

Effect of COVID-19 Pandemic on Diagnosis and Treatment Delays in Primary Bladder Cancer in Turkey: Single-Institution Experience, 36 Month Screening

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Abstract

Objective: The pandemic caused delays in the diagnosis and treatment of many diseases, and bladder cancer is one of them. The aim of this study is to investigate the effect of the pandemic on primary bladder cancer by comparing the pre- and post-coronavirus disease 2019 pandemic within an 18-month spectrum, based on March 2020 in patients with primary bladder cancer who applied to our clinic.

Methods: Only patients operated for primary bladder tumors were included in the study, they were divided into two groups as those who underwent surgery before and after the 18-month period. Those operated before March 2020 were classified as group A, those operated after March 2020 were classified as group B. The characteristics of the two groups, such as age, gender, smoking status, tumor size, tumor multiplicity, and pathological stage, were compared.

Results: The existing bladder tumor was examined according to its size, tumor multiplicity and pathological stage, and it was observed that there were significant differences between the groups ($p < 0.05$).

Conclusion: Delays in the diagnosis of diseases such as bladder cancer may cause to progression of the disease.

Keywords: COVID-19, bladder cancer, bladder cancer follow-up

INTRODUCTION

Bladder cancer is a significant cause of morbidity and mortality. The tumor-node-metastasis staging system combined with tumor grade guides us in terms of treatment management. Without a doubt, stage is one of the most important prognostic factor in bladder cancer (1). The tumor stage has a one-to-one relationship with the depth of the tumor in the muscle. The time the patient will receive treatment is very important in increasing the muscle depth and in the progression of the stage. Delays in bladder cancer treatment are likely to worsen the prognosis of patients (2).

In the period since the beginning of 2020, the coronavirus disease of 2019 (COVID-19) continues to spread all over the world and still has not been brought under control. The disease has progressed very rapidly and continues to spread on a global scale despite all the precautions taken. After the World Health Organization declared a pandemic on March 11, 2021, radical changes occurred in the provision of healthcare. Many healthcare professionals had to focus on their COVID-19 patients (3-5). As the pandemic flared up, non-COVID-19 patients in hospitals began to be unable to receive adequate and fast health care. Lockdowns, restrictions, and stay-at-home calls have reduced the number of hospital admissions of non-COVID-19



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patients. The focus of almost all healthcare institutions and healthcare professionals on the struggle against COVID-19 has led to a prolongation of the diagnosis and treatment times of some diseases such as cancer (6). As a result of this situation, it can be thought that the diagnosis of many patients with bladder cancer is delayed, and thus the pandemic contributes poorly to the prognosis of bladder cancer.

The aim of this study is to investigate the effect of the pandemic on primary bladder cancer by comparing the pre- and post-COVID-19 pandemic within an 18-month spectrum, based on March 2020, in patients with primary bladder cancer who visited our clinic. In healthcare institutions and healthcare professionals, an increase in bladder cancer stage should be expected compared to the pre-COVID-19 period, due to the decrease in the hospital admissions due to the increased workload and the recommendations of the governments to stay at home.

METHODS

Study Design

This study was conducted at Sakarya Training and Research Hospital. The data of all patients who were registered in the urology department of our institution and operated due to a bladder tumor between September 2018 and September 2021 were collected from their medical documents. The files of 1,075 patients who underwent surgery for bladder tumor were reviewed. These patients were included in the study according to certain criteria. Only patients operated for primary bladder tumors were included in the study. If the operated individuals required ReTUR after the first operation, the pathology report with advanced stage was taken into consideration, and if the pathological stage was reported the same, it was counted. The patient needed ReTUR but decided not to have the operation voluntarily or if the patient wanted to continue his treatment in another center was excluded from the study. Regardless of the pathological diagnosis of the patient, if there was metastasis on imaging, the patient was grouped assuming a minimum T2 bladder tumor. If the patient underwent radical cystectomy without a pathological diagnosis of T2, the pathology report of the radical cystectomy material was considered.

The above-mentioned criteria were considered and 218 primary bladder tumor patients were included in the study. Based on the date of March 2020, when the first COVID-19 case was seen in Turkey, the patients were divided into 2 groups: as those who underwent surgery before and after the 18-month period. Those operated before March 2020 were classified as group A, and those operated after March 2020 were classified as group B (Figure 1).

The characteristics of the 2 groups, such as age, gender, smoking status, tumor size, tumor multiplicity, and pathological stage, were compared. The size written in the operation note by the surgeon performing the operation was accepted as the tumor size. Information about tumor multiplicity was also obtained from the operation note. Smoking status was analyzed as 3 different conditions: as never smoker, ex-smoker, and active smoker. The pathological stage was divided into non-muscle-invasive bladder cancer (NMIBC) and muscle-invasive bladder cancer (MIBC) and then analyzed.

