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Original Scientific Paper

A COMPARISON OF PROSTATE BIOPSIES PERFORMED BEFORE AND DURING THE COVID-19 PANDEMIC

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SUMMARY – Prostate cancer is the most common cancer in men in developed countries, and prostate biopsy is the gold standard for diagnosis. However, the COVID-19 pandemic disrupted medical examinations, potentially leading to delays in diagnostic investigations, particularly for vulnerable oncology patients. This study included a total of 2796 patients. Biopsies were performed from 2018 to 2021, with a division into pre-pandemic (2018-2019) and pandemic (2020-2021) periods. To compare the two period and yearly data, we used the Chi-square test and the Cochran-Armitage trend test, respectively. During the pandemic period, there was a 26.47% decrease in prostate biopsies compared with pre-pandemic years. The percentage of patients diagnosed with GS 3+3 adenocarcinomas decreased by 37.93% and by 17.66% for GS ≥3+4 (p=0.0164). The percentage of decrease for systematic biopsy was 37.85%, while the percentage of targeted+systematic biopsy increased by 57.89% (p<0.0001). Although the Department of Urology of the UHC Zagreb continued to perform prostate biopsies during the COVID-19 pandemic without interruption, there was a noticeable decrease in the number of biopsies. However, during the pandemic period, we observed an increased proportion of targeted biopsies and a subsequent increase in the proportion of higher-grade adenocarcinoma (GS ≥3+4). The long-term impact of the reduced number of biopsies and prostate cancer diagnoses is yet to be determined, but we believe that this study could be a good starting point for further investigations on this topic.

Key words: *prostate cancer; prostate biopsy; COVID-19; pandemic*

Introduction

Prostate cancer is currently the most common cancer in men both worldwide and in the Republic of Croatia[1,2]. Risk factors are not clearly defined, but the most important are age, race, and hereditary factors[3]. The symptoms of localized prostate cancer are nonspecific or sparse[4]. The gold standard for diagnosing prostate cancer is a prostate biopsy[5]. For many years, conventional systematic biopsies guided by transrectal ultrasound (TRUS) have been widely accepted as the standard biopsy technique, but with the development of new technology and its implementation in medicine, targeted biopsies dependent on multiparametric magnetic resonance imaging have become the new method of choice. The advantages they provide are a greater detection rate of clinically significant prostate cancer and a reduced detection rate of clinically insignificant cancers, thus reducing overdiagnosis and overtreatment[6-12].

In the last few months of 2019, an unfamiliar coronavirus was diagnosed as the origin of pneumonia cases in

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Wuhan, a city in the Hubei Province of China. It spread across China, resulting in an epidemic, followed by an increasing number of cases in other countries throughout the world. In February 2020, the World Health Organization labeled the disease as COVID-19, which stands for coronavirus disease 2019[13]. The rapidly expanding COVID-19 pandemic impacted all areas of life, social interactions, and other normal activities, including medical examinations, which were commonly seen as potential places of danger[14-17]. Furthermore, health care for oncology patients may have been disrupted due to pandemic through suspensions in diagnostic examinations and postponed cancer diagnoses because of a lower level of cancer screening[18]. Moreover, the Centers for Disease Control and Prevention released guidance on delaying nonessential procedures and postponing routine clinical visits as part of the initial mitigation strategies for the COVID-19 pandemic[19].

The aim of this study was to evaluate the impact of the COVID-19 pandemic on prostate cancer diagnoses and the number of prostate biopsies in a high-volume hospital.

Methods

In this retrospective study, we evaluated the number and results of prostate biopsies at the department of Urology, University Hospital Center Zagreb, during 4 years (2018-2021). The cohort was divided into 2 separate periods, the pre-pandemic period (2018-2019) and the pandemic period (2020-2021). We compared the total number of biopsies (systematic and targeted), the results (positive, negative+HGPIN/ASAP), the Gleason scores of positive biopsies (3+3, ≥3+4), and number of patients that underwent biopsies by age group (≤65 years, >65 years) performed in 2020 and 2021 with the number and results of biopsies performed in 2018 and 2019. The percentage decrease before and during the pandemic period was calculated as percentage decrease = $(N_{pandemic} - N_{control})/N_{control}$. Statistical data processing was performed using MedCalc Statistical Software version 20.0.4 (MedCalc Software Ltd, Ostend, Belgium).

