

## IMPACT OF COVID-19 PANDEMIC ON THE STRUCTURE OF PATIENTS UNDERGOING SURGICAL TREATMENT FOR URO-ONCOLOGICAL INDICATIONS

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The aim of this retrospective study was to examine the impact of the COVID-19 pandemic on the structure of patients who had undergone operative treatment for oncological indications at the Urology Clinic of the University Clinical Center Niš in the period from March 2018 to June 2022. The following operations were included: nephrectomy for kidney cancer, nephroureterectomy for upper urothelial cancer, prostatectomy for prostate cancer, cystectomy for bladder cancer, orchiectomy for testicular cancer and penectomy for penile cancer. Data were taken on the number of operations, patients' age and gender and postoperative histopathological findings. Depending on the time the surgery was performed, patients were divided into two groups: the preCOVID group - procedures carried out before the start of the pandemic (March 1, 2018 – March 1, 2020) and the COVID group - procedures carried out after the start of the pandemic (June 2020 – June 2022). A total of 569 investigated operations were performed, 320 before and 249 after the beginning of the pandemic. Nephrectomies were the most frequently performed procedures in both study groups. During the pandemic, a significant decrease in number of prostatectomies and nephrectomies was registered. The proportion of prostatectomies was significantly lower in the COVID group, while the proportion of cystectomies significantly increased. The frequency of stage T4 bladder cancer was significantly higher during the pandemic, while the frequency of stage T3a was significantly lower. When we consider the results of tumor stages after all operative procedures in our study, significantly more patients with T4 stage were registered during the pandemic, the majority with bladder cancer.

*Acta Medica Medianae 2024; 63(1): 47-55.*

**Key words:** COVID-19 pandemic, urologic surgical procedures, urologic cancers

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### Introduction

The rapid spread of the Coronavirus disease (COVID-19) caused by the new Beta Coronavirus SARS-CoV-2, has significantly threatened the functioning of the entire health system (1). The great and urgent need for hospital and human capacities in the treatment of COVID-19 patients has led to a rapid overload of health institutions all over the world. In this way, diagnostic and therapeutic procedures for patients who needed medical treatment due to other diseases and conditions were postponed in most cases,

especially at the beginning of the pandemic (2). Fear of viral transmission, the implementation of epidemiological measures, as well as the reduced availability of medical practitioners at all levels of health care were the most common reasons why non-COVID patients did not regularly attend medical examinations (3, 4). This was especially the case with the elderly population, which was more susceptible to serious illness from COVID-19 (5). Considering that a significant part of uro-oncology patients consists of this geriatric population, the pandemic has also affected their treatment (6).

In the Republic of Serbia, the first case of COVID-19 was officially registered on March 6, and the epidemic of this disease was declared on March 19, 2020 (7). Since then, the statistical curve of patients who suffered or died from COVID-19 has been changing, with several registered waves, and the last one recorded in March 2022 (8). Since the beginning of the epidemic, a large number of COVID patients have been hospitalized at the University Clinical Center

Niš. The first, sudden hospital patient admission was recorded in March and April 2020, when the capacities of the University Clinical Center Niš, including the Clinic of Urology, were designated for the treatment of COVID patients. During that period, only emergency procedures were carried out at our institution. After that, we started the strategy of conducting also elective, oncological procedures.

### Aim

This study aimed to examine the impact of the COVID-19 pandemic on the structure of patients who had undergone surgical treatment for oncological indications at the Clinic of Urology of the University Clinical Center Niš. In this sense, we compared the number of performed uro-oncological surgical procedures, as well as post-operative, histopathological findings between the period before and the period during the pandemic.

