

Follow-up care of 12 months of patients with bladder cancer in Spain

the EMPARO-CU study group

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Follow-up care of 12 months of patients with bladder cancer in Spain

A multicenter prospective cohort study

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Abstract

The therapeutic approach of bladder cancer strongly determines its prognosis. We describe the treatments and outcomes for a Spanish cohort of patients with bladder cancer for the first 12 months after diagnosis and identify the factors that influenced the decision to undergo the treatment received. We conducted a multicenter, prospective, cohort study including primary bladder cancer patients during the first 12 months after diagnosis. The clinical outcomes were performance status (ECOG), adverse events and any cause of mortality. We stratified the analysis by factors that might influence the treatments received. We conducted univariate and multivariable logistic regression models to assess which patient and tumor characteristics were associated with receiving adjuvant treatment in the subgroup of noninvasive bladder cancer patients. In total, 314 patients were included (85% men; 53.8% >70 years) in 7 tertiary Spanish hospitals; 82.2% had a noninvasive urothelial bladder cancer (NMIBC). Patients received mostly surgery plus adjuvant therapy (67.7%). BCG (32.8% patients) was the most frequently administered adjuvant therapy, followed by intravesical chemotherapy (17.8% patients) and radiotherapy (10.8%). The variability of administered treatments among hospitals was low. Patients with NMIBC were more likely to receive adjuvant therapy if they had a higher educational level, some comorbidities and a high-grade tumor. The number of fully active patients (ECOG 0) significantly decreased during the first year of follow-up from 58% to 36% (OR: 2.41, 95%CI 1.82–3.20); at 12-month follow-up 10.8% patients had died from any cause. In conclusion, most of the patients had a NMIBC. Surgery alone or plus adjuvant therapy were the commonest curative options of bladder cancer. BCG therapy was the adjuvant therapy most frequently administered. Higher educational level, presence of comorbidities and a high-grade tumor were associated with adjuvant therapy. Patient performance status was worsening over time. Almost 1 of 10 patients died during the first year of follow-up.

Abbreviations: BCG = bacilli of Calmette-Guerin, BMI = body mass index, CI = confidence intervals, ECOG = eastern cooperative oncology group, NMIBC = non-invasive urothelial bladder cancer, OR = odds ratios, QoL = quality of life, TURB = transurethral resection of the bladder, WHO = World Health Organization.

Keywords: bladder neoplasms, cohort study, male urogenital diseases, multicenter study, multivariable analysis

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

This study was approved by the Ethics Committee of Hospital de la Santa Creu i Sant Pau (Barcelona), Fundació Puigvert (Barcelona), Hospital 12 de Octubre (Madrid), Hospital Ramón y Cajal (Madrid), Hospital Universitario Donostia (San Sebastián), Hospital Nuestra Señora del Mar (Barcelona), Hospital Virgen de las Nieves (Granada), Consorcio Hospital General Universitario de Valencia and Basque Country Ethics Committee

Previously to inclusion in this study, all patients were informed about the study, they accepted to participate and signed the consent form.

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1. Introduction

Bladder cancer is the fourth most commonly diagnosed cancer in the European Union in men, and the 12th in women, with an incidence of 55.4 and 12.1/100,000 person per year, respectively.^[1] It is the fifth cancer with higher mortality with an incidence of 31/100,000 people per year for both sexes.^[1] In Spain it is globally, the fifth most commonly diagnosed cancer with an incidence of 37.8/100,000 people per year and mortality rate of 11/100,000 people per year.^[1]

In general, symptoms start with hematuria (around 90% of the cases), the tumor is confined to the bladder, and the most common histological type is urothelial cell carcinoma.^[2] Prognosis of bladder cancer depends not only on patient and tumor characteristics, but also on the capability of the health-care system to identify the disease and treat the patients in a timely manner and to perform an adequate follow-up as well. The follow-up of patients with bladder cancer remains complicated due to the high frequency of recurrence and progression after treatment.^[3–5] Although there are guidelines about diagnosis and treatment procedures, little is known regarding how bladder cancer patients are treated in a prospective follow-up with a representative large cohort in multiple centers.

