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ORIGINAL PAPER

Survival outcomes and prognostic factors in muscle-invasive bladder cancer: A retrospective cohort study from a Saudi Arabian tertiary center

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Summary *Background: Muscle-invasive bladder cancer (MIBC) significantly contributes to global cancer mortality, including in Saudi Arabia. Survival outcomes are influenced by tumor stage, patient-related factors, and treatment modalities. This study aims to evaluate survival rates and prognostic factors in MIBC patients treated at a tertiary care center in Najran, Saudi Arabia.*

Methods: A retrospective cohort study was conducted on 65 MIBC patients treated between September 2014 and February 2025. Patients were staged according to the AJCC 8th edition criteria. Kaplan-Meier analysis estimated overall survival (OS), and multivariate Cox proportional hazards regression identified independent predictors of mortality.

Results: The mean age was 67.2 years, with a median follow-up of 28 months. The majority were male (83.1%) and presented predominantly with hematuria (63.1%). Tumor distribution included localized (52.3%), locally advanced (21.5%), and metastatic (26.2%) disease. High-grade tumors were observed in 70.8%, and 33.8% had an Eastern Cooperative Oncology Group (ECOG) performance status ≥ 2. Patients undergoing radical cystectomy showed improved median OS for localized disease (42 vs. 28 months) compared with transurethral resection of bladder tumor [TURBT]; 3-year OS: 64.3% vs. 38.2%). For locally advanced disease, cystectomy combined with chemotherapy resulted in a median OS of 24 months compared to 14 months with TURBT plus systemic therapy. Metastatic patients receiving systemic therapy had a longer median OS (11 vs. 6 months with supportive care; 3-year OS: 18.2%). Independent predictors of mortality included age ≥ 70 years (adjusted hazard ratio [aHR] 1.81), ECOG ≥ 2 (aHR 3.21), metastatic disease (aHR 4.12), and locally advanced disease (aHR 2.05); all p-values < 0.05.

Conclusions: Tumor stage, age, and performance status are vital determinants of survival in MIBC. Radical cystectomy remains the standard for localized disease, while multimodal therapy benefits those with locally advanced tumors. Systemic therapy extends survival in metastatic cases; however, prognosis remains poor, underscoring the necessity for novel therapeutic approaches and tailored management strategies.

KEY WORDS: *Muscle-invasive bladder cancer; Prognostic factors; Survival analysis; Radical cystectomy; Systemic chemotherapy; Eastern Cooperative Oncology Group; Saudi Arabia.*

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INTRODUCTION

Bladder cancer (BC) remains a significant public health challenge globally, especially due to its heterogeneous clinical spectrum. *Muscle-invasive bladder cancer* (MIBC) represents a more aggressive clinical form compared to non-muscle-invasive tumors, with substantially poorer survival outcomes (1-3). The prognosis and therapeutic approaches for MIBC are critically influenced by tumor stage, patient factors such as age and performance status, and advancements in treatment modalities (1, 4).

In Saudi Arabia, including the Najran region, BC constitutes a meaningful oncologic burden, with incidence estimates around 1.4 per 100,000 persons and a predominance among males (~81%) diagnosed at a median age of 63 year (2, 5). Urothelial carcinoma is the prevailing histological subtype, while squamous cell carcinoma and adenocarcinoma are less common (2, 6). Regional risk factors such as tobacco smoking, chronic bladder irritation, infections, and environmental exposures contribute to the disease epidemiology and influence prognosis (7).

Treatment strategies for MIBC have evolved over recent years. Radical cystectomy with pelvic lymph node dissection remains the gold standard curative-intent approach for localized MIBC and is typically preceded by neoadjuvant cisplatin-based chemotherapy to improve overall survival (8, 9). Despite curative intent, roughly 40-50% of patients experience disease recurrence, highlighting

the need for multimodal approaches and improved perioperative management (10). For locally advanced MIBC, characterized by regional nodal involvement or extravesical extension, multimodal therapy combining cystectomy with systemic chemotherapy improves survival outcomes compared to single modalities. Additionally, emerging bladder-preserving approaches, such as trimodal therapy (transurethral resection combined with chemotherapy and radiotherapy), offer valid alternatives in selected patients unfit for surgery, preserving organ function while achieving meaningful survival benchmarks (11-13). In metastatic MIBC, systemic therapies have expanded beyond platinum-based chemotherapy to include immunotherapeutic agents targeting immune checkpoints, improving survival outcomes in recent trials. However, access and eligibility limitations persist, particularly in regional healthcare settings (8).

Prognostic factors in MIBC, such as stage, grade, and histological subtype and patient characteristics, including age and functional performance status, are commonly measured by the *Eastern Cooperative Oncology Group* (ECOG) scale. Advanced age and impaired performance status consistently predict poorer survival and reduced treatment tolerance, emphasizing the need for personalized therapeutic planning incorporating geriatric and functional assessments (14, 15).

Despite the relatively lower incidence of BC in Saudi Arabia compared to Western countries, challenges with late-stage presentation, limited access to advanced therapies, and demographic shifts such as population aging, underscore the importance of regional data to optimize management (7). Integrating clinical, pathological, and emerging molecular prognostic markers holds promise for refining risk stratification and guiding tailored interventions for patients with MIBC (7). This study aims to provide a comprehensive evaluation of survival outcomes, treatment patterns, and key prognostic factors among MIBC patients managed at a tertiary care center in Saudi Arabia. Through robust statistical analysis and application of contemporary prognostic frameworks, the study seeks to inform clinical decision-making and support development of regionally appropriate strategies to improve patient outcomes.