### Material and Methods

The retrospective study included data on oncological surgical procedures performed at the Clinic of Urology, University Clinical Center Niš between March 2018 and June 2022. The following procedures were included in the study: nephrectomy for renal cancer, nephroureterectomy for upper urothelial cancer, prostatectomy for prostate cancer, cystectomy for bladder cancer, orchiectomy for testicular cancer and penectomy for penile cancer. Data on the number of procedures, patients' age and gender, as well as postoperative, histopathological tumor stage, grade and type were taken into account. Depending on the time the surgery was performed, patients were divided into two groups: the pre-COVID group - procedures carried out in the period before the pandemic (March 1, 2018 – March 1, 2020) and the COVID group - procedures carried out during the period of the COVID-19 pandemic (June 1, 2020 – June 1, 2022). March and April 2020 were not included in the study, because only emergency procedures were performed during that period.

Data analysis was performed using the MedCalc program (version 22). The Chi-square test was used to test the statistical significance of absolute frequency differences between samples. The comparison of arithmetic means of two samples was performed by Student's t-test. A p-value < 0.05 was considered statistically significant.

### Results

A total of 569 uro-oncological surgical procedures were performed at the Clinic of Urology, University Clinical Center Niš during the

study period, 320 in the period before and 249 during the COVID-19 pandemic. No statistically significant difference was observed in terms of age and gender distribution between patients of both groups who underwent the same surgical procedures. The total number of operations, as well as their number by group, is shown in Figure 1. The most frequently performed surgical procedures in both groups were nephrectomies. In relation to the pre-pandemic period, during the pandemic the largest and statistically significant decrease was registered in the number of prostatectomies (by 47.7%,  $p = 0.0003$ ), followed by nephrectomies (by 37.3%,  $p = 0.0015$ ). A decrease was also registered in the number of nephroureterectomies (by 24.1%). Operations with an increase in number during the pandemic were cystectomy (by 38%) and orchiectomy (by 7.8%). The number of operations for penile cancer was identical before and during the pandemic (Figure 1). Figure 2 shows a comparative view of the structure of surgical procedures between the examined groups. The proportion of prostatectomies in relation to the total number of operations was significantly lower in the COVID group compared to the pre-COVID group ( $p = 0.0134$ ). On the other hand, the percentage of cystectomies increased significantly during the COVID-19 pandemic ( $p = 0.0004$ ). The proportion of other procedures by group did not differ significantly.

In our research, stage T1a renal cancer was more prevalent before the pandemic compared to the pandemic period, but this difference was not statistically significant. The frequency of stage T1b and T2 was similar in both studied groups. On the other hand, a higher percentage of stage > T2 was registered during the pandemic compared to the pre-pandemic period (35.1% vs. 27.9%), but without a significant difference. Also, no significant difference was observed between the examined groups in terms of the histopathology type, as well as kidney cancer grade (Table 1). When it comes to prostate cancer, the prevalence of tumor stage and Gleason score did not significantly differ between the examined groups. The incidence of locally advanced prostate cancer (T3–4) was similar between the pre-COVID and COVID groups (41.9% vs. 40%) (Table 2). The distribution of tumor stage in testicular cancer was similar in both studied groups. The ratio of seminoma to non-seminomatous testicular cancer was 1 : 1 before the pandemic, while a slight increase in the number of non-seminomatous tumors was recorded afterwards (Table 3). No significant difference was observed regarding the stage and grade of penile cancer (Table 4).