We therefore conducted a prospective cohort study of Spanish bladder cancer patients. Baseline characteristics, diagnostic and therapeutic intervals in this cohort were previously published.^[2] Quality of life (QoL) of this cohort was also reported.^[6] In this article, we presented patient-important outcomes and treatments received during the first 12-months follow-up after diagnosis. Our first objective was to describe the clinical outcomes and treatments received by bladder cancer patients during the first 12-month-follow-up after diagnosis. Secondly, we aim to identify factors associated with the prescription of adjuvant treatment in patients with non-muscle-invasive bladder cancer.

2. Methods

We performed a multicenter, prospective cohort study in patients with a newly diagnosed bladder cancer in Spain from October 2010 to September 2011. Methods were previously published.^[2] The research ethics committees from the 7 tertiary participating hospitals approved the protocol. Consecutive bladder cancer patients were identified from the urology and oncology departments. The eligibility criteria were: being diagnosed of bladder cancer during the study period; being diagnosed and treated at the participating hospitals; and agree to participate and signing the informed consent form.

The information sources were medical records and structured interviews with patients (baseline, at 6 and 12 months of follow-up). The collected data were: socio-demographics, body mass index (BMI), Charlson co-morbidity index, Eastern Cooperative Oncology Group/WHO performance status (ECOG/WHO), bladder biopsy pathology reports, Tumor lymph Nodes Metastases stage, received treatments, patient-reported adverse events, disease status and mortality.

2.1. Statistical analysis

We performed a descriptive analysis stratified by received treatment (only surgery or surgery with any adjuvant therapy). We analyzed the following variables: age, sex, BMI, educational level, ECOG/WHO status, Charlson index, primary tumor, tumor in situ (Tis) associated, tumor histological grade, number of tumors, and largest tumor size.

Using European organization of research and treatment of cancer and urological club for oncological treatment risk tables for recurrence and progression,^[7–9] the following variables were categorized: age (<60, 60–70, ≥71 years), BMI (≤24.9, 25–29.9, ≥30), educational level (illiterate-primary, secondary-subjects

with high school or 10–14 years of schooling-, post-secondary-subjects with university degree or post-graduate studies corresponding to 15 years or more of schooling-), Charlson index (0, 1, 2, ≥3), number of tumors (1, ≥2) and largest tumor size (<30 mm, ≥30 mm). We obtained mean and standard deviation for continuous variables (age and BMI) and relative and absolute frequencies for categorical variables.

In addition, we imputed missing values for variables with missing data using the Multiple Imputation by Chained Equations method, where each variable has its own imputation model.

We performed a subgroup analysis selecting only the non-muscle-invasive urothelial carcinomas cases (Ta, Tis, stage T1). Univariate and multivariate logistic regression models were constructed to assess associations between clinical and demographic variables (independent variables) and any adjuvant treatment (intravesical Bacilli of Calmette-Guérin -BCG-, chemotherapy, and radiotherapy administered up to 1 year after diagnosis) received after surgery (dependent variables). Specifically, independent variables considered as potentially associated with adjuvant treatment were age, sex, BMI, education level, performance status, Charlson index, primary tumor, Tis associated with Ta or T1, tumor histology grade, size and number of tumors.

Repeated measures of performance status (ECOG/WHO) within participants (at baseline, 6 months and 12 months) were analyzed using generalized estimating equation models where each patient has 1 value of performance status for each period. An autoregressive correlation structure was chosen. We tested the presence of a linear trend of deterioration of performance status overtime, by introducing time to assessment (at baseline, 6 months and 12 months) as independent variable in the model, and any deterioration of performance status (Yes/No) as dependent variable.

Odds ratios (OR) with 95% confidence intervals (CI) were used as association estimates. Level of significance was set to $\alpha = 0.05$. The statistical software used was SPSS, v24.0 (SPSS INC., Chicago, IL) and Stata, v14.1 (College Station, TX: StataCorp LP).

3. Results

Three-hundred and fourteen patients from 347 recruited patients with a first diagnosis of bladder cancer fulfilled the inclusion criteria. During 12 months follow-up after diagnosis 34 (10.8%) patients died and 5 (1.6%) were losses of follow-up (Fig. 1). The reasons of death were bladder cancer progression (15 patients), other non-neoplasm diseases (6 patients), and unknown causes (13 patients).