Categorical data were the period of performed biopsies (before or during the pandemic period), Gleason score (3+3, ≥3+4), biopsy results (positive, negative (including HGPIN and/or ASAP)), and the chosen biopsy method (SB or TB+SB). Chi-square test was used for calculations between the two observed periods. The Cochran-Armitage trend test was used for calculating the trend during the four observed years for Gleason score groups 3+3 and ≥3+4 and for SB and TB+SB. A two-tailed p value of 0.05 or less was taken as statistically significant.

Results

There were 798 prostate biopsies performed during 2018, 804 in 2019, 556 in 2020, and 638 patients underwent prostate biopsy in 2021.

In the pandemic period, there were 553 positive biopsies (261 in 2020, 292 in 2021), 490 negative biopsies (234 in 2020, 256 in 2021), and 151 precancerous lesions (HGPIN, ASAP) (61 in 2020 and 90 in 2021) compared with 743 positive biopsies (373 in 2018, 370 in 2019), 665 negative biopsies (325 in 2018, 340 in 2019), and 194 precancerous lesions (100 in 2018, 94 in 2019) in the pre-pandemic period. There was a 25.58% decrease when comparing positive biopsies in the pandemic and pre-pandemic periods, and 25.38% decrease for negative biopsies, including ASAP and HGPIN (p=0.9730) (**Table 1**).

Table 1. Number of prostate biopsies, percentage of decrease, and p value

	Pre pandemic N	Pandemic N	Decrease	p value
Total	1602	1194	25.47%	
Gleason 3+3	290	180	37.93%	0.0164
Gleason ≥3+4	453	373	17.66%	
SB	1395	867	37.85%	<0.0001
TB+SB	207	327	-57.98%	
Age ≤65 years	640	442	30.93%	0.1155
Age >65 years	962	752	21.83%	
Positive biopsy	743	553	25.58%	0.9730
Negative biopsy (including HGPIN and ASAP)	859	641	25.38%	

In the pandemic period, there were 180 patients with adenocarcinomas with GS 3+3 (90 in 2020, 90 in 2021) and 373 patients with GS≥3+4 (171 in 2020, 202 in 2021) compared with 290 patients with GS 3+3 (144 in 2018, 146 in 2019) and 453 patients with GS>=3+4 (229 in 2018, 224 in 2019) in the pre-pandemic period. This represents a decrease of 37.93% between the pandemic and pre-pandemic periods for GS 3+3 and a decrease of 17.66% for GS≥3+4 (p=0.0164).

In 2018 there were 38.61% adenocarcinomas with GS 3+3 and 39.46% in 2019. On the other hand, in 2020 that percentage fell to 34.48% and to 30.82% in 2021 (**Figure 1**). The Cochran-Armitage trend test showed statistical significance for this decreasing trend (p=0.020).

A comparison of the number of SB and TB+SB during these four years was also performed. In the pandemic period ,867 patients underwent SB (440

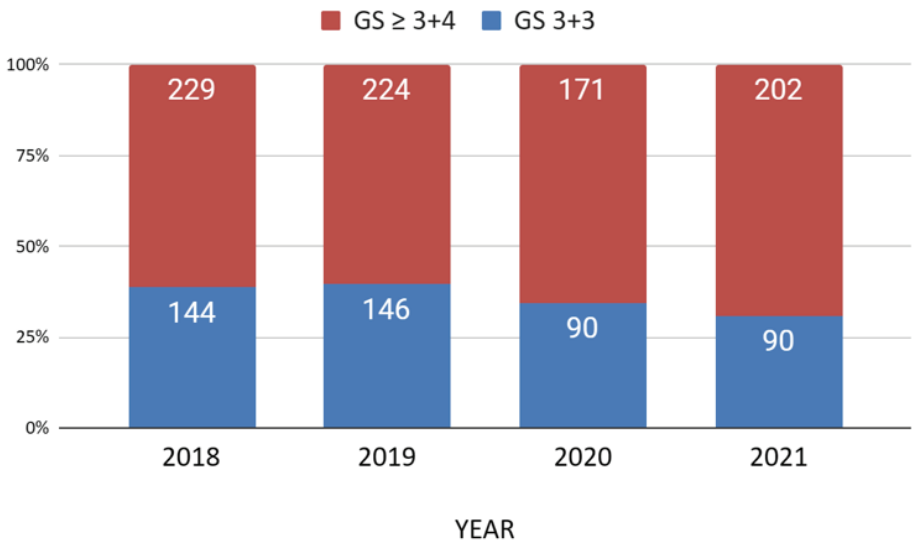

Figure 1. Number of patients with Gleason score 3+3 and Gleason score ≥3+4 showing the trend during 2018–2021. Cochrane Armitage test for trend p=0.020.