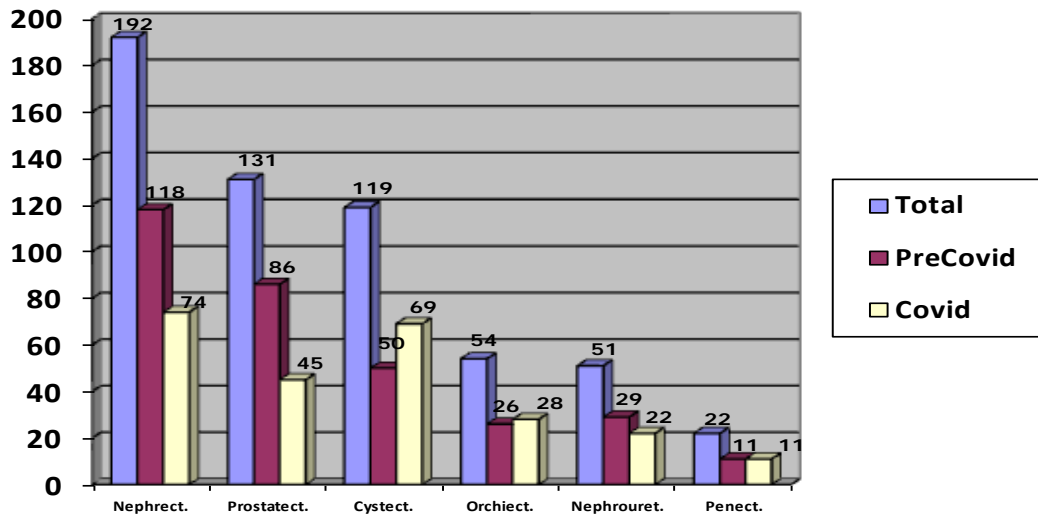


Figure 1. Number of operative procedures in total and by groups

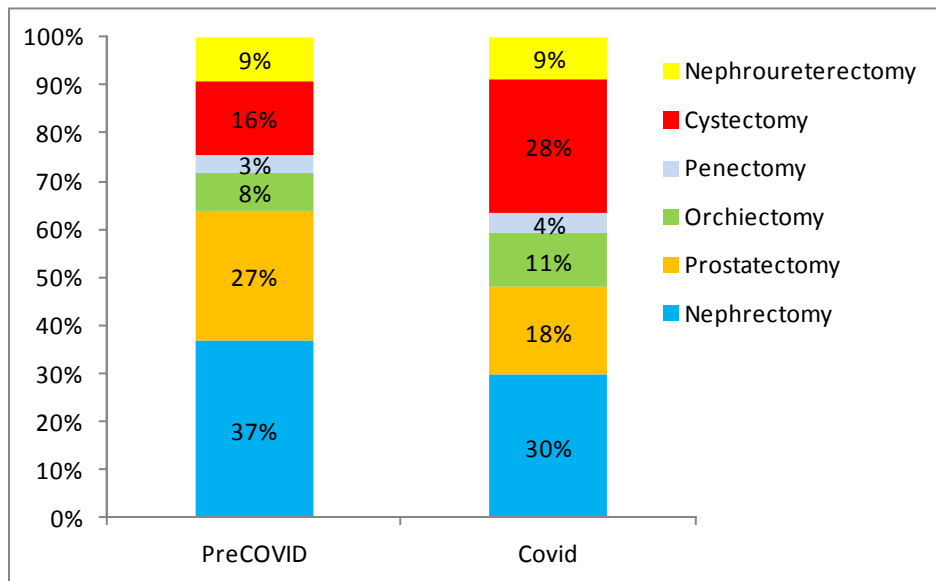


Figure 2. Comparative view of the percentage of surgical procedures between the examined groups

**Table 1.** Characteristics of patients who underwent nephrectomy

	PreCOVID group	COVID group	p-value
Number of patients	118	74	0.0015
Age (years)	61.4 ± 12.5	59.7 ± 13	0.3676
Gender			
Male	67 (56.8%)	41 (55.4%)	0.8522
Female	51 (43.2%)	33 (44.6%)	
Tumor stage			
T1a	37 (31.4%)	18 (24.3%)	0.2955
T1b	29 (24.6%)	19 (25.7%)	0.8644
T2a	19 (16.1%)	5 (6.8%)	0.0574
T2b	3 (2.5%)	6 (8.1%)	0.0765
T3a	29 (24.6%)	25 (33.8%)	0.1684
T3b	/	/	
T3c	/	/	
T4	1 (0.8%)	1 (1.3%)	0.7385
Tumor grade			
G1	20 (16.9%)	12 (16.2%)	0.8948
G2	61 (51.8%)	33 (44.6%)	0.3394
G3	24 (20.3%)	14 (18.9%)	0.8105
G4	13 (11%)	15 (20.3%)	0.0778
Tumor type			
ccRCC	103 (87.3%)	61 (82.4%)	0.3548
chRCC	1 (0.8%)	2 (2.7%)	0.3143
pRCC	13 (11.1%)	10 (13.5%)	0.6051
other	1 (0.8%)	1 (1.4%)	0.7385

