

Survival Analysis and Prognosis Factors of Urothelial Bladder Carcinoma in Moroccan Patient

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Abstract

Introduction: Urothelial bladder carcinoma (UBC) is a major urological malignancy with heterogeneous clinical outcomes. Data on survival and prognostic factors in North African populations remain limited. This study aimed to evaluate overall survival and identify prognostic clinicopathological factors in a cohort of Moroccan patients with UBC. **Materials and Methods:** We conducted a retrospective cohort study including 124 patients diagnosed with urothelial bladder carcinoma at Ibn Rochd University Hospital, Casablanca, between 2020 and 2022. Overall survival was estimated using the Kaplan-Meier method and compared using the log-rank test. Prognostic factors were assessed using univariate and multivariate Cox proportional hazards regression models. Median follow-up was estimated using the reverse Kaplan-Meier method. **Results:** During a median follow-up of 28.14 months, 34 patients (27.4%) died. The median overall survival was not reached, and the estimated overall survival rate at last follow-up was 65.9% (95% CI: 57.47-74.52%). Patients with non-muscle-invasive bladder cancer (NMIBC) showed significantly better survival than those with muscle-invasive bladder cancer (MIBC) (log-rank $p = 0.004$). In univariate analysis, tumour stage, tumour grade, and histological subtype were significantly associated with overall survival. In multivariate Cox regression analysis, tumour stage remained the only independent prognostic factor. Compared with Tis/Ta tumours, patients with T2 disease (HR = 2.82, 95% CI: 1.35-5.89; $p = 0.006$) and T3 disease (HR = 6.39, 95% CI: 2.25-18.12; $p < 0.001$) had a significantly increased risk of death. **Conclusion:** In this Moroccan cohort, tumour stage was the primary independent predictor of overall survival in urothelial bladder carcinoma. These findings highlight the critical importance of early diagnosis and accurate pathological staging and provide baseline survival data that may support future multicentre studies and improved risk stratification in the region.

Keywords: Urothelial Carcinoma of Bladder, Non-muscle-invasive bladder carcinoma, Muscle-invasive bladder carcinoma

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Introduction

Bladder cancer has become a major public health problem whose incidence is constantly increasing, with an incidence of 573,000 new cases and a mortality of 212,536 deaths in 2020, according to Globocan data [1]. It ranks 10th among the world's most frequent cancers, with the increase shared between Southern Europe, Western Europe and America [1].

Urothelial carcinoma of the bladder accounts for 90% of bladder cancers, with 75% of cases belonging to the non-muscle-invasive form (NMIBC) and the remaining 25% to muscle-invasive urothelial carcinoma [2]. NMIBC is characterized by high rate of recurrence after a transurethral resection (TURBT) of Tumour, with 70% of 5 years' recurrence rate, due to incomplete

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resection or non-detectable Tumours by a cystoscopy. Furthermore a progression to muscle-invasive form is noticeable in 10 to 20% cases [3, 4].

In Morocco, bladder cancer ranks 8th when considering both sexes with a gross incidence of 2,268 new cases in 2020 and a mortality of 1,268 cases per (100 000 people) and 4th if we only consider men with an incidence of 10.2 and a mortality of 5.8 (ASR) per 100 000 people [2, 4]. The management of this pathology constitutes a major challenge, both in terms of prognostic diagnosis and patient monitoring. A good understanding of the histopathological distribution, risk factors as well as survival in terms of UBC can help reduce the extent of the psychosocial and health consequences of this pathology.

The objective of this present work is to analyse a series of Moroccan patients affected with a urothelial carcinoma of bladder (UBC), diagnosed at the Ibn Rochd University Hospital Center of Casablanca, through a description of clinico-pathological factors, and evaluation of their impact on survival.

Materials and Methods

Study design and population

This retrospective cohort study included 124 patients diagnosed with UBC and managed at Ibn Rochd University Hospital, Casablanca, between January 2020 and December 2022. Eligible patients were adults with histologically confirmed urothelial carcinoma of the bladder and available clinical, pathological, and follow-up data. Patients with non-urothelial histology or incomplete survival information were excluded. The study was conducted in accordance with institutional ethical standards.

Clinical and pathological data collection

Demographic and clinical data were extracted from medical records, including age at diagnosis, sex, smoking status, and tumour characteristics. Smoking status was recorded as active, passive, or non-smoker based on available clinical documentation.