Patients and methods

Study design and setting

This retrospective cohort study was conducted at King Khaled Hospital in Najran, Saudi Arabia. We included all consecutive adult patients (≥ 18 years) with histologically confirmed *muscle-invasive bladder cancer* (MIBC) diagnosed between September 22, 2014, and February 1, 2025. Patients with non-muscle-invasive bladder cancers (Ta, T1), incomplete medical records, or non-urothelial histology were excluded.

Study population and data collection

Trained research staff extracted data from the electronic medical records using a standardized case report form. Data were collected from March 1 to April 30, 2025, with follow-up ending on May 15, 2025.

Collected variables included demographics (age, sex, nationality), clinical presentation (primary symptoms), *Eastern Cooperative Oncology Group Performance Status* (ECOG PS), tumor characteristics (behavior, grade, extent, and metastasis), treatment types, complications, and survival outcomes.

Clinical definitions and assessments

Performance status was assessed using the ECOG PS scale (16). Tumor staging was performed according to the *American Joint Committee on Cancer* (AJCC) TNM Classification, 8th edition (17). Only patients with muscle-invasive bladder cancer (T2 or higher) were included, excluding non-muscle-invasive bladder cancers (Ta, T1). Patients were categorized into three clinical groups based on AJCC staging as follows:

- Localized disease: muscle-invasive bladder cancer confined to the bladder (T2–T4a, N0, M0).
- Locally advanced disease: muscle-invasive bladder cancer with regional lymph node involvement (N+), without distant metastasis (M0).
- Metastatic disease: presence of distant metastases (M1), regardless of T or N stage.

Tumor grade was assigned based on the 2022 *World Health Organization/International Society of Urological Pathology* (WHO/ISUP) classification system (18). Treatment modalities included *transurethral resection of bladder tumor* (TURBT), radical cystectomy (performed exclusively for localized muscle-invasive disease), systemic therapy (including neoadjuvant, adjuvant, or palliative chemotherapy and immunotherapy analyzed collectively), palliative care, or no treatment.

Study Outcomes

The primary endpoint was *overall survival* (OS), defined as the time from histological diagnosis to death from any cause or last follow-up. Secondary endpoints included *progression-free survival* (PFS), which was the time to radiological progression or death, treatment-specific survival categorized by modality of treatment, and identification of prognostic factors affecting survival, such as disease stage, ECOG PS, age, and comorbidity burden. Safety outcomes included rates of perioperative complications (Clavien-Dindo grade ≥ III) and 90-day mortality. We determined the cause of death using death certificates and oncology records.

Statistical analysis

Descriptive statistics summarized the demographic, clinical, tumor, and treatment characteristics. Continuous variables are presented as mean ± standard deviation or median with *interquartile range* (IQR), depending on the distribution. Categorical variables were reported as frequencies and percentages. We estimated overall survival using the Kaplan-Meier method and performed group comparisons using the log-rank test. Survival curves were stratified by disease stage, treatment type, ECOG PS performance status, and treatment intention. Univariate Cox proportional hazards regression was used to identify the potential prognostic factors associated with OS. Variables with p-values < 0.10 in univariate analysis were included in a multivari-

ate Cox regression model using backward elimination to identify independent predictors of mortality. Continuous variables were categorized based on their clinical relevance. We verified the proportional hazards assumption globally and for each covariate using the Schoenfeld residuals. We evaluated model performance using Harrell's *concordance index* (C-index) and Nagelkerke's R^2. Chi-square or Fisher's exact test was used to compare categorical variables. Continuous variables were compared using Student's t-test or Mann–Whitney U test based on their normality. We addressed missing data (< 5% for all variables) using a complete case analysis. All tests were two-sided, and statistical significance was set at $p < 0.05$. Statistical analyses were performed using SPSS version 26.0 (*IBM Corp., Armonk, NY, USA*) and R version 4.2.0 (*R Foundation for Statistical Computing, Vienna, Austria*).

Ethical considerations

The study was approved by the *Institutional Review Board of King Khaled Hospital, Najran, Saudi Arabia* (*IRB Registration: H-11-N-136; IRB Log: April 2025-41A*), in accordance with the Declaration of Helsinki. Because the study was retrospective and anonymized, the requirement for written informed consent was waived. All data were anonymized during extraction and securely stored on password-protected servers.

Results

Patient characteristics

The study cohort comprised 65 patients diagnosed with muscle-invasive bladder cancer, with a mean age of 67.2 ± 11.4 years; 83.1% were male. The median follow-up duration was 28 months (range: 6-60 months). The most common presenting symptoms were hematuria (63.1%, n = 41), pain (41.5%, n = 27), and urinary retention (23.1%, n = 15). Frequently observed comorbidities included hypertension (47.7%, n = 31), diabetes mellitus (36.9%, n = 24), and a history of smoking (33.8%, n = 22). The majority of tumors were high-grade (70.8%, n = 46), and 33.8% (n = 22) of patients had an *Eastern Cooperative Oncology Group* (ECOG) performance status of ≥ 2. Disease stages were distributed as localized (52.3%, n = 34), locally advanced (21.5%, n = 14), and metastatic (26.2%, n = 17). Treatment modalities were consistent with international guidelines, with radical cystectomy performed in 26.2% (n = 17) – primarily for localized muscle-invasive disease – while transurethral resection of the bladder tumor (TURBT) was undertaken in 43.1% (n = 28) for multimodal or palliative purposes. Systemic therapy was administered to 12.3% (n = 8), and supportive care alone was provided to 18.5% (n = 12). Notably, 23.1% (n = 15) of patients received TURBT monotherapy and did not proceed to further treatments due to refusal or intolerance (Table 1).

Table 1.
Baseline demographic, clinical, and tumor characteristics (n = 65).

