Acta Clin Croat (Suppl. 2) 2023; 62:33-36
doi: 10.20471/acc.2023.62.s2.5

Original Scientific Paper

UROTHELIAL CARCINOMA BEFORE AND DURING THE COVID-19 PANDEMIC IN CROATIA – A SINGLE-CENTER STUDY

Marin Glavčić[1], Ivona Ćudina[2], Pero Hrabač[3,6], Goran Glavčić[4] and Marijana Ćorić[5,6]

[1]Department of Orthopedics and Traumatology, Dubrava University Hospital, Zagreb, Croatia;
[2]Zagreb-West Health Center, Zagreb, Croatia;
[3]Andrija Štampar Teaching Institute of Public Health, Zagreb, Croatia;
[4]Department of Surgery, Sestre milosrdnice University Hospital Center, Zagreb, Croatia;
[5]Department of Pathology and Cytology, Zagreb University Hospital Center, Zagreb, Croatia;
[6]University of Zagreb School of Medicine, Zagreb, Croatia

SUMMARY – The aim of this study was to compare the number of newly diagnosed, histopathologically confirmed cases of urothelial carcinoma before and during the COVID-19 pandemic at the Zagreb University Hospital Center. We retroactively collected and analyzed 300 histopathologically confirmed urothelial carcinoma between January 1, 2019, and December 31, 2020, at the Department of Pathology and Cytology, Zagreb University Hospital Center. Our results showed that during the COVID-19 pandemic, there was a statistically significant decrease (p=0.001; χ2-test) in the number of newly diagnosed, histopathologically confirmed cases of urothelial carcinoma at the Zagreb University Hospital Center. There was a decrease in the absolute number of newly diagnosed urothelial carcinoma by 25.8% in the observed time of the pandemic (March 19, 2020 to December 31, 2020) as compared to the same period of the previous year (March 19, 2019 to December 31, 2019). Our study is the first study of this type based on the number of newly diagnosed urothelial carcinoma in Croatia. Observing the early period of the pandemic, our results provide important foundation for future monitoring and long-term consequences of the pandemic on the morbidity and mortality of urothelial carcinoma.

Key words: *COVID-19; Croatia; Pandemic; Urothelial carcinoma*

Introduction

The World Health Organization classified COVID-19 (coronavirus disease 2019) as a pandemic after more than 200,000 cases in more than 160 countries[1]. During the pandemic, Croatia's healthcare and hospital systems underwent significant modifications. Hospital work was adjusted to epidemiologic conditions, focusing on COVID-19 protection[2,3]. Zagreb University Hospital Center (UHC) is the most significant health center and the only national hospital in Croatia, demonstrating its size and significance[4].

Urothelial carcinoma is the most common type of bladder cancer, also known as transitional cell carcinoma (TCC). These cancers begin in the urothelial cells that line the bladder interior. Urothelial cells also line other parts of the urinary tract, including the renal pelvis, the ureters, and the urethra. Tumors in these areas are sometimes found in people with bladder cancer, so the entire urinary tract must be examined for tumors[5,6].

The aim of this study was to assess the impact of the COVID-19 pandemic on the number of patients who presented to hospital for further diagnostics of suspected urothelial carcinoma. The findings could

Correspondence to: *Marin Glavčić, MD,* Dubrava University Hospital, Av. Gojka Šuška 6 , HR-10000 Zagreb, Croatia
E-mail: maringlavcic@gmail.com

change the way in which hospital services respond during this and future epidemics or similar events.

Materials and Methods

In this retrospective study, we included patients with histopathologically verified urothelial carcinoma, which were obtained by biopsy, transurethral resection (TUR), or other surgical procedures and sent for analysis to the Department of Pathology and Cytology, Zagreb UHC between January 1, 2019 and December 31, 2020. Other surgical procedures include radical cystectomy, partial cystectomy, nephroureterectomy, and distal resection of the ureter.

Patients with histopathologically verified malignant alterations of the urothelial cells other than urothelial carcinoma were excluded from the study, as were patients whose histopathologic samples were sent from other institutions.

We used March 19, 2020 as the beginning of the pandemic since it was when the official decisions of the Headquarters were made to prevent the spread of coronavirus infection in the Republic of Croatia. The implemented measures had an impact on the functioning of healthcare services.

We compared data in two different ways. In the first scenario, we observed and compared two asymmetric periods: the period before the Crisis Headquarters' decisions (January 1, 2019 to March 18, 2020; below referred to as the 'pre-COVID period'); and the period following the Crisis Headquarters' decisions (March 19, 2020 to December 31, 2020; below referred to as the 'pandemic period'). These comparisons allowed us to cover more patients and thus obtain more credible statistical results.