Pathological data were obtained from routine pathology reports generated at the time of diagnosis. The classification of tumours was established in accordance with the World Health Organisation's (WHO) classification, as published in 2016, and staged using the TNM classification of the UICC/AJCC (2016). Full TNM staging (T, N, and M categories) was reported when available. Non-invasive Tumours were defined as papillary urothelial lesions without detrusor muscle invasion, while invasive Tumours were characterised by detrusor muscle invasion confirmed by histopathological examination, both types of Tumours were included in the study cohort.

Due to the retrospective nature of the study, certain pathological parameters including, lymphovascular invasion, perineural invasion, margin status, and histological variants of urothelial carcinoma were not consistently documented in the original pathology reports and could not be reliably extracted. To avoid misclassification or incomplete reporting, these variables

were not included in the analysis.

Carcinoma in situ (CIS) was recorded only when explicitly reported in pathology findings. Systematic bladder mapping or random biopsies were not routinely performed in all patients during the study period, which may have influenced the observed frequency of CIS.

Treatment modalities

Treatment strategies were recorded based on available clinical documentation and included transurethral resection of bladder tumour (TURBT), intravesical therapy, radical cystectomy, systemic chemotherapy, radiotherapy, or combinations thereof. Given the heterogeneity of treatment approaches and the limited number of outcome events within each subgroup, treatment variables were described descriptively but were not incorporated into multivariable survival models.

Survival outcome and statistical analysis

Overall survival (OS) was defined as the time from histological diagnosis to death from any cause or last follow-up. Patients alive at last contact were censored. Follow-up duration was estimated using the reverse Kaplan-Meier method.

Survival curves were generated using the Kaplan-Meier method and compared using the log-rank test. Univariate and multivariate Cox proportional hazards regression models were used to evaluate associations between clinicopathological variables and OS. Given the limited number of events, multivariable modelling was restricted to clinically relevant covariates to reduce overfitting and collinearity. TNM stage categories were simplified for regression analyses to improve model stability.

Because the analyses were exploratory and the number of events was limited, formal assessment of proportional hazards assumptions and advanced model performance metrics were not systematically performed. Results are therefore interpreted as hypothesis-generating.

Results

Characteristics of patients

The study population comprised 124 patients diagnosed between 2020 and 2022. The median age at diagnosis was 64 years (range: 35-89), with 53.2% of patients (n = 66) aged over 64 years (Figure 1). The cohort showed a marked male predominance, with a male-to-female ratio of 8.53:1 (111/13) (Figure 2A).

Regarding lifestyle factors, active smoking was highly prevalent, while passive smoking and non-smoking status were observed in only a small proportion of patients (Figure 2B). Histopathological evaluation revealed a predominance of high-grade tumours (66.1%) compared with low-grade tumours (Figure 2C), reflecting the aggressive pathological profile of this hospital-based cohort.

Despite this high-grade predominance, most tumours were classified as non-muscle-invasive (65.9%), including Ta/Tis lesions (35.5%) and T1 tumours (29.8%), whereas

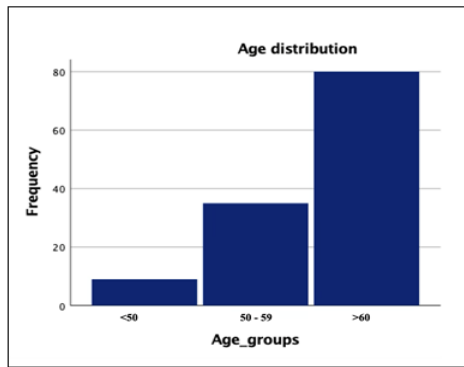


Figure 1. Age Distribution of Patients at the Time of Diagnosis

muscle-invasive tumours represented a smaller subset of cases (Figure 2D). As only one patient presented with carcinoma in situ (Tis), this case was grouped with Ta tumours for descriptive and survival analyses.

Table 1 summarizes the full TNM distribution of the cohort. For Cox proportional hazards modelling, tumours were categorized using a simplified MMSD-based stage grouping to reduce collinearity and ensure statistical robustness: Stage I (T1N0M0), Stage II (T2N0M0), Stage III (T3N0M0), and Stage IV (T4N0M0 or any N+ or M+ disease). Table 2 presents the distribution of patients according to treatment modality.

Overall, these findings confirm a strong male predominance and a high prevalence of active smoking, consistent with known epidemiological patterns of urothelial bladder carcinoma. Furthermore, the coexistence of high-grade pathology with predominantly non-muscle-invasive disease underscores the critical importance of early detection, high-quality transurethral resection, and risk-adapted surveillance strategies.