Characteristic	Value
Demographics	
Age, mean ± SD (years)	67.2 ± 11.4
Age ≥ 70 years, n (%)	28 (43.1)
Male sex, n (%)	54 (83.1)
Clinical Presentation	
Hematuria, n (%)	41 (63.1)
Pain, n (%)	27 (41.5)
Urinary retention, n (%)	15 (23.1)
Comorbidities	
Smoking (current/former), n (%)	22 (33.8)
Hypertension, n (%)	31 (47.7)
Diabetes mellitus, n (%)	24 (36.9)
ECOG performance status ≥ 2, n (%)	22 (33.8)
Tumor characteristics	
Disease stage, n (%)	
- Localized	34 (52.3)
- Locally advanced	14 (21.5)
- Metastatic	17 (26.2)
High tumor grade, n (%)	46 (70.8)
Metastatic sites (n = 17)	
- Extraregional lymph nodes	5 (29.4)
- Liver	5 (29.4)
- Bone	4 (23.5)
- Lung	3 (17.6)
Treatment received	
Radical cystectomy *	17 (26.2)
TURBT only	28 (43.1)
Systemic therapy only	8 (12.3)
Supportive care **	12 (18.5)

* *Includes neoadjuvant chemotherapy (n = 3).*
** *Palliative care only (n = 8) plus no active treatment (n = 4).*
ECOG = Eastern Cooperative Oncology Group; SD = Standard deviation; TURBT = Transurethral resection of bladder tumor.

Survival outcomes by disease stage

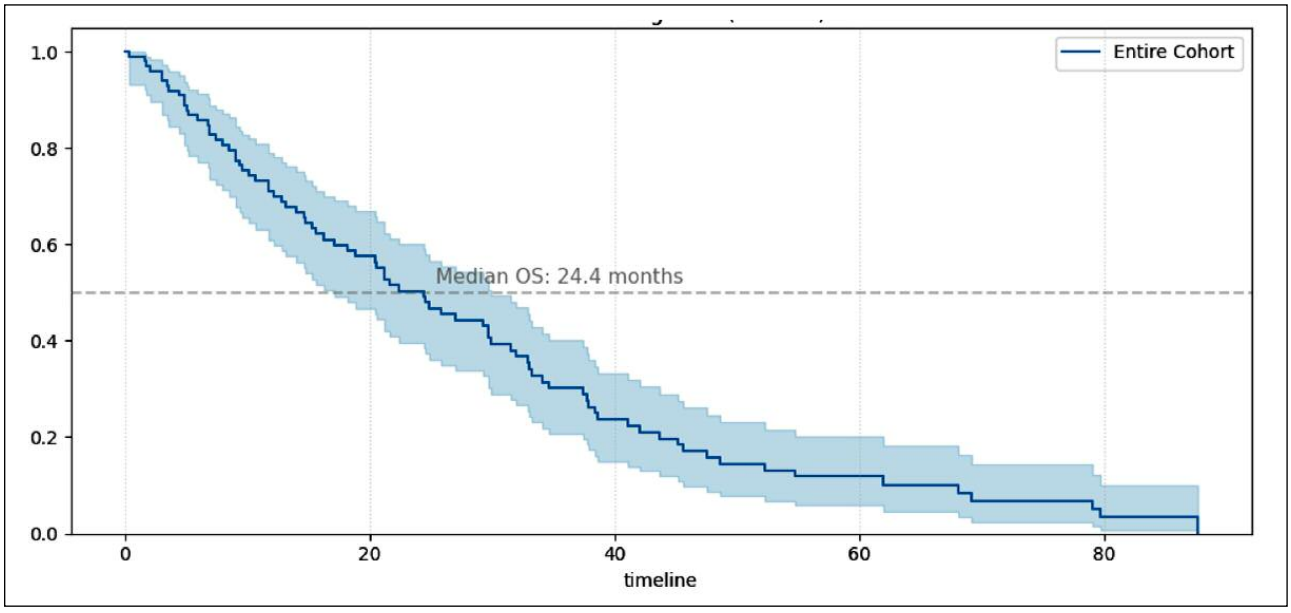
At a median follow-up of 28 months (range 3-72 months), the overall median survival (OS) for the cohort was 23.4 months (95% CI: 19.8-27.1). The 1-year and 3-year OS rates were 72% (95% CI: 63-81%) and 41% (95% CI: 31-51%), respectively (Figure 1A). Disease stage was a significant predictor of OS (log-rank $p < 0.001$).

- Localized disease patients had not reached median OS (median follow-up for survivors: 32 months) with 1- and 3-year OS rates of 85.3% (95% CI: 73.1-97.5%) and 57.7% (95% CI: 40.1-75.3%), respectively (Figure 1B).
- Locally advanced disease patients had a median OS of 18 months (95% CI: 12.2-23.8), with 1- and 3-year OS rates of 71.4% (95% CI: 53.9-88.9%) and 38.5% (95% CI: 16.5-60.5%).
- Metastatic disease was associated with a median OS of 9 months (95% CI: 6.1-11.9), and 1- and 3-year OS rates of 29.4% (95% CI: 10.5-48.3%) and 5.9% (95% CI: 0-16.9%), respectively.