The majority of bladder cancer patients were men (85.0%), older than 70 years of age (53.8%, median age 71.7, range: 36–100), overweight or obese (67.6%, median BMI 26.6, range: 15.6–49.8), had low level of education (52.9%) and had some comorbidities (64.0%) (Table 1).

The most frequently recorded co-morbidities were other cancers (21.7%), diabetes (21.0%), congestive heart failure (17.8%), chronic pulmonary disease (15.9%), renal disease (11.1%), myocardial infarction (8.9%), peripheral vascular disease (5.4%), cerebrovascular disease (5.1%), liver disease (4.1%) and others (4.8%).

Two-hundred sixteen (68.8%) patients underwent surgery with some adjuvant therapy (32.8% intravesical BCG, 17.8% intravesical chemotherapy, 10.8% radiotherapy or systemic chemotherapy, 7.4% non-specified) and, 91 (29.0%) patients were treated with only surgery (Transurethral resection of the bladder -TURB- and/or radical cystectomy) (Table 1). In general, TURB alone or surgery plus intravesical BCG were the usual treatments in all hospitals, except in hospital E, which treated their patients most commonly with TURB or surgery plus intravesical

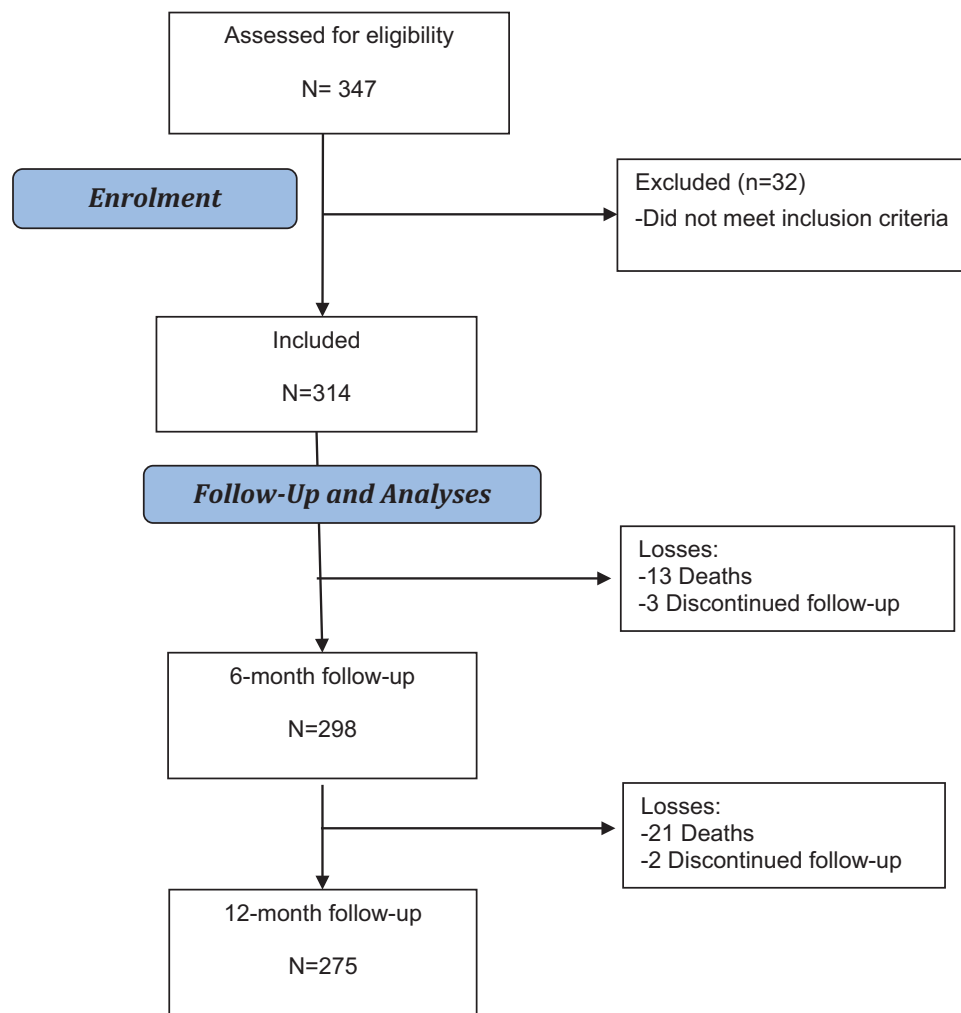


Figure 1. Flow diagram of the bladder cancer cohort follow-up.

chemotherapy (Supplementary material, TS1, <http://links.lww.com/MD/H647>).

