ORIGINAL ARTICLES

UDC: 616.98-036.21::578.834]:616-006-052- 08
DOI: https://doi.org/10.2298/VSP211018024K

Covid-19's impact on radiotherapy in the Republic of Srpska

Uticaj Covid-19 na radioterapiju u Republici Srpskoj

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Abstract

Background/Aim. Coronavirus disease 2019 (COVID-19) significantly affects patients with any type of chronic disease, especially the ones with neoplasm. The aim of this study was to investigate the impact of the COVID-19 pandemic on the weekly number of external beam (EB) radiotherapy (RT) (EBRT) fractions and monthly brachytherapy (BT) applications without intentional hypofractionation. We also investigated how the pandemic affected the number of EBRT patients younger or older than 70 years. **Methods.** The Affidea Radiotherapy Center, Banja Luka (BL RT Center), provides RT to the population (1.15 million) of the Republic of Srpska (Bosnia and Herzegovina). We analyzed the period of 14 months before the onset and the same period during COVID-19. **Results.** The average weekly number of EBRT fractions from January 2019 to the end of February 2020 was 680.5 [standard deviation (SD) 67.4], and from March 2020 to the end of April 2021, it was 617.1 (SD 96.4). During April 2020, the weekly number of the EBRT decreased by 67.9% compared to the same period in 2019, while in March 2021, it fell by 42.4%. Paired samples *t*-test showed that the occurrence of the COVID-19 pandemic had a statistically significant effect [$t(60) = 4.627$, $p < 0.05$] on the reduction in the number of weekly EBRT fractions in the BL RT Center. When comparing number of EBRT patients over 70 years old to those fewer than 70 years old, the decrease was 16.3% vs. 1.6%, respectively. The Wilcoxon signed-rank test revealed that the COVID-19 pandemic had a statistically significant effect ($Z = -2.42$, $p = 0.016$) on reducing the number of monthly BT applications. **Conclusion.** A statistically significant decline in EBRT and BT was observed in BL RT Center for the first fourteen months of the pandemic. The "waves" of the pandemic "closed" the medical wards needed for the diagnosis and therapy of oncology patients and converted them into COVID-19 wards. Therefore, some oncology patients who would have had an indication for RT never received it.

Key words:
age factors; brachytherapy; covid-19; epidemiology; radiotherapy; radiotherapy dosage.

Apstrakt

Uvod/Cilj. Bolest prouzrokovana koronavirusom 2019 (*coronavirus disease* 19 – COVID-19) utiče na bolesnike sa bilo kojim tipom hronične bolesti, a posebno na one sa malignitetima. Cilj studije bio je da se utvrdi uticaj pandemije COVID-19 na broj nedeljnih frakcija radioterapije (RT) sa spoljašnjim zračenjem (EBRT) i mesečne brahiterapijske (BT) aplikacije, bez namernog hipofrakcionisanja, kao i njen uticaj na broj bolesnika podvrgnutih EBRT, mlađih ili starijih od 70 godina. **Metode.** Centar za radioterapiju *Affidea* u Banjoj Luci (BL RT centar), pruža RT stanovništvu (1,15 miliona) Republike Srpske (Bosna i Hercegovina). Analizirali smo period od 14 meseci pre početka COVID-19 i isti period za vreme COVID-19. **Rezultati.** Prosečni sedmični broj EBRT frakcija u periodu od januara 2019. do kraja februara 2020. iznosio je 680,5 [standardna devijacija (SD) 67,4], a od marta 2020. do kraja aprila 2021, 617,1 (SD 96,4). Tokom aprila 2020., sedmični broj EBRT frakcija smanjio se 67,9% u odnosu na isti period 2019., dok je u martu 2021. godine pao za 42,4%; *t*-test uparenih uzoraka pokazao je da je pojava pandemije COVID-19 imala statistički značajan učinak [$t(60) = 4.627$, $p < 0,05$], na smanjenje broja sedmičnih EBRT frakcija u BL RT centru. Smanjenje broja bolesnika podvrgnutih EBRT starijih od 70 godina u odnosu na mlađe od 70 godina, iznosilo je 16,3% naspram 1,6%, redom. *Wilcoxon* rang test otkrio je da je pandemija COVID-19 imala statistički značajan učinak na smanjenje broja mesečnih BT aplikacija ($Z = -2,42$, $p = 0,016$). **Zaključak.** Za prvih 14 meseci pandemije primećen je statistički značajan pad EBRT i BT u BL RT centru. „Talasi" pandemije „zatvarali" su odeljenja potrebna za dijagnostiku i terapiju onkoloških bolesnika i pretvarali ih u COVID-19 odeljenja. Zbog toga pojedini onkološki bolesnici nikada nisu dobili RT koja im je bila indikovana.