**Table 2.** Characteristics of patients who underwent prostatectomy

	PreCOVID group	COVID group	p-value
Number of patients	86	45	0.0003
Age (years)	61.3 ± 4.7	60.9 ± 5.3	0.6588
Tumor stage			
T2a	10 (11.6%)	4 (8.9%)	0.6312
T2b	10 (11.6%)	5 (11.1%)	0.9300
T2c	30 (34.9%)	18 (40%)	0.5653
T3a	16 (18.6%)	7 (15.6%)	0.6643
T3b	20 (23.3%)	10 (22.2%)	0.8940
T4	/	1 (2.2%)	
Gleason score (GS)			
GS 6	27 (31.4%)	20 (44.4%)	0.1407
GS 7	48 (55.8%)	19 (42.2%)	0.1410
GS 8	10 (11.6%)	4 (8.9%)	0.6312
GS 9	1 (1.2%)	2 (4.5%)	0.2349

**Table 3.** Characteristics of patients who underwent orchiectomy

	PreCOVID group	COVID group	p-value
Number of patients	26	28	0.7877
Age (years)	34.5 ± 14.7	33.9 ± 13.1	0.8746
Tumor stage			
T1	10 (38.5%)	11 (39.3%)	0.9510
T2	14 (53.8%)	16 (57.1%)	0.8093
T3	2 (7.7%)	1 (3.6%)	0.5128
T4	/	/	
Tumor type			
Seminoma	13 (50%)	13 (46.4%)	0.7949
Non-seminoma	13 (50%)	15 (53.6%)	

**Table 4.** Characteristics of patients who underwent penectomy

	PreCOVID group	COVID group	p-value
Number of patients	11	11	0.8890
Age (years)	66.8 ± 9.6	67.4 ± 10.3	
Tumor stage			0.4028
T1	6 (54.6%)	4 (36.4%)	0.6770
T2	5 (45.4%)	6 (54.6%)	
T3	/	1 (9.1%)	
T4	/	/	
Tumor grade			0.3496
G1	4 (45.5%)	2 (18.2%)	0.1797
G2	6 (54.5%)	9 (81.8%)	
G3	1 (9.1%)	/	
G4	/	/	0.8890

The prevalence of stage  $\leq$  T2 bladder urothelial cancers between the pre-COVID and COVID groups was not significantly different (36% vs. 28.9%,  $p = 0.4198$ ). However, the frequency of T4 stage was significantly higher in the COVID group ( $p = 0.0342$ ), whereby 1/3 of the patients in this group had this stage of the disease. Also, when we consider the proportion of patients with stage  $\geq$  T3b, there is an even greater statistical significance between the COVID and pre-COVID group (59.5% vs. 34%,  $p = 0.0064$ ). In our study, two cases of stage T4b after cystectomy were registered, both in the COVID group. On the other hand, in the period before the pandemic, there were significantly more patients with stage T3a ( $p = 0.0124$ ). The incidence of high-grade bladder cancer was higher during the pandemic, but with

no statistical significance (Table 5). There was no significant difference in tumor stage or grade for upper urothelial cancer. However, the only case of the T4 stage was recorded during the pandemic (Table 6).

