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Source / Izvornik: **Acta clinica Croatica, 2024, 63., 40 - 44**

Journal article, Published version
Rad u časopisu, Objavljena verzija rada (izdavačev PDF)

https://doi.org/10.20471/acc.2024.63.s2.6

Permanent link / Trajna poveznica: https://urn.nsk.hr/urn:nbn:hr:184:531797

Acta Clin Croat (Suppl. 2) 2024; 63:40-44
doi: 10.20471/acc.2024.63.s2.6

Original Scientific Paper

IMPACT OF THE COVID PANDEMIC ON PROSTATE CANCER DIAGNOSIS AND TREATMENT: RESULTS FROM A CROATIAN TERTIARY REFERRAL CENTER

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SUMMARY – The COVID-19 pandemic had a negative impact on the treatment of diseases other than COVID. The aim of our study was to demonstrate the impact it had on the diagnosis and treatment of patients with prostate cancer. By reviewing the work performed at the Clinic of Urology of the Clinical Hospital Centre Rijeka, we compared the following data for the period before the pandemic (2018) and the period during the pandemic (2021): number of prostate biopsies performed, number of newly-diagnosed cancers, PSA levels at biopsy, waiting time from the diagnosis to start of the treatment, stage of disease at biopsy and stage after prostatectomy, and finally the treatment options used. The results confirm the hypothesis that the pandemic had a negative impact on both diagnosis and treatment. The number of newly-diagnosed patients decreased by 37.24%, which correlates with a lower number of all prostate biopsies. We also noted a longer time to the start of the treatment for patients and an increase in poorer pathohistological outcomes after radical prostatectomy. Due to the higher disease stages, radiotherapy and chemotherapy were used more frequently.

Key words: *COVID-19; prostate cancer; treatment*

Introduction

The recent outbreak of a novel coronavirus infection that began in Wuhan, China, in mid-December 2019 and quickly spread around the world soon became the largest pandemic of the 21st century, known as COVID -19[1]. As such, it had a major impact on health systems around the globe, causing delays in non-emergency medical care, especially in the early months of 2020, mainly to prevent infections and maintain clinical capacity for patients with COVID-19. The World Health Organization (WHO) and its European office showed that between February and August 2020, 92% of countries in the European Region reported some form of disruption in health services[2]. As a result, there have been significant delays in cancer diagnosis and suboptimal treatment reported worldwide[3].

In Croatia, the first COVID -19 patient was diagnosed in late February 2020. From March 19, 2020, lockdown and social distancing measures were implemented by the Croatian government. As the number of infected patients increased, elective, non-urgent procedures and treatments were often postponed[4]. Fear of infection also led patients to postpone outpatient clinic visits, resulting in a 10.3% decrease in

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cancer diagnoses in 2020 compared with the previous year[5].

Prostate cancer is one of the most important public health problems in Croatia, as it is the most common malignancy in men, with its incidence increasing over the years[6]. It is a heterogeneous disease that can range from low-risk localized cancer to metastatic disease at the time of the diagnosis. Treatment options depend on the diagnosis previously confirmed by prostate biopsy, subsequent computed tomography (CT scan) and/or magnetic resonance imaging (MRI) of the abdomen and pelvis, and bone scintigraphy[7]. Considering that the COVID -19 pandemic had a significant impact on the day-to-day functioning of our health care system by reducing the number of outpatient examinations, at which most tumors are diagnosed, the question arose as to how many men had prostate cancer that was not diagnosed in a timely manner? With this question in mind, we decided to conduct a retrospective study in which we compared the data from one year before the pandemic (2018) and one year during the pandemic (2021) at the Clinical Hospital Center of Rijeka (CHC Rijeka) to assess the true impact of COVID-19 on: 1) the number of patients diagnosed with prostate cancer, 2) the time difference between the biopsy and the beginning of the treatment, and 3) the treatment option chosen.

Patients and methods

This retrospective study included 329 patients at CHC Rijeka who underwent prostate biopsy in the year before the COVID-19 pandemic (January 1st – December 31st of 2018) and 193 patients in the year during the pandemic (January 1st – December 31st of 2021). We used the hospital database to collect the following information: time of the biopsy, prostate specific antigen (PSA) before the biopsy, time of the pathohistological diagnosis, treatment option selected (radical prostatectomy with or without lymphadenectomy, hormonal therapy, surgical castration, radiotherapy, chemotherapy), tumor stage, and lymph node involvement after prostatectomy.

