



Frequency of Medical Checkups and Clinical Procedures in Oncology Patients Before and During the Coronavirus Pandemic (Covid-19) in the Department of Gynaecology and Obstetrics of the University Hospital Centre Zagreb

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Abstract

Introduction. At the end of 2019, an epidemic caused by a coronavirus broke out in China. A certain number of female cancer patients neglected their regular oncology treatment during the pandemic, at first because of quarantine, and later due to their incompetence in applying online medicine. The majority of cancer patients demand permanent care and diagnostic/therapeutic procedures. The coronavirus pandemic (COVID-19) led to numerous check-up cancellations and surgery postponements in healthcare, yet it is unknown to what extent it has affected the healthcare of female cancer patients.

Aim. To determine the frequency of check-ups and clinical procedures that female cancer patients underwent prior to and during the coronavirus (COVID-19) epidemic.

Methods. Gathering data on the number of clinical procedures in cancer patients was conducted through the hospital information system (BIS) of the Department of Gynaecology and Obstetrics of KBC Zagreb in the period of two years. The study group included female cancer patients during one year of the pandemic (March 11, 2020 to March 11, 2021), and the control group consisted of female cancer patients during the period of one year preceding the pandemic.

Results. In the Department of Obstetrics and Gynaecology of KBC Zagreb there were less laparoscopic procedures (LPSC) in 2020 than in 2019, with 24.6% less procedures administered in 2020. There were also fewer other gynaecological procedures in 2020, however, the difference was not statistically significant $p > 0.05$. In the same period in Zagreb in 2020 there were 13.9% fewer patients treated for cancer than in 2019. Also in 2020, there were statistically significantly fewer patients treated throughout Croatia $p < 0.001$, with a decrease of 16.3%.

Conclusion. All aspects of healthcare, from diagnostics and therapy to research, have been distressed by the emergence of COVID-19. During the crisis caused by this disease, healthcare workers dealt with the problem of thorough and rapid reorganisation of the system, not only with the purpose of treating newly infected patients, but also in trying to maintain the quality of healthcare for cancer patients. The adjustment of the healthcare system with timely organisation in the Department of Obstetrics and Gynaecology managed to preserve the level of quality healthcare for its female cancer patients. For the future it would be necessary to prepare action plans which will assure adequate health care service without decreasing number of examinations.

Introduction

The coronavirus is a virus that belongs to the group of enveloped and non-segmented ribonucleic (RNA) viruses in the family Coronaviridae, order Nidovirales. The coronavirus has been known since 1967, when round viruses with spikes resembling a crown were observed under an electron microscope. Its appearance is from time to time, with symptoms of an acute febrile illness of the upper respiratory system, similar to a cold (1). COVID-19 is an infectious disease caused by the then-unknown SARS-CoV-2 coronavirus, which appeared in Wuhan at the end of 2019, and shortly thereafter an epidemic was declared in the People's Republic of China, and the virus began to spread throughout the world (1,2). The coronavirus pandemic was declared by the World Health Organization (WHO) on March 11, 2020. The first case of infection with the coronavirus in Croatia was recorded on February 25, 2020 (3). Since the beginning of the pandemic caused by the SARS-CoV-2 virus, over 8,500 people have died of cancer in Croatia (4). Considering the high mortality rate, the fight against cancer is by all standards a national strategic and security issue, and in the context of the COVID-19 crisis, it becomes an even greater challenge. The benefit of disease control should be evaluated in the context of the potential risk of complications and death related to COVID-19 (4). The health system faced a major problem in the reorganization of health care, with an extraordinary public health situation, and oncology patients and their care in the first weeks and months, until the system was reorganized, were deprived of chemotherapy, radiation, or postponement of operations. The WHO gave a recommendation at the beginning of the epidemic to postpone everything possible. In the Department of Obstetrics and Gynaecology of KBC Zagreb, which was also affected by the earthquake due to the pandemic, the implementation of therapy and surgery was not in operation for several days, until the staff, due to their own efforts, came up with a solution and provided conditions for work, care and treatment of patients in improvised premises. In a short period of time, hospital employees were faced with numerous challenges, private, business, uncertain forecasts, and the impossibility of forecasting and planning, which is of great importance for good health care