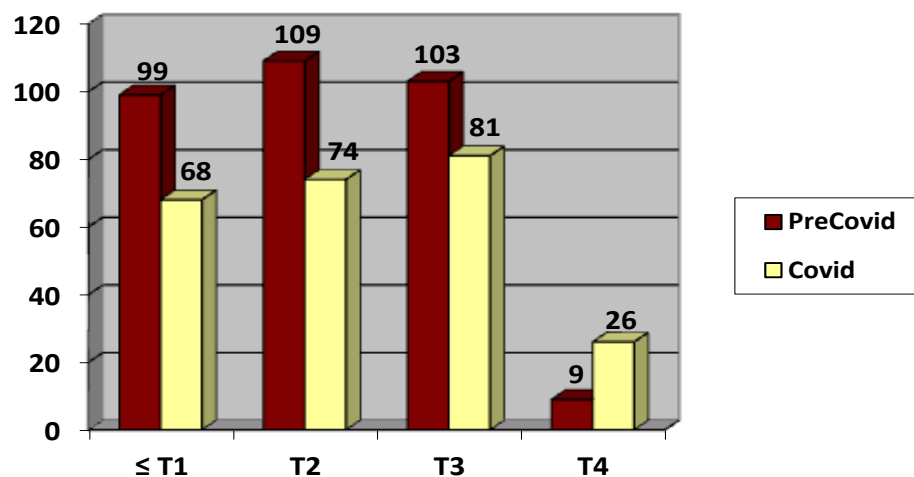
When we consider the results of tumor stages after all operative procedures in our study, the COVID group had significantly more patients with T4 stage compared to the pre-COVID group ( $p = 0.0002$ ). The distribution of other tumor stages was similar between the examined groups (Figure 3). The largest number of stage T4 tumors was verified after cystectomy (23 cases), while one case each was recorded after nephrectomy, nephroureterectomy and prostatectomy.

**Table 5.** Characteristics of patients who underwent cystectomy

	PreCOVID group	COVID group	p-value
Number of patients	50	69	0.0824
Age (years)	66.7 ± 10.4	65.4 ± 9.6	0.4828
Gender			
Male	39 (78%)	57 (82.6%)	0.5315
Female	11 (22%)	12 (17.4%)	
Tumor stage			
T1	5 (10%)	9 (13%)	0.6125
T2a	4 (8%)	3 (4.3%)	0.4053
T2b	9 (18%)	8 (11.6%)	0.3263
T3a	15 (30%)	8 (11.6%)	0.0124
T3b	9 (18%)	18 (26.1%)	0.3005
T4	8 (16%)	23 (33.4%)	0.0342
Tumor grade			
Low grade	11 (22%)	8 (11.6%)	0.1277
High grade	39 (78%)	61 (88.4%)	

**Table 6.** Characteristics of patients who underwent nephroureterectomy

	PreCOVID group	COVID group	p-value
Number of patients	29	22	0.3317
Age (years)	63.4 ± 6.2	62.8 ± 5.8	0.7265
Gender			
Male	18 (62.1%)	14 (63.6%)	0.9096
Female	11 (37.9%)	8 (36.4%)	
Tumor stage			
Ta	9 (31%)	6 (27.3%)	0.7725
T1	3 (10.3%)	1 (4.55%)	0.4500
T2	5 (17.3%)	3 (13.6%)	0.7285
T3	12 (41.4%)	11 (50%)	0.5440
T4	/	1 (4.55%)	
Tumor grade			
Low grade	15 (51.7%)	8 (36.4%)	0.2797
High grade	14 (48.3%)	14 (63.6%)	

