

# Optimal management for initially diagnosed Ta high grade bladder cancer.

## What does matter for intravesical recurrence?

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### Objectives:

The aim of this study were to evaluate the oncological outcome and impact of each treatment affecting intravesical recurrence in patients who newly diagnosed Ta high grade (TaHG) non-muscle invasive bladder cancer (NMIBC).

### Methods:

We retrospectively evaluated TaHG bladder cancer patients who newly diagnosed by transurethral resection (TUR) from January 2007 through October 2018 in the Sapporo Medical University Urologic Consortium. Primary endpoint was intravesical recurrence and secondary endpoint was treatment options affecting intravesical recurrence. We excluded patients having prior history of bladder cancer. Tumor grade was determined according to 1973 WHO and 2004 WHO/ISUP grading system.

### Results:

We included 390 patients, with a mean age of 73 years. Mean follow up period was 30.5 months after TUR. Of them, 111 patients (28.5%) experienced intravesical recurrence.

Second TUR was performed for 255 patients (65.4%) and immediate intravesical chemotherapy was done for 167 patients (42.8%). Two-hundred sixty patients (66.7%) underwent induction intravesical instillation therapy.

Two-year recurrence free survival rate was 76.2%. According to multivariate analysis, treatment options reducing intravesical recurrence risk were immediate intravesical instillation and induction intravesical instillation therapy ( $P = 0.003$ ,  $P = 0.03$ , respectively). Contrarily, second TUR did not impact on intravesical recurrence ( $P = 0.12$ ).

### Conclusions:

Approximately one-third of the patients with newly diagnosed TaHG bladder cancer developed intravesical recurrence during 3 years. Immediate and induction intravesical chemotherapy were critical management to reduce the risk of intravesical recurrence.

## Aim

## Patients characteristics

## Intravesical recurrence rate

## Which treatment option can reduce the risk of intravesical recurrence ?

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- To evaluate appropriate treatment option for reducing intravesical recurrence in newly diagnosed TaHG bladder cancer.

## Patients and Methods

- Patients who newly diagnosed TaHG bladder cancer.
- Period: From January 2007 through October 2018
- Design: Multicenter retrospective study
- Institutional review board number 302-162

## Exclusion criteria

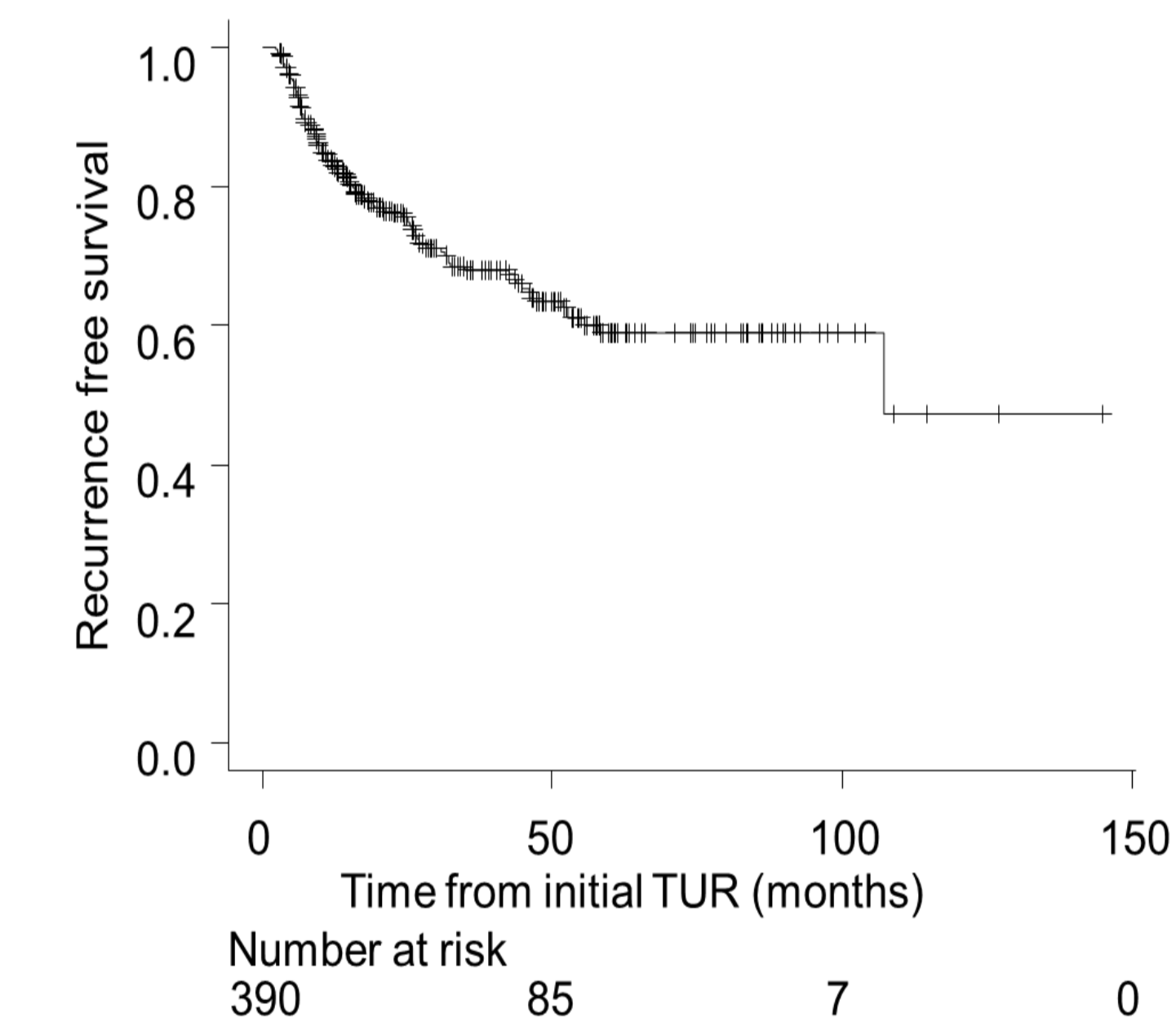
- Prior history of bladder cancer.
- Radiographically suspicious of muscle invasive bladder cancer.