(4). The pandemic evidently had a great impact on the care and concern of already at-risk groups, and one of them is certainly those suffering from malignant diseases (4,5). Oncology patients have a greater tendency for a more severe form of the disease, considering the immune system that is compromised by cancer, and the method of treatment that is carried out. During the COVID-19 pandemic, the care of oncology patients had two, at first glance, opposite goals: to prevent or reduce the possibility of infection with the SARS-CoV-2 coronavirus, and to maintain the continuity of oncology treatment in such a way that conditions during the pandemic do not lead to worse treatment outcomes (6). It has been observed that oncology patients have an increased risk of secondary complications of COVID-19, which is not surprising given that they are often in an immunocompromised state (7). Oncology patients in relation to the SARS-CoV-2 virus pandemic can be divided into two groups: oncology patients with inactive oncological disease, who are in relatively long control monitoring and without the use of immunosuppressive therapy, and oncology patients with metastatic disease who are undergoing active oncological treatment. Oncology patients who have completed their immunosuppressive treatment relatively recently are certainly at a higher risk of having a more severe or complex clinical picture in case of infection with the coronavirus (8). The worst scenario would be that during the COVID-19 pandemic, we diagnose oncology patients later, in a more severe stage of the disease, treat them less effectively and consequently they have increased mortality from cancer (9). Chemotherapy at the time of COVID-19 infection should be prescribed in a smaller dose, taking care to achieve an equally successful method of controlling the disease, and oncology patients on hormone therapy should not have significant changes in the therapeutic principles of treatment, except for the fact that less frequent controls would be recommended (10-14). In cases of newly diagnosed infection with the SARS-CoV-2 virus, the accepted strategy of oncological treatment should be revised in oncology patients, and the further course of treatment should be individualized (15-17).

On the other hand, from an epidemiological point of view, there were a number of potential dangers for patients with a malignant disease, but also for the health system, i.e. health workers (18-23). The facts that should be taken into account in the organization

of oncology care during the COVID-19 pandemic were that in case of infection with the SARS-CoV-2 virus, patients with a malignant disease have a higher risk of developing a more severe clinical status and a poor outcome compared to the healthy population (24-32). During the pandemic, it was necessary to limit gynaecological examinations only in cases of newly diagnosed malignant tumors of the genital organs or in patients who developed an acute condition during treatment or follow-up (32,33).

It was necessary to preserve the quality of life of patients who are in the terminal phase of the disease through a multidisciplinary approach and the cooperation of hospice services. Communication and consultation via telephone and video link enable a quick exchange of information and suggestions for the implementation of care (32,33,34).

Aim

Through retrospective analysis of data collected during the first year of the pandemic, and data collected during one year immediately before the pandemic, the goal was to gain insight into quantitative differences in the health care of oncology patients at the Department of Obstetrics and Gynaecology, University Hospital Centre Zagreb. The main goal was to examine the frequency of diagnostic/therapeutic procedures in oncology patients before and during the coronavirus (COVID-19) pandemic, and to investigate whether there is a negative relationship between the impact of the pandemic on the quality of health services and care in oncology patients.

Methods

Design

An observational study was conducted to monitor the frequency of control examinations and clinical procedures in a group of oncology patients during the pandemic, and the results were compared with the incidence of control examinations and clinical procedures during an earlier period. The research was conducted using the hospital information system (BIS) of KBC Zagreb. BIS is a program that covers segments of medical documentation management, economic aspects and other business records. The use and maintenance of the hospital's IT system increase the level of quality of health care and safety for the patient in case of complications, given the fast and accessible program of recorded data. In order for the hospital IT system to be effective and successful, it should be operated by trained personnel with the availability of technical and programming support.