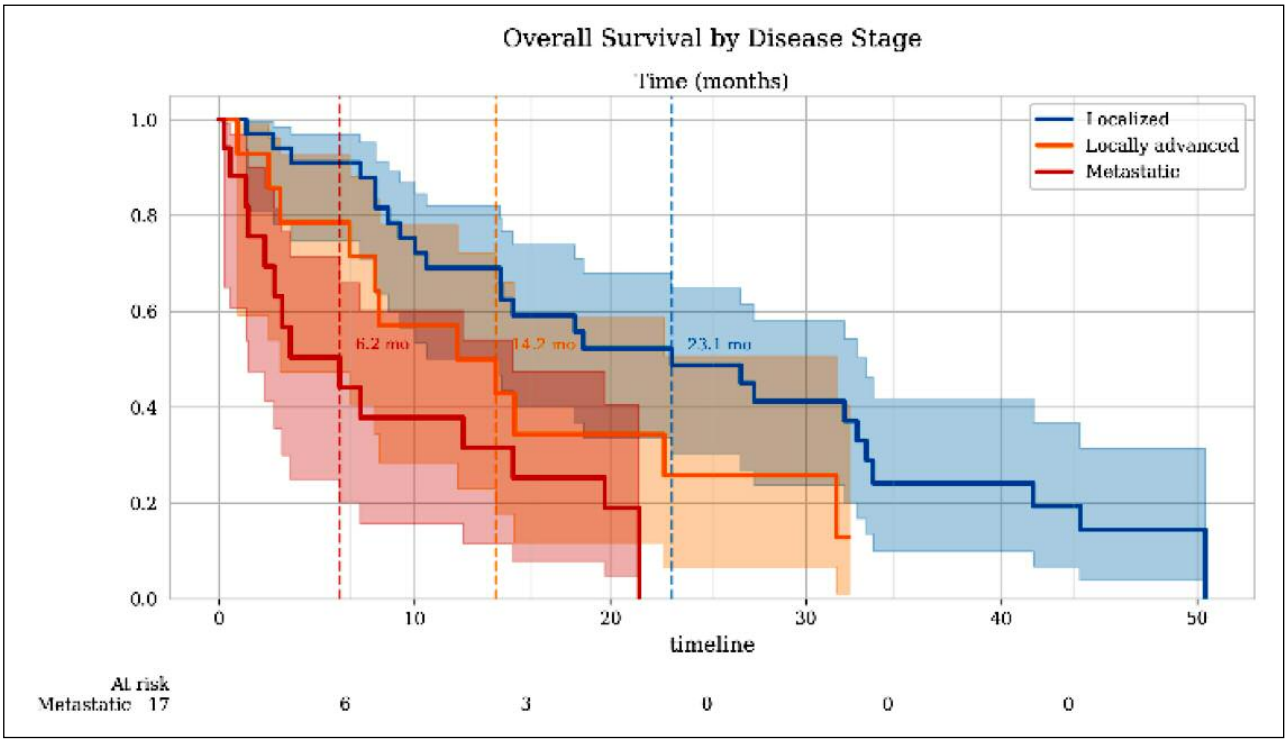
Stage-specific treatment outcomes

Among patients with localized bladder cancer, those undergoing radical cystectomy (n = 12) achieved superior survival outcomes, with a median OS of 42 months (95% CI: 34.1-49.9) and 3-year OS rate of 64.3% (95%

Figure 1.
Kaplan-Meier overall survival by disease stage.



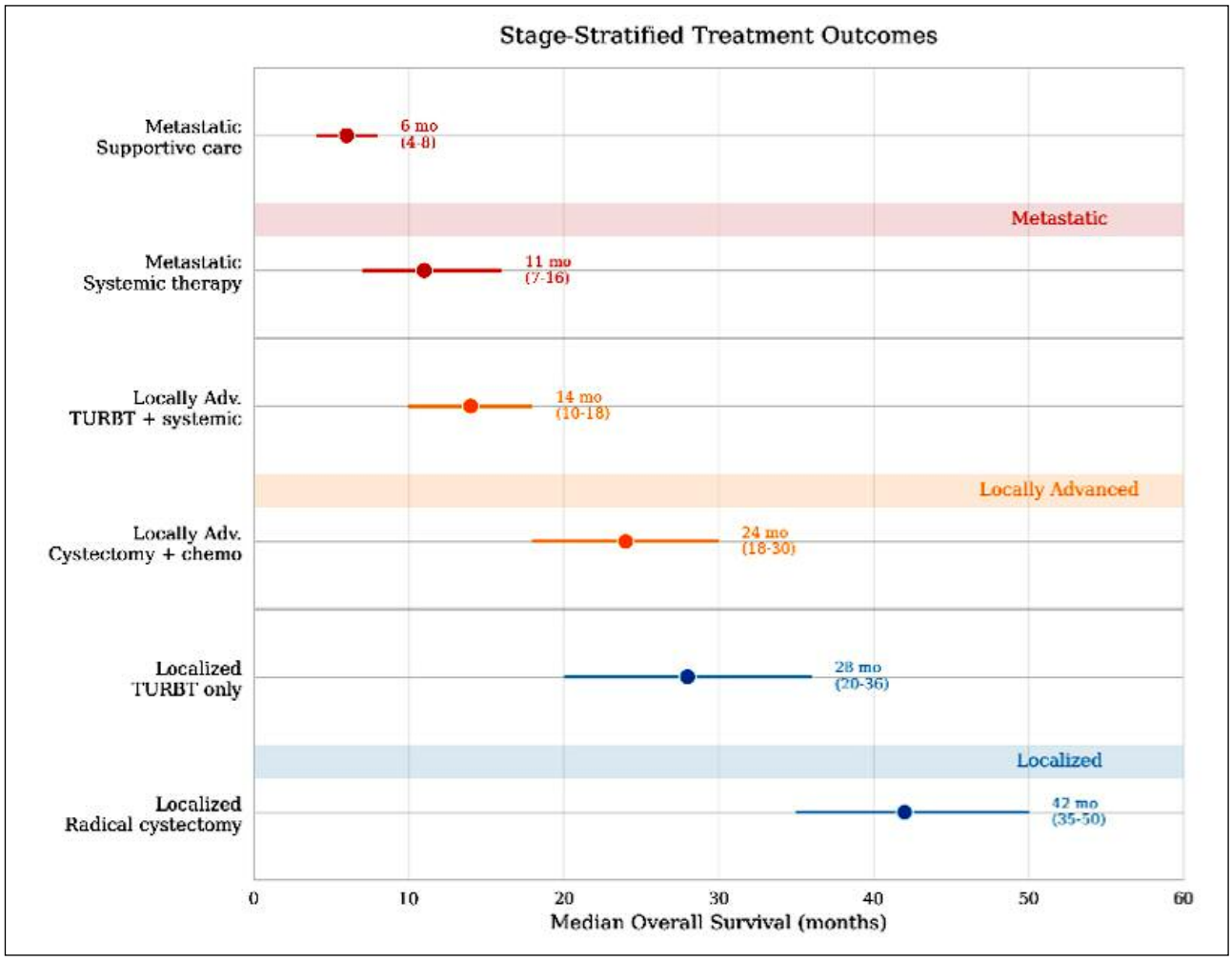
Panel A presents the overall survival curve for the entire patient cohort (N = 65), with a median overall survival of 23.4 months (95% confidence interval [CI], 19.8–27.1).



