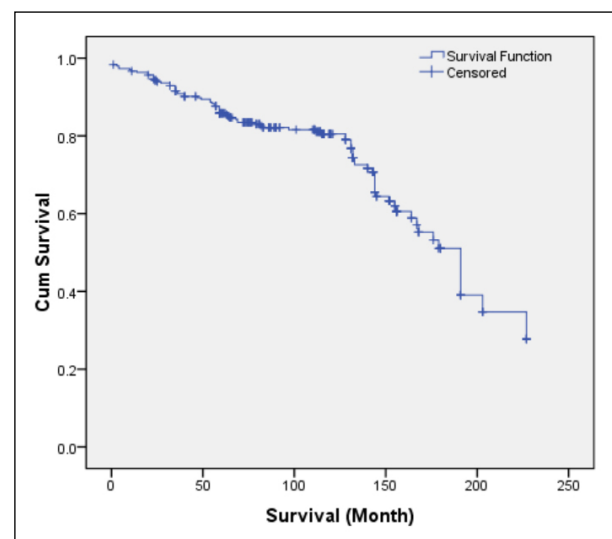
Univariate Cox regression analysis revealed that ECOG performance status (2 vs. 0: HR 5.29, p < 0.001; 1 vs. 0: HR 3.80, p < 0.001), non-ileal conduit urinary diversion (HR 4.21, p < 0.001), high-grade tumors (HR 9.50, p < 0.001), advanced stage (Stage

II vs. Tis: HR 5.16, p < 0.001; Stage IV vs. Tis: HR 6.10, p < 0.001), lymph node positivity (HR 11.95, p < 0.001), and squamous cell carcinoma histology (HR 16.78, p < 0.001) were significantly associated with increased mortality (Table 3).

However, multivariate Cox regression analysis demonstrated that only non-ileal conduit urinary diversion (HR 5.21, p = 0.003), Stage II (HR 2.56, p = 0.047), Stage IV

**Figure 1.**

*Kaplan-Meier estimates of overall survival for Yemeni patients who underwent radical cystectomy.*



**Table 3.**

*Univariate Cox regression analysis of factors associated with overall survival in muscle-invasive bladder cancer patients undergoing radical cystectomy.*

Variable	Subgroup	N (%)	Hazard ratio (95% CI)	P-value
ECOG performance status	0	131 (43.7)	Ref	
	1	110 (36.7)	3.80 (1.89-7.64)	< 0.001
	2	59 (19.7)	5.29 (2.58-10.85)	< 0.001
Urinary diversion type	Ileal conduit diversion	287 (95.7)	Ref	
	Non-ileal conduit diversion	13 (4.3)	4.21 (2.31-7.67)	< 0.001
Tumor grade	Low grade	270 (90.0)	Ref	
	High grade	30 (10.0)	9.50 (5.87-15.37)	< 0.001
Pathological stage	Tis	57 (19.0)	Ref	
	I	37 (12.3)	0.03 (0.00-0.27)	0.002
	II	131 (43.7)	5.16 (2.24-11.90)	< 0.001
	III	42 (14.0)	2.28 (0.87-5.99)	0.095
	IV	33 (11.0)	6.10 (2.64-14.13)	< 0.001
Lymph node status	Negative	202 (67.3)	Ref	
	Positive	98 (32.7)	11.95 (7.11-20.08)	< 0.001
Histological type	Urothelial carcinoma	246 (82.0)	Ref	
	Squamous cell carcinoma	42 (14.0)	16.78 (10.09-27.91)	< 0.001
	Other	12 (4.0)	4.00 (1.99-8.03)	< 0.001
Gender	Female	116 (38.7)	Ref	
	Male	184 (61.3)	0.95 (0.61-1.46)	0.800
Smoking status	No	114 (38.0)	Ref	
	Yes	186 (62.0)	0.86 (0.55-1.33)	0.496
Age (year)	Mean (SD)	67.6 (4.8)	0.97 (0.93-1.01)	0.159

ECOG = Eastern Cooperative Oncology Group; HR = Hazard Ratio; CI = Confidence Interval; SD = Standard Deviation. Ref = Reference.  
\*Other\* in Histological Type includes Adenocarcinoma and Mixed Carcinoma.

(HR 2.76,  $p = 0.050$ ), lymph node positivity (HR 2.92,  $p = 0.022$ ), and squamous cell carcinoma histology (HR 3.09,  $p = 0.022$ ) remained significantly associated with overall mortality. While ECOG performance status and

high-grade tumors did not achieve statistical significance in the multivariate model, the aforementioned factors demonstrated a significant independent impact on patient mortality (Table 4) (Figure 2 A-F).