**Figure 3.** Distribution of tumor stages after all operative procedures

## Discussion

There was a 22.2% decrease in the number of uro-oncological surgical procedures during the pandemic, compared to the pre-pandemic period. A number of studies by other authors have also registered a decrease in the number of uro-oncological procedures during the pandemic. A large retrospective study in the United Kingdom, which included more than 110 thousand uro-oncological procedures, registered a decrease of 7.6% (9). In our study, nephrectomies due to renal cancer were the most frequently performed procedures in both investigated time periods. However, almost 40% more nephrectomies were performed before the pandemic. Renal cancer is often asymptomatic, especially in the lower stages

of the disease, and is often discovered as an incidental finding during radiological, systematic examinations (10). The reduced availability of radiological examinations, as well as the reduced number of systematic examinations during the pandemic, could be one of the reasons why a smaller number of kidney tumors, especially those of smaller diameter, were diagnosed in this period. In our study, the percentage of stage T1a tumors was higher in the pre-pandemic compared to the pandemic period, but this difference is not statistically significant. At the beginning of the pandemic, the European Association of Urologists (EAU) recommended that nephrectomy for renal cancer stage < T2 can be safely delayed for 3 months. On the other hand, treatment of advanced renal cancer, especially those with

associated venous thrombosis, should not be delayed (11). In our study, a higher percentage of stage > T2 was registered during the pandemic compared to the pre-pandemic period, but the difference was not significant. Similar results were also shown in a study by Turkish authors. They recorded a decrease in the number of nephrectomies by almost 50% during the pandemic, with a similar ratio of tumor stage and grade as in our study (12). On the other hand, some studies did not record a significant decrease in the number of nephrectomies during the pandemic period (9, 13).

Patients with prostate cancer are also often asymptomatic, and timely diagnosis largely depends on regular screening. Studies have shown that fewer men reported for prostate cancer screening during the pandemic (14, 15). At the beginning of the COVID-19 pandemic, EAU guidelines recommended that radical prostatectomy in patients with low-, intermediate-, and even in some cases high-risk cancers can be postponed, without a clearly defined time distance (11). The fact is that an alternative modality of treatment (hormonal and radiation therapy), which requires less direct contact with medical personnel and does not require hospitalization of the patient, was a safer treatment option when it comes to the risk of viral transmission. This was certainly one of the important reasons why patients chose this treatment modality instead of radical prostatectomy (16). In our study, the largest and statistically significant decrease in the number of procedures during the pandemic was recorded in radical prostatectomies. The aforementioned study in the United Kingdom has also recorded the greatest decrease in the number of radical prostatectomies among all uro-oncological procedures (9). Other studies also registered a decrease in the number of prostatectomies of up to 50%, with no difference in the stage and grade of tumors before and during the pandemic (12, 17).

One of the main results of our study concerns the data on performed cystectomies for bladder cancer. The proportion of cystectomies, unlike other operations, increased significantly during the pandemic period. Significantly more stage  $\geq$  T3b bladder cancers were registered in the COVID group, which were also registered in more than half of the cystectomy cases in this group. In about 1/3 of the cases in COVID group, cystectomy was performed in patients with bladder cancer stage T4. Total, painless hematuria is generally the main clinical sign in patients with bladder cancer and its presentation is often intermittent. The author's experience shows that patients who were later diagnosed with bladder cancer, often ignored the initial appearance of painless hematuria and came for an examination only after the recurrent or massive hematuria, which delayed diagnosis and treatment even for several months. The pandemic also affected

