

How has the COVID-19 pandemic affected patients with primary bladder cancer?

¿Cómo ha afectado la pandemia de COVID-19 a los pacientes con cáncer de vejiga primario?

Ali K. Yildiz^{1*}, Berat C. Ozgur², Arif S. Bayraktar², Demirhan O. Demir³,
and Omer G. Doluoglu²

¹Department of Urology, Ankara City Hospital, Ankara; ²Department of Urology, Ankara Training and Research Hospital, Ankara; ³Department of Urology, Karabuk University, Karabuk. Turkey.

Abstract

Purpose. The COVID-19-induced effects of primary bladder cancer (BC) patients have not yet been clarified. The aim of this study was to investigate the effects of the pandemic on the diagnosis, treatment, and follow-up of primary BC patients. **Material and methods.** A retrospective single-center analysis was made of all patients who underwent diagnostic and surgical procedures due to primary BC between November 2018 and July 2021. A total of 275 patients were identified and allocated to one of the groups: Pre-COVIDBC (BC diagnosed before the COVID-19 pandemic) or COVIDBC (during the pandemic). **Results.** The BC patients diagnosed during the pandemic were mostly at higher stages (T2) ($p = 0.04$), the risk of non-muscle invasive BC (NMIBC) was higher ($p = 0.02$), and recurrence and progression scores were increased ($p = 0.001$) compared to patients diagnosed before the pandemic. The time to surgery from diagnosis ($p = 0.001$) and symptom duration ($p = 0.04$) were significantly prolonged during the pandemic and the rate of follow-up significantly decreased ($p = 0.03$). **Conclusions.** The study results highlight the significant increase in muscle invasive BC and the very high risk of NMIBC in patients presenting during the COVID-19 pandemic.

Keywords: Bladder cancer. COVID-19. Pandemic. Tumor stage. Grade. Transurethral resection.

Resumen

Antecedentes. Los efectos inducidos por la COVID-19 en pacientes con cáncer de vejiga primario no están aclarados actualmente. **Objetivo.** Investigar los efectos de la pandemia en el diagnóstico, el tratamiento y el seguimiento del cáncer de vejiga primario. **Método.** Se realizó un análisis retrospectivo unicéntrico de todos los pacientes que se sometieron a procedimientos diagnósticos y quirúrgicos por cáncer primario de vejiga durante noviembre de 2018 y julio de 2021. Se incluyeron 275 pacientes en el estudio. Los pacientes fueron asignados a uno de dos grupos: pre-COVIDBC (antes de la pandemia) o COVIDBC (durante la pandemia). **Resultados.** Los pacientes con cáncer de vejiga diagnosticados durante la pandemia se encontraban en su mayoría en estadios más altos (T2) ($p = 0.04$), el grupo de riesgo era más alto en el cáncer de vejiga no invasivo del músculo ($p = 0.02$), y la recurrencia y las puntuaciones de progresión aumentaron ($p = 0.001$) en comparación con antes del período pandémico. Además, el tiempo hasta la cirugía desde el diagnóstico ($p = 0.001$) y la duración de los síntomas ($p = 0.04$) aumentaron considerablemente durante la pandemia, y la tasa de seguimiento disminuyó significativamente

*Correspondence:

Ali K. Yildiz
E-mail: alikaanyildiz@gmail.com

Date of reception: 14-03-2022

Date of acceptance: 07-08-2022

DOI: 10.24875/CIRU.22000204

Cir Cir. 2023;91(2):204-211

Contents available at PubMed

www.cirugiyacirujanos.com

0009-7411/© 2022 Academia Mexicana de Cirugía. Published by Permanyer. This is an open access article under the terms of the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

($p = 0.03$). **Conclusiones.** Destaca el aumento significativo del cáncer de vejiga invasivo del músculo y del cáncer de vejiga no invasivo del músculo de muy alto riesgo durante la pandemia.

Palabras clave: Cáncer de vejiga. COVID-19. Pandemia. Estadio tumoral. Grado. Resección transuretral.

Introduction

The rapid spread of coronavirus disease-2019 (COVID-19), caused by a novel beta-coronavirus known as severe acute respiratory syndrome 2 (SARS-CoV-2), has had a dramatic impact on both people and health system worldwide¹. The number of people infected with SARS-CoV-2 created intensive demand for health-care systems with limited resources resulting in decreased capacity, a rapid depletion of health-care service systems, and made the hospitals a source of viral transmission.