Ethics

The conducted research was in accordance with the Nuremberg Code and the Declaration of Helsinki, where care was taken to respect personal integrity. At the 182nd session of the University Hospital Centre Zagreb Ethics Committee, held on May 10, 2021, a request for approval of the research entitled: "Frequency of control examinations and clinical procedures in oncology patients before and during the coronavirus pandemic (COVID-19) in the Department of Obstetrics and Gynaecology of the University Hospital Centre Zagreb - a two-year retrospective study" was considered. The Ethics committee agreed with the conduct of the mentioned research, given that the mentioned research does not contradict the ethical principles.

Data collection

The research group consisted of oncology patients treated during one year, from the beginning of the pandemic (March 11, 2020 to March 11, 2021), and the control group consisted of oncology patients treated during the previous period of one year before the pandemic, in 2019. After the approval of the Ethical Committee of KBC Zagreb to conduct research, BIS was approached. The research was conducted at the Clinic for Women's Diseases and Childbirth, KBC Zagreb from March 2020 to March 2021. The research collected descriptive data on the number of performed gynaecological procedures, in patients of the research and control groups, in the Department of Gynaecological Oncology of the Clinic for Women's Diseases and Childbirth of the KBC-Zagreb, Petrova 13. Data was collected on the number of performed diagnostic/therapeutic procedures; laparotomies, laparoscopic procedures, total laparoscopic hysterectomies, minor procedures, conizations and Lletz conizations, vulvectomies, hysteroscopies, modified radical hysterectomies, surgical procedures with the use of a laparoscope for vaginal removal of the uterus, combined procedures with hysteroscope and laparoscope, cervical amputations, and vaginal hysterectomies.

Statistics

In order to determine whether there was a statistically significant change in the frequency of performing of certain gynaecological procedures in oncology patients at the Clinic for Women's Diseases and Childbirth between 2019 and 2020, chi-square "goodness-of-fit" tests were conducted. According to the collected data from all regional offices of the Republic of Croatia in the Oncology Department of the Clinic for Women's Diseases and Childbirth of the KBC Zagreb; from the outpatient clinic for the control of patients treated for cancer, and for the sake of comparison, the same tests were used to compare and record the number of patients treated for cancer

between 2019 and 2020, for the city of Zagreb and the whole of Croatia. Two-tailed tests and an alpha value of 5% were used. Statistical processing was performed in SPSS, version 26.0 (2018, IBM Corp., Armonk, N.Y., USA).

Results

During 2019, which preceded the pandemic, a data on a total of 672 oncology patients was collected, who were the control group; while during the first year of the pandemic (2020), a total of 616 oncology patients, who were the research group, were collected over a period of one year. For the less frequently performed procedures (LAVH, hysc+lpsc, Amputation, Vag. Hyst.), the power of the performed test is extremely low, and there was little or no chance that the test would reveal statistically significant differences, but for the sake of data completeness, those test results are also listed. The laparoscopy (LPSC)

procedure at the KBC Zagreb Obstetrics and Gynaecology Clinic was performed statistically significantly less often in 2020 than in 2019 ($\chi^2(1)=4.78$ $p=0.029$), with 24.6% fewer procedures performed in 2020. Other gynaecological procedures did not differ statistically significantly according to the frequency of performed procedures in 2019 and 2020 ($p>0.05$).

For the sake of comparison, from the available data, there were 13.9% fewer patients treated for cancer in Zagreb in 2020 than in 2019. This difference is statistically significant ($\chi^2(1)=28.52$ $p<0.001$).

Also in 2020, there were statistically significantly fewer female patients treated throughout Croatia ($\chi^2(1) = 81.65$ $p<0.001$), with a decrease of 16.3% (Table 2).