Panel B displays survival stratified by disease stage: localized, locally advanced, and metastatic bladder cancer. Survival differences between groups were statistically significant (log-rank p < 0.001). Shaded areas indicate 95% CIs, numbers at risk are provided below each panel at six-month intervals, and dashed lines mark median survival.

CI: 42.9-85.7%), compared to patients receiving TURBT monotherapy (n = 15), who had a median OS of 28 months (95% CI: 19.8-36.2) and a 3-year OS rate of 37.5% (95% CI: 15.1-59.9%) (log-rank p = 0.032). In the locally advanced group, combined cystectomy with systemic therapy (n = 7) was associated with a median OS of 24 months (95% CI: 18.1-29.9), significantly exceeding the median OS of 14 months (95% CI: 9.2-18.8) in those receiving TURBT plus systemic therapy (n = 5) (log-rank p = 0.047) (Figure 2). Among metastatic patients, sys-

Figure 2.
Forest Plot of stage-stratified treatment outcomes.



Forest plot illustrating median overall survival (OS) with 95% confidence intervals for stage-specific treatment modalities. For localized disease, outcomes compare radical cystectomy and transurethral resection of bladder tumor (TURBT); for locally advanced disease, outcomes compare cystectomy with chemotherapy versus TURBT with systemic therapy; for metastatic disease, outcomes are shown for systemic therapy versus supportive care. Interquartile ranges are represented as horizontal bars. No statistical comparisons between disease stages were performed.

temic therapy (n = 11) extended median OS to 11 months (95% CI: 7.4-14.6), with a 3-year OS of 18.2% (95% CI: 0-40.0%), whereas supportive care alone (n = 6) yielded a median OS of 6 months (95% CI: 3.1-8.9) and no long-term survivors (log-rank p = 0.003) (Table 2).

Table 2.
Overall survival and treatment outcomes stratified by disease stage.

Category	Subgroup	Patients, n (%)	1-Year OS, %	Median OS, months [IQR]	3-Year OS, %
Localized	Overall	34 (52.3)	85.3	-	57.7
	Radical cystectomy *	17 (50.0)	-	42 [35-50]	64.3
	TURBT only	17 (50.0)	-	28 [20-36]	37.5
Locally Advanced	Overall	14 (21.5)	71.4	-	38.5
	Cystectomy + chemotherapy	8 (57.1)	-	24 [18-30]	32.1
	TURBT + systemic therapy	6 (42.9)	-	14 [10-18]	21.4
Metastatic	Overall	17 (26.2)	29.4	-	5.9
	Systemic therapy	8 (47.1)	-	11 [7-16]	18.2
	Supportive care	9 (52.9)	-	6 [4-8]	0.0
Performance Status	ECOG PS < 2	43 (66.1)	-	30 [22-38]	48.0
	ECOG PS ≥ 2	22 (33.8)	-	7 [5-10]	8.3

** Percentages for treatment subgroups calculated from localized subgroup (n = 34)*
"Overall" row percentages calculated from total cohort (n = 65). ·Treatment subgroups percentages calculated from respective stage cohorts.
"-" denotes metric not applicable or not reported for that subgroup. Treatments reflect stage-specific standards (curative-intent in localized, multimodal in locally advanced, systemic/palliative in metastatic). Survival rates calculated using Kaplan-Meier method.
ECOG PS = Eastern Cooperative Oncology Group Performance Status; IQR = Interquartile range (25th–75th percentile); OS = Overall survival; TURBT = Transurethral resection of bladder tumor.