Results of overall survival of patients across histological type

During a median follow-up of 28.14 months, overall survival was analyzed using the Kaplan-Meier method. The median overall survival was not reached in the overall cohort. The estimated overall survival rate at last follow-up was 65.9% (95% CI: 57.47-74.52%).

Kaplan-Meier survival analysis demonstrated significant differences in overall survival according to histological type, tumour grade, and TNM stage. Patients with NMIBC showed significantly better survival compared with those with muscle-invasive bladder cancer (MIBC) (log-rank $p = 0.004$) (Figures 3 and 4).

At the end of follow-up, the estimated overall survival rate was higher in patients with NMIBC (72.8%) than in those with MIBC (42.9%). Due to the limited number of events and the heterogeneity of treatment modalities, survival analyses were not further stratified by treatment.

Univariate and multivariate analysis

Univariate Cox proportional hazards regression identified several variables significantly associated with overall survival. Patients with MIBC had a higher risk of death compared with those with non-muscle-invasive

disease (HR = 2.60, 95% CI: 1.32-5.21; $p = 0.005$). High tumour grade was also associated with poorer survival (HR = 3.79, 95% CI: 1.46-9.82; $p = 0.006$). Increasing tumour stage showed a strong adverse effect on overall survival, with progressively higher hazard ratios observed from T1 to T3 (all $p < 0.05$).

In multivariate Cox regression analysis including clinically relevant covariates, tumour stage remained the only independent prognostic factor for overall survival. Compared with Tis/Ta tumours, patients with T2 disease had a significantly increased risk of death (HR = 2.82, 95% CI: 1.35-5.89; $p = 0.006$), as did those with T3 disease (HR = 6.39, 95% CI: 2.25-18.12; $p < 0.001$). Other variables, including histological subtype and tumour grade, did not retain independent significance after adjustment (Tables 3 and 4).

Discussion

Urothelial carcinoma of the bladder remains the most common urological malignancy worldwide and is associated with substantial morbidity and mortality [5]. As with smoking, for instance, whose adverse prognosis and impact on recurrence-free survival have been definitively demonstrated [6, 7]. Understanding prognostic clinical and pathological factors is essential for improving patient stratification and management. In Morocco, data on survival outcomes in urothelial bladder carcinoma are limited, which underscores the relevance of the present study.

The primary objective of this work was to evaluate the prognostic impact of clinical and pathological variables on overall survival in a Moroccan cohort of patients with urothelial bladder carcinoma. Using Kaplan-Meier survival estimates and Cox proportional hazards modelling, we aimed to identify factors associated with survival outcomes while accounting for potential confounding variables.

Our principal finding is that tumour stage emerged as the only independent prognostic factor for overall survival

Table 1. Distribution of TNM Stages in the Study Cohort. (UICC/AJCC, 2016).

TNM stage	Patients (n)	Patients (%)
Stage T		
Ta	44	35.48
T1	38	30.64
T2a	32	25.80
T2b	1	0.80
T3a	4	3.22
T4a	5	4.03
Stage N		
N0	123	99.19
N2	1	0.80
Stage M		
M0	120	96.77
Mx	4	3.22

Table 2. Treatment Modalities in the Study Cohort

Treatment modality	Patients (n)	Patients (%)
Surgery (TURBT/ Cystectomy / Cysto-prostatectomy)	84	67.70
Surgery + BCG	12	9.70
Surgery + Chemotherapy (adjuvant/neoadjuvant)	13	10.50
Surgery + Concomitant Radio-chemotherapy	13	10.50
Surgery + Radiotherapy	2	1.60

BCG: Bacillus Calmette-Guerin; TURBT: transurethral resection of bladder tumour

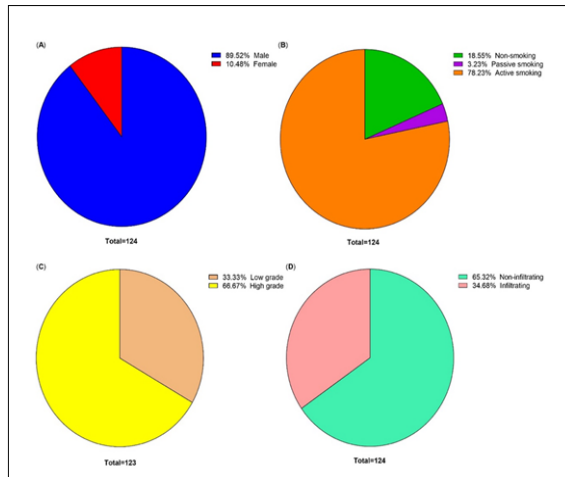


Figure 2. Distribution of Sex (A), Smoking Status (B), Tumour Grade (C), and Tumour Invasion Status (D) in the Study Cohort

in multivariate analysis. Patients with higher-stage disease experienced significantly worse outcomes compared with those with non-muscle-invasive tumours. This observation is consistent with extensive literature demonstrating that depth of tumour invasion remains the most powerful determinant of prognosis in urothelial bladder carcinoma [8-10]. These findings highlight the central importance of accurate staging at diagnosis.