Data were processed using descriptive statistics. Continuous variables were presented as median (minimum and maximum values), whereas categorical variables were reported with absolute frequencies and percentages. Normality of the distribution of variables was tested using the Shapiro-Wilk test. The Mann-Whitney test was used to compare differences between continuous variables. The Pearson chi-square test was used to assess the difference in the distribution of a categorical variable between the two independent year-related groups. The significance level was set at $p<0.05$. Statistical analysis was performed using Stata 14[8].

Results

There was a 41.35% reduction in all prostate biopsies (193 vs. 329) with a 37.24% reduction (150 vs. 239) in newly diagnosed prostate cancers in 2021, during the pandemic, compared with 2018, a pre-pandemic year (**Figure 1**). The median pre-biopsy PSA level in

Figure 1. Number of newly diagnosed patients with prostate cancer per month in 2018 and 2021.

2021 was significantly different (10.8 vs. 9.44 ng/mL, p=0.0316). In 2021, the median time between the biopsy and beginning of the therapy was 98 days (min 6, max 438), thus significantly longer than the median of 83 (min 10, max 712) days in 2018 (p=0.0010). When comparing the Gleason score at the time of the diagnosis, we found no statistical difference between the years (p=0.773) (**Table 1**). More chemotherapy was used in 2021 (5.52% vs. 0.86%, p=0.006). Radiotherapy was also used more frequently (33.79% vs. 23.28%, p=0.026). There were no statistical differences between the years regarding the remaining treatment options – radical prostatectomy with or without lymphadenectomy, surgical castration, and hormonal therapy (**Table 2**). A total of 202 patients underwent radical prostatectomy. There were significant differences in the tumor stage (T stage) determined in the prostatectomy specimen (p=0.011). There was a higher percentage of pT3A (16.18% vs. 14.18%) and pT3B (33.82% vs. 13.43%) in 2021 compared with 2018, while the percentage of pT2A (1.47% vs. 2.24%), pT2B (1.47% vs. 3.73%), and pT2C (47.06% vs. 66.42%) was lower (**Table 3**). Regarding the lymph node involvement, there was no significant difference in nodal stage (N stage) in prostatectomy with lymphadenectomy specimens between the two years (p=0.260).

Discussion

With this study, we have shown that the COVID-19 pandemic has placed a burden on our health care sys-

Table 1. Distribution of patients with prostate cancer depending on the Gleason score at diagnosis in 2018 and 2021 N (%), p=0.773

Gleason score	2018 (236 patients) N (%)	2021 (149 patients) N (%)
10 (5+5)	2 (1%)	1 (1%)
9 (5+4)	14 (6%)	4 (2%)
9 (4+5)	27 (11%)	15 (10%)
8 (5+3)	3 (1%)	1 (1%)
8 (4+4)	37 (16%)	22 (15%)
8 (3+5)	2 (1%)	3 (2%)
7 (4+3)	52 (22%)	34 (23%)
7 (3+4)	76 (32%)	57 (38%)
6 (3+3)	23 (10%)	12 (8%)

Table 2. Chosen treatment options in patients with prostate cancer 2018 vs. 2021, N (%)

Treatment (377 patients)	2018 (232 patients) N (%)		2021 (145 patients) N (%)	
	Treated	Not treated	Treated	Not treated
Chemotherapy	2 (0.86%)	230 (99.14%)	8 (5.52%)	137 (94.48%)
Radiotherapy	54 (23.28%)	178 (76.72%)	49 (33.79%)	96 (66.21%)
Radical prostatectomy	136 (58.62%)	96 (41.38%)	72 (49.66%)	73 (50.34%)
Radical prostatectomy with lymphadenectomy	80 (34.48%)	152 (65.52%)	57 (39.31%)	88 (60.69%)
Hormonal therapy	117 (50.43%)	115 (49.57%)	83 (57.24%)	62 (42.76%)
Surgical castration	41 (17.67%)	191 (82.33%)	18 (12.41%)	127 (87.59%)