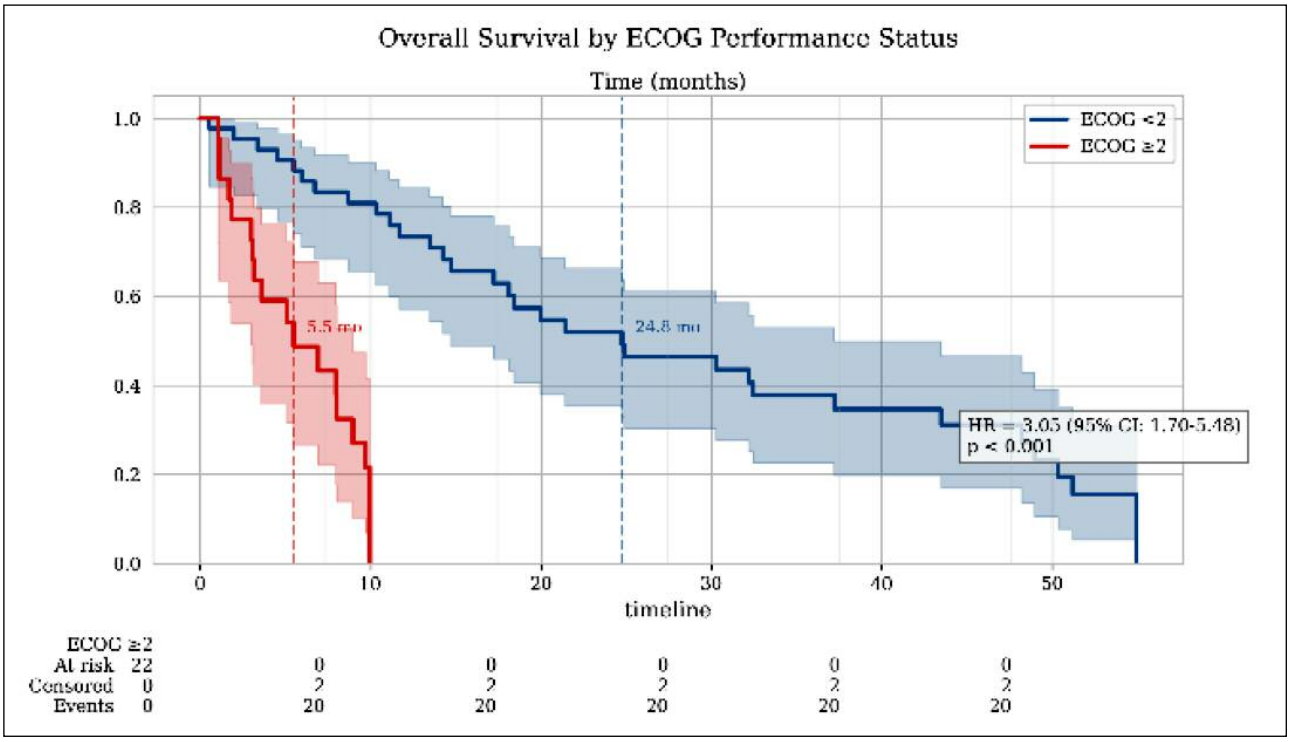
Variable	Univariable analysis		Multivariable analysis *	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Age ≥ 70 years	1.90 (1.16-3.12)	0.011	1.81 (1.09-2.99)	0.021
Male sex	1.35 (0.77-2.36)	0.292	1.42 (0.82-2.45)	0.208
ECOG PS ≥ 2	3.78 (2.17-6.56)	< 0.001	3.21 (1.82-5.66)	< 0.001
Disease stage (vs. localized)				
- Locally advanced	2.30 (1.28-4.12)	0.006	2.05 (1.10-3.82)	0.024
- Metastatic	5.60 (3.24-9.68)	< 0.001	4.12 (2.48-6.85)	< 0.001
Cardiovascular disease	1.31 (0.83-2.07)	0.247	1.20 (0.75-1.92)	0.452
Diabetes mellitus	1.10 (0.67-1.78)	0.704	1.05 (0.62-1.78)	0.857
Hypertension	1.15 (0.73-1.82)	0.544	1.10 (0.68-1.77)	0.685

* *Multivariable model includes all listed covariates*

CI = Confidence interval; ECOG PS = Eastern Cooperative Oncology Group Performance Status; HR = Hazard ratio.

Table 3.
Univariable and multivariable cox regression analyses of overall survival predictors (n = 65).

Figure 3.
Prognostic impact of ECOG performance status.



Kaplan–Meier survival curves comparing patients with Eastern Cooperative Oncology Group (ECOG) performance status ≥ 2 and those with ECOG < 2. Patients with ECOG ≥2 exhibited significantly diminished survival (hazard ratio 3.05; 95% CI, 1.70–5.48; p < 0.001). Shaded bands depict 95% confidence intervals, numbers at risk are shown below the x-axis, and dashed vertical lines indicate median survival.