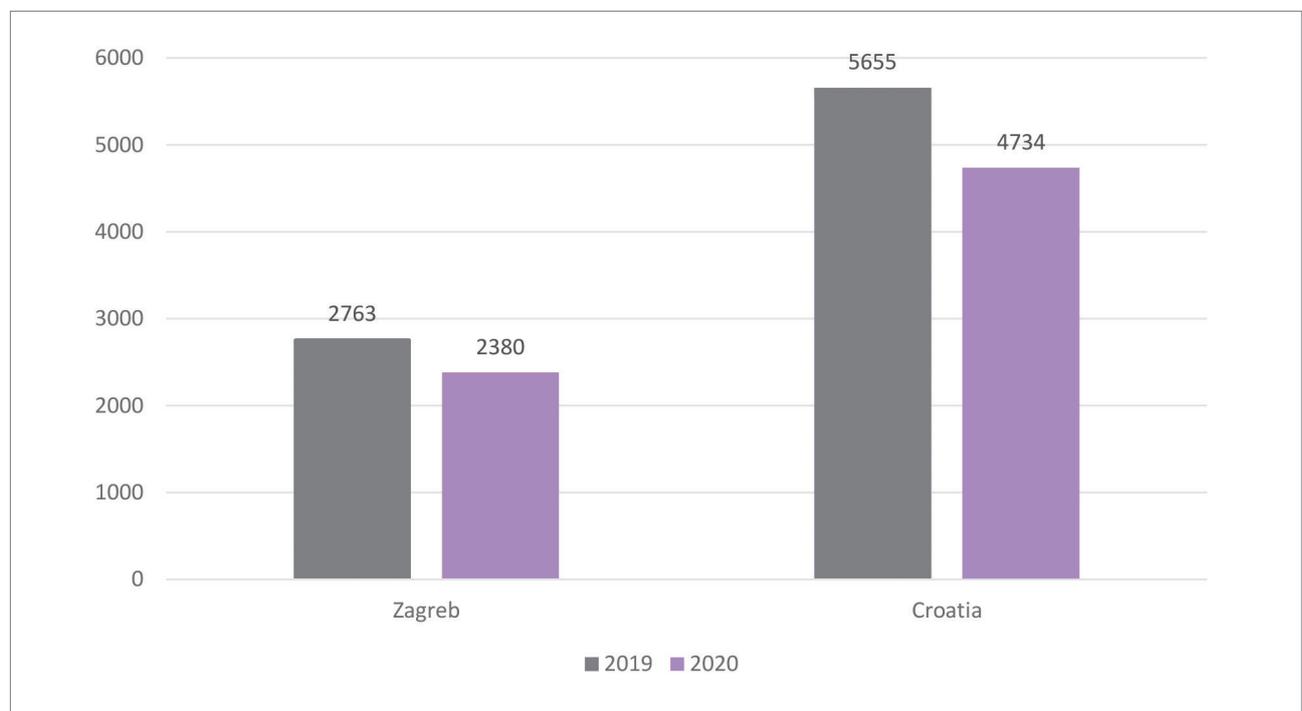
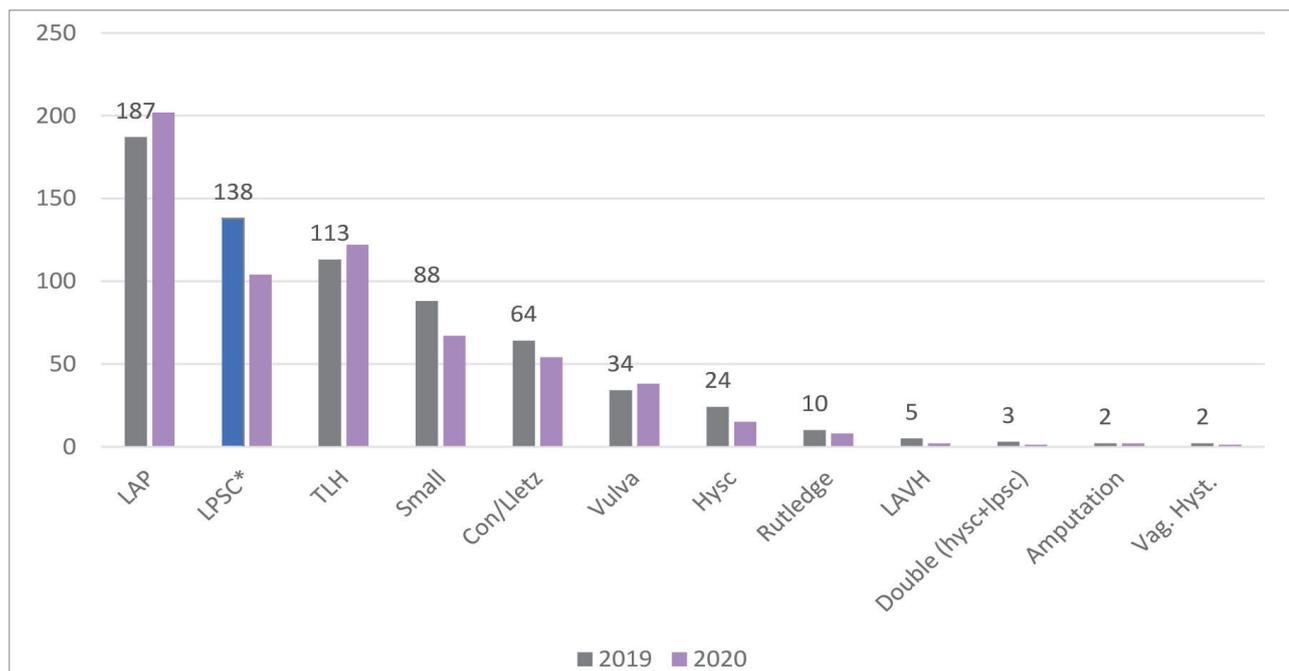