Statistical Analysis

Data were analyzed using SPSS 20.0 software (SPSS, Version 20.0; International Business Machines Corp, Armonk, NY). Chi-square and t-tests were used for statistical analysis. Distribution was analyzed using the Shapiro-Wilk test. Variables with normal distribution were analyzed using a Student's t-test. Chi-square test was used for the analysis of qualitative data. $P < 0.05$ value was defined as statistically significant.

RESULTS

There were 124 and 94 patients in groups A and B, respectively. Characteristics of all patient, before and after the outbreak of COVID-19 are shown in (Table 1). The mean age in group A and B were 64.6 ± 7.6 and 63.4 ± 9.4 , respectively. There was no statistically significant difference between the 2 groups ($p = 0.327$). When groups A and B were compared based on gender, it was seen that there was no statistical difference between the groups ($p = 0.209$). When the patients were examined according to their

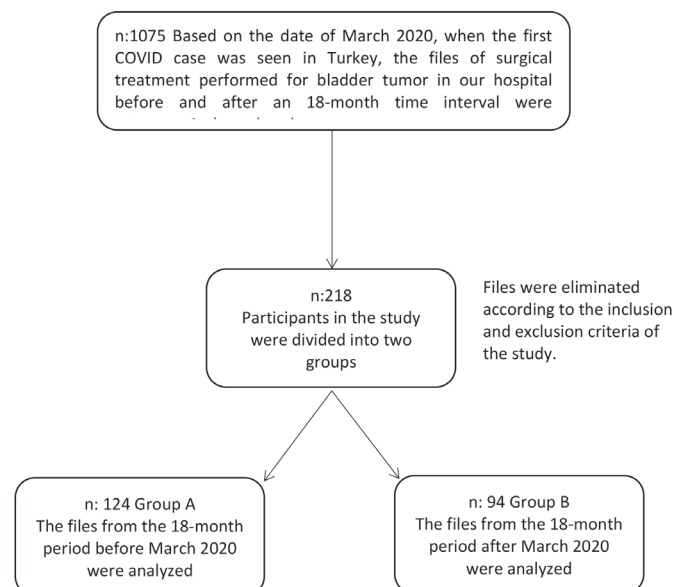


Figure 1. Study algorithm

Table 1. Characteristics of all patients before and after the outbreak of COVID-19

Parameters	Grup A (n=124)	Grup B (n=94)	p value
Age	64.6±7.6	63.4±9.4	0.327 ^a
Gender			
Male	106	86	0.209 ^b
Female	18	8	
Smoking status			
None	11	5	0.122 ^b
Past smoker	44	24	
Active smoker	69	65	
Tumor size (centimeters)	3.5±2.5	4.49±2.5	0.04^a
Multiplicity			
Single	84	38	<0.01 ^b
Multipl	40	56	
Pathologic stage			
PLUMP ^c ,Ta,T1 (NMIBC ^d)	99	64	0.048^b
T2 (MIBC ^e)	25	30	
^a Variables with normal distribution were analyzed using Student's t-test ^b Chi-square test was used for the analysis of qualitative data. ^c Papillary urothelial neoplasm with low malignant potential ^d Non-muscle invasive bladder cancer ^e Muscle-invasive bladder cancer			

smoking use, no significant difference was observed between never-smokers, past smokers, and active smokers ($p=0.122$).

The existing bladder tumor was examined according to its size, tumor multiplicity, and pathological stage, and significant differences were observed between the groups. The tumor diameter was recorded in centimetres, with the size noted by the surgeon who performed the operation. The mean tumor diameter was calculated as 3.5 ± 2.5 cm for group A and 4.49 ± 2.5 cm for group B. It was found that tumors in group B were statistically significantly larger in tumor diameters ($p=0.04$). The groups were compared according to whether the tumor in the bladder was multiple or single. For group A, the number of patients with a single tumor was 84, and the number of patients with multiple tumors was 38. For group B, the number of patients with a single tumor was 40, and the number of patients with multiple tumors was 56. Multiple tumors were more common in group B, and there was a statistically significant difference between the two groups ($p<0.01$). The pathological stages of the patients were examined as NMIBC and MIBC. It was seen that the number of NMIBCs for group A was 99 and the number of MIBC was 25. For group B, the number of NMIBC was 64 and the number of MIBC was 30. A statistically significant difference was observed in the

comparison between the groups. It was observed that tumoral stages were more advanced in group B ($p=0.048$).