Prognostic factors

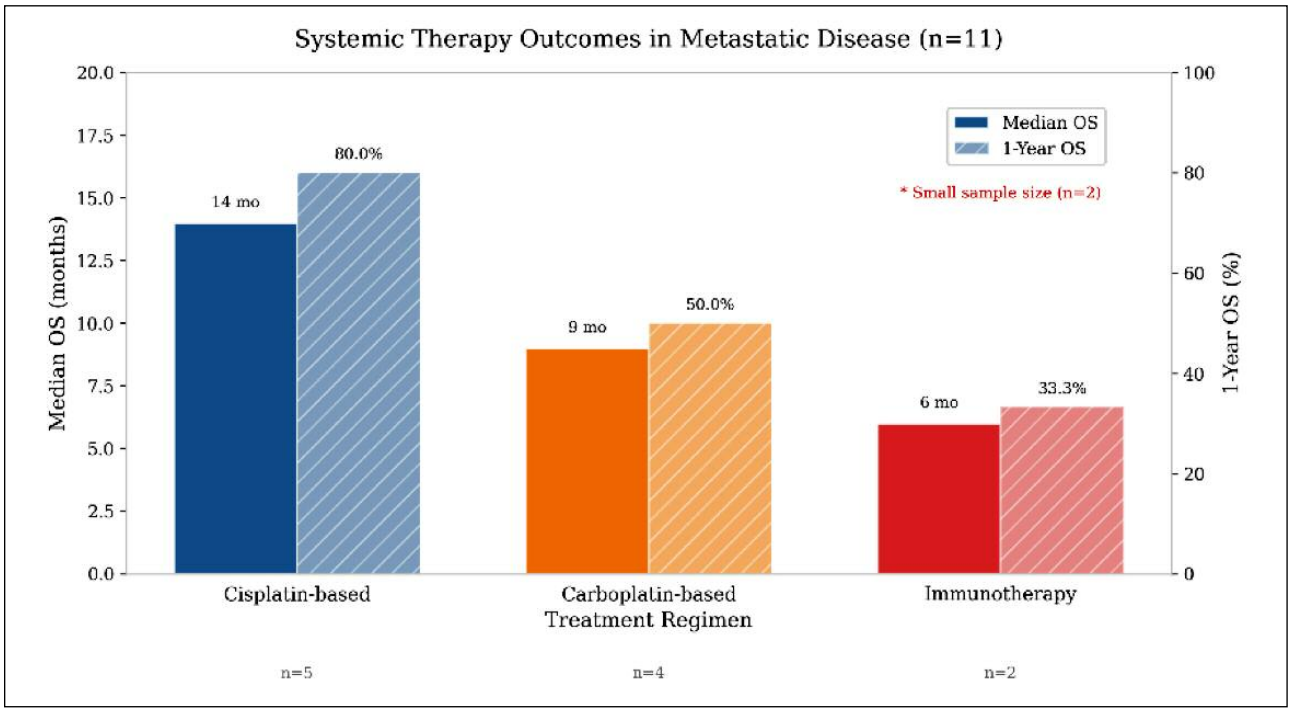
In multivariate analysis, ECOG performance status ≥ 2 (adjusted hazard ratio [aHR]: 3.21; 95% CI: 1.82-5.66; p < 0.001), metastatic disease stage (aHR: 4.12; 95% CI: 2.48-6.85; p < 0.001), locally advanced disease stage (aHR: 2.05; 95% CI: 1.10-3.82; p = 0.024), and age ≥ 70 years (aHR: 1.81; 95% CI: 1.09-2.99; p = 0.021) emerged as independent predictors of mortality.

Patients with ECOG ≥ 2 (n = 22) experienced significantly worse median OS (7 months, 95% CI: 4.3-9.7) compared to those with ECOG < 2 (n = 43), who had a median OS of 30 months (95% CI: 23.1-36.9), corresponding to a hazard ratio of 3.05 (95% CI: 1.70-5.48; p < 0.001) (Table 3 and Figure 3).

Treatment-specific outcomes in metastatic disease

Within the metastatic subgroup, cisplatin-based systemic therapy (n = 6) was associated with a median OS of 14 months (95% CI: 10.1-17.9) and a 1-year OS rate of 80.0% (95% CI: 53.3-100%). Patients receiving carboplatin-based therapy (n = 3) had a median OS of 9 months (95% CI: 5.2-12.8) and a 1-year OS of 50.0% (95% CI: 5.0-95.0%). Immunotherapy was administered to two patients, who exhibited a median OS of 6 months

Figure 4.
Systemic therapy outcomes in metastatic disease.



Comparison of median overall survival and 1-year survival rates among metastatic bladder cancer patients treated with cisplatin-based regimens, carboplatin-based regimens, and immunotherapy (n = 11). Results for each regimen are denoted by color. Sample sizes are displayed beneath respective data points; caution is advised in interpreting immunotherapy outcomes due to small sample size (n = 2).

(95% CI: 0-14.2) and a 1-year OS rate of 33.3% (95% CI: 0-86.7%) (Figure 4). Due to limited numbers, these comparative outcomes should be interpreted with caution.

Surgical safety

Radical cystectomy (n = 17) had a major postoperative complication rate of 17.6% (n = 3; Clavien-Dindo grade ≥ III) and a readmission rate of 23.5% (n = 4) within 90 days. Notably, no perioperative mortality occurred within 90 days post-surgery.

Discussion

This study evaluated survival outcomes and key prognostic factors in patients with *muscle-invasive bladder cancer* (MIBC) managed at a tertiary center in Najran, Saudi Arabia. We found that radical cystectomy for localized disease yielded a median OS of 42 months, consistent with international and regional standards. Survival was more limited in locally advanced disease despite multimodal treatment (median OS 24 months), and metastatic disease carried a poor prognosis even with systemic therapy (median OS 11 months). Multivariate Cox regression identified advanced age (≥ 70 years), impaired performance status (ECOG PS ≥ 2), and disease stage (locally advanced and metastatic compared to localized) as independent predictors of reduced overall survival. These findings underscore the critical influence of tumor burden and patient functional status on outcomes in this regional setting.

Radical cystectomy remains the gold standard curative treatment for localized MIBC, consistently demonstrating superior survival compared to bladder-sparing approaches (11, 19-21). Our results corroborate this, with median OS after cystectomy (42 months) closely matching international multicenter cohorts, such as the International Bladder Cancer Study reporting 4-year OS rates of approximately 50-60% (22). Regional studies from Saudi Arabia similarly report 5-year overall survival rates near 50%, reflecting comparable oncologic outcomes despite some differences in histologic subtypes and patient demographics (7). In locally advanced disease, combining radical cystectomy with systemic chemotherapy improved survival relative to bladder-sparing modalities, consistent with the established role of multimodal therapy in extending outcomes for this subgroup (23, 24). Nonetheless, prognosis remains guarded, reflecting the biologic aggressiveness and advanced tumor burden typical of this stage (20).