Figure 1. Representation of female patients treated for cancer in 2019 and 2020 in Zagreb and throughout Croatia

Table 1. Descriptive data on the frequency of implementation of certain gynaecological procedures in 2019 and 2020 and the results of chi-square "goodness-of-fit" tests

Gynaecological procedure	2019		2020		X ²	p
	f	%	f	%		
LAP	187	48.1	202	51.9	0.58	0.447
LPSC	138	57	104	43	4.78	0.029
TLH	113	48.1	122	51.9	0.35	0.557
Small	88	56.8	67	43.2	2.85	0.092
Con/Lletzt	64	54.2	54	45.8	0.85	0.357
Vulva	34	47.2	38	52.8	0.22	0.637
Hysc	24	61.5	15	38.5	2.08	0.150
Rutledge	10	55.6	8	44.4	0.22	0.637
LAVH	5	71.4	2	28.6	1.29	0.257
Double (hysc+lpsc)	3	75	1	25	1.00	0.317
Amputation	2	50	2	50	0.00	1
Vag. Hyst.	2	66.7	1	33.3	0.33	0.564

Note: f - frequency, % - percentage of the total number of procedures in both years, χ^2 - chi-square test result (degrees of freedom are 1), p - statistical significance; Gynaecological procedures: LAP - laparotomy, LPSC - laparoscopy, TLH - total laparoscopic hysterectomy, Small - small procedures, Con/Lletzt - miniconization, Vulva - vulvectomy, Hysc - hysteroscopy, Rutledge - modified radical hysterectomy, LAVH - surgical procedure of using a laparoscope in vaginal removal of the uterus, Double (hysc+lpsc) - hysteroscopy with laparoscopy, Amputation - amputation, Vag. Hyst. - vaginal hysterectomy.

