

Delayed cystoscopy follow-up of non-muscle invasive bladder cancer during the COVID-19 pandemic may increase recurrence rates but not progression rates

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ABSTRACT

Background This study aimed to investigate whether there is a difference in recurrence and progression rate before and after the pandemic in patients who applied for bladder cancer and/or were followed-up-treatment-operated in the urology clinic during the pandemic.

Material and Methods A total of 116 non-muscle invasive bladder cancer (NMIBC) patients with delayed cystoscopy and 90 control patients with timely cystoscopy were included in the study between June and July 2020. Demographic data of the patients were recorded. Recurrences and progression scores were calculated and grouped according to these scores. The cystoscopy delay time was calculated from the planned cystoscopy time to the performed cystoscopy time. The recurrence and progression status of the patients were recorded, and a comparison was made between the two groups.

Results The median age was 63.6 years (interquartile range [IQR] 35–85) in the delayed cystoscopy group and 67.3 (25-87) in the control group. In the delayed cystoscopy group, 29 (25%) patients had tumour recurrence on follow-up cystoscopy, and 3 (10.34%) patients had tumour progression on subsequent TUR-BT. The mean cystoscopy delay time is 89.27 ± 27.35 days. As a result of the chi-square analysis performed on the group with 10-17 recurrence points found a statistically significant relationship between the experimental and control groups ($\chi^2 = 5.792$; $p = .016$; $p < 0.05$). As a result of the chi-square analysis between the experimental and control groups according to the progression score groups, no statistically significant correlation was found between the experimental and control groups ($p > 0.05$).

Conclusions In this study, we reported that superficial bladder cancers with low recurrence scores could wait 3-6 months, but delaying 3-6 months in cases with a recurrence score of 10 or more increases the recurrence rate.

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Keywords: Bladder cancer, delay, follow-up, recurrence, progression.



INTRODUCTION

The severe acute respiratory syndrome coronavirus-2, shortly named coronavirus disease 2019 (COVID-19), caused by a beta coronavirus, was declared a pandemic by the World Health Organization in March 2020, affecting millions of individuals worldwide.¹ It is predicted that the second wave or other similar pandemics may occur. Treatment of other diseases was postponed for a certain period due to the exceeding capacity of the health system against the risk of transmission. In response, professional organisations suggested re-prioritizing surgical cases, especially to avoid delays in the diagnosis and treatment of cancer patients.²

Bladder cancer (BC) is the seventh most commonly diagnosed cancer in the male population worldwide.³ Approximately 75% of patients with BC present with a disease confined to the mucosa (stage Ta, carcinoma in situ [CIS]) or submucosa (stage T1).⁴ This is called non-muscle invasive bladder cancer (NMIBC). NMIBC has a high probability of recurrence and progression. The recurrence and progression rates at five-year follow-ups were 78% and 45%, respectively.⁵ Uro-oncologists worldwide have been troubled during the COVID-19 era, as it is well known that delays in managing bladder cancer can have deleterious effects.⁶ It is essential to

achieve the management of bladder cancer in such kinds of pandemic diseases. We aimed to investigate whether there is a difference in recurrence and progression rate before and after the pandemic in patients who applied for bladder cancer and/or were followed-up-treatment-operated in the urology clinic during the pandemic.

MATERIAL AND METHODS

Here, we presented a multicenter study with the contribution of Urology Clinics. Ethics committee approval of the study was obtained (HNEAH-KAEK 2020/139), and written consent was obtained from all patients. One hundred and sixteen patients with NMIBC bladder cancer who underwent delayed cystoscopy and TUR-T between June and July 2020 were included in the study whose cystoscopy was postponed due to the pandemic. Also, 90 NMIBC patients who underwent timely control cystoscopies were included as a control group. Patients with muscle-invasive bladder cancer, patients not yet diagnosed with bladder cancer, patients with residual tumours in their first operation, and patients who did not accept participation were excluded from the study. Delays starting from the scheduled date of cystoscopy

Table 1. Weighting used to calculate disease recurrence and progression scores.

