

Original article

DOI: 10.5633/amm.2024.0105

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

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

The aim of this retrospective study is to examine the impact of the Covid-19 pandemic on the structure of patients who, due to oncological indications, underwent operative treatment at the Urology Clinic of the University Clinical Center Nis 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, patient age and gender and postoperative histopathological findings. Operative procedures were divided in two groups: preCovid group - procedures carried out before the start of the pandemic (March 1, 2018 - March 1, 2020) and 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 frequency of stage T3a was significantly lower. When we consider 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.

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

Originalni rad

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UTICAJ COVID 19 PANDEMIJE NA STRUKTURU PACIJENATA PODVRGNUTIH OPERATIVNOM LEČENJU
ZBOG URO-ONKOLOŠKIH INDIKACIJA

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UTICAJ COVID 19 PANDEMIJE NA STRUKTURU PACIJENATA PODVRGNUTIH OPERATIVNOM LEČENJU
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Cilj ove retrospektivne studije je da ispita uticaj pandemije Covida 19 na strukturu pacijenata koji su zbog onkoloških indikacija bili podvrgnuti operativnom lečenju na Klinici za urologiju UKC Niš u vremenskom periodu od marta 2018. do juna 2022. godine. U istraživanje su uključeni 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, starosnoj dobi i polu pacijenata, kao i postoperativnom, histopatološkom nalazu. Operativne procedure su podeljene u dve grupe: preCovid grupa – procedure sprovedene u vremenskom periodu pre početka pandemije (01. mart 2018. – 01. mart 2020. godine) i Covid grupa – procedure sprovedene u periodu nakon početka pandemije Covida 19 (jun 2020. – jun 2022. godine). Urađeno je ukupno 569 ispitivanih, uro-onkoloških operacija, i to 320 u periodu pre i 249 nakon početka pandemije. Nefrektomije su bile najčešće sprovedene procedure u obe ispitivane grupe. Tokom pandemije registrovan je statistički značajan pad broja prostatektomija i nefrektomija. Udeo prostatektomija bio je statistički značajno manji u Covid grupi, dok je udeo cistektomija statistički značajno porastao. Učestalost T4 stadijuma karcinoma mokraćne bešike bila je statistički značajno veća tokom pandemije, dok je učestalost T3a stadijuma bila značajno manja. Kada uzmemo u obzir rezultate tumorskih stadijuma nakon svih operativnih procedura u našoj studiji, značajno više pacijenata sa T4 stadijumom registrovano je tokom pandemije, većina sa karcinomom mokraćne bešike.

Ključne reči: Covid 19 pandemija, urološke operacije, karcinomi u urologiji

INTRODUCTION

The rapid spread of Covid 19 disease, caused by the new betacoronavirus 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 was postponed in most cases, especially at beginning of 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 is consisted 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 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 in the University Clinical Center Nis. The first, sudden hospital patient admission was recorded in March and April 2020, when the capacities of University Clinical Center Nis, including Clinic of Urology, were designated to 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

The aim of this study was to examine the impact of the Covid 19 pandemic on the structure of patients who underwent surgical treatment due to oncological indications at Clinic of Urology at University Clinical Center Nis. In this sense, we compared the number of performed uro-oncological, surgical procedures, as well as post-operative, histopathological findings between the time 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 Nis between March 2018. until 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, patient age and gender, as well as postoperative, histopathological tumor stage, grade and type were taken into account. Procedures were divided in two groups: preCovid group - procedures carried out in the period before the pandemic (1st March 2018. – 1st March 2020) and Covid group - procedures carried out during the period of the Covid 19 pandemic (1st June 2020. – 1st June 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 Clinic of Urology, University Clinical Center Nis 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 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 pandemic ($p=0.0004$). The proportion of other procedures by group did not differ significantly.