**Table 4.** Multivariate Cox regression analysis of factors associated with overall mortality in muscle-invasive bladder cancer patients undergoing radical cystectomy.

Variable	Subgroup	Hazard Ratio (95% CI)	p-value
ECOG Performance Status	0	Ref	
	1	1.95 (0.79-4.83)	0.148
	2	1.75 (0.72-4.26)	0.217
Urinary Diversion Type	Ileal conduit diversion	Ref	
	Non-ileal conduit diversion	5.21 (1.75-15.47)	0.003
Tumor Grade	Low Grade	Ref	
	High Grade	0.60 (0.29-1.25)	0.175
Pathological Stage	Tis	Ref	
	I	0.02 (0.00-0.23)	0.001
	II	2.56 (1.01-6.48)	0.047
	III	2.58 (0.95-7.00)	0.062
	IV	2.76 (1.00-7.61)	0.050
Lymph Node Status	Negative	Ref	
	Positive	2.92 (1.17-7.31)	0.022
Histological Type	Urothelial Carcinoma	Ref	
	Squamous Cell Carcinoma	3.09 (1.18-8.10)	0.022
	Other	0.09 (0.03-0.29)	< 0.001

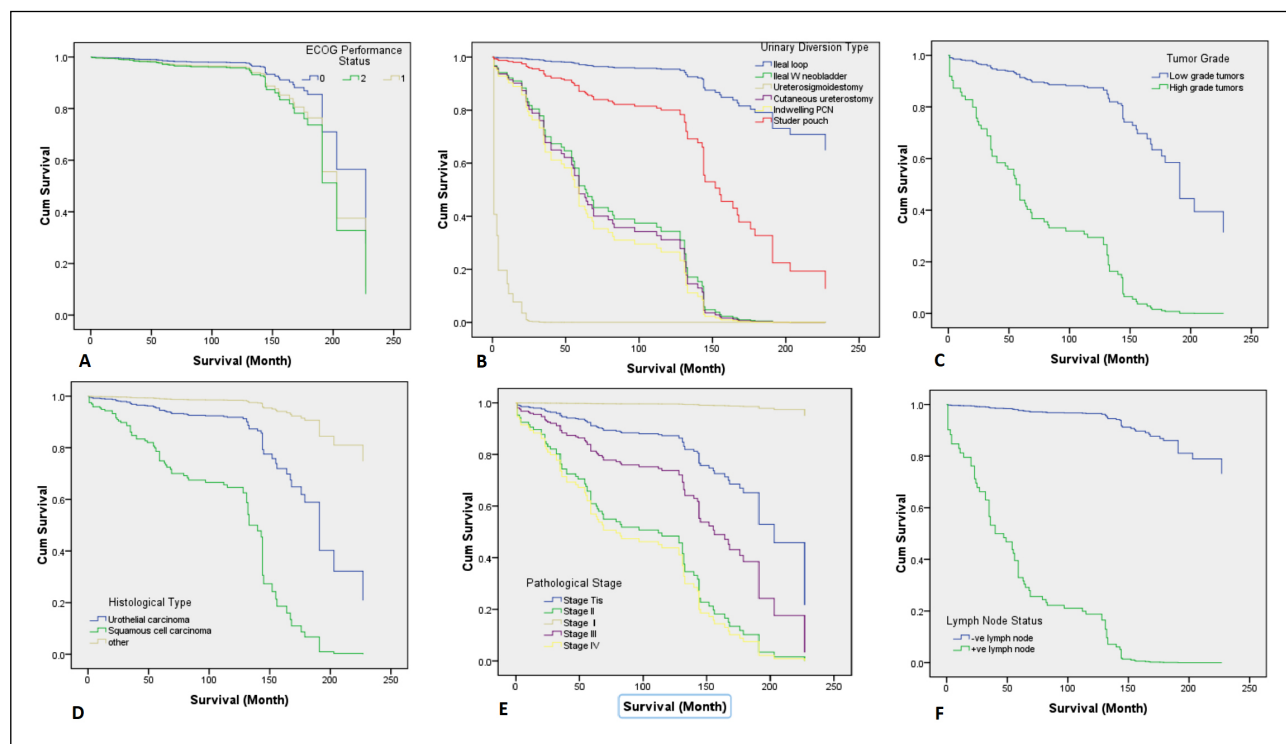
ECOG = Eastern Cooperative Oncology Group; HR = Hazard Ratio; CI = Confidence Interval; SD = Standard Deviation. Ref = Reference.