Risks of delayed diagnosis and treatment differ between different genitourinary tumors; some require more rapid intervention than others, including high-grade bladder cancer (BC), advanced renal cell carcinoma, testicular cancer, and penile carcinoma². As urothelial cancer progresses rapidly, it is important to prioritize the timely care of these cancers. Urology associations and reference centers have released recommendations to give information about urological care during the COVID-19 pandemic. It is essential that urologists prioritize patient safety with a balance between potential delays in the diagnosis and treatment of urological conditions and the related additional burden on health-care resources and the risk of exposure to COVID-19³. While it has been targeted to preserve health-care resources due to the burden created by the pandemic, the risk of delayed treatment of cancer has emerged. Consequently, the transformation of health-care services and increased interest of the population in avoiding disease exposure have resulted in reduced numbers of hospital presentations.

The effect of the outbreak on BC patients due to decreased presentation at emergency rooms and urology clinics is unclear. The European Association of Urology (EAU) Guidelines Office Rapid Reaction Group published a guideline to adapt the EAU recommendations for the COVID-19 period⁴. According to this guideline, four priority groups were established, and a certain time of delay to treatment was specified for each patient group based on their priority.

The aim of this study was to identify how the COVID-19 pandemic influenced the oncological outcomes of primary BC, tumor stage and grade, symptom duration, time to surgery from diagnosis, pre-operative clinical characteristics, and post-operative follow-up.

Material and methods

Approval for this single-center and retrospective study was granted by the Local Ethics Committee and all procedures were in accordance with the Declaration of Helsinki. It was planned to enroll all patients who underwent a transurethral resection of bladder tumor (TURBT) procedure for the primary BC between November 2018 and July 2021. Our center is a reference hub for COVID-19 patients and has been providing healthcare to a large patient population since the beginning of the pandemic. Bladder tumors were defined as urothelial carcinoma detected in post-operative pathology specimens. The study exclusion criteria were defined as a history of urinary system tumor, chronic kidney disease, or anemia.

The patients were allocated to one of the groups: Pre-COVIDBC or COVIDBC. The COVIDBC group consisted of patients diagnosed between March 2020 and July 2021 (during the COVID-19 pandemic), and the Pre-COVIDBC group consisted of patients diagnosed between November 2018 and March 2020 (before the COVID-19 pandemic).

After the pre-operative diagnosis of BC, all patients were prepared for surgery regardless of risk. No patient was referred to another center as our hospital was able to manage all BC cases during the pandemic. The surgery was performed under spinal anesthesia and by the same anesthesia team. All TURBT procedures were performed by an experienced surgeon (more than 100 cases).

A record was made of demographic baseline data and tumor characteristics, including gender, age, the American Society of Anesthesiologists score, body mass index, hydronephrosis grade, hemoglobin, serum creatinine, tumor side, tumor count, tumor size, and tumor localization. It was planned to repeat the initial cystoscopy at the end of the 3rd month in all patients.

Patients without follow-up were defined as those who were not admitted for cystoscopy control within the first 6 months. Early cystectomy was recommended for suitable very high risk patients, and 3rd month cystoscopy follow-up was recommended for patients not suitable for surgery or those who declined surgical treatment. Incomplete resection was defined as visible tumor tissue left after the TURBT procedure.

In the patients who presented with primary bladder tumor, T-stage, tumor grade, and the presence of carcinoma *in situ* (CIS) were evaluated. The EAU non-muscle invasive bladder cancer (NMIBC) risk stratification was applied to NMIBC patients using these data and the two groups were compared. The 2006 European Organization for Research and Treatment of Cancer (EORTC) scoring model (tumor count, tumor size, number of recurrences in the last year, T-stage, presence of CIS, and tumor grade) was used for EORTC recurrence and progression scores. Comparisons were made between the groups in respect of time to TURBT operation from diagnosis, rate of follow-up, symptom duration, microscopic and macroscopic hematuria, incomplete resection, duration of surgery, duration of post-operative hospital stay, and complications.

The data were analyzed using IBM SPSS Statistics v.26[®]. Conformity of the continuous variables to normal distribution was assessed using the Kolmogorov–Smirnov tests and P-P plot tests. The variables showing normal distribution were presented as mean ± standard deviation values, and those not showing normal distribution as median (minimum-maximum) values. Categorical variables were presented as number (n) and percentage (%). Comparisons of categorical variables between the groups were made using Pearson’s Chi-square and Fischer’s Exact Test. The tests were specified according to the smallest theoretical frequency with Fisher’s Exact Test used in case of < 5 and Pearson’s Chi-square Test > 5. Continuous variables were compared using the Independent Samples t-test for normally distributed data, and the Mann–Whitney U-test was applied to non-normally distributed data. $p < 0.05$ was considered statistically significant.