**Figure 2. Representation of certain gynaecological procedures in 2019 and 2020 at the Department of Obstetrics and Gynaecology, University Hospital Zagreb****Table 2. Descriptive data on the number of female patients treated for cancer in regional offices during 2019 and 2020, and the results of chi-square "goodness-of-fit" tests**

Area	2019		2020		X ²	p
	f	%	f	%		
Zagreb	2763	53.7%	2380	46.3%	28.52	<0.001
Croatia	5655	54.4%	4734	45.6%	81.65	<0.001

Discussion

During the global pandemic of the COVID-19 disease, the Republic of Croatia, like the rest of the world, was exposed to extraordinary measures to prevent the spread of the infection, which had profound consequences on the life of the entire society, as well as on the availability of oncology care (35-38). The consequences of isolation measures on the timely detection, diagnosis, treatment and outcomes of oncology patients at the Department of Obstetrics and Gynaecology are still being analyzed. During the escalation of the SARS-CoV-2 virus pandemic, health systems in Europe and the world came under great pressure. The questions related to the impact of the epidemic on oncology patients and the steps in the prevention and treatment of malignant tumors, and how will COVID-19 affect the expected outcomes of treatment, and how to improve the results of treatment, were discussed at numerous gatherings, congresses and professional meetings around the world, which gather experts who exchanged experiences, results and offered effective methods of oncology care in one place. Research on the impact of the COVID-19 pandemic on cancer treatment, conducted by the Initiative of Pharmaceutical and Biotechnology Companies in six Eastern European countries, including Croatia, showed that there was a drop in the number of patients treated by oncologists/haematologists. Other researchers point us to a significant drop in the number of cancer diagnoses and the number of diagnostic procedures during the epidemic; confirmed a significant difference in the frequency of diagnostic procedures and interventions before and after the start of the pandemic (35,36). Stah et al. found that 1218 exams (cancer prevention program) were performed in the pre-pandemic period and 857 in the pandemic period, a 29.6% decrease (37). If we compare our results with Stah et al., and decrease of 16.3% we can conclude that our action measures gave some results (Table 2) (37). This retrospective research during the first year of the pandemic precisely showed the immediate negative impact of the pandemic on the number of diagnostic procedures performed, on a smaller number of therapeutic procedures, as well as, in accordance with the results, on the consequent worse outcome of the treatment of oncology patients at the Clinic for Women's Diseases

and Childbirth of the KBC Zagreb. According to an insight into the recorded data, the number of diagnostic and therapeutic procedures during the first year of the pandemic (Table 1) recorded 24.6% fewer laparoscopic procedures in 2020 than in 2019, before the pandemic ($\chi^2(1)=4.78, p=0.029$); which means statistically significantly less laparoscopies compared to 2019. Other gynaecological procedures did not differ statistically significantly according to the frequency of application in 2019 and 2020 ($p>0.05$), although there were fewer of them. Thus, small procedures, conization/LETZ (Loop Excision of the Transformation Zone-LETZ) biopsy of the cervix, hysterectomy, Rutledge, LAVH (Laparoscopic Assisted Vaginal Hysterectomy-LAVH), hysterectomy+LPSC and vaginal hysterectomy were less prevalent during the pandemic year 2020, than during 2019, but without a statistically significant difference. During the pandemic year 2020, there were slightly more laparotomies, TLH (Total Laparoscopic Hysterectomy) and vulvectomies, but without a statistically significant difference compared to 2019, while cervical amputations were equally represented during 2019 and 2020. Such results, with a slightly higher frequency and more extensive procedures during the pandemic year, can be interpreted as a result of a direct connection due to the spread of the underlying disease and the need for surgical intervention as quickly as possible, despite the pandemic. Thus, other relatively small interventions according to the scope of surgical treatment were less common during the year of the pandemic, but without a statistically significant difference. In Table 1 (Descriptive data on the frequency of certain gynaecological procedures in 2019 and 2020, and the results of chi-square "goodness-of-fit" tests), as well as the graphic display (Figure 2) shows the frequency and order of all represented diagnostic and therapeutic procedures of oncology patients at the Department. The most common procedures were laparotomies, while the least common were vaginal hysterectomies. According to the results of the Department, there were indicators of a total of fewer number of treated gynaecological/oncological patients at the level of Zagreb, but also significantly fewer number of treated gynaecological/oncological patients in the whole of Croatia. Thus, in Zagreb in 2020, during the pandemic, there were 13.9% fewer patients treated for cancer than in 2019. That difference was statistically significant ($\chi^2(1)=28.52, p<0.001$). Also, in 2020, there was statistically significantly fewer number of treated patients at the