Three hundred and two patients (96.2%) had a urothelial cell carcinoma. In 258 (82.2%) patients the bladder cancer was non-muscle-invasive; 33.1% of tumors were multiple and 29.6% large size (≥ 30 mm). A low number of patients had positive lymph nodes (5.0%) and distance metastases (3.2%) (Table 2).

Among patients with a non-muscle-invasive bladder cancer, the factors significantly associated to receive any adjuvant therapy were educational level, Charlson index and tumor histology grade. Patients with higher studies (secondary or post-secondary studies) were more likely to receive adjuvant therapy than those who had a lower educational level (OR: 2.93, 95%CI 1.09–7.89; OR: 9.88, 95%CI 2.18–44.78, respectively) (Table 3). Patients with Charlson index 1 or 2 received adjuvant therapy more frequently than those who did not have any comorbidity (OR 3.28, 95%CI 1.05–10.27; OR: 4.81, 95%CI 1.37–16.88, respectively). Furthermore, patients with high-grade carcinoma were more likely to receive adjuvant therapy than those who had a lower grade carcinoma (OR: 4.85, 95%CI 1.65–14.26).

Considering all included patients, performance status (ECOG) was worsening over time (Fig. 2). Comparing with basal performance status, the number of fully active patients (ECOG 0) decreased significantly during the first year of follow-up from 58% to 36% (OR: 2.41, 95%CI 1.82–3.20).

Concerning the disease condition at 12-month-follow-up, 33.3% of patients had persistence or progression of the disease,

5% died from progression of bladder cancer and 10.8% had died from any cause (Table 4).

One hundred-eight (34.4%) patients suffered treatment-related adverse events, mostly related to surgery and systemic chemotherapy (Supplementary material, TS2, <http://links.lww.com/MD/H648>).

4. Discussion

Overall, 314 patients, mainly men older than 70 years, were recruited over 1-year in our prospective cohort from 7 tertiary Spanish hospitals. All patients received surgery, either alone (1 third) or with adjuvant therapy (more than two thirds). One third of patients received BCG that was the most frequent adjuvant therapy administered, followed by intravesical chemotherapy and radiotherapy or systemic chemotherapy.

We found 82% of patients had non-muscle-invasive urothelial bladder cancer (NMIBC); they were more likely to receive adjuvant therapy if they had a high-grade carcinoma, higher level of studies and 1 or 2 co-morbidities. Previous studies showed an association between a high grade NMIBC and the risk of progression or recurrence.^[5] We did not find studies with information about study co-morbidities and educational level as predictors for receiving adjuvant therapy. However, other cancers it has been shown association of high level of studies with the likelihood of receiving adjuvant therapy.^[10]

In addition, our study reveals that there was not a significant variability among centers in the indications of the different

Table 1
Patient characteristics by treatment received.

	All patients N = 314	Only surgery		Surgery and adjuvant therapy			Surgery plus non-specified adjuvant therapy N = 23	Unknown Treatment N = 7
		TURB N = 82	TURB & radical cystectomy N = 9	Intravesical chemotherapy N = 56	BCG intravesical N = 103	Radiotherapy or systemic chemotherapy N = 34		
	n (%)	n	n	n	n	n	n	n
Age at presentation								
<60 yrs	61 (19.4)	20	2	14	16	3	3	3
60-70 yrs	84 (26.8)	18	2	19	26	10	7	2
≥71 yrs	169 (53.8)	44	5	23	61	21	13	2
Missing	0 (0.0)	0	0	0	0	0	0	0
Sex								
Men	267 (85.0)	67	8	43	93	30	20	6
Women	47 (15.0)	15	1	13	10	4	3	1
Body mass index								
≤24.9	87 (27.7)	22	2	15	27	7	9	5
25 to 29.9	149 (47.5)	41	3	26	50	19	9	1
≥30	63 (20.1)	17	1	14	19	7	4	1
Unknown	15 (4.7)	2	3	1	7	1	1	0
Educational level								
Illiterate- primary	166 (52.9)	53	3	22	57	16	11	4
Secondary	103 (32.8)	23	3	19	34	15	8	1
Post- secondary	40 (12.7)	5	3	14	11	3	3	1
Unknown	5 (1.6)	1	0	1	1	0	1	1
Charlson index score								
0	113 (36.0)	35	3	20	35	7	10	3
1	61 (19.4)	14	3	15	19	7	2	1
2	69 (22.0)	15	1	9	24	11	8	1
≥3	71 (22.6)	18	2	12	25	9	3	2