Results

Evaluations were made of a total of 275 patients diagnosed with bladder tumor between November 2018 and July 2021 (147 before the COVID-19 pandemic and 128 during the COVID-19 pandemic). The demographic characteristics and pre-operative clinical

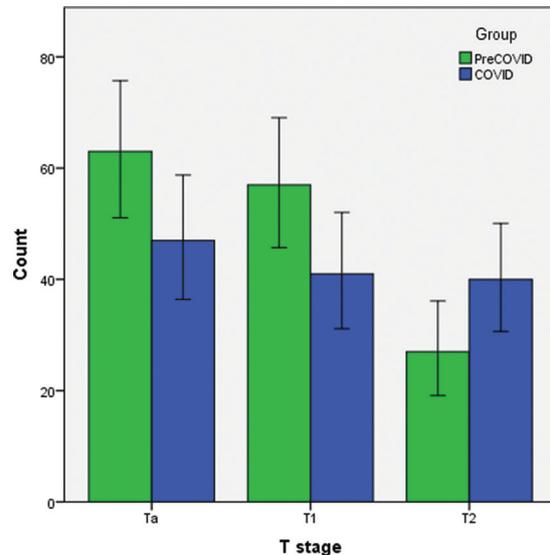


Figure 1. Tumor stage was Ta in 63 (42.9%), T1 in 57 (38.8%) and T2 in 27 (18.4%) of the 147 patents in the Pre-COVIDBC group, and Ta in 47 (36.7%), T1 in 41 (32.0%), and T2 in 40 (31.3%) of the 128 patients in the COVIDBC group (Chi-square test, $p = 0.04$). Each error bar is constructed using a 95% confidence interval of the count.

data are listed in Table 1. Newly diagnosed BC cases showed a 13% decrease during the COVID-19 pandemic compared to before COVID-19.

Regarding the oncological outcomes of all the BC patients, the study results confirmed an overall significant increase in higher tumor stages (T2) during the pandemic compared to before the pandemic, with significantly fewer Ta tumors ($p = 0.04$). The incidence of higher stage tumors (T2) was 18.4% pre-pandemic compared to 31.3% during the pandemic, and the rate of Ta tumors decreased during the pandemic compared to the pre-pandemic period (36.7% vs. 42.9%) (Fig. 1). A significant difference was determined in tumor count between the pre-pandemic and pandemic periods (1.4 ± 0.6 vs. 1.6 ± 1.0 ; $p = 0.02$). In patients with BC, no adverse oncological outcomes concerning tumor grading could be detected in the comparisons of the pre-pandemic and pandemic periods. The surgical findings, intraoperative data, and tumor characteristics are shown in Table 2.

Of the 208 NMIBC patients, the COVIDBC group included 88 and the Pre-COVIDBC group included 120. The clinical findings and follow-up results of both groups are listed in Table 3. Based on the EAU NMIBC risk stratification, these results demonstrate a significant increase in very high-risk patients during the pandemic compared to pre-pandemic, with a significant

Table 1. Demographic characteristics and pre-operative data

	Pre-COVIDBC (n = 147)	COVIDBC (n = 128)	p - value
Age (years)	64.7 ± 13.4-66 (31-87)	63.5 ± 12.5-65 (22-92)	0.4
BMI (kg/m ²)	27.3 ± 2.6-27.6 (20.2-34.3)	27.0 ± 2.3-27.5 (22.0-32.7)	0.5
Gender			0.3
Male	123 (83.7)	112 (87.5)	
Female	24 (16.3)	16 (12.5)	
ASA score			0.1
1	11 (7.5)	16 (12.5)	
2	70 (47.6)	67 (52.3)	
3	66 (44.9)	45 (35.2)	
Hematuria			0.04*
Gross hematuria	103 (70.1)	106 (82.8)	
Mic. hematuria	22 (15.0)	12 (9.4)	
No hematuria	22 (15.0)	10 (7.8)	
Hydronephrosis			0.05*
Grade 0	128 (87.1)	100 (78.1)	
Grade 1	6 (4.1)	12 (9.4)	
Grade 2	9 (6.1)	14 (10.9)	
Grade 3	4 (2.7)	2 (1.6)	
Hemoglobin (gr/dL)	14.0 ± 2.3-14.5 (8.4-18.6)	14.1 ± 2.0-14.4 (7.6-17.8)	0.7
Serum creatinine (mg/dL)	1.26 ± 1.20-1.0 (0.6-9.1)	1.20 ± 1.16-0.9 (0.5-8.8)	0.7
Time from diagnosis to treatment (day)	12 ± 6-12 (3-34)	30 ± 21-27 (3-96)	0.001*
Symptom duration (weeks)	7.3 ± 6.9-1 (0.5-12)	9.1 ± 7.5-1 (0.5-18)	0.04*