Factor	Recurrence	Progression
Number of tumours		
Single	0	0
2-7	3	3
≥8	6	6
Tumor diameter		
<3 cm	0	0
≥3 cm	3	3
Prior recurrence rate		
Primary	0	0
≤1 recurrence/year	2	2
>1 recurrence/year	4	2
Category		
Ta	0	0
T1	1	4
Concurrent CIS		
No	0	0
Yes	1	6
Grade		
G1	0	0
G2	1	0
G3	2	5
Total Score	0-17	0-23

CIS: carcinoma in situ.

according to the EAU follow-up protocol were recorded as “cystoscopy delay time.” The definition of recurrence was characterised by the presence of a tumour on follow-up cystoscopy. TUR-computed tomography (CT) was planned under general or spinal anaesthesia when recurrence was detected, and the pathological features of the tumour were noted. Transurethral resection of the tumours was performed with the bipolar resectoscope with three urologists with at least five years of experience, and the pathologic specimens were evaluated by two uro-pathologist.

The recurrence and progression scores of these 116 cases were determined in the EAU 2020 Guideline’s NMIBC (TaT1 and CIS) section.5 To predict short- and long-term risks of bladder cancer recurrence and progression in patients, the EORTC Genito-Urinary Cancer Group developed a scoring system and risk tables. The scoring system was based on the six most significant clinical and pathological factors: the number and diameter of tumours, prior recurrence rate, category (ta, T1) of tumours, concurrent CIS, and grade of tumours. The total recurrence and progression scores ranged between 0-17 and 0-23, respectively (Table 1).

Statistical analysis

Guideline values were compared statistically with the data in our study. The data analysis was done with IBM SPSS 25, and the frequency and percentage values of the variables were given. The differences between variables were analysed using the chi-square test. A *p* - value of < 0.05 was considered statistically significant in the study.

RESULTS

The median age was 63.6 years (interquartile range [IQR] 35-85) in the delayed cystoscopy group and 67.3 (25-87) in the control group. The initial pathology of 73 (62.9%) patients was Ta, and 43 (37.1%) was T1. In the delayed cystoscopy group, 29 (25%) patients had tumour recurrence on follow-up cystoscopy, and 3 (10.34%) patients had tumour progression on subsequent TUR-BT. The mean cystoscopy delay time was 89.27 ± 27.35 days. Demographic characteristics were shown in Table 2.

There was no recurrence of 13 patients who scored 0 points, 8 (15.1%) recurrence of 53 patients who

scored 1 to 4, 11 (28.9%) recurrence of 38 patients who scored 5 to 9, 10 (83.3%) recurrence of 12 patients who scored 10 to 17 occurred. Eight patients who scored 10 -17 had T1 tumours, 1 had Ta high-grade CIS, and 1 Had TaG1 5 cm tumour. As a result of the chi-square analysis between the experimental and control groups regarding recurrence scores, no correlation was found between the experimental and control groups regarding the scores of recurrence 0, recurrence 1-4, and recurrence 5-9 (*p* < 0.05). As a result of the chi-square analysis performed in the group with 10-17 recurrence points, a statistically significant relationship was found between the experimental and control groups ($\chi^2 = 5.792$; *p* = 0.016; *p* < 0.05) (Table 3).

The progression score was shown in Table 3. There was no progression of 13 patients who scored 0 points, 1 (2.38%) progression of 41 patients who scored 2 to 6, 1 (3.33%) progression of 38 patients who scored 7 to 13, 1 (3.33%) progression of 31 patients who scored 14 to 23 occurred. As a result of the chi-square analysis between the experimental and control groups according to the progression score groups, no statistically significant correlation was found between the experimental and control groups for progression 0, progression 2-6, progression 7-13, and progression 14-23 scores (*p* > 0.05).

DISCUSSION

At the end of this study, we found that the recurrence rates increased in the patient group with a high recurrence score for cystoscopy delay, but it did not show any change in the progression rates.

COVID-19 has developed into a worldwide health problem affecting millions of individuals and has created many problems for patients who have bladder cancer in receiving care. There is no information about

Table 2. Demographic characteristics of the patients.

	Delayed cystoscopy group	Control group
Age (years)	63.6 (35-85)	67.3 (25-87)
Gender (male/female)	105/11	73/17
Initial pathology		
Ta	73 (62.9%)	50 (55.6%)
T1	43 (37.1%)	40 (44.4%)

Table 3. Comparison of recurrence rates of groups according to recurrence scores.