Surgery plus non-specified adjuvant therapy: the patient received an adjuvant therapy but it was not possible to identify whether it was intravesical chemotherapy or BCG intravesical or radiotherapy or systemic chemotherapy. Unknown Treatment: it was not possible to know what kind of treatment the patient underwent after surgery.

BCG = Bacilli of Calmette-Guerin, TURB = Transurethral resection of the bladder.

therapeutic alternatives, except for 1 hospital that preferably administered intravesical chemotherapy as adjuvant therapy. In this hospital more than 88% of patients had a NMIBC and intravesical chemotherapy is an option of this stage of cancer.^[11,12]

Our results showed that bladder cancer has important health consequences during the 12 months after the diagnosis, partly due to adverse events related to treatments (more than a third of patients suffered adverse events) and persistence or progression of the disease (1 of every 4 patients) and, 1 of every 10 patients died of any cause of mortality. Furthermore, the number of fully active patients decreased significantly during the first year of follow-up after diagnosis.

We published QoL of the subgroup of patients with a NIMBC that underwent TUR with or without intravesical therapy.^[6] QoL was measured by the Health Survey Short Form-36 version 2 and the Bladder Cancer Index. The results showed that physical and mental health remained quite stable during 12-month follow-up although with a subtle decline, urinary and bowel function improved, but sexual function worsened. Differences between QoL and performance status of our study could be attributed to the fact that QoL was analyzed only in a subgroup of patient and did not include tumor stages II, III, and IV and patients that underwent cystectomy.

Our study might have been exposed to some limitations due to potential information bias. However, to minimize this bias the information was prospectively obtained from hospital records and from patients through the use of structured interviews. Other limitation was the relatively short follow-up time of the study, which did not allow for estimates of long-term impact of this entity.

We have not identified any published prospective multicenter study focused on incident cases of bladder cancer and their treatment during the first year after diagnosis. Previously published observational studies focused on a specific cancer stage and were retrospective in design.^[9,12-14] Other studies, based on database registries,^[14-16] have focused on prognosis factors for recurrence or progression^[14] or on preventive measures like the influence of diet and lifestyle on recurrence and the relationship between progression of NMIBC and genetic profiles.^[17]

5. Conclusions

Based on our results, the first year after diagnosis of bladder cancer has important health consequences in terms of treatments used, disability of the patients and mortality. Surgery with adjuvant therapy was the main curative options received after the diagnosis of non-muscle invasive bladder cancer. BCG therapy was the most frequently administered adjuvant treatment. Higher educational level, presence of 1 or 2 comorbidities and a high-grade tumor were associated with more frequent adjuvant therapy in NMIBC.

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Table 2**Tumor characteristics by treatment received.**