(*) Statistically significant difference.

Data are shown as mean ± SD, median (minimum-maximum) values and number (n) and percentage (%).

BMI: body mass index; ASA: the American Society of Anesthesiologist.

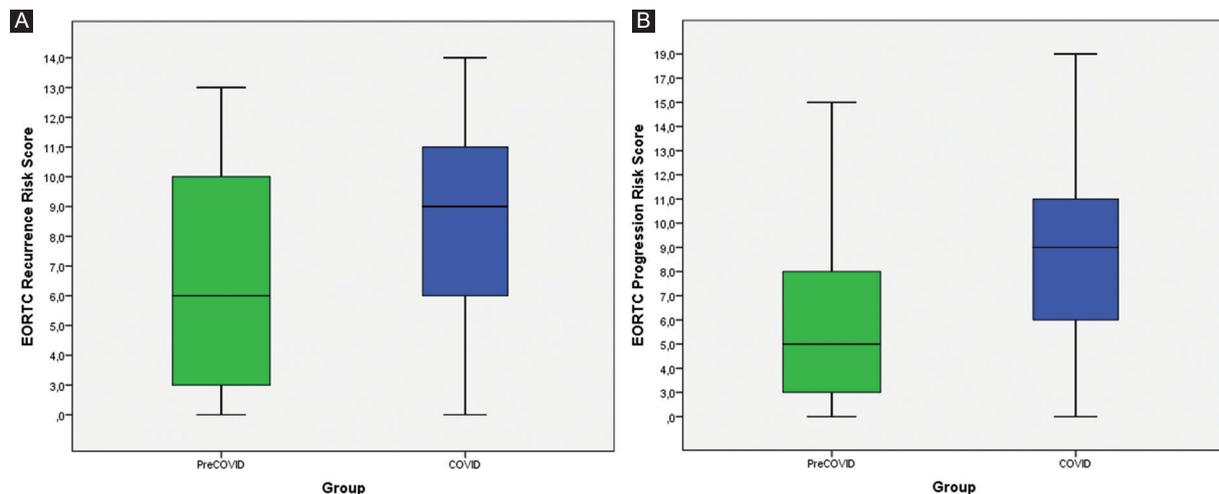


Figure 2. Scores of recurrence and progression of bladder cancer were assessed according to the EORTC scoring system. **A:** EORTC recurrence score was median (min-max, lower-upper quartile), 6 (0-13, 3-10) for the Pre-COVIDBC group, and 9 (0-14, 6-11) for the COVIDBC group (Mann–Whitney U-test, $p = 0.001$), **B:** EORTC progression score was median (min-max, lower-upper quartile), 5 (0-15, 3-8) for the Pre-COVIDBC group, and 9 (0-19, 6-11) for the COVIDBC group (Mann–Whitney U-test, $p = 0.001$).