In the second scenario, we observed and compared two symmetric periods: the period following the Crisis Headquarters's decisions (March 19, 2020) and up to the end of the year (below referred to as the 'later period'); and the same period in 2019 (below referred to as the 'earlier period'). These comparisons allowed us to compare the absolute numbers of newly diagnosed urothelial carcinoma cases detected between the same periods in those two years.

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

Results

During the period observed, 300 patients with histopathologically confirmed urothelial carcinoma were diagnosed by biopsy, TUR, or other surgical resection and analyzed at the Zagreb UHC (211 before *vs*. 89 after the pandemic had been proclaimed). In this research, the patient mean age was 69.7 years in the pre-COVID period and 70.0 in the pandemic period. There was no statistically significant difference in the patient mean age between the pre-COVID and pandemic period (p=0.79; Student's t-test). In both periods, there were more male than female patients (173 *vs*. 38 in pre-COVID and 71 *vs*. 18 in the pandemic period). There was no statistically significant difference (p=0.65; χ^2-test).

The number of patients with histopathologically confirmed urothelial carcinoma diagnosed and analyzed at the Zagreb UHC showed a statistically significant decrease (p=0.001; χ^2-test) during the COVID 19 lockdown period. We also divided data into 'earlier period' and 'later period' in order to be able to compare absolute statistics and assess the actual percentage of decline (see Materials and Methods section). When the absolute numbers of confirmed urothelial carcinoma obtained by TUR, surgical resections, and needle biopsies were evaluated, there was a total decrease by 25.8% in the number of urothelial carcinomas during the pandemic period (120 carcinomas in the pre-COVID period and 89 carcinomas in the pandemic period).

When comparing positive findings of urothelial carcinoma by individual categories in the pre-COVID and pandemic periods, positive urothelial carcinoma samples by surgical resections decreased by 53.4% (59 *vs*. 28 procedures, respectively), those by TUR increased by 18.2% (44 *vs*. 52 procedures respectively) and by needle biopsies decreased by 47.0% (17 *vs*. 9 procedures, respectively) in the pandemic period.

Discussion

The COVID-19 pandemic has had an impact on hospitals all over the world. Non-emergency care has been reduced or postponed in many hospitals[7]. Furthermore, government restrictions encouraged people

to stay at home and avoid non-emergency hospital visits. This has contributed to people's fear of hospitals and their avoidance or postponement of hospital visits for non-emergency care.

Our research results showed a statistically significant decrease in the total number of histopathologially confirmed urothelial carcinomas during the COVID-19 pandemic compared to the pre-pandemic period. We observed a decrease in histopathologically confirmed urothelial carcinoma by surgical resections and needle biopsies during time-identical periods in 2019 and 2020, while there was an increase in histopathologically confirmed urothelial carcinoma by TUR in 2020 compared to the previous year.

A large Danish study compared data from the National Cancer Registry from February to May 2020 to the same period in the preceding five years. The authors describe a 42% decrease in newly diagnosed prostate cancers[8]. In Sweden, a comparable study reported a 36% decrease in the number of newly diagnosed cases of prostate cancer in 2020 compared to the previous year[9]. The findings of studies conducted in Denmark and Sweden support the findings of our research.

Zagreb UHC is a tertiary care institution that treats patients from all over the Republic of Croatia. Therefore, it is not possible to unambiguously define the initial population from which the cases originated. Thus, it is not possible to calculate the disease incidence in the entire population. It is only possible to determine changes in the use of health care in the specified hospital and clinically relevant characteristics of patients.

During the study period, there were two significant events the impact of which on change in the number of searches in 2020 should not be overlooked. The first was the earthquake that hit Zagreb on March 22, 2020[10], and the second was reorganization of the Dubrava University Hospital into the Center for COVID-19 Patients[11]. Therefore, some of those who would have been treated in Dubrava University Hospital sought hospital aid in Zagreb UHC because it is not only the largest hospital in Croatia but also the hospital closest to the Dubrava University Hospital.

To the best of our knowledge, this is the first study of this kind based on the number of urothelial cancer searches in the Republic of Croatia. Observing the pandemic in its early stages, our findings provide important guidelines for future monitoring and long-term effects of the pandemic on urothelial cancer morbidity and mortality.

Conclusion

Our results showed that during the COVID-19 pandemic, there was a statistically significant decrease ($p=0.001$; χ^2-test) in the number of newly diagnosed, histopathologically confirmed cases of urothelial carcinoma at the Zagreb UHC. Observing the same periods (March 19 to December 31) of 2019 and 2020, we found a decrease in the absolute number of newly diagnosed urothelial carcinoma by 25.8%.