	All patients N = 314 n (%)	Only surgery		Surgery and adjuvant therapy			Surgery & non-specified adjuvant therapy N = 23 n	Unknown treatment N = 7 n
		TURB N = 82 n	TURB & radical cystectomy N = 9 n	Intravesical chemotherapy N = 56 N	BCG intravesical N = 103 n	Radiotherapy or systemic chemotherapy N = 34 n		
Tumor histology								
Adenocarcinoma	9 (2.9)	5	0	0	2	0	1	1
Urothelial cell carcinoma	302 (96.2)	77	9	56	100	33	22	5
Squamous cell carcinoma	1 (0.3)	0	0	0	0	0	0	1
Others	0 (0.0)	0	0	0	0	0	0	0
Unknown	2 (0.6)	0	0	0	1	1	0	0
Number of tumors								
1 tumor	170 (54.1)	47	2	46	39	20	14	2
≥2 tumors	104 (33.1)	22	4	5	54	12	6	1
Missing	40 (12.8)	13	3	5	10	2	3	4
Largest Tumor Size (mm)								
<30 mm	148 (47.2)	44	4	24	52	13	9	2
≥30 mm	93 (29.6)	20	2	19	25	15	10	2
Missing	73 (23.2)	18	3	13	26	6	4	3
Primary tumor (T)								
Ta	107 (34.1)	45	0	31	27	0	4	0
Tis	10 (3.2)	0	2	1	6	0	1	0
T1	141 (44.9)	37	1	24	69	4	6	0
T2a	27 (8.6)	0	5	0	1	14	5	2
T2b	18 (5.7)	0	1	0	0	9	5	3
T3a	2 (0.6)	0	0	0	0	0	1	1
T3b	3 (1.0)	0	0	0	0	2	1	0
T4a	6 (1.9)	0	0	0	0	5	0	1
T4b	0 (0.0)	0	0	0	0	0	0	0
Tis associated								
Yes	24 (7.6)	1	2	1	14	3	2	1
No	273 (87.0)	76	7	53	81	30	20	6
Missing	17 (5.4)	5	0	2	8	1	1	0
Lymph nodes (N)								
N0	298 (95.0)	82	9	56	103	23	20	5
N1	7 (2.2)	0	0	0	0	6	1	0
N2	7 (2.2)	0	0	0	0	3	2	2
N3	2 (0.6)	0	0	0	0	2	0	0
Distant metastasis (M)								
M0	304 (96.8)	82	9	56	103	27	21	6
M1	10 (3.2)	0	0	0	0	7	2	1
TNM stage								
0a	107 (34.1)	45	0	31	27	0	4	0
0is	10 (3.2)	0	2	1	6	0	1	0
I	140 (44.6)	37	1	24	69	4	5	0
II	37 (11.8)	0	6	0	1	18	8	4
III	2 (0.6)	0	0	0	0	0	2	0
IV	18 (5.7)	0	0	0	0	12	3	3

Surgery plus non-specified adjuvant therapy: the patient received an adjuvant therapy but it was not possible to identify whether it was intravesical chemotherapy or BCG intravesical or radiotherapy or systemic chemotherapy. Unknown Treatment: it was not possible to know what kind of treatment the patient underwent after surgery.

BCG = Bacilli of Calmette-Guérin, TNM = tumor lymph nodes metastases, TURB: transurethral resection of the bladder.

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Table 3

Probability of receiving any adjuvant treatment in patients with non-muscle-invasive urothelial carcinoma: univariate and multivariate logistic regression models.