DISCUSSION

After the outbreak of the COVID-19 pandemic in 2020, there have been major changes in the management of world health systems (7). Many healthcare organizations have been taking care of COVID-19 patients, and accordingly, dramatic decreases have been observed in the number of healthcare professionals dealing with non-COVID-19 diseases. Some health institutions shut down their operating theaters or reduced their capacity. Some operating rooms were converted into intensive care units. As the COVID-19 pandemic progressed, the number of non-COVID-19 patients examined by physicians decreased, so the diagnoses of diseases decreased, and the necessary treatments were interrupted (8). The duration of use and reporting of some tests, such as computed tomography and ultrasonography, which are required to diagnose non-COVID-19 patients, have been prolonged because of the excess of patients. In addition, patients' admissions to the hospital decreased. With some restrictions and closures imposed by the governments, individuals without an emergency disease had problems in applying to health institutions (7). In some diseases, delay in applying to health institutions can be tolerated, but in diseases such as cancer, which may progress rapidly, delay in seeing a doctor may cause serious damage to the progression of the disease and accordingly to human health.

In our study, based on March 2020, the date of the first COVID-19 case in Turkey, we scanned the period 18 months before and 18 months after this date. In these periods, we evaluated the factors that may affect the course of the disease, such as the stage, tumor size, and multiplicity of primary bladder cancer cases. The reason why we included primary bladder cancer in our study because the patients with a diagnosis are already in a follow-up protocol and that they will not have any problems in applying to the health institution, even if there is a pandemic. However, it can be assumed that even if primary bladder cancer has symptoms such as hematuria, it is possible to delay applications to health institutions because of the pandemic and stay-at-home suggestions. Therefore, it is not wrong to conclude that primary bladder tumors may progress more aggressively during the pandemic period.

Delays in cancer diagnosis due to the disruptions in the health system during the pandemic were shared with some publications in the literature. As an example, in a study conducted in the United Kingdom published by Maganty et al. (9), it has been revealed

that the death rate from breast, colorectal, lung, and esophageal cancers increases as a result of decreased screening during the closure times of the pandemic period. Li et al. (7) examined the diagnosis and treatment delays of urological diseases of the COVID-19 pandemic in their single-center but large patient population publication in China where they examined urological diseases. In the post-COVID-19 outbreak period, the rate of use of beds in the hospital due to urological disease decreased by 44.8%. Despite this, the rate of hospitalization due to urological malignancies was found to be statistically significantly increased ($p < 0.01$) (7). In a newly published multicenter study in Turkey, the effects of delaying cystoscopic surveillance on recurrence and progression in NMIBC patients during the COVID-19 pandemic were investigated. This multicenter study showed significant increases in recurrence and progression after delay in follow-up cystoscopies in the patients with NMIBC (3). In the study published by Wallace et al. (2) on delay in diagnosis of bladder cancer, it was shown that a shorter delay resulted in a lower tumor stage and a 5% better 5-year survival.

In addition to the effects of the COVID-19 pandemic itself on people, changes in the functioning of the health system and on human behavior indirectly have negative effects on human health due to delays in the diagnosis and treatment of non-COVID-19 diseases. Additionally, as a result of studies conducted in China, it has been shown that patients with cancer are more negatively affected by COVID-19, and this may lead to worse outcomes in these patients compared with the normal population (10). However, delaying an established treatment for cancer may also have negative consequences for the chance of a cure. May have a significant impact on the prognosis of the disease. Due to the general morbidity and life-threatening aggressive nature of bladder cancer, it is necessary to adapt to the COVID-19 period in order to evaluate patients who may have bladder cancer and to make a diagnosis without delay.

Study Limitations

Our findings must be considered in the context of several limitations. First of all, this is a single-center retrospective study with a small sample size. The local based intensity of the pandemic was not considered. Different results may be found in different regions. Secondly, carcinoma in situ was not considered because of lack of data. Third, we do not know whether the patients included in the study did not go to the doctor for examination because of the pandemic. If they have not seen a doctor for any reason other than the pandemic, statistical differences may occur. Fourth, as the distance of the patients

from the health centers where they live increases, it can be expected that their access to health services will be more delayed than the patients who live in city centers during the pandemic. In the study, the distance of the residential areas of the patients and the health center was not questioned. Fifth, although T1 and Ta have different progression risks, they were not compared by making two separate groupings.

CONCLUSION

In conclusion, it is inevitable that the pandemic, which causes radical changes in health systems globally and increases the workload in health facilities, will prevent non-COVID-19 patients from receiving quality and uninterrupted health services. Delays in the diagnosis of diseases such as bladder cancer, which can be quickly diagnosed and controlled with the right treatment, may cause many bladder cancer cases to be undetected, and consequently the progression of the disease. Continuing screening and using cancer diagnostic tests in health systems will enable us to prevent patients from being harmed by cancer during the pandemic.

Ethics

Ethics Committee Approval: This study was conducted at Sakarya Training and Research Hospital. The data of all patients who were registered in the urology department of our institution and operated due to a bladder tumor between September 2018 and September 2021 were collected from their medical documents.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: R.B.D., Design: Y.M.A., Data Collection or Processing: F.H., Analysis or Interpretation: A.G., Literature Search: R.B.D., H.S.K., K.D., F.H., Writing: Y.M.A.

Conflict of Interest: No conflict of interest was declared by the authors.

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