References

1. Coronavirus disease (COVID-19) outbreak [Internet] World Health Organisation (WHO) [cited 2020 Jul 20]. Available from: https://experience .arcgis.com/experience/ 685d0ace-521648f8a5beeeee1b9125cd
2. Spinelli A, Pellino G. COVID-19 pandemic: perspectives on an unfolding crisis. Br J Surg. 2020;107(7):785-7. https://doi.org/10.1002/bjs.11627
3. Helgeland J, Telle KE, Grøsland M, Huseby BM, Håberg S, Lindman ASE. Admissions to Norwegian hospitals during the COVID-19 pandemic. Scand J Public Health. 2021;(Sep 2020):1-8. https://doi.org/10.1177/14034948211000813
4. O nama. [Internet]. Klinički bolnički centar Zagreb [cited 2021 Jul 27]. Avaliable from: https://www.kbc-zagreb.hr/o-nama.aspx. (in Croatian)
5. American Society of Clinical Oncology [Internet]. Bladder Cancer: Introduction; 2017 [Cited 2022 Apr 21]. Available from: www.cancer.net/cancer-types/bladder-cancer/introduction.
6. National Cancer Institute [Internet]. Bladder Cancer Treatment (PDQ®) – Patient Version [Cited 2022 Apr 21]. Available from: www.cancer.gov/types/bladder/patient/bladder-treatment-pdq.
7. Nepogodiev D, Omar OM, Glasbey JC, Li E, Simoes JFF, Abbott TEF, *et al*. Elective surgery cancellations due to the COVID-19 pandemic: global predictive modeling to inform surgical recovery plans. Br J Surg [Internet]. 2020 Oct 1 [cited 2022 Apr 21];107(11):1440-9. Available from: /pmc/articles/PMC7272903/. https://doi.org/10.1002/bjs.11746
8. Skovlund CW, Friis S, Dehlendorff C, Nilbert MC, Mørch LS. Hidden morbidities: drop in cancer diagnoses during the COVID-19 pandemic in Denmark. Acta Oncol. 2021;60:20-3. https://doi.org/10.1080/0284186x.2020.1858235
9. Fallara G, Sandin F, Styrke J, Carlsson S, Lissbrant IF, Ahlgren J, *et al*. Prostate cancer diagnosis, staging, and treatment in Sweden during the first phase of the COVID-19 pandemic. Scand J Urol. 2021; 55(3):184-91. https://www.tandfonline.com/action/journalInformation?journalCode=isju20. https://doi.org/10.1080/21681805.2021.1910341
10. Wikipedia: the free encyclopedia [Internet]. St. Petersburg (FL): Wikimedia Foundation, Inc. 2001 – Potres u Zagrebu; [Cited 2021 Jul 29]. Available from: https://hr.wikipedia.org/wiki/Potres_u_Zagrebu_2020.
11. NOVOSTI I OBAVIJESTI. [Internet]. KB Dubrava; 2020 [Cited 2021 Jul 28]. Avaliable from: https://eadu.kbd.hr/?page_id=12186

Sažetak

UTJECAJ PANDEMIJE COVID-19 NA NOVODIJAGNOSTICIRANE UROTELNE KARCINOME

M. Glavčić, I. Ćudina, P. Hrabač, G. Glavčić i *M. Ćorić*

Cilj ovog istraživanja bio je usporediti broj novodijagnosticiranih, patohistološki potvrđenih slučajeva urotelnog karcinoma prije i tijekom pandemije COVID-19 u KBC-u Zagreb. Na Kliničkom zavodu za patologiju i citologiju KBC-a Zagreb retroaktivno smo prikupili i obradili ukupno 300 patohistološki potvrđenih urotelnih karcinoma. Naši rezultati pokazuju da je tijekom pandemije COVID-19 došlo do statistički značajnog smanjenja (p=0,001; χ^2-test) broja novodijagnosticiranih, patohistološki potvrđenih slučajeva urotelnog karcinoma u KBC-u Zagreb. Uočen je pad apsolutnog broja novodijagnosticiranih urotelnih karcinoma za 25,8% u promatranom vremenu pandemije (19. ožujka 2020. do 31. prosinca 2020.) u odnosu na isto razdoblje prošle godine (19. ožujka 2019. do 31. prosinca 2019.). Prema našim saznanjima, ovo je prva studija ovog tipa temeljena na broju novodijagnosticiranih urotelnih karcinoma u Hrvatskoj. Promatrajući rano razdoblje pandemije, naši rezultati daju važne temelje za buduće praćenje i dugoročne posljedice pandemije na pobol i smrtnost od urotelnog karcinoma.

Ključne riječi: *COVID-19; Hrvatska; Pandemija; Urotelni karcinom*