



TRENDS IN PROSTATE CANCER DIAGNOSIS DURING THE COVID-19 PANDEMIC: SINGLE-INSTITUTION EXPERIENCE

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SUMMARY – The aim of this study was to compare the number of biopsy and surgical procedures on prostate, as well as the number of newly diagnosed, histologically confirmed cases of prostate cancer during the COVID-19 pandemic at Zagreb University Hospital Center (UHC). We retrospectively collected and processed a total of 1344 histopathologic findings of the prostate at the Zagreb UHC. Our results show that during the COVID-19 pandemic, there was a statistically significant decrease in the absolute number of biopsy and surgical procedures on prostate at Zagreb UHC, and so was the number of newly diagnosed, histologically confirmed cases of prostate cancer. During the observed time of the pandemic (March 19, 2020 to December 31, 2020), there was a 37.5% decrease in the absolute number of newly diagnosed prostate cancer cases compared to the same period of the previous year (March 19, 2019 to December 31, 2019). To our knowledge, this is the first study of this kind that is based on the number of prostate cancer diagnoses in Croatia. By observing the early period of the pandemic, our results provide important guidelines for monitoring and understanding the long-term consequences of the pandemic on the prostate cancer morbidity and mortality.

Key words: *COVID-19; Histopathologic findings; Pandemic; Prostate cancer*

Introduction

Coronavirus disease 2019 (COVID-19) was declared a pandemic by the World Health Organization (WHO) at the time when over 200,000 cases were detected in more than 160 countries¹. During the pandemic, fundamental changes were made in Croatia considering health care and hospital system. Hospital work had adapted to the epidemiologic circumstances, with focus on protection against COVID-19.

The Zagreb University Hospital Center (UHC) is the largest health center in the Republic of Croatia and it is the only hospital with the status of national hospital, which testifies to its size and importance².

Almost all prostate cancers are histologically adenocarcinomas. The histologic grade of prostate cancer is determined by the Gleason score that represents the degree of differentiation of cancer. In 2014, the International Society of Urological Pathology (ISUP) proposed a new classification of prostate cancer, which is based on a modified Gleason system. It divides carcinomas into 5 grading groups³. The goal of this ISUP 2014/WHO 2016 new classification was to make a more precise and simple division of prostate

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cancer and reduce the number of over-treated indolent cancers⁴.

Prostate cancer is the second most common malignant disease in men worldwide, with 1,276,106 new cases *per year*, causing 3.8% of all malignant deaths in 2018⁵. Data in Croatia do not differ much from data in the world. According to data from the 2019 Croatian Health Statistics Yearbook and the 2018 Cancer Incidence Bulletin in Croatia, during these periods, prostate cancer was the most common newly diagnosed tumor in males^{6,7}, with a total of 13,952 new cases of all malignant changes⁷.

Materials and Methods

This retrospective study included patients whose histopathologic prostate materials were obtained by biopsy or surgical resection and sent for analysis to the Department of Pathology and Cytology, Zagreb UHC between January 1, 2019 and December 31, 2020. We excluded patients whose histopathologic samples were sent from other hospitals and patients with histologically confirmed non-malignant changes of the prostate.

March 19, 2020 was taken as the beginning of the pandemic since it was when the official decisions of the Crisis Headquarters were made to prevent the spread of coronavirus infection in the Republic of Croatia. The given measures affected functioning of the healthcare services.

Data were compared in two different ways. We firstly observed and compared two asymmetric

periods, i.e., the period before the Crisis Headquarters decisions (January 1, 2019 to March 18, 2020, below referred to as 'pre-COVID period'); and the period following the Crisis Headquarters decisions (March 19, 2020 to December 31, 2020, below referred to as 'pandemic period'). This comparison was used to cover more patients and thus obtain more credible statistical results.

In the second scenario, we observed and compared two symmetric periods, i.e., the period following the Crisis Headquarters decisions (March 19, 2020) until the end of the year (below referred to as 'later period'); and the same period in 2019 (below referred to as 'earlier period'). This comparison allowed us to compare absolute numbers of newly diagnosed prostate cancer findings between the later and earlier period.

Inference statistics were performed using Statistica software (data analysis software system, version 13; TIBCO Software Inc., 2018; <http://tibco.com>). The level of statistical significance was set at 0.05. The normality of distribution for the variables measured by the ratio scale was examined by the Kolmogorov-Smirnov test. The χ^2 -test was used to test differences between the observed groups for nominal variables and Student's t-test for proportional variables that followed normal distribution.