Although tumour grade and histological subtype (NMIBC vs. MIBC) were significantly associated with survival in univariate analyses, these variables did not retain independent significance in multivariate models. This likely reflects collinearity between grade, histological subtype, and tumour stage, as higher-grade tumours are

more frequently associated with deeper invasion. In cohorts with limited sample size and event numbers, tumour stage often captures most of the prognostic information, attenuating the independent effects of correlated variables.

The median age at diagnosis in our cohort was 64 years, which is comparable to previous Moroccan studies and slightly lower than that reported in Western populations [11, 12]. While increasing age has been associated with poorer survival in several population-based studies [8, 13, 14], age did not independently predict overall survival in our analysis. This may be explained by the relatively homogeneous age distribution of the cohort, limited statistical power, and potential confounding by comorbidities and treatment selection [15].

A marked male predominance was observed, with a male-to-female ratio of 8.53:1, consistent with epidemiological patterns reported in North Africa and other regions [13, 16]. Biological hypotheses have suggested sex-related differences in urothelial carcinogenesis, including hormonal influences and differential mutational burden [17-19]. However, in our study, sex was not significantly associated with overall survival, aligning with findings reported by Doshi et al. [17], although other studies have described sex-specific survival differences, particularly when stratified by muscle invasion [8, 9, 20].

Tobacco smoking was highly prevalent in our cohort, reflecting its established role as a major etiological factor in urothelial bladder carcinoma [6, 21]. Despite this, smoking status was not significantly associated with overall survival. This lack of association may be attributable to the absence of detailed smoking exposure data, such as pack-years, duration of smoking, and time

Table 3. Univariate Cox Proportional Hazards Regression Analysis for Overall Survival

Variable		Hazard ratio (HR)	95% CI	p-value
Sex (Male)		HR = 0.92	[0.32 - 2.6]	0.87
Age (>64 years)		HR= 1.85	[0.92 - 3.72]	0.08
Tobacco	Passif	HR= 2.67	[0.63 - 11.24]	0.17
	Actif	HR= 1.2	[0.46 - 3.12]	0.7
Grade (HG)		HR= 3.79	[1.46 -9.84]	0.006
Stage TNM	T1	HR = 5.22	[1.7- 15.9]	0.004
	T2	HR= 6.82	[2.20 - 21.12]	0.001
	T3	HR= 12.02	[2.64 - 54.51]	0.001
	T4	HR= [NR]	[NR]	0.98

HR: hazard ratio; CI: confidence interval; HG: high grade. HR and 95% CI for T4 could not be reliably estimated due to the low number of events in this category; NR: not reached. Note: The hazards ratio estimate for stage T4 could not be calculated due to an insufficient number of events.

Table 4. Multivariate Cox Proportional Hazards Regression Analysis for Overall Survival

Variable		Adjusted HR	95% CI	p-value
Sex (Male)		HR = 0.85	[0.42 - 1.73]	0.66
Age (>64 years)		HR= 1.24	[0.85 - 1.81]	0.25
Tobacco	Passif	HR= 1.31	[0.48 - 3.60]	0.59
	Actif	HR= 0.98	[0.56 - 1.73]	0.96
Grade (HG)		HR= 0.7	[0.36 -1.34]	0.28
Stage TNM	T1	HR = 1.72	[0.88 - 3.34]	0.1
	T2	HR= 2.82	[1.35 - 5.89]	0.006
	T3	HR= 6.39	[2.25 - 18.12]	< 0.001
	T4	HR= 3.47	[0.73 - 16.39]	0.116

HR: hazard ratio; CI: confidence interval. Adjusted HRs were obtained from a multivariate Cox proportional hazards model including age, sex, smoking status, tumour grade, histological subtype, and TNM stage.