Table 1. Clinicopathological characteristics of the TaHG bladder cancer patients in this study

	Patients (n = 390)
Age (y, mean ± SD)	73.2 ± 10.5
history of smoking	
Yes	235 (60.3%)
No	155 (39.7%)
Gender	
Female	81 (20.8%)
Male	309 (79.2%)
History of UUTCa	
Yes	46 (11.8%)
No	344 (88.2%)
Multiplicity	
Solitary	202 (51.8%)
Multiple	188 (48.2%)
Papillary tumor	
Yes	378 (96.9%)
No	12 (3.1%)
Tumor stalk	
Yes	259 (66.4%)
No	131 (33.6%)
1973 WHO grade	
Grade 2	162 (41.5%)
Grade 3	228 (58.5%)
Concomitant CIS	
Yes	56 (14.4%)
No	334 (85.6%)
Tumor size	
Less than 30mm	321 (82.3%)
30mm or more	69 (17.7%)
Immediate intravesical instillation	
Yes	167 (42.8%)
No	223 (57.2%)
Induction intravesical instillation	
Yes	260 (66.7%)
No	130 (33.3%)
Second TUR	
Yes	255 (65.4%)
No	135 (34.6%)
Follow up period (months, mean ± SD)	30.5 ± 26.3

CIS: Carcinoma in situ, UUTCa: Upper Urinary Tract carcinoma

Figure 1. Intravesical recurrence free survival rate of all patients.



Mean follow up period was 30.5 ± 26.3 months. Intravesical recurrence was observed in 111 patients (28.5%). In the entire cohort, 2 and 3-year intravesical recurrence free survival rate was 76.2% and 68.1%, respectively (figure 1).