Table 2. Surgical and tumor characteristics

	Pre-COVIDBC (n = 147)	COVIDBC (n = 128)	p - value
Tumor size (cm)	2.1 ± 1.4-2 (0.3-10)	2.4 ± 1.8-2 (0.5-14)	0.1
Tumor count	1.4 ± 0.6-1 (1-6)	1.6 ± 1.0-1 (1-8)	0.02*
Tumor site			0.6
Right	58 (39.5)	51 (39.8)	
Left	51 (34.7)	39 (30.5)	
Bilateral	38 (25.9)	38 (29.7)	
Tumor number			0.5
Solitary	25 (49.0)	30 (56.6)	
Multiple	26 (51.0)	23 (43.4)	
Tumor localization			0.5
Lateral	106 (72.1)	90 (70.3)	
Posterior	11 (7.5)	16 (12.5)	
Anterior	10 (6.8)	6 (4.7)	
Neck-Trigone	13 (8.8)	8 (6.3)	
Dome	7 (4.8)	8 (6.3)	
Tumor stage			0.04*
Ta	63 (42.9)	47 (36.7)	
T1	57 (38.8)	41 (32.0)	
T2	27 (18.4)	40 (31.3)	
Tumor grade			0.2
PUNLMP	62 (42.2)	41 (32.0)	
Low	30 (20.4)	28 (21.9)	
High	55 (37.4)	59 (46.1)	
CIS (concomitant)			0.3
Present	18 (12.2)	21 (16.4)	
Not present	129 (87.8)	107 (83.6)	
Complete resection			0.8
Present	132 (89.8)	116 (90.6)	
Not present	15 (10.2)	12 (9.4)	
Complication			0.9
Hematuria	8 (5.5)	7 (5.5)	
Post-operative fever	6 (4.0)	6 (4.7)	
Not present	133 (90.5)	115 (89.8)	
Operation time (min)	27.8 ± 14.0-25 (10-120)	29.4 ± 15.3-25 (15-115)	0.3
Hospitalization time (days)	1.3 ± 0.6-1 (1-6)	1.2 ± 0.4-1 (1-4)	0.001*

(*) Statistically significant difference.
Data are shown as mean ± SD, median (minimum-maximum) values and number (n) and percentage (%).
PUNLMP: Papillary urothelial neoplasm of malignant potential; CIS: Carcinoma *in situ*.

decrease in low-risk patients (p = 0.02). When NMIBC was evaluated, the incidence of very high-risk patients increased by 11.5% (18.2% vs. 6.7%) during the pandemic compared to pre-pandemic, and low-risk patients decreased by 14.2% (25.0% vs. 39.2%). In respect of the recurrence and progression scores of NMIBC patients, the study results showed a significantly higher EORTC recurrence (median [min-max],

Table 3. NMIBC clinical and follow-up data results

	Pre-COVIDBC (n = 120)	COVIDBC (n = 88)	p - value
EAU NMIBC risk group			0.02*
Low	47 (39.2)	22 (25.0)	
Intermediate	19 (15.8)	16 (18.2)	
High	46 (38.3)	34 (38.6)	
Very high	8 (6.7)	16 (18.2)	
EORTC recurrence score	6.3 ± 3.9-6 (0-13)	7.8 ± 3.0-9 (0-14)	0.001*
EORTC progression score	5.4 ± 4.1-5 (0-15)	8.6 ± 3.4-9 (0-19)	0.001*
Follow-up			0.03*
Present	97 (80.8)	60 (68.2)	
Not present	23 (19.2)	28 (31.8)	

(*) Statistically significant difference.
Data are shown as mean ± SD, median (minimum-maximum) values and number (n) and percentage (%).
EAU: European Association of Urology; NMIBC: Non-muscle invasive bladder cancer; EORTC: European Organization for Research and Treatment of Cancer.

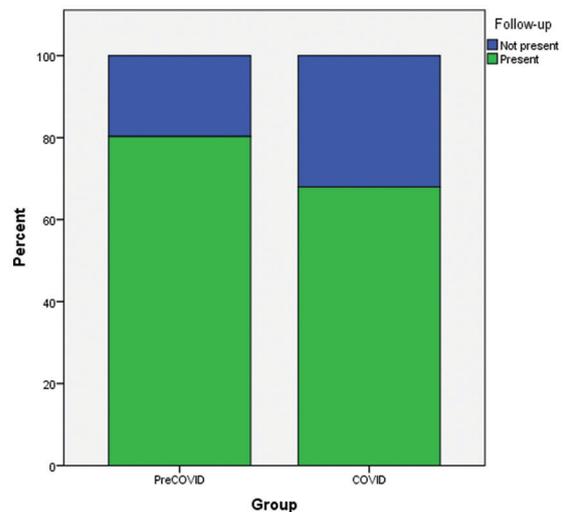


Figure 3. During post-operative follow-up, the rate of presentation for the first control in the Pre-COVIDBC and COVIDBC groups was 80.8% and 68.2%, respectively (Chi-square test, p = 0.03).

9 [0-14] vs. 6 [0-13]) and progression score (median [min-max], 9 [0-19] vs. 5 [0-15]) during the pandemic than before the pandemic (p = 0.001) (Fig. 2). A significant difference was determined between the groups in respect of the follow-up rates (pre-pandemic: 80.8% vs. pandemic: 68.2%; p = 0.03) (Fig. 3).