## DISCUSSION

The study provides a comprehensive evaluation of the management and outcomes of MIBC in Yemen over a period of 16 years. The data collected from patients indicate a median overall survival of 191 months, with 1-year, 3-year, 5-year, and 10-year survival probabilities of 99%, 93%, 88%, and 82%, respectively.

Additionally, the result identified non-ileal conduit diversion, advanced stages of disease, lymph node positivity, and squamous cell carcinoma histology as significant independent predictors of overall mortality in bladder cancer patients. In contrast to studies in Western countries, which have reported 5-year survival rates of 54.5%-68% in bladder cancer patients who underwent radical cystectomy (15, 16), the current study achieved a 5-year survival rate of 88%. This suggests that appropriate patient selection and surgical interventions can lead to comparable outcomes in diverse healthcare settings, despite geographical and infrastructural challenges. In general, findings indicate that RC demonstrates efficacy in controlling local recurrence, evidenced by a five-year DFS rate of 74% (17). Conditional survival analysis revealed that a

**Figure 2.** Kaplan-Meier analysis of overall survival probability in Yemeni patients undergoing radical cystectomy, stratified by: (A) ECOG performance status; (B) Urinary diversion type; (C) Tumor grade; (D) Histological type; (E) Pathological stage; (F) Lymph node status.



longer survivorship after surgery leads to an increase in OS and CSM-free survival probability in patients with MIBC. For instance, patients who were alive at 1 year after RC had 70% and 74% 5-year conditional OS and CSM-free survival rates, respectively, whereas patients who survived 5 years after surgery had 85% and 92% 5-year conditional OS and CSM-free survival rates (18, 19). These findings underscore the importance of optimizing surgical management in MIBC to improve patient prognosis in diverse healthcare settings. Radical cystectomy remains the gold standard for MIBC treatment due to its association with improved survival outcomes (5). However, the results of this study suggest that appropriate surgical interventions can lead to comparable outcomes in diverse healthcare settings, despite geographical and infrastructural challenges.

Our study conducted in Yemen elucidates the significant prevalence of *squamous cell carcinoma* (SCC), which can be attributed to the country's high rates of schistosomiasis. Among the cases analyzed, urothelial carcinoma emerged as the most prevalent pathology, accounting for 82.5% of all instances, thereby corroborating findings from global studies that consistently identify urothelial carcinoma as the predominant variant of bladder cancer (9).

Nonetheless, the 13.5% prevalence of SCC within our cohort warrants attention, particularly in the context of research emerging from regions with endemic schistosomiasis, a well-established risk factor for SCC. Notably, *Al-Samawi et al.* (10) reported that 17% of bladder cancer cases in Yemen were classified as SCC. Furthermore, the literature indicates that SCC of the bladder is associated with increased aggressiveness and inferior survival outcomes, including diminished progression-free and cancer-specific survival, when compared to the urothelial histological subtype (20-22). Furthermore, metastatic SCC is observed to respond inadequately to systemic treatments and radiotherapy (22). Concordant with previous findings, the SCC histopathological subtype in our study was significantly associated with elevated overall mortality. These observations underscore the pressing imperative for the development of targeted screening and management strategies aimed at addressing the distinct risk factors endemic to regions affected by schistosomiasis.

While our study demonstrates promising overall and DFS rates, the reported 31.2% post-operative complication rate, including 7 cases of 30-day post-operative mortality, underscores the imperative for enhanced post-operative care and monitoring. This complication rate is consistent with findings from other reports, such as a systematic review by *Novara et al.*, which reported a post-RC complication range of 20% to 30% (23). Similarly, *Katsimperis et al.* identified gastrointestinal (20%), infections (17%), and ileus (14%) complications as the most frequent, with the majority classified as Clavien I-II (45%) (24). *Zakaria et al.* reported an overall complication rate of 30.6%, encompassing both early and late events, with a 90-day (Clavien grade III-IV) complication rate of 20.9% (25). These elevated complication rates may stem from disparities in healthcare infrastructure, patient management protocols, and adherence to surgical guidelines. Addressing these issues through refined surgical techniques, optimized pre-operative patient prepara-

tion, and improved post-operative care has the potential to reduce the complication rate in Yemeni patients.