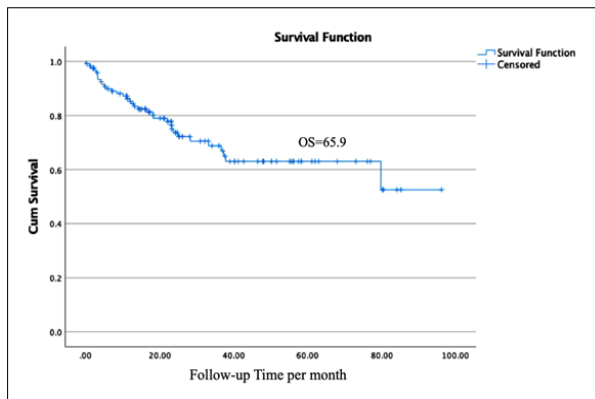


Figure 3. Kaplan-Meier Curve of Overall Survival in the Study Cohort

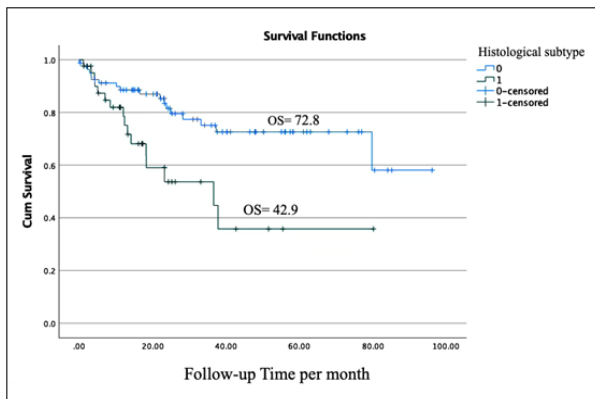


Figure 4. Kaplan-Meier Overall Survival According to Histological Type (NMIBC vs MIBC).

since cessation, which have been shown to influence survival outcomes in other studies [22-24]. Consequently, the prognostic impact of smoking on survival should be interpreted with caution in this cohort.

In addition to the prevailing risk factors, consideration should be given to regional epidemiological trend. Since 2004, indigenous transmission of urinary schistosomiasis has been interrupted in Morocco, with reported cases now mainly imported. Studies conducted in the post-elimination phase show a predominance of *Schistosoma Haematobium*, a parasite classically associated with squamous cell carcinoma of the bladder. This epidemiological situation could explain the current predominance of urothelial

carcinomas observed in this study [25, 26].

Regarding pathological findings, CIS was infrequently reported. This low frequency likely reflects routine clinical practice during the study period, as systematic bladder mapping or random biopsies were not consistently performed. As a result, CIS may have been underdiagnosed, and its prognostic significance could not be adequately evaluated in this analysis.

Treatment strategies in this cohort were heterogeneous, reflecting real-world clinical practice. Although treatment modalities were described, they were not incorporated into multivariable survival models due to limited event numbers within treatment subgroups. Treatment likely interacts with tumour stage and patient characteristics to influence outcomes; however, this effect could not be reliably assessed in the present study.

Several limitations should be acknowledged. The retrospective, single-center design and relatively small sample size limited statistical power and model complexity. The limited number of events may have contributed to wide confidence intervals and reduced stability in multivariable analyses. Additionally, formal assessment of proportional hazards assumptions and advanced model performance metrics was not performed, and results should therefore be considered exploratory.

Despite these limitations, this study provides valuable baseline survival data for Moroccan patients with urothelial bladder carcinoma and, to our knowledge, represents one of the first analyses comparing survival between non-muscle-invasive and muscle-invasive disease in this population. These findings underscore the importance of early diagnosis, accurate staging, and standardized pathological reporting and provide a foundation for future multicentre studies incorporating detailed pathology and treatment data.

In conclusion, urothelial bladder carcinoma represents a major public health concern in Morocco. In this retrospective cohort study, we identified tumour stage as the primary independent prognostic factor for overall survival, with significantly poorer outcomes observed in patients with muscle-invasive and higher-stage disease. Although tumour grade and histological subtype were associated with survival in univariate analyses, their prognostic impact did not persist after adjustment for

stage.

These findings underscore the critical importance of early detection, accurate pathological staging, and appropriate risk stratification in the management of urothelial bladder carcinoma. Despite its limitations, including the retrospective design and limited sample size, this study provides valuable baseline survival data for Moroccan patients and highlights the need for larger, multicenter studies incorporating standardized pathology reporting and detailed treatment information to refine prognostic assessment and guide clinical decision-making.

Acknowledgments

Statement of Transparency and Principles

- The authors declare no conflict of interest.
- The study was approved by the Research Ethics Committee of the authors' affiliated institution. (Committee Code: 2026/RSI/22, Date : 21-01-2026).
- The study data are available upon reasonable request.
- All authors contributed to the implementation of this research.

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