level of the whole of Croatia ($\chi^2(1) = 81.65, p < 0.001$), with a decrease of 16.3%. The same results are shown graphically (Figure 1) for the city of Zagreb and the whole of Croatia, where it is evident that there were statistically significantly less represented and treated gynaecological/oncology patients during the 2020 pandemic in Zagreb and Croatia than in 2019. Cancer patients mostly accept the new situation and its impact on the healthcare system, and are most often inclined to accept all suggested preventive measures, even though there is an increasing need for psychological support. Most hospitals have adapted by reserving their capacities in intensive care units for potential complications of COVID-19 (35). Continuation of regular operations would call into question the possibility of treatment for all patients who need intensive care, i.e. mechanical ventilation. Due to the potential burden on the system, the number of elective operations, which also include primary tumor operations, has been significantly reduced (38). Liang et al., as well as many other researchers, report an increased incidence of complications in oncology patients from COVID-19 (20). Considering the relatively small number of studies that investigated the impact of SARS-CoV-2 infection on oncology patients with malignant diseases, conclusions are drawn from cohort analyses. In general, older oncology patients with significant comorbidities or recent surgical procedures had a higher probability of needing hospital treatment, a higher risk of developing a more severe clinical picture and death from COVID-19 (39). With a retrospective insight into the results of the Clinic for Women's Diseases and Childbirth during the first year of the pandemic and one year before the pandemic, we had consistent results, like the vast majority of researchers who, in the conducted studies, emphasized the need to reduce the intensity or postpone specific oncological treatment whenever possible, considering on the risk of infection for patients. The risk of disease progression due to delaying therapy increases with the duration of the pandemic, which can have negative consequences for oncology patients (40-42). The rapid spread of severe acute respiratory syndrome caused by the SARS-CoV-2 coronavirus required urgent and coordinated health care, and maintaining continuity of care for diseases other than COVID-19 (42). The European Society for Medical Oncology (ESMO) approved three different levels of access to treatment (high, medium, low) for patients with gynaecological cancer, who are particu-

larly at risk of complications caused by COVID-19, due to age and the prevalence of comorbidities (43). Frey et al report that more than one-third of gynaecologic cancer patients at three affiliated hospitals in New York experienced a delay, change, or cancellation of treatment during the first two months of the COVID-19 pandemic (44). These changes in the treatment plan are a direct correlation and consequence of the overloading of the health system by the spread of the pandemic (44,45). Our experiences and retrospective research through the first year of the pandemic in the Clinic for Women's Diseases and Childbirth of the KBC Zagreb showed similar problems in the organization of health care for oncology patients, as in most other oncology centres worldwide. Through timely organization and a selective approach, it was possible to maintain the continuity of the necessary procedures and diagnostics, which resulted in minor deviations from the usual approach to such patients.

Conclusion

All aspects of healthcare, from diagnostics and therapy to research, were affected by the emergence of COVID-19. During the crisis caused by this disease, health workers deal with the problem of a thorough and rapid reorganization of the system not only for the purpose of taking care of newly infected persons, but also to avoid causing a loss of quality of treatment for other patients. The treatment of malignant diseases of gynaecological patients is one segment that requires continuity even in the era of the pandemic, considering the nature of the disease itself and the impact on survival, which is made possible by specific oncological treatment.