patients with non-muscle-invasive bladder cancer, who delayed cystoscopic examinations during the follow-up, which influenced their further treatment (18, 19). At the beginning of the COVID pandemic, most of the relevant uro-oncology organizations considered that the necessary diagnostics in patients with total, painless hematuria should not be postponed, but there were also those who recommended that it could be postponed for 1–2 months (11). It is known that delaying a cystectomy for  $\geq$  12 weeks increases the chance of tumor stage progression and decreases survival in patients with muscle-invasive carcinoma (20). The results of other studies on the pandemic impact on the treatment of bladder cancer patients are various. In the study by Romanian authors, significantly more cystectomies, as well as stage T3 and T4 bladder cancers, were registered during the pandemic compared to the pre-pandemic period (21). Other studies also registered an increase in the number of cystectomies, but without a significant difference in tumor stage (12, 17). In the study by Brument M. et al., a decrease in the number of cystectomies by 2.4% was recorded (9). When it comes to upper urothelial cancer, our study results are different compared to cancer of the lower urothelium. The percentage of nephroureterectomies was identical in both investigated time periods in our study. Although the only T4 stage was registered in the COVID group, there was no statistically significant difference comparing the other stages between the pre-COVID and COVID groups. The percentage of high-grade tumors was higher during the pandemic but without statistical significance. A study by Japanese authors also showed no significant difference in tumor stage after nephroureterectomy before and during the pandemic (22). In our study, there was no difference in terms of tumor stage and grade between the examined groups when it comes to testicular and penile cancers. The results of other studies are similar to our results (12, 23).

## Conclusion

During the pandemic, a decrease in the total number of uro-oncological surgical procedures was recorded, of which a statistically significant decrease was registered in the number of prostatectomies and nephrectomies. Unlike other procedures, the percentage of cystectomies increased significantly during the pandemic period. In this period, significantly more bladder cancers of stage  $\geq$  T3b and significantly fewer cancers of stage T3a were registered. When we consider the results of tumor stages after all procedures in our study, significantly more patients with T4 stage were registered during the pandemic, most of them with bladder cancer.

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Originalni rad

UDC: 616.98:578.834]:616.6-006-089

doi: 10.5633/amm.2024.0105

## UTICAJ COVID-19 PANDEMIJE NA STRUKTURU BOLESNIKA PODVRGNUTIH OPERATIVNOM LEČENJU ZBOG UROONKOLOŠKIH INDIKACIJA

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Cilj ove retrospektivne studije bio je da ispita uticaj pandemije COVID-19 na strukturu bolesnika koji su zbog onkoloških indikacija bili podvrgnuti operativnom lečenju na Klinici za urologiju Univerzitetskog kliničkog centra u Nišu u periodu od marta 2018. godine do juna 2022. godine. Istraživanjem su bili obuhvaćeni sledeći operativni zahvati: nefrektomija zbog karcinoma bubrega, nefroureterektomija zbog karcinoma gornjeg urotela, prostatektomija zbog karcinoma prostate, cistektomija zbog karcinoma mokraćne bešike, orhiektomija zbog tumora testisa i amputacija penisa zbog karcinoma penisa. Uzeti su podaci o broju operacija, godinama starosti i polu bolesnika, kao i postoperativni histopatološki nalazi. Operativne procedure podeljene su u dve grupe: pre COVID grupa uključila je procedure sprovedene pre početka pandemije (1. mart 2018. godine – 1. mart 2020. godine), a COVID grupa one sprovedene nakon početka pandemije COVID-19 (jun 2020. godine – jun 2022. godine). Urađeno je ukupno 569 uroonkoloških operacija – 320 pre početka pandemije i 249 nakon početka pandemije. U obema ispitivanim grupama najčešće sprovedene procedure bile su nefrektomije. Statistički značajan pad broja prostatektomija i nefrektomija registrovan je u toku pandemije. Udeo prostatektomija bio je statistički značajno manji u COVID grupi, dok je udeo cistektomija u njoj statistički značajno porastao. Učestalost T4 stadijuma karcinoma mokraćne bešike bila je statistički značajno veća tokom pandemije, a učestalost T3a stadijuma značajno manja. Rezultati u vezi sa tumorskim stadijumima, dobijeni nakon svih operativnih procedura ispitanih u ovoj studiji, pokazali su da je značajno više bolesnika sa T4 stadijumom registrovano u toku pandemije: pritom, u većini slučajeva radilo se o karcinomu mokraćne bešike.

*Acta Medica Medianae 2024; 63(1):47-55.*

**Ključne reči:** COVID-19 pandemija, urološke operacije, karcinomi u urologiji

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