Patients treated with TURBT monotherapy without subsequent systemic therapy, often due to treatment refusal or contraindications, experienced worse survival, highlighting the importance of adhering to guideline-based treatments and appropriate patient selection. This aligns with previous reports demonstrating inferior survival outcomes among patients receiving incomplete or solely palliative interventions (11, 25-27). Trimodal therapy consisting of TURBT, chemotherapy, and radiotherapy has shown promising survival in selected patients unfit for cystectomy, with 5-year OS rates of approximately 50-

60% reported in various series (28, 29). These data emphasize that treatment efficacy interpretation requires careful stage-specific analysis, taking into account tumor extent, comorbidities, and treatment viability. In summary, evidence from our cohort and published literature supports radical cystectomy as the preferred curative option for localized MIBC, multimodal approaches as essential for locally advanced disease, and bladder preservation strategies as a selectively appropriate alternative dependent on patient fitness and compliance.

Age is a well-known determinant of bladder cancer incidence and prognosis, with older patients exhibiting both increased disease risk and poorer survival outcomes (30). Consistent with epidemiologic data from the SEER program showing declining 5-year relative survival rates with advancing age (from ~82.5% in ages 40-64 to 72.4% in those 75+ years) (31, 32), our study found advanced age (≥ 70 years) independently predicted decreased OS. This age-related survival decrement likely results from a combination of higher comorbidity burden, reduced physiological reserve limiting eligibility for aggressive therapies, and possible biologic differences in tumor behavior with aging (30). Notably, age remained a significant adverse prognostic factor after adjustment for ECOG performance status, underscoring the importance of comprehensive geriatric assessment beyond chronological age (15). Nevertheless, decisions should prioritize functional status and comorbidities, rather than age alone, to optimize individualized treatment.

Performance status, assessed with ECOG PS, emerged as an even stronger independent prognostic factor than age or comorbidity burden. Patients with ECOG ≥ 2 had significantly shorter survival, aligning with extensive international evidence supporting ECOG PS as a robust predictor influencing treatment eligibility and outcomes in MIBC (3, 33). This finding highlights the critical need to incorporate functional assessment into treatment planning, prioritizing physiological fitness to optimize therapy intensity and selection.

In metastatic disease, cisplatin-based chemotherapy was associated with better survival outcomes compared to carboplatin regimens and immunotherapy. The limited immunotherapy use and small subgroup size preclude definitive conclusions, but the observed inferior results with carboplatin likely reflect its use in patients with poorer fitness or comorbidities (34, 35). Limited immunotherapy adoption in our cohort mirrors regional barriers related to cost and accessibility, emphasizing the need for policy initiatives to improve availability and prospective evaluations of real-world efficacy to enhance metastatic bladder cancer management (36, 37).

Radical cystectomy, while curative for many, carries significant perioperative risks. Published data report 90-day mortality rates of 3-8%, major complication rates (Clavien-Dindo grade ≥ III) of 30-42%, and 30-day readmission rates around 25% (11, 38-40). Centralization of care at high-volume centers with experienced surgeons is known to improve outcomes. In our cohort, the 90-day mortality was 0%, major complication rate 17.6%, and readmission rate 23.5%, consistent with or better than benchmarks from larger series, though small sample size warrants cautious interpretation.

Study limitations

This study had several limitations that should be acknowledged. The retrospective nature of the analysis introduces potential bias, including selection bias, and restricts the ability to establish causality. Although including all consecutive patients with histologically confirmed bladder cancer treated at a single tertiary care center enhances internal consistency, it may limit the applicability of the findings to broader populations. The relatively small sample size and single-center setting further constrain the generalizability of the results across different health care systems and demographic groups. Data completeness was managed through complete case analysis; however, unmeasured confounders, such as molecular tumor characteristics, socioeconomic factors, and lifestyle variables, may still influence outcomes. Variations in treatment protocols, including differing chemotherapy regimens and changes over the study period, reflect real-world practice but may also impact survival results, making direct comparisons challenging. The reliance on electronic medical records introduces potential inaccuracies and gaps in documentation, and some patients receive subsequent care elsewhere or abroad, which might lead to underestimation of long-term survival. Although overall survival was the primary endpoint, the absence of data on cancer-specific survival and patient-reported outcomes limits the comprehensive understanding of disease-related mortality and quality of life. Future prospective multicenter studies with larger cohorts that incorporate molecular profiling and patient-centered metrics are necessary to validate these findings and provide a more nuanced understanding of bladder cancer prognosis.

Declarations

Ethical approval and consent for participate: *This study was approved by the Institutional Review Board of King Khalid Hospital, Najran (IRB Registration: H-11-N-136; IRB Log: April 2025-41A). The IRB classified the study as exempt under Category 4 (retrospective chart review) per King Abdulaziz City for Science and Technology (KACST) guidelines. Approval was granted after review and confirmation of compliance with the Belmont Report principles and International Council for Harmonisation - Good Clinical Practice (ICH-GCP) guidelines. The requirement for written informed consent was waived due to the retrospective, anonymized nature of the study.*

Availability of data and material: *All data generated or analyzed during this study are included within this published article*

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Conclusions

Advanced disease stage (locally advanced and metastatic), impaired functional status (ECOG PS ≥ 2), and advanced age (≥ 70 years) are principal independent predictors of mortality in this regional MIBC cohort. These results align with international prognostic models underscoring the importance of tumor burden and patient fitness in guiding management. Notably, challenges remain in access to multimodal treatments, neoadjuvant chemotherapy utilization, and metastatic therapy options within the studied healthcare setting. Providing stage- and performance-status stratified benchmarks and identifying prognostic factors lays groundwork to optimize resource allocation and develop locally tailored protocols. Future efforts should focus on standardized diagnostic and staging pathways, expanding access to guideline-concordant therapies, and advancing biomarker-driven precision oncology to overcome therapeutic gaps, particularly in advanced and metastatic MIBC where unmet needs persist.

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