Table 3. pT stage in prostatectomy specimens, N (%), p=0.010

pT stage		
(203 patients)	2018 (134 patients) N (%)	2021 (69 patients) N (%)
pT2A	3 (2.24%)	1 (1.47%)
pT2B	5 (3.73%)	1 (1.47%)
pT2C	89 (66.42%)	32 (47.06%)
pT3A	19 (14.18%)	11 (16.18%)
pT3B	18 (13.43%)	23 (33.82%)

tem, particularly in patients with prostate cancer. A combination of restrictions, delays in non-emergent hospital procedures, and general fear of contracting the virus led to a decrease in outpatient examinations[9,10]. Accordingly, fewer prostate biopsies were performed. Although the number of prostate biopsies was lower, the percentage of prostate cancer diagnoses based on the biopsies was not statistically different in the two years. In 2021, we reported a 37.24% decrease in prostate cancer diagnoses. Several published studies have shown similar results, namely a decrease of approximately one-third in patients with newly-diagnosed cancer when comparing a pre-pandemic and a pandemic year[11,12]. In addition, Deukeren et al. reported a 17% decrease in the first wave of COVID-19 (January to May 2020) in the Netherlands, followed by a steady rebound in numbers in the second half of 2020[13]. We also found an increase in PSA levels before biopsy, most likely due to patients not reporting in time. Barreras et al. reported an increase in initial PSA levels in their patients. However, they explained it as a result of better triage of patients for the biopsy[14]. Although we did not observe a difference in the distribution of patients in terms of staging at the time of the diagnosis (Gleason score of the biopsy specimen) in these two years, we had more patients with higher tumor stage detected in the prostatectomy specimen in 2021. This can be explained with the fact that, on average, patients waited longer to start their treatment than in the pre-pandemic period because of the temporary restructuring of the healthcare system[15]. Our results are consistent with those of Nyk et al., who found an association between the ongoing pandemic and an increase in adverse pathologic findings in patients treated with radical prostatectomy[16]. Our results are also consistent with the previously mentioned study by Barreras et al., who reported an increase in tumor stage after prostatectomy[14]. Although we found a difference in T stage between the two years, there was no statistical difference in terms of the nodal involvement. Consequently, we had an increase in patients treated with radiotherapy and chemotherapy. The number of patients in whom radical prostatectomy, hormonal therapy, and/or surgical castration were indicated did not differ significantly between the two years. A study conducted in the Netherlands also showed no difference in the number of radical prostatectomies performed in the pandemic 2020, but the time between the diagnosis and the treatment for their patients was shorter. The study also reported that more patients were treated with radiotherapy and hormonal therapy[13].

Conclusion

This retrospective study of patients with prostate cancer at CHC Rijeka confirmed the negative effect of the COVID-19 pandemic on oncologic patients. We found a decrease in the number of prostate biopsies, an increase in pre-biopsy PSA levels, a longer time between diagnosis and treatment, and a worse pathologic outcome in patients who underwent radical prostatectomy during the 2021 pandemic year. To prevent similar outcomes and reduce the negative impact on our oncology patients in a potential future pandemic, we should increase focus on finding appropriate guidelines for timely diagnosis and treatment of patients in need.

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Sažetak

UTJECAJ COVID PANDEMIJE NA DIJAGNOZU I LIJEČENJE RAKA PROSTATE: REZULTATI IZ HRVATSKOG TERCIJARNOG REFERENTNOG CENTRA

I. Bukša, K. Smolić, A. Srok, J. Španjol i *K. Krpina*

COVID-19 pandemija negativno je utjecala na liječenje ne-COVID bolesti. Cilj našeg istraživanja je pokazati utjecaj iste na dijagnostiku i liječenje bolesnika oboljelih od karcinoma prostate. Pretražujući arhivu Klinike za urologiju Kliničkog bolničkog centra Rijeka usporedili smo sljedeće podatke za prepandemijsku 2018. i pandemijsku 2021. godinu: broj biopsija prostate, broj novodijagnosticiranih karcinoma, vrijednosti PSA pri upućivanju na biopsiju, vrijeme čekanja od postavljanja dijagnoze do početka liječenja, stadij bolesti na temelju bioptata i stadij na temelju uzorka nakon prostatektomije te korištene oblike liječenja. Rezultati potvrđuju hipotezu negativnog utjecaja pandemije na dijagnostiku i liječenje. Postotak novodijagnosticiranih bolesnika smanjio se za 37.24% što korelira s manjim brojem biopsija prostate. Također primijetili smo produljeni vremenski period do početka liječenja bolesnika te porast lošijih patohistoloških rezultata nakon radikalne prostatektomije. Sukladno lošijem stadiju bolesti, nešto učestalije se primjenjivala radioterapija i kemoterapija u nastavku njihova liječenja.

Ključne riječi: *COVID-19, Karcinom prostate, Terapija*