Results

In the observed period from January 1, 2019 to December 31, 2020, a total of 1344 prostate samples were analyzed. Most findings (n=767; 57.1%) were

Table 1. Number of biopsies and prostate surgeries performed by weeks of 2019 and 2020

2019						2020					
1-10	11-20	21-30	31-40	41-50	51-53	1-10	11-20	21-30	31-40	41-50	51-53
1	20	11	13	15	22	4	15	12	12	14	10
17	12	19	2	16	10	8	6	13	8	6	4
7	19	26	7	20	10	10	1	22	9	11	7
10	23	16	6	12		19	8	7	8	8	
14	14	13	10	11		17	7	15	13	7	
17	17	14	14	13		16	7	7	7	7	
19	9	15	10	15		23	15	18	8	5	
21	16	11	15	13		19	12	11	7	6	
15	22	15	19	16		21	11	10	11	14	
12	13	17	23	20		26	6	15	9	5	

Results are shown in different colors, from green, which represents the lowest number of biopsies, to red, which represents the highest number of prostate biopsies performed.

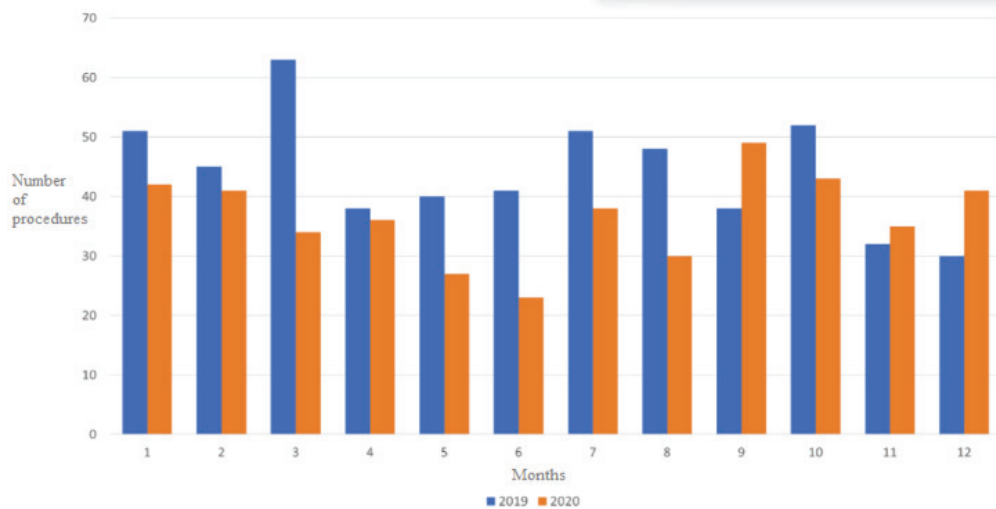


Fig. 1. Number of biopsies and surgical procedures performed on prostate by months in 2019 and 2020.

obtained in 2019, while the remaining 577 (42.9%) examinations were performed in 2020. The number of performed biopsies and prostate surgeries performed by weeks in 2019 and 2020 is shown in Table 1. There was a noticeable trend of decline in the number of histopathologic findings after the first 11 weeks of 2020, which corresponds to the date of pandemic proclamation in the Republic of Croatia. The downward trend in the number of examinations is even

more noticeable when visually displayed at the level of month in the year, which is shown in Figure 1. The difference was statistically significant again ($p < 0.001$; χ^2 -test), but given the smaller number of considered categories (12 months instead of 53 weeks as analyzed earlier), this result is more credible than the previous one. The decline in the number of histopathologic findings by months in 2020 is visible in almost all months with the exception of August when an increase

Table 2. Results of prostate histologic examination

	Histopathologic finding		n
	Malignant	Benign	
Pandemic period	869 (91.4%)	82 (8.6%)	951
Pre-COVID period	342 (87.0%)	51 (3.0%)	393
Total	1211	133	1344

Table 3. Distribution of Gleason score in two asymmetric periods: pandemic and pre-COVID

	Gleason score					n
	6	7	8	9	10	
Pandemic period	280 (32.6%)	468 (54.4%)	60 (7.0%)	43 (5.0%)	9 (1.1%)	860
Pre-COVID period	91 (26.7%)	196 (57.5%)	26 (7.6%)	24 (7.0%)	4 (1.2%)	341
Total	371	664	86	67	13	1201

in the number of prostate examinations was observed in 2020 compared to 2019.

According to the results, there were statistically significantly ($p=0.0150$; χ^2 -test) less benign and malignant findings during the pandemic period compared to the pre-COVID period (Table 2).