	Only surgery n (%)	Surgery plus any adjuvant therapy n (%)	Risk of having any adjuvant treatment	
			Univariate model OR (95% CI)	Multivariate model aOR (95% CI)
All patients*	80(32.3)	168(67.7)		
Age at presentation				
<60 yrs	18(22.5)	31(18.5)	1.00 reference	1.00 reference
60 to 70 yrs	18(22.5)	51(30.4)	1.65 (0.75-3.63)	2.15 (0.63-7.31)
≥71 yrs	44(55.0)	86(51.2)	1.13 (0.57-2.25)	1.31 (0.39-4.35)
Sex				
Men	65(81.3)	145(86.3)	1.00 reference	1.00 reference
Women	15(18.8)	23(13.7)	0.69 (0.34-1.40)	0.90 (0.29-2.80)
Body mass index (BMI) at presentation				
≥30	16(20.8)	33(20.6)	1.00 reference	1.00 reference
25 to 29.9	39(50.6)	83(51.9)	1.03 (0.51-2.09)	1.19 (0.43-3.29)
≤24.9	22(28.6)	44(27.5)	0.97 (0.44-2.13)	0.46 (0.14-1.58)
Educational level				
Illiterate-primary	51(64.6)	80(48.5)	1.00 reference	1.00 reference
Secondary	22(27.8)	57(34.5)	1.65 (0.90-3.02)	2.93 (1.09-7.89)
Post-secondary	6(7.6)	28(17.0)	2.97 (1.15-7.69)	9.88 (2.18-44.78)
Performance status (ECOG/WHO) at presentation				
Fully active	48(60.0)	102(60.7)	1.00 reference	1.00 reference
Restricted or worse	32(40.0)	66(39.3)	0.97 (0.56-1.67)	1.00 (0.41-2.45)
Charlson index score at presentation				
0	36(45.0)	58(34.5)	1.00 reference	1.00 reference
1	14(17.5)	36(21.4)	1.60 (0.76-3.36)	4.81 (1.37-16.88)
2	11(13.8)	33(19.6)	1.86 (0.84-4.14)	3.28 (1.05-10.27)
≥3	19(23.7)	41(24.4)	1.34 (0.68-2.66)	1.76 (0.59-5.26)
Primary tumor (T)				
Ta	43(55.1)	61(38.1)	1.00 reference	1.00 reference
T1	35(44.9)	99(61.9)	1.99 (1.15-3.45)	1.76 (0.71-4.39)
Tis associated				
No	73(96.1)	142(89.3)	1.00 reference	1.00 reference
Yes	3(3.9)	17(10.7)	2.91 (0.83-10.26)	0.96 (0.08-11.20)
Tumor histology grade				
Low grade papillary urothelial carcinoma	72(92.3)	100(62.5)	1.00 reference	1.00 reference
High grade papillary urothelial carcinoma	6(7.7)	60(37.5)	7.20 (2.95-17.57)	4.85 (1.65-14.26)
Number of tumors				
1 tumor	45(66.2)	91(59.9)	1.00 reference	1.00 reference
≥ 2 tumors	23(33.8)	61(40.1)	1.31 (0.72-2.38)	0.96 (0.39-2.34)
Largest tumor size (mm)				
<30 mm	43(68.3)	80(62.5)	1.00 reference	1.00 reference
≥30 mm	20(31.7)	48(37.5)	1.29 (0.68-2.45)	1.45 (0.62-3.38)

*Ten patients were excluded due they had missing information about adjuvant treatment. OR: odd ratio; it shows for example the probability of receiving any adjuvant treatment ifr patients have secondary or post-secondary studies as compared to illiterate-patients or those with primary studies. aOR: adjusted odd ratio; it shows the probability of receiving any adjuvant treatment adjusted for other variables in the specified model. 95% CI: 95% Confidence Interval. In bold type when confidence interval is significant.

ECOG = eastern cooperative oncology group, WHO = World health organization.