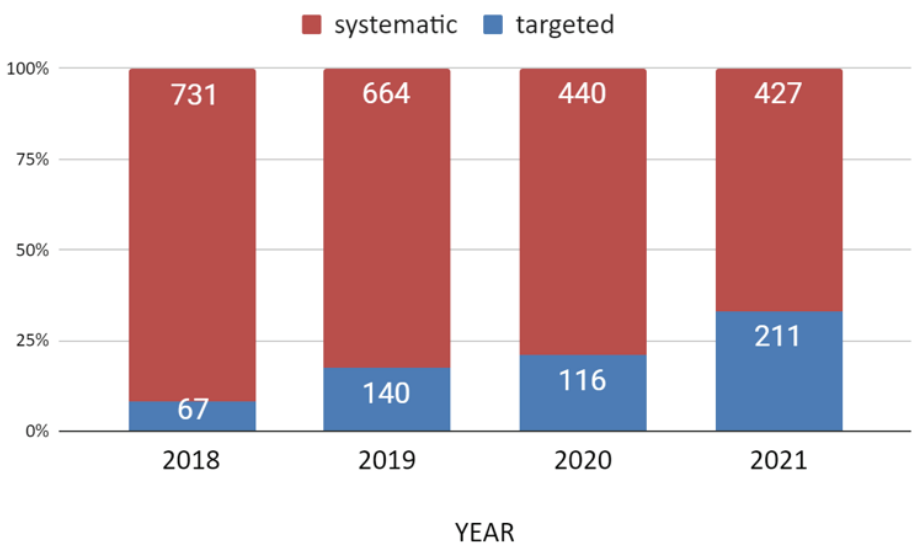

Figure 2. Number of systematic and targeted+systematic prostate biopsies showing the trend during 2018–2021. Cochrane Armitage test for trend p<0.0001.

in 2020, 427 in 2021) and 327 patients underwent TB+SB (116 in 2020, 211 in 2021), compared with 1395 SB (731 in 2018, 664 in 2019) and 207 TB+SB (67 in 2018, 140 in 2019) in the pre-pandemic period. There was a decrease of 37.85% between the pandemic and pre-pandemic numbers of SB and an increase of 57.98% for TB+SB ($p<0.001$) (**Table 1**).

In 2018, 8.40% of all biopsies were targeted, whereas there were 17.41% targeted biopsies in 2019. However, in 2020 that percentage rose to 20.86% and to 33.07% in 2021 (**Figure 2**). There was a notable increasing trend for TB+SB with Cochran-Armitage trend test ($p<0.0001$).

Data were analyzed for the difference between the number of patients younger and older than 65 years who underwent prostate biopsy in the pandemic and pre-pandemic periods. In the pandemic period, there were 442 patients aged ≤65 years (210 in 2020, 232 in 2021), compared with 640 patients aged ≤65 years in the pre-pandemic period (311 in 2018, 329 in 2019). This represents a decrease of 30.93% for patients aged ≤65 years and 21.83% for patients older than 65 years ($p=0.1155$).

Discussion

It is well-known that health services were reduced worldwide during the COVID-19 pandemic[20]. Oncology patients experienced significant impacts as well[21]. Although the Department of Urology at the UHC Zagreb was one of the few departments that continued to perform prostate biopsies without interruption during the lockdown period, there were still significantly fewer biopsies.