Discussion

In this study, comparisons were made of patients with the primary bladder tumor who presented at

hospital either during or before the COVID-19 pandemic. In the group that presented during the COVID-19 pandemic, T stage showed a significant increase in favor of T2 (MIBC) compared to the group that presented before the pandemic and there was a significant increase in the ratio of NMIBC high-risk patients according to the EAU risk stratification. The duration of symptoms and time to surgery from diagnosis at presentation were significantly prolonged. In contrast, the rate of follow-up showed a significant decrease during the COVID-19 pandemic.

The COVID-19 pandemic increased the burdens on health-care systems, primarily in the emergency rooms and intensive care units, leading to delays in many diagnoses and treatment procedures. Diagnostic pathways have been interrupted in cancers, especially in those that have screening programs such as prostate, colorectal, or cervical cancers. A decrease of 77%, 62%, and 26% has been reported in newly diagnosed prostate, colorectal, and breast cancers, respectively, during the COVID-19 pandemic compared to before the pandemic and for newly diagnosed BC, there has been seen to be a significant decrease of 66%⁵. In the present study, a 13% decrease was detected in newly diagnosed BC cases over the 17-month period during the pandemic compared to the same time span before the pandemic.

The TNM classification for BC was updated in 2017 by the Union for International Cancer Control⁶. In a study evaluating NMIBC patients using the new TNM classification, 5-year disease-specific survival (DSS) was found to be 98.5% in TaG1 patients and 88.7% in T1G3 patients⁷. In another study evaluating MIBC patients, 5-year DSS after radical cystectomy was found to be 75-80% in organ-restricted T2 patients⁸. Muscle invasion in BC is an important prognostic factor for mortality. In the present study, a significant difference was determined between the groups in terms of T stage ($p = 0.04$), but not for the presence of CIS ($p = 0.2$). There was an increase in the high grade rate, but this increase was not statistically significant ($p = 0.3$). A substantial proportion of the primary BC patients who presented during the COVID-19 pandemic had lower Ta and higher T2 (MIBC) stages. As a result, it was thought that such patients may have poor prognostic factors in the medium/long term in terms of progression and DSS due to hospital presentation at an advanced stage during the pandemic.

According to the EAU NMIBC risk stratification, a significant difference was detected between the groups in terms of EORTC risk stratification with a

substantial increase in the rate of very high-risk patients observed during the pandemic ($p = 0.02$). There are scoring systems for estimation of recurrence and progression in NMIBC patients. In a previous study, tumor count, tumor size, number of recurrences in a year, tumor T class, presence of CIS, and tumor grade were reported as critical prognostic factors for risk scores⁹. In the present study, factors that influence recurrence and progression were evaluated and scores were calculated. The EORTC recurrence score was median (min-max), 9 (0-14) for the COVIDBC group, and 6 (0-13) for the Pre-COVIDBC group. The EORTC progression score was 9 (0-19) for the COVIDBC group and 5 (0-15) for the Pre-COVIDBC group, with a significant difference determined between the groups for both scores ($p < 0.01$ for both). A significant increase in NMIBC very high-risk patient rate, recurrence, and progression score can result in serious oncological consequences without the early treatment or regular follow-up.

In BC patients, the progression rate increases with disease duration, indicating that a delay in presentation or treatment may cause a progression in the disease stage. In the present study, symptom duration at initial presentation was found to be significantly longer during the COVID-19 pandemic compared to the pre-pandemic group ($p = 0.04$). The reasons for the delay in admission to the hospital during the 17-month pandemic period may have been patient anxiety, the prolongation of the referral period, and the longer waiting time in the hospital or the cancellation of appointments, but for whatever reason, further prolongation of this process may lead to the possibility of disease progression.