However, it is more interesting to observe differences before and after March 19, 2020 (pre-COVID and pandemic periods). Median ages for the two mentioned periods were almost identical, i.e., 66.5 years in the pre-COVID period and 66.4 in the pandemic period ($p=0.922$; t -test). Gleason value was determined for 1201 (99.2%) of 1211 patients with prostate cancer. There was no statistically significant difference when observing Gleason values in the two asymmetric periods ($p=0.274$; χ^2 -test) (Table 3).

Discussion

The COVID-19 pandemic produced an unprecedented disruption in the ways of delivering and receiving health care services. Non-emergency care and procedures were on a lower list of priorities while reorganizing hospitals as COVID-19 centers⁸. The impact of COVID-19 was multifactorial, including change in people's behavior, limitation of public transport and healthcare availability, and also arising from people's fear of hospitals and healthcare centers.

The results of this study showed a significant decrease in the absolute number of biopsy and surgical procedures of the prostate in the Zagreb UHC. Also, a decrease in the absolute number of newly diagnosed, histologically confirmed cases of prostate cancer at the same institution was observed.

There was a decrease in the absolute number of prostate examinations in the later period by 35.4%. When only carcinomas are observed, the absolute number of malignant prostate findings decreased by 37.5% in the later period.

A similar finding was recorded in a retrospective study conducted at the Verona University Hospital in Italy, which showed how COVID-19 had deeply affected all aspects of prostate cancer care, including early diagnosis, treatment and staging⁹.

In this study, we did not find statistically significant deviations of Gleason score in the two periods observed. We believe that with continuation of the pandemic and the same trend of decreasing numbers of newly diagnosed malignant diseases, there is a high

possibility of newly diagnosed patients with prostate cancer in higher rather than lower stages of the disease.

During the observed period, two significant events took place the impact of which on change in the number of diagnostic procedures in 2020 should be considered. The first was the Zagreb earthquake on March 22, 2020¹⁰, and the second was reorganization of the Dubrava University Hospital into a COVID-19 treating center¹¹. There is the possibility that reorganization of Dubrava University Hospital led to some influxes of patients from there to Zagreb UHC. This trend could have altered some numbers in the later stages of our study and falsely increased the number of procedures in 2020.

To the best of our knowledge, our study is the first of this kind based on the number of prostate cancer changes and characteristics in the Republic of Croatia. Our research could potentially be a solid basis for future monitoring of prostate cancer and long-term effects of the pandemic on morbidity and mortality.

Zagreb UHC is a tertiary care institution and the only hospital in the country with the status of a national hospital. Therefore, it is impossible to define the initial population from which the histopathologic findings come. Therefore, it is not possible to calculate changes in the incidence in the entire population of our country.

Conclusion

Our results show that during the COVID-19 pandemic, there was a statistically significant decrease in the number of biopsy and surgical procedures on the prostate at Zagreb UHC, as well in the number of newly diagnosed, histologically confirmed cases of prostate cancer. A 37.5% drop in the absolute number of prostate cancer was detected in the observed period during the pandemic relative to the same period in 2019.

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Sažetak

COVID-19 I DIJAGNOSTIKA TUMORA PROSTATE U KBC-u ZAGREB

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Cilj ovoga istraživanja bio je usporediti broj biopsijskih i kirurških zahvata na prostati, kao i broj novodijagnosticiranih, patohistološki potvrđenih slučajeva karcinoma prostate tijekom pandemije COVID-19 u Kliničkom bolničkom centru Zagreb. Retrogradno smo prikupili i obradili ukupno 1344 patohistoloških nalaza prostate na Kliničkom zavodu za patologiju i citologiju KBC-a Zagreb. Naši rezultati pokazuju da je tijekom pandemije COVID-19 došlo do statistički značajnog pada apsolutnog broja biopsijskih i kirurških zahvata na prostati, kao i broja novodijagnosticiranih, patohistološki potvrđenih slučajeva karcinoma prostate. Uočen je pad apsolutnog broja novodijagnosticiranih karcinoma prostate za 37,5% u promatranom vremenu pandemije (od 19. ožujka do 31. prosinca 2020. godine) u odnosu na isto razdoblje u prethodnoj godini (od 19. ožujka do 31. prosinca 2019. godine). Prema našim spoznajama ovo je prvo istraživanje ovakvog tipa temeljeno na broju pretraga karcinoma prostate na području Republike Hrvatske. Promatrajući rano razdoblje pandemije naši rezultati donose važne smjernice u budućem praćenju i dugoročnim posljedicama pandemije na pobol i smrtnost karcinoma prostate.

Ključne riječi: *COVID-19; Patohistološki nalaz; Pandemija; Karcinom prostate*