While numerous studies have investigated the impact of *orthotopic neobladder* (ON) and *ileal conduit* (IC) diversions on *health-related quality of life* (HRQoL) in bladder cancer patients, the influence of orthotopic neobladder on cancer control remains less defined. A systematic review found no significant difference in quality of life between continent and incontinent urinary diversions. However, orthotopic neobladder may offer HRQoL advantages through the preservation of body image (26). In contrast, the impact of orthotopic neobladder on survival outcomes has been less extensively studied. *Yossepowitch et al.* (27) reported improved cancer-specific and overall survival with orthotopic neobladder compared to ileal conduit, though this significance was not maintained after stratification by disease stage (confined vs. non-confined). In contrast to this finding, *Su et al.* observed superior 5-year survival rates with orthotopic neobladder across all and specific T stages (28). After employing propensity score matching to mitigate baseline differences, orthotopic neobladder was identified as a protective factor for overall survival; however, subgroup analysis revealed that this benefit was primarily observed in patients with pathological T2 stage disease (28). Consistent with previous research, non-ileal conduit diversion was associated with increased overall mortality in our study.

Our findings underscore the significance of certain prognostic factors in bladder cancer patients. Specifically, advanced tumor stage, lymph node involvement, and squamous cell carcinoma histology emerged as independent predictors of overall mortality. These factors likely contribute to a poorer prognosis through several mechanisms. Advanced stage disease often indicates a more extensive local invasion and a higher likelihood of distant metastasis, rendering curative treatment more challenging. Moreover, lymph node positivity signifies regional spread of the malignancy, further decreasing the likelihood of successful local control and increasing the risk of systemic dissemination. Notably, squamous cell carcinoma is a less common histological subtype of bladder cancer that is frequently associated with more aggressive biological behavior and a decreased responsiveness to standard platinum-based chemotherapy regimens, contributing to its association with increased mortality.

These results align with prior reports (29-32); and further emphasize the critical role of accurate staging, comprehensive pathological assessment, and individualized treatment strategies that consider the unique characteristics of each patient's disease.

#### **Implications for future care**

The substantial morbidity associated with MIBC, coupled with the challenges identified in this study, highlights the need for a comprehensive cancer management program in Yemen. Interdisciplinary collaboration among urologists, medical oncologists, and primary care providers is essential to optimize treatment pathways and improve patient outcomes. Furthermore, enhanced public health education focusing on early detection and timely intervention may significantly improve survival rates.

### Study limitations

This study is subject to several limitations. The single-surgeon design potentially restricts the generalizability of the findings. The retrospective methodology introduces inherent selection bias and the potential for data inconsistencies. The relatively small sample size limits statistical power and the feasibility of conducting robust subgroup analyses. Variability in follow-up duration may impact the assessment of long-term outcomes. The absence of standardized treatment protocols could contribute to variability in post-operative results, while reliance on clinical documentation for complication reporting may lead to underreporting. Finally, the lack of comparative data from other institutions and the absence of several factors that may affect survival, such as chemotherapy, limits the contextualization of these findings within the broader landscape of bladder cancer management. Future multi-center, randomized controlled trials incorporating diverse treatment protocols are recommended to address these limitations and further refine our understanding of MIBC management in this context.

### CONCLUSIONS

This study highlights the urgent need for improved bladder cancer care in Yemen. Late-stage diagnosis and sub-optimal surgical methods critically affect survival. Addressing these issues requires prioritizing early detection and standardized surgical techniques to develop effective care pathways for MIBC patients.

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### DECLARATIONS

**Ethical approval:** The study was conducted in accordance with the Declaration of Helsinki and received ethical approval from the Ethics Research Committees of the General Military Hospital, Sana'a, Yemen, with ID: 0015, on April 15, 2024. Due to the retrospective nature of the study, the ethics committee did not require patient consent for chart review, and all data were encrypted and kept anonymous.

**Availability of data and material:** All the data was included in this study.

**Competing interests:** The author declares no potential conflict of interest.

**Funding:** None.

**Authors' contributions:** All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis, and interpretation, or all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

**Acknowledgments:** None.

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### Correspondence

Khaled Al-Kohlany  
kalkohlani@gmail.com

Majdi Al-Shami  
MajdiAlshami@gmail.com

Department of Urology, General Military Hospital, Sana'a, Yemen

Amal Al-Maleki  
majdi.alshami@yahoo.com  
Department of Obstetrics and Gynecology, Palestine Hospital for Motherhood and Childhood, Sana'a, Yemen

Hani Hussein  
drhani01@gmail.com  
Department of Urology, 22 MAY Typical Specialized Surgical Center, Sana'a, Yemen

Faisal Ahmed (Corresponding Author)  
fmaaa2006@yahoo.com  
Department of Urology, School of Medicine, Ibb University, Ibb, Yemen