When comparing the pre-pandemic and pandemic periods, there was a 25.47% decrease in the total number of prostate biopsies performed. Several other studies have reported a similar decrease; for the example, a 37.9% decrease in the number of prostate biopsies between the pre-pandemic period and the first few months of the pandemic period was reported by Kaufman et al., and a 27.32% decrease was reported by Kieling et al. when comparing 2019 and 2020[18,22]. Furthermore, on the national level, the Croatian national cancer registry reported a decrease of 20% in diagnosis of prostate cancer in 2020 compared with 2019, which is in accordance with our results[2].

Further analysis showed that there was a significantly higher decrease in diagnosed adenocarcinomas with GS 3+3 in the pandemic period, compared with GS ≥3+4(37.93% vs. 17.66%). Similarly to our study, this trend was also reported by Gurel et al[23]. Additionally, this trend can be observed yearly in the analyzed period (**Figure 1**). One possible explanation for this may be that there were fewer general medical examinations during the pandemic, and fewer patients opted for opportunistic screening. Examined patients tended to experience voiding problems or to have positive family history. This can explain the higher proportion of GS ≥3+4.

When we compared the methods employed in prostate biopsies between the pre-pandemic and pandemic periods, there was a decrease of 37.85% in the number of SB and a large increase of 57.98% in TB+SB. This increased utilization of targeted biopsies can also explain the observed decrease in the number of GS 3+3 adenocarcinomas. The increase in the proportion of targeted biopsies was probably due to increased availability of mpMRI, avoiding invasive tests during the pandemic period, but also because it was recognized as the method of choice, especially in the pandemic period. This trend is shown in **Figure 2**, and it will be interesting to see if it continues in the following years, if the pandemic is not the only reason for the increase in the number of mpMRIs.

Pandemic periods certainly represent periods of challenge for the medical system. Despite the challenges posed by the pandemic, the urology department at UHC Zagreb remained active in performing prostate biopsies. However, the reduction in diagnostic tests and patient referrals resulted in a noticeable drop in the number of biopsies performed. The increased use of mpMRI and targeted biopsies has been beneficial and is expected to continue in the post-pandemic period. The long-term impact of the pandemic-related decrease in the number of biopsies and diagnoses of prostate cancer remains to be seen in the coming years.

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Sažetak

USPOREDBA BIOPSIJA PROSTATE PRIJE I ZA VRIJEME COVID-19 PANDEMIJE

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Karcinom prostate je najčešći rak kod muškaraca u razvijenim zemljama danas, a zlatni standard za dijagnozu istog je biopsija prostate. Međutim, COVID-19 pandemija negativno je utjecala na kontinuitet liječničkih pregleda, što je rezultiralo potencijalnim kašnjenjem dijagnostičke obrade, osobito za skupinu najugroženijih onkoloških pacijenata. Naša studija istražuje utjecaj pandemije na dijagnosticiranje karcinoma prostate i stope biopsija u centru s velikim brojem pacijenata.

U istraživanje je obuhvaćeno ukupno 2796 bolesnika. Biopsije su izvođene od 2018. do 2021. godine, a podijeljene su na grupe predpandemijskog (2018.-2019.) i pandemijskog (2020.-2021.) razdoblja. Za usporedbu razdoblja i godišnjih podataka upotrijebili smo chi-kvadrat test, a Cochrane-Armitage test korišten je za računanje trenda.

U razdoblju pandemije broj biopsija prostate smanjio se za 26.47% u odnosu na godine prije pandemije. Postotak bolesnika s dijagnosticiranim adenokarcinomom GS 3+3 smanjio se za 37.93%, a za GS ≥3+4 17.66% (p=0.0164). Postotak smanjenja za shematsku biopsiju iznosio je 37.85% dok se korištenje ciljane+shematske biopsije povećalo za 57.89% (p<0.0001).

Iako je Klinika za urologiju KBC-a Zagreb kontinuirano izvodila biopsije prostate tijekom pandemije COVID-19, primjetan je pad broja biopsija. Međutim, primijetili smo povećanje udjela ciljanih biopsija i naknadni porast udjela adenokarcinoma GS ≥3+4 za vrijeme trajanja pandemije. Dugoročni učinak smanjenog broja biopsija i dijagnoza karcinoma prostate tek treba utvrditi, ali vjerujemo da bi ova studija mogla biti dobra polazna točka za daljnja istraživanja ove teme.

Ključne riječi: *karcinom prostate, biopsija prostate, COVID-19, pandemija*