In the present study, the time between diagnosis and TURBT surgery in the COVIDBC and Pre-COVIDBC groups was 30 ± 21 days and 12 ± 6 days, respectively, and the difference between the groups was significant ($p < 0.01$). All patients diagnosed with pre-operative BC were prepared for surgery under the same conditions without risk classification, and no patient was referred to an external center. This eliminated the paradoxically more rapid access to care for some high-risk patients. All surgeries were performed in our center, but as in many centers, due to the decrease in the number of operation rooms during the pandemic period, there was a decrease in the average number of surgeries per day. This resulted in a prolongation of the time between diagnosis and operation. The literature on NMIBC investigating the effects of delayed intravesical treatment is limited, although

in a study which compared early cystectomy with late cystectomy in high-risk NMIBC patients, it was found that a lengthy delay may influence survival and that cancer-specific survival (CSS) might be reduced in patients with cystectomy delayed for 13 months or longer¹⁰. However, in respect of MIBC, there are numerous studies which have investigated the potential outcomes of delayed surgery. In a study of MIBC patients, it was found that a delay in treatment of longer than 10 weeks is associated with poor CSS and overall survival (OS) outcomes¹¹. These results suggest that even though the delayed times in the current study were shorter than the stage progression times in the literature, due to the limited surgical capacity during the COVID-19 pandemic, prolonging the time from diagnosis to surgery even more than stated in the available data may result in poor survival outcomes in BC patients.

The EAU Guidelines Office Rapid Reaction Group has published a guideline that evaluates disease priorities to adapt EAU recommendations for the COVID-19 pandemic⁴. In the present study, it was planned to repeat the initial cystoscopy at the end of the 3rd month in all patients and patients without follow-up were defined as those who were not admitted for cystoscopy control within the first 6 months. The rate of follow-up was 68.2% and 80.8% in the COVIDBC group and Pre-COVIDBC group, respectively ($p = 0.03$). The 3rd month control after TURBT is an important prognostic indicator for recurrence and progression¹². Not implementing this may prevent the prediction of recurrence and progression during follow-up visits and may cause poor oncological outcomes by leading to delayed early diagnosis and treatment.

The diagnosis of BC is usually made after the examination of patients presenting with gross hematuria (GH) or microscopic hematuria. GH as the presenting symptom in newly diagnosed BC patients has been found to be associated with higher pathological stage¹³. In the present study, the rate of presenting with GH in the COVIDBC and Pre-COVIDBC groups was 82.8% and 70.1%, respectively, with a significantly higher rate detected during COVID-19 pandemic ($p = 0.04$). This was supported by the significantly higher pathological stages. Obstructive nephropathy (ON) is a common cause of acute kidney insufficiency (AKI), accounting for 5-10% of overall AKI cases, and up to 22% in an older population^{14,15}. In cases where AKI is associated with malignancy, ON-induced AKI is seen in nearly 10% of cases¹⁶ with higher mortality

than that seen in patients without ON¹⁷. In the present study, data on ON were investigated and a significant difference was detected between the COVIDBC and Pre-COVIDBC groups in terms of the degree of hydronephrosis ($p = 0.04$). These data suggest that the prevalence of ON may have increased in the diagnosis of primary BC during the pandemic period and higher morbidity and mortality rates may have been due to AKI. Although the rates of GH and ON substantially increased during the COVID-19 pandemic, no difference was determined in terms of presenting hemoglobin and creatinine values ($p = 0.7$ for both).

The most important limitations of the present study were the short follow-up period to standardize the factors that influence tumor recurrence and progression, and the retrospective evaluation of patients diagnosed before the COVID-19 pandemic. A larger population with longer follow-up is required to prove whether the pandemic had additional adverse effects on survival outcomes. Multicentric studies are needed to increase the sample size and obtain more conclusive results. However, during the pandemic, it was not possible to conduct a multicentric study, since only certain centers performed the surgery and follow-up of urological oncology cases and our center was a COVID-19 reference center.

Conclusions

The results of this study demonstrated that the number of newly diagnosed primary BC patients decreased during the COVID-19 pandemic compared to before the pandemic. BC patients diagnosed during the pandemic were mostly at higher stages (T2) and higher risk in NMIBC patients. The increase in muscle invasive (T2) BC and high-risk NMIBC patients can be considered to have increased subsequent morbidity and mortality rates. The recurrence and progression scores and time to surgery from diagnosis also substantially increased. Therefore, the importance of the early surgical intervention should be emphasized and care must be taken not to delay the treatment period. There is also a need for more awareness of alternative treatments for patients who do not accept or are not suitable for early cystectomy. Symptom duration on presentation was significantly longer, and there was a considerable increase in the prevalence of GH and obstructive nephropathy on presentation. During the pandemic, the rate of follow-up significantly decreased among BC patients. The transformation of health-care services and increased attention of the population to

avoid disease exposure during the pandemic might have led to the decrease in hospital presentations and prolonged time to surgery from diagnosis.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflicts of interest