	Delayed cystoscopy group	Control group	P - value
Recurrence score 0			1.000
-	13	14	
+	0	0	
Recurrence score 1-4			0.591
-	45	19	
+	8	3	
Recurrence score 5-9			0.702
-	27	27	
+	11	9	
Recurrence score 10-17			0.016
-	2	11	
+	10	7	

the direct effect of COVID-19 and stress factors on the formation or progression of bladder cancer. It becomes an important issue to check our routine in managing bladder cancer. Long-term BC-specific mortality rates are around 1-2%, and active surveillance for recurrent low- and intermediate-risk NMIBCs is an important management option.^{7,8} Marcq *et al.*⁹ reported the role of active surveillance in low-grade non-muscle invasive bladder cancer (NMIBC) (Ta, T1a, < 1 cm, < 5 lesions) revealed a 15% upgrading and 10% upstaging at a median follow-up of 32 months. According to a combined analysis of 2,596 patients from seven EORTC Trials, the number of tumours, tumour size, and the prior recurrence rate are the most important prognostic factors for recurrence rate, T category, grade, and the presence of CIS for progression rate.⁵ Due to the very low recurrence and progression rates of NMIBC, active surveillance protocols have been tried to be developed. In a study in which 186 NMIBC patients were followed for a median of 72 months,

progression was detected in only 2%.¹⁰ In another study, no muscle invasion progression was observed in the follow-up of 122 patients.¹¹ In light of these findings, although it was reported that the cystoscopy interval could be opened in NMIBC follow-ups, in our study, it was found that there was a significant increase in recurrence rates, especially when the cystoscopies of patients with high recurrence scores were delayed.

In the literature, it is reported that it is safe to defer cystoscopy and transurethral resection of bladder tumour (TURBT) for recurrence in patients with known low-grade NMIBC bladder tumours during the COVID-19 pandemic.^{6,12,13} A recent multicenter study determined that delaying the cystoscopy for more than three months resulted in a 4.8-fold increase in tumour recurrence and a 6.7-fold increase in progression.¹⁴ In our study, we observed that a delay of 3-6 months would not cause trouble in the NMIBC group with a recurrence score of 9 or less, in line with the literature.

Table 4. Comparison of progression rates of groups according to progression scores.

	Delayed cystoscopy group	Control group	P-value
Progression score 0			1.000
-	13	14	
+	0	0	
Progression score 2-6			0.695
-	40	18	
+	1	0	
Progression score 7-13			0.508
-	30	30	
+	1	0	
Progression score 14-23			0.737
-	30	27	
+	1	1	

We found that the delay in the cystoscopy suture had a significant effect on recurrence in the risky group with a recurrence score of 10-17. It was determined that there was no difference in the groups with recurrence scores between 0,1-4 and 5-9, but there was a statistically significant difference between the rates we obtained from the study and the rates determined in the Guideline in the group with a recurrence score between 10-17. There was no statistically significant difference between the progression rate in our study and the guideline ($p > 0.05$) (Table 4). Progression rates are consistent with our study, literature, and guideline rates.

The limitation of this study is that it was conducted with a limited number of cases and in a limited time. Another limitation of the study is that cancer-specific and overall survival could not be evaluated due to these patients' lack of long-term follow-up.

CONCLUSIONS

A prevailing consensus within the literature substantiates the admissible deferment of the treatment and subsequent surveillance of NMIBC by a span of 3 to 6 months, particularly in the context of exigent circumstances such as the COVID-19 pandemic or similar periods. This study presents noteworthy findings, indicating that NMIBC instances characterised by diminished recurrence scores may endure the postponement of 3 to 6 months with discernible prudence. Nonetheless, it is imperative to state that the deferment of a similar duration in cases where the recurrence score reaches or surpasses 10 shows a marked escalation in the recurrence rate, thereby underscoring the imperative of judicious clinical discretion in such scenarios.

Highlights

•**What's known:** NMIBC has a high probability of recurrence and progression. The recurrence and progression rates at five-year follow-ups were 78% and 45%, respectively.

•**What's new:** NMIBC bladder cancers with low recurrence scores can wait 3-6 months, but delaying 3-6 months in cases with a recurrence score of 10 or more increases the recurrence rate.

Conflict of Interest

The author(s) declared no potential conflicts of in-

terest with respect to the research, authorship, and/or publication of this article.

Ethical Approval

The protocol of the study was approved by the Medical Ethics Committee of Haydarpaşa Training and Research Hospital, İstanbul, Turkey. (Decision number: HNEAH-KAEK 20207139-22902, date: 13.07.2020).

Authors' Contribution

Study Conception: YB; Study Design: YB, AÇ; Literature Review: YB, AÇ; Critical Review: YB, AÇ; Data Collection and/or Processing: YB, AÇ; Analysis and/or Data Interpretation: YB, AÇ; Manuscript preparing: YB, AÇ.

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