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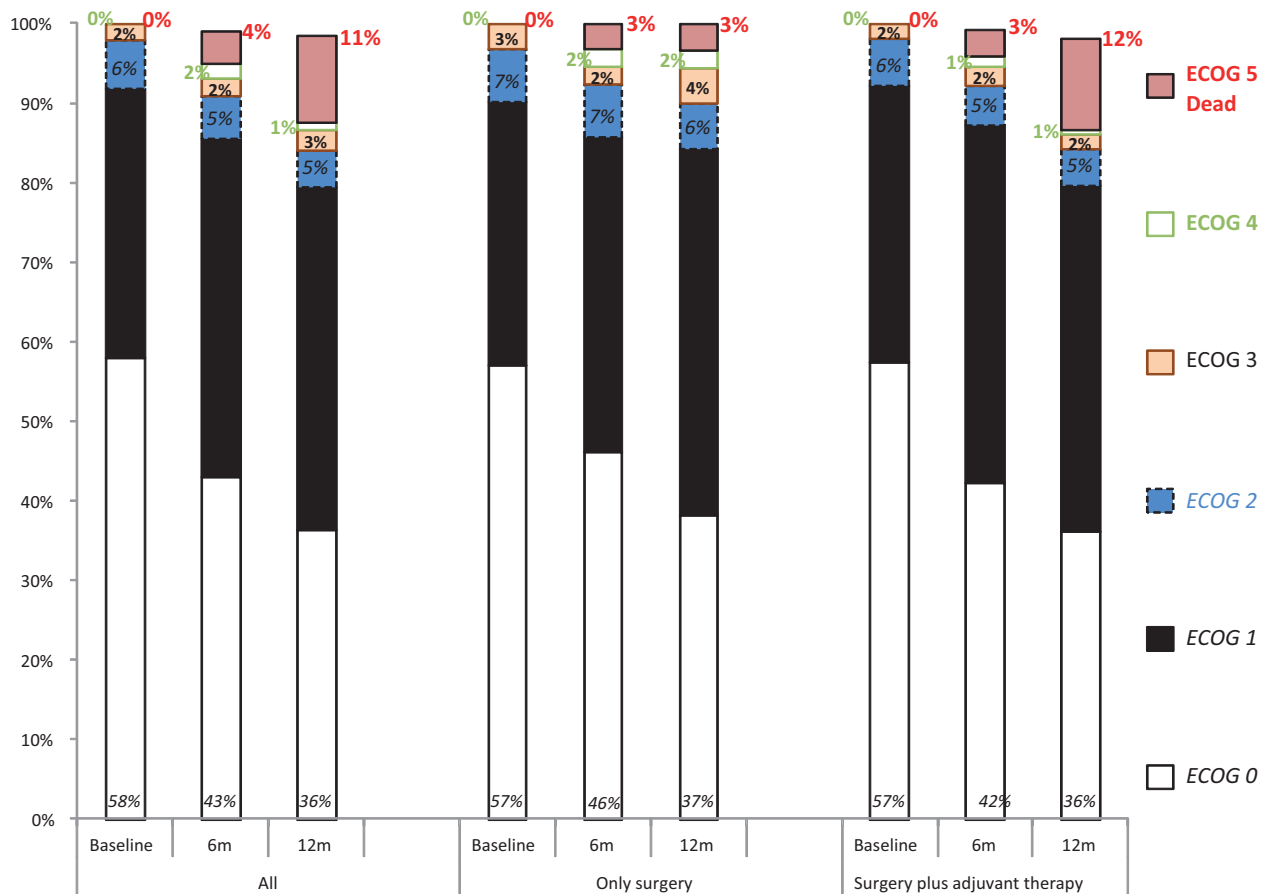


Figure 2. Performance status (ECOG/WHO) over the study follow-up by treatment received. ECOG = eastern cooperative oncology group, WHO = World health organization.

Table 4

Disease status and patient survival by initial treatment at 12 months of follow-up.

	Only surgery			Surgery and adjuvant therapy			Surgery & non-specified adjuvant therapy N = 23	Unknown treatment N = 7
	All patients N = 314	TURB N = 82	TURB & radical cystectomy N = 9	Intravesical chemotherapy N = 56	BCG intravesical N = 103	Radiotherapy or systemic chemotherapy N = 34		
	n (%)	n (%)	n (%)	n(%)	n(%)	n(%)		
Disease status at 12 months								
No evidence of remaining disease	226(72.0)	65 (79.34)	8 (88.9)	49 (87.5)	84 (81.6)	10 (29.4)	9 (39.1)	1 (1.4)
Local disease	31(9.9)	11 (13.4)	0	6 (10.7)	10 (9.7)	3 (8.8)	1 (4.4)	0
Regional disease	5(1.6)	0	0	0	3 (2.9)	1 (3.0)	1 (4.4)	0
Metastasis	37 (11.8)	3 (3.6)	1 (11.1)	1 (1.8)	5 (4.8)	16 (47.0)	7 (30.4)	4 (5.7)
Unknown	15 (4.7)	3 (3.6)	0	0	1 (1.0)	4 (11.8)	5 (21.7)	2 (2.9)
Survival at 12 months								
Live	275 (87.6)	76 (92.7)	8 (88.9)	54 (96.4)	98 (95.1)	25 (73.5)	12 (52.2)	2 (2.9)
Dead	34 (10.8)	4 (4.9)	1 (11.1)	2 (3.6)	5 (4.8)	9 (26.5)	9 (39.1)	4 (5.7)
Missing	5(1.6)	2 (2.4)	0	0	0	0	2 (8.7)	1 (1.4)

Only percentages for cases above 9 are shown. Surgery plus non-specified adjuvant therapy: the patient received an adjuvant therapy but it was not possible to identify whether it was intravesical chemotherapy or BCG intravesical or radiotherapy or systemic chemotherapy. Unknown Treatment: it was not possible to know what kind of treatment the patient underwent after surgery. BCG = Bacilli of Calmette-Guérin, TURB = transurethral resection of the bladder.

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