Authors declared no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

References

- Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of Coronavirus disease 2019 in China. *N Engl J Med.* 2020;382:1708-20.
- Kutikov A, Weinberg DS, Edelman MJ, Horwitz EM, Uzzo RG, Fisher RI. A war on two fronts: cancer care in the time of COVID-19. *Ann Intern Med.* 2020;172:756-8.
- Heldwein FL, Loeb S, Wroclawski ML, Sridhar AN, Carneiro A, Lima FS, et al. A systematic review on guidelines and recommendations for urology standard of care during the COVID-19 pandemic. *Eur Urol Focus.* 2020;6:1070-85.
- Ribal MJ, Cornford P, Briganti A, Knoll T, Gravas S, Babjuk M, et al. European association of urology guidelines office rapid reaction group: an organisation-wide collaborative effort to adapt the European association of urology guidelines recommendations to the Coronavirus disease 2019 era. *Eur Urol.* 2020;78:21-8.
- De Vincentiis L, Carr RA, Mariani MP, Ferrara G. Cancer diagnostic rates during the 2020 'lockdown', due to COVID-19 pandemic, compared with the 2018-2019: an audit study from cellular pathology. *J Clin Pathol.* 2021;74:187-9.
- UICC International Union Against Cancer. In: Brierley JD, Gospodarowicz MK, Wittekind C, editors. *TNM Classification of Malignant Tumors.* 8th ed. New York: Wiley-Blackwell and UICC; 2017. p. 263.
- Cambier S, Sylvester RJ, Collette L, Gontero P, Brausi MA, van Andel G, et al. EORTC nomograms and risk groups for predicting recurrence, progression, and disease-specific and overall survival in non-muscle-invasive stage Ta-T1 urothelial bladder cancer patients treated with 1-3 years of maintenance *Bacillus Calmette-Guérin.* *Eur Urol.* 2016;69:60-9.
- Malkowicz SB, van Poppel H, Mickisch G, Pansadoro V, Thüroff J, Soloway MS, et al. Muscle-invasive urothelial carcinoma of the bladder. *Urology.* 2007;69(1 Suppl):3-16.
- Sylvester RJ, van der Meijden AP, Oosterlinck W, Witjes JA, Bouffoux C, Denis L, et al. Predicting recurrence and progression in individual patients with stage Ta T1 bladder cancer using EORTC risk tables: a combined analysis of 2596 patients from seven EORTC trials. *Eur Urol.* 2006;49:466-5; discussion 475-7.
- Jäger W, Thomas C, Haag S, Hampel C, Salzer A, Thüroff JW, et al. Early vs delayed radical cystectomy for 'high-risk' carcinoma not invading bladder muscle: delay of cystectomy reduces cancer-specific survival. *BJU Int.* 2011;108(8 Pt 2):E284-8.
- Boeri L, Soligo M, Frank I, Boorjian SA, Thompson RH, Tollefson M, et al. Delaying radical cystectomy after neoadjuvant chemotherapy for muscle-invasive bladder cancer is associated with adverse survival outcomes. *Eur Urol Oncol.* 2019;2:390-6.
- Holmang S, Johansson SL. Stage Ta-T1 bladder cancer: the relationship between findings at first followup cystoscopy and subsequent recurrence and progression. *J Urol.* 2002;167:1634-7.
- Ramirez D, Gupta A, Canter D, Harrow B, Dobbs RW, Kucherov V, et al. Microscopic haematuria at time of diagnosis is associated with lower disease stage in patients with newly diagnosed bladder cancer. *BJU Int.* 2016;117:783-6.
- Chávez-Iñiguez JS, Navarro-Gallardo GJ, Medina-González R, Alcantar-Vallín L, García-García G. Acute kidney injury caused by obstructive nephropathy. *Int J Nephrol.* 2020;2020:8846622.
- Akposso K, Hertig A, Couprie R, Flahaut A, Alberti C, Karras GA, et al. Acute renal failure in patients over 80 years old: 25-years' experience. *Intensive Care Med.* 2000;26:400-6.
- Cohen EP, Krzesinski JM, Launay-Vacher V, Sprangers B. Onco-nephrology: Core Curriculum 2015. *Am J Kidney Dis.* 2015;66:869-83.
- Soares M, Salluh JI, Carvalho MS, Darmon M, Rocco JR, Spector N. Prognosis of critically ill patients with cancer and acute renal dysfunction. *J Clin Oncol.* 2006;24:4003-10.