Based on this retrospective research, it can be concluded:

- the overall number of diagnostic/therapeutic interventions during the pandemic is lower, from which it can be indirectly concluded that due to the pandemic and the limited number of control examinations, fewer diagnoses were made on time

- during the year of the pandemic, statistically significantly fewer laparoscopic procedures were performed than during the year preceding the pandemic
- in total, during the year of the pandemic, a smaller number of other diagnostic/therapeutic procedures were performed, but still without a statistically significant difference, thanks to the good reorganization of the health care system

All available and conducted studies have indicated a reduced total number of diagnostic/therapeutic procedures, with a reduced intensity or delay of specific oncological treatment, whenever possible considering the risk of infection for oncology patients. Most hospitals have adapted by reserving their capacities in intensive care units for potential complications caused by COVID-19.

For the future, it would be necessary to prepare action plans which will assure adequate health care service without decreasing the number of examinations.

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UČESTALOST KONTROLNIH PREGLEDA I KLINIČKIH POSTUPAKA KOD ONKOLOŠKIH PACIJENATA PRIJE I ZA VRIJEME PANDEMIJE BOLESTI COVID-19 U KLINICI ZA ŽENSKÉ BOLESTI I PORODE KBC-a ZAGREB

Sažetak

Uvod. Krajem 2019. u Kini je izbila epidemija izazvana koronavirusom. Određeni broj oboljelih od raka zanemario je redovito onkološko liječenje tijekom pandemije, najprije zbog karantene, a kasnije zbog nestručnosti u primjeni *online* medicine. Većina onkoloških bolesnika zahtijeva stalnu njegu i dijagnostičko-terapijske postupke. Pandemija bolesti COVID-19 dovela je do brojnih otkazivanja pregleda i odgađanja operacija u zdravstvu, no nije poznato u kojoj je mjeri utjecala na zdravstvenu skrb žena oboljelih od raka.

Cilj. Utvrditi učestalost pregleda i kliničkih zahvata kojima su bile podvrgnute oboljele od raka prije i tijekom pandemije bolesti COVID-19.

Metode. Prikupljanje podataka o broju kliničkih postupaka u onkoloških bolesnika provedeno je kroz bolnički informacijski sustav (BIS) Klinike za ženske bolesti i porode KBC-a Zagreb u razdoblju od dvije godine. Ispitnu skupinu činile su oboljele od raka tijekom jedne godine pandemije (od 11. ožujka 2020. do 11. ožujka 2021.), a kontrolnu skupinu činile su oboljele od raka tijekom godine dana prije pandemije.

Rezultati. U Klinici za ženske bolesti i porode KBC-a Zagreb bilo je manje laparoskopskih zahvata (LPSC) 2020. nego 2019., s 24,6 % manje obavljenih zahvata 2020. Manje je bilo i ostalih ginekoloških zahvata 2020., ali razlika nije statistički značajna ($p > 0,05$). U Zagrebu je u istom razdoblju 2020. od karcinoma liječeno 13,9 % manje pacijenata nego 2019. Također je 2020. statistički značajno manje liječenih u cijeloj Hrvatskoj ($p < 0,001$), uz pad od 16,3 %.

Zaključak. Svi aspekti zdravstvene skrbi, od dijagnostike i terapije do istraživanja, pogođeni su pojavom bolesti COVID-19. Tijekom krize izazvane ovom bolešću zdravstveni su se djelatnici uhvatili ukoštac s problemom temeljite i brze reorganizacije sustava, ne samo u svrhu liječenja novooboljelih nego i u nastojanju da održe kvalitetu zdravstvene skrbi za oboljele od raka. Prilagodбом zdravstvenog sustava pravodobnom organizacijom Klinika za ženske bolesti i porode uspjela je očuvati razinu kvalitete zdravstvene zaštite svojih onkoloških bolesnica. Za budućnost bi bilo potrebno izraditi akcijske planove koji će osigurati adekvatnu zdravstvenu uslugu bez smanjenja broja pregleda.

Ključne riječi: koronavirus, pandemija, onkološki bolesnici, pregled, klinički postupci