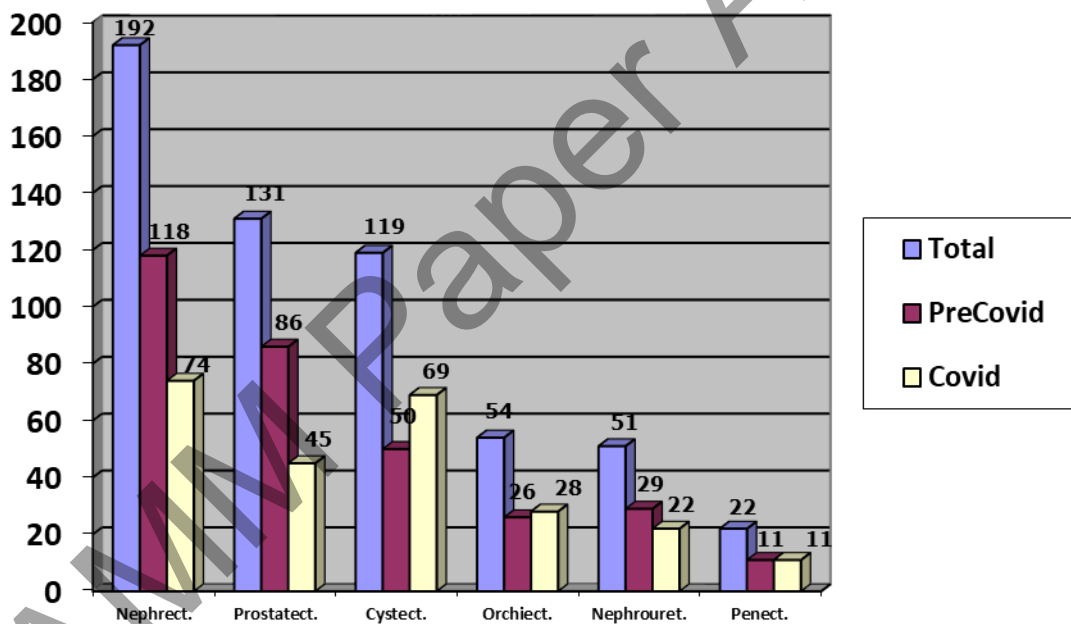


Figure 1. Number of operative procedures in total and by groups

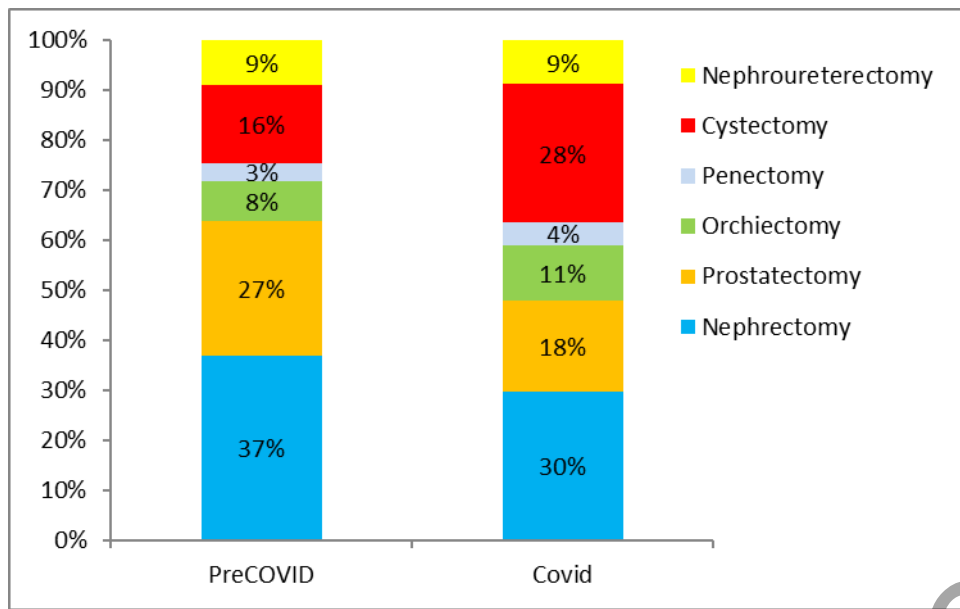


Figure 2. Comparative view of the percentage of surgical procedures between the examined groups

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 preCovid 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).

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			

Seminomal	13 (50%)	13 (46.4%)	0.7949
Non-seminomatous	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 preCovid 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 without statistical significance (Table 5). When it comes to upper urothelial cancer, there was no significant difference in stages, as well as tumor grade. However, the only case of T4 stage was recorded during the pandemic (Table 6).

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
T4a	8 (16%)	21 (30.5%)	0.0714
T4b	/	2 (2.9%)	
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%)	

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.

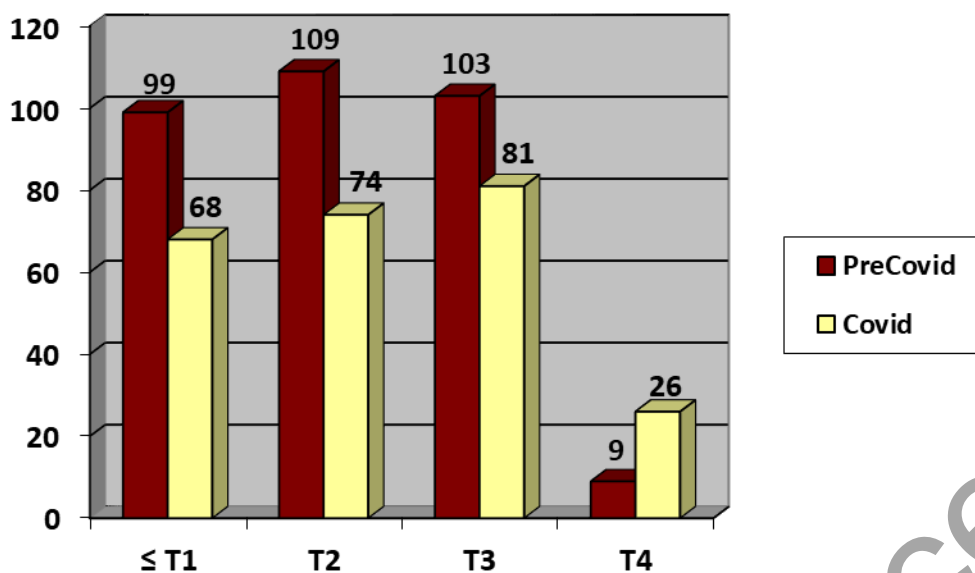


Figure 3. Distribution of tumor stages after all operative procedures

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, percentage of stage T1a tumors was higher in pre-pandemic compared to the pandemic period, but this difference is not statistically significant. At the beginning of the

pandemic, an 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, there were also studies that did not record a significant decrease in the number of nephrectomies in 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 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 have 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 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 at 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 gave a recommendation that it could be postponed for 1-2 months (11). It is known that delaying a cystectomy for ≥ 12 weeks increases the chance of tumor stage progression and decrease survival in patients with muscle-invasive carcinoma (20). The results of other studies on 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 the 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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AMM Paper Accepted