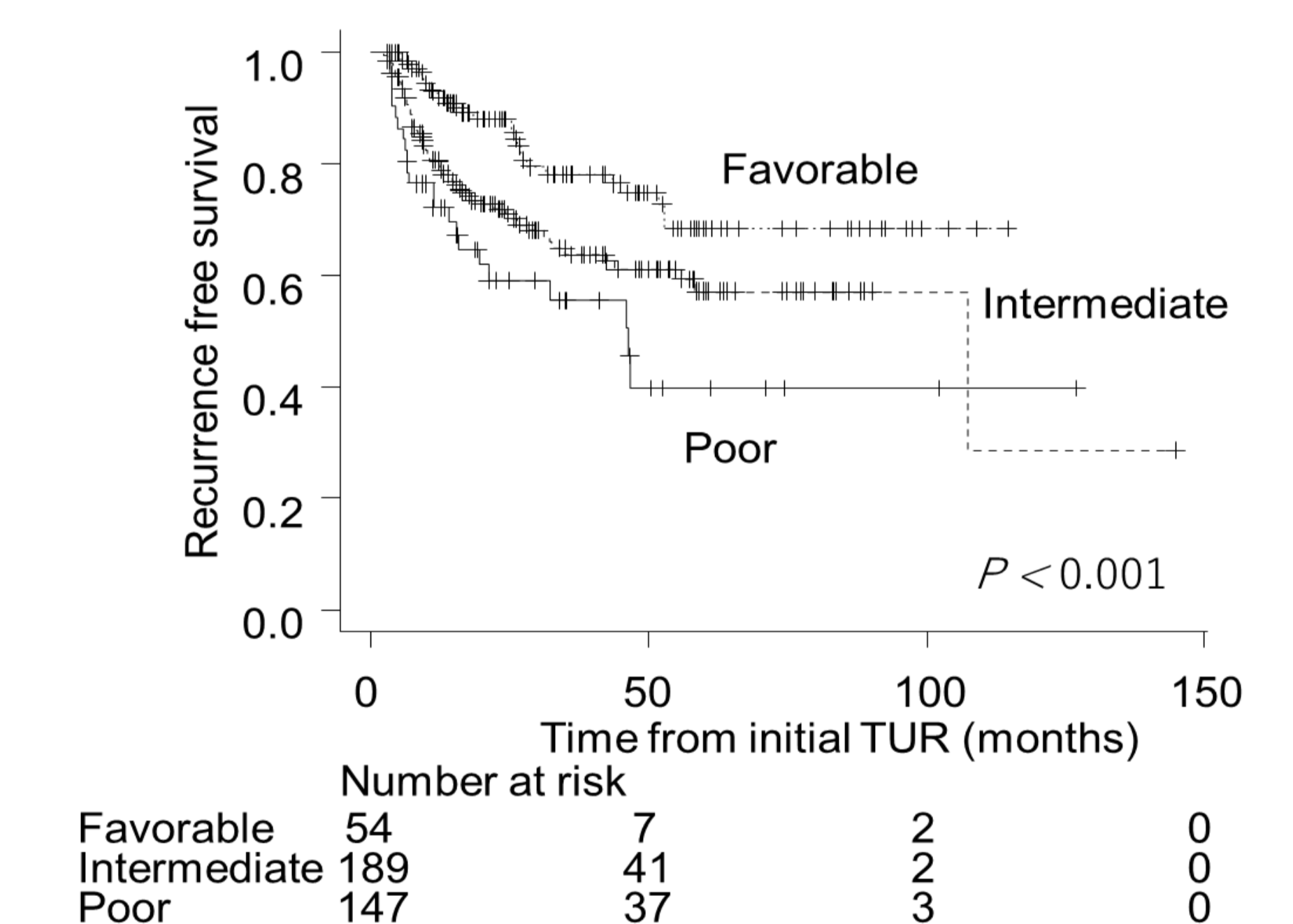
Table 2. Risk factors affecting intravesical recurrence according to treatment options

	Univariate		Multivariate	
	OR (95% CI)	P	HR (95% CI)	P
Second TUR (Yes)	0.67 (0.44-1.01)	0.053	0.70 (0.46-1.09)	0.12
Immediate intravesical instillation (Yes)	0.58 (0.40-0.85)	0.004	0.56 (0.39-0.82)	0.003
Induction intravesical instillation (Yes)	0.59 (0.41-0.87)	0.007	0.65 (0.44-0.96)	0.03

OR, odds ratio; HR, hazard ratio.

To determine treatment option reducing intravesical recurrence in TaHG NMIBC patients, we performed uni-, and multivariate analysis (table 2). Accordingly, immediate intravesical instillation of THP and induction intravesical treatment including THP, MMC, and BCG statistically decreased intravesical recurrence. In contrast, second TUR did not achieve statistical power for reducing intravesical recurrence in the cohort.

Figure 2. Intravesical recurrence free survival rate according to the risk classification.



We classified the patients according to the risk for intravesical recurrence from the aspect of treatment options. The risk factors were no immediate intravesical instillation and no induction intravesical treatment. Patients with 2 risks were categorized as Poor risk, 1 risk factor as intermediate risk, no risk factor as favorable risk group. Figure 2 shows intravesical recurrence free survival according to the risk model (Log-rank test,  $P < 0.001$ ).

## Conclusion

Among patients who newly diagnosed TaHG bladder cancer, approximately one-third of patients developed intravesical recurrence during 3 years. From the aspect of treatment options, immediate intravesical chemotherapy and induction intravesical instillation therapy were the key managements to reduce intravesical recurrence risk.

**Conflict of Interest**  
The authors have nothing to disclose.