Ključne reči:
životno doba, faktor; brahiterapija; covid-19; epidemiologija; radioterapija; radioterapija, doziranje.

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Introduction

The Coronavirus disease 2019 (COVID-19) pandemic is an entirely new experience for "modern" society that has drastically affected all aspects of life, especially the health care system. The treatment of oncology patients has become a real challenge under the influence of several "waves" of the pandemic. In addition to having infected patients, we have also had many infected health workers. Any contact with an infected person (private or at work) leads to a two-week quarantine, further reducing the number of medical staff in hospitals [1]. Radiotherapy (RT) teams are adopting new work procedures and the use of protective equipment in order to minimize the risk of infecting medical staff and patients while at the same time optimizing the treatment and care of oncology patients. Many RT centers followed the recommendation to use a hypofractionated RT (breast, prostate, palliative treatments, etc.), thus reducing the number of hospital visits [2]. Some RT centers split their staff into teams to make physical segregation and avoid the risk of infection among them. When possible, the number of medical control checks and consultations has been reduced, and telephone communication has been switched on. This has reduced the number of patients in most healthcare systems (outside the COVID-19 departments) [3].

Oncology patients are especially endangered because they need timely diagnosis and treatment therapy, primarily RT with surgery and systemic therapy [4, 5]. Pandemic "waves" have reduced the capacity of most departments in hospitals, making it harder for cancer patients to get to RT, especially during those periods. This evident impact of the COVID-19 pandemic on the health care system, including the RT services, was the subject of several studies [4, 6,] which show a quantitative decline in the number of patients per age and diagnosis.

The COVID-19 reached the Republic of Srpska (RS, Bosnia and Herzegovina) on March 5, 2020, when a patient in Banja Luka (BL), who had traveled in from Italy, tested positive. For this epidemiological retrospective study, we assume that the pandemic began on March 1, 2020.

The aim of this epidemiological study was to investigate the impact of COVID-19 on the weekly number of external beam RT (EBRT) fractions and monthly brachytherapy (BT) applications in the BL RT Center, including the age of the patients and the treatment site.

Methods

BL RT Center Affidea provides EBRT and BT services to all insured persons of the Health Insurance Fund of the RS. The Center has two Varian True Beam (Varian, Medical Systems, Palo Alto, California) linear accelerators (Linac), one Varian DHX Linac, and one Varian GammaMed plus™ iX BT high dose rate (HDR) unit. In routine clinical EBRT practice, we use 3D conformal radiotherapy (3DCRT), intensity-modulated radiotherapy (IMRT), and volumetric modulated arc therapy (VMAT) treatment techniques. In BT applications, gynecologic (GYN) cancer predominates. Patients were irradiated from Monday to Friday during one 8-h shift (260 working days per year). The estimated population and the total number of new cancer cases in the RS in 2016 were 1,157,516 and 5,786, respectively. Table 1 presents new cancer cases by leading primary sites and by sex in the RS during 2016 [7].

Table 1
New cancer cases by leading primary sites and sex, in the Republic of Srpska (RS), during 2016 [7]

Sex	Patients (%)
Male	
trachea and lungs	16.8
colon and rectum	12.6
prostate	9.5
bladder	7.0
stomach	5.2
kidney	3.1
liver	2.8
Female	
breast	16.4
colon and rectum	8.8
cervix	7.0
trachea and lungs	6.1
uterus	4.3
ovary	4.3
thyroid gland	4.0

For this epidemiological retrospective study, we assume that the pandemic began on March 1, 2020. We analyzed the number of weekly EBRT fractions and monthly BT applications in the period before (period 0: January 2019 – end of February 2020, which is the period with the largest number of EBRT fractions) and during the onset of COVID-19 in BL RT Center (period 1: March 2020 – end of April 2021). We also investigated the influence of COVID-19 on the number of EBRT patients per treatment site, younger and older than 70 years. Both periods had 14 months, i.e., 61 weeks.

Statistical analysis

Results are presented as median and arithmetic mean values with standard deviation (SD). Relative error (RE) was used to determine the percentage difference in the change in quantity. The Kolmogorov-Smirnov test was applied to assess the normality of the continuous studied data (> 50 measurements for EBRT data). The Shapiro-Wilk normality test was applied in the case of a smaller measurement sample (< 20 measurements for BT data).

The strength of the association between independent factor (presence of COVID-19) and EBRT fraction per week or BT applications (dependent factor) was determined by using parametric one-tailed paired samples *t*-test for normal distribution of data differences and nonparametric Wilcoxon signed-rank test when the data differences did not have a normal distribution [8]. All the analyses were estimated at a minimal $p < 0.05$ level of statistical significance. Complete statistical analysis of data was done with the statistical software package, SPSS Statistics 23 (IBM, Armonk NY, USA).

Results

External beam radiotherapy

Figure 1 presents the mean value of the number of EBRT fractions working per day in the period 2016–2021.

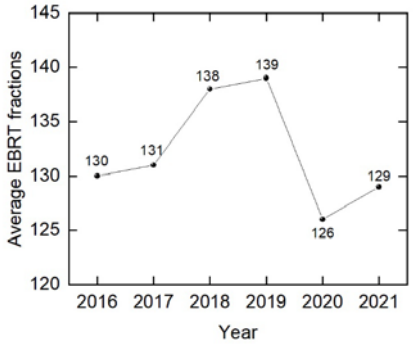

Fig. 1 – Average number of EBRT fractions working per day in the period 2016–2021.
EBRT – external beam radiotherapy.

The total weekly number of EBRT fractions in the period 2019–2021 in the BL RT Center is shown in Figure 2.

The relative difference between the weekly number of EBRT fractions for 2020 and 2021 compared to 2019 is shown in Figure 3.

Descriptive statistical analysis was performed for period 0 (n_0 = 61 weeks, when we consider that there was no influence of COVID-19 on the number of EBRT fractions) and period 1 (n_1 = 61 weeks, the period when the pandemic was present); the results are shown in Table 2.

The applied Kolmogorov-Smirnov normality test (p = 0.2) indicates the normal distribution of the values of differences (n_0-n_1) of weekly EBRT fractions (mean 63.4, SD 107). Therefore, a parametric one-tailed paired-samples t-test was performed [t (60) = 4.627, p < 0.05].

We compared the number of patients older than 70 years, younger than 70 years, and the total number of EBRT patients by the most common treatment sites (Table 3).

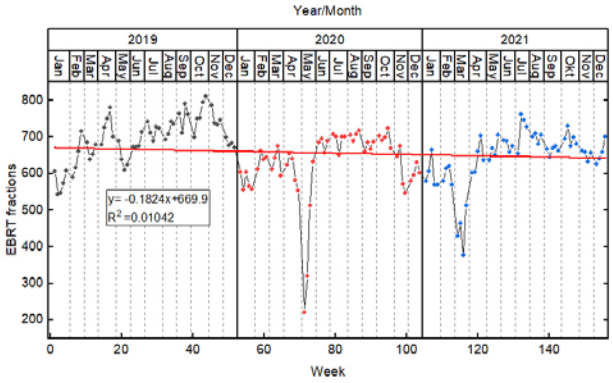

Fig. 2 – Weekly number of external beam radiation therapy (EBRT) patients in the period 2019–2021.

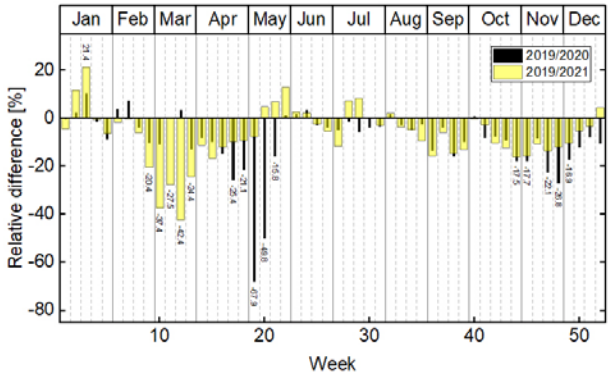

Fig. 3 – Relative difference of the weekly number of external beam radiation therapy (EBRT) fractions for 2020 and 2021 in relation to the year 2019.

Table 2

Descriptive statistics by 61 weekly external beam radiotherapy (EBRT) fractions before and during the COVID-19 pandemic

COVID -19	Number of weeks	EBRT/week	
		mean ± SD	min–max
Before	61	680.5 ± 67.4	543–811
During	61	617.1 ± 96.4	221–724

COVID-19 – corona virus disaese 2019; SD – standard deviation.

Table 3

Difference according to the treatment site for patients older than 70 years, younger than 70 years, and in total all patients (for 14 months before and during the COVID-19 pandemic)

Diagnosis sites	Number of RT	Difference (percentages)
Skin		
patients > 70 years		
before COVID-19	25	
during COVID-19	4	-84
patients < 70 years		
before COVID-19	13	
during COVID-19	5	-61.5
total		
before COVID-19	38	
during COVID-19	9	-76.3
GYN*		
patients > 70 years		
before COVID-19	101	
during COVID-19	61	-39.6
patients < 70 years		
before COVID-19	259	
during COVID-19	204	-21.2
total		
before COVID-19	360	
during COVID-19	265	-23.4
Breast		
patients > 70 years		
before COVID-19	128	
during COVID-19	90	-29.7
patients < 70 years		
before COVID-19	345	
during COVID-19	275	-20.3
total		
before COVID – 19	473	
during COVID – 19	365	-22.8
Lung		
patients > 70 years		
before COVID-19	91	
during COVID-19	77	-15.4
patients < 70 years		
before COVID-19	162	
during COVID-19	133	-17.9
total		
before COVID-19	253	
during COVID-19	210	-17
Stomach		
patients > 70 years		
before COVID-19	11	
during COVID-19	10	-9.1
patients < 70 years		
before COVID-19	30	
during COVID-19	27	-10
total		
before COVID-19	41	
during COVID-19	37	-9.8
Prostate		
patients > 70 years		
before COVID-19	130	
during COVID-19	113	-13.1
patients < 70 years		
before COVID-19	74	
during COVID-19	83	+12.2
total		
before COVID-19	204	
during COVID-19	196	-3.9

Table 3 (continued)

Diagnosis sites	Number of RT	Difference (percentages)
Bladder		
patients > 70 years		
before COVID-19	22	
during COVID-19	23	+4.5
patients < 70 years		
before COVID-19	11	
during COVID-19	14	+27.3
total		
before COVID-19	33	
during COVID-19	37	+12.1
Colo-rectum		
patients > 70 years		
before COVID-19	75	
during COVID-19	78	+4.0
patients < 70 years		
before COVID-19	128	
during COVID-19	130	+1.6
total		
before COVID-19	193	
during COVID-19	208	+7.8
Bone		
patients > 70 years		
before COVID-19	141	
during COVID-19	119	-15.6
patients < 70 years		
before COVID-19	203	
during COVID-19	237	+16.7
total		
before COVID-19	344	
during COVID-19	356	+3.5
Head and neck**		
patients > 70 years		
before COVID-19	64	
during COVID-19	69	+7.8
patients < 70 years		
before COVID-19	151	
during COVID-19	151	0
total		
before COVID-19	215	
during COVID-19	220	+2.3
Brain		
patients > 70 years		
before COVID-19	65	
during COVID-19	45	-30.8
patients < 70 years		
before COVID-19	142	
during COVID-19	165	+16.2
total		
before COVID-19	207	
during COVID-19	210	+1.4
Total		
patients > 70 years		
before COVID-19	931	
during COVID-19	779	-16.3
patients < 70 years		
before COVID-19	1,699	
during COVID-19	1,672	-1.6
total		
before COVID-19	2,630	
during COVID-19	2,451	-6.8

COVID-19 – corona virus disease 2019; Before COVID-19 – period from January 2020 to March 2020; during COVID-19 – period from March 2020 to May 2020; RT – radiotherapy; * – cervical, corpus uteri cancer, ovarian, uterine, vaginal, and vulvar cancers; ** – head and neck, hypopharynx, larynx, supraglottis, lip and oral cavity, nasal cavity and sinuses, nasopharynx, oropharynx, pharynx, salivary glands, and thyroid gland cancers.

Note: only the most common places were analyzed.

Brachytherapy applications

The total number of annual BT applications in the previous six years is shown in Figure 4.

The total monthly number of BT applications between 2019 and 2021 is shown in Figure 5.

Figure 6 shows the relative difference between the monthly numbers of BT applications for 2020 and 2021 in relation to 2019.

Descriptive statistical analysis was performed for period 0 (n_0 = 14 months, when we consider that there was no influence of COVID-19 on the number of EBRT fractions) and period 1 (n_1 = 14 months, the period when the pandemic was present); the results are shown in Table 4.

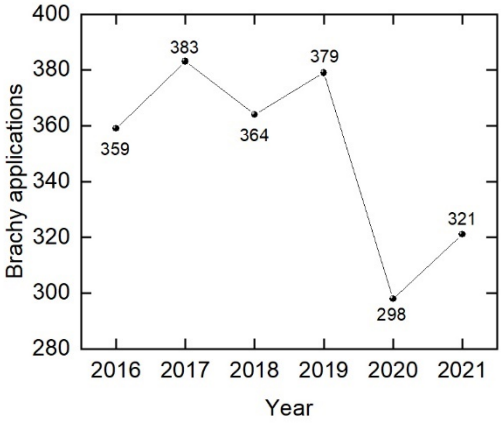

Fig. 4 – Average number of brachytherapy (Brachy) applications in the period 2016–2021.

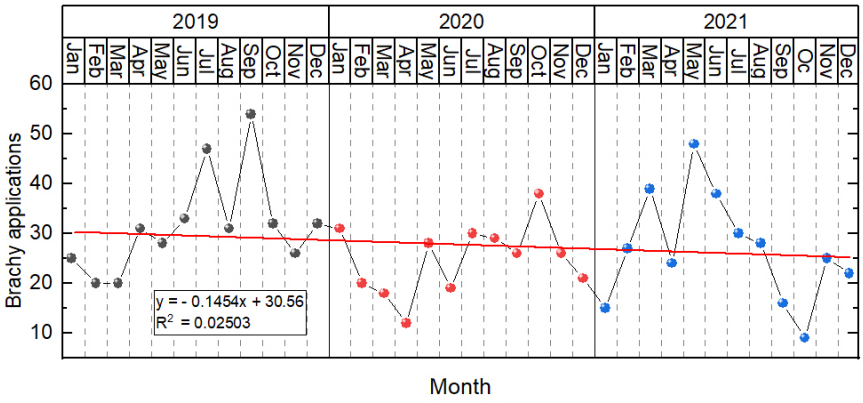

Fig. 5 – Monthly number of brachytherapy (Brachy) applications for the period January 2019 – December 2021.

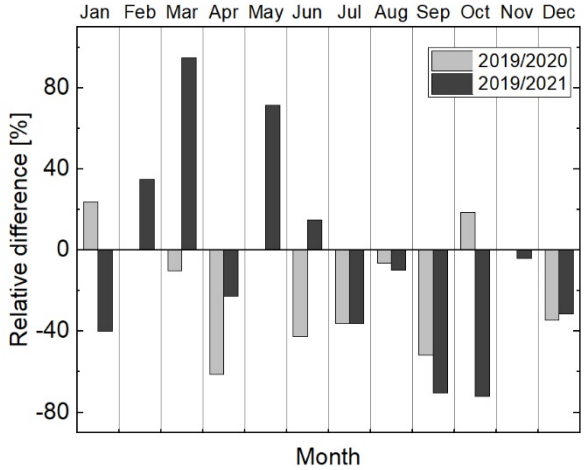

Fig. 6 – Relative difference of the monthly number of brachytherapy applications for 2020 and 2021, in relation to 2019.

Table 4

Descriptive statistics of brachytherapy (BT) applications for period before and during COVID-19

COVID -19	Number of months	BT/month	
		median	min–max
Before	14	31	20–54
During	14	26	12–39

COVID-19 – corona virus disaese 2019.

The result of the Shapiro-Wilk normality test performed for the values of the differences of the monthly BT applications (mean 5.9, SD 9.0) of the previously mentioned period (n_0-n_1) was significant (p = 0.009), which indicates that there is no normal distribution of the obtained results. Therefore, a nonparametric Wilcoxon signed-rank test was performed (for data of 28-month BT applications; Z = - 2.42, p = 0.016).

Discussion

External beam radiotherapy

The average number of daily irradiated EBRT patients in the BL RT Center grew from 2016–2019 and experienced a sharp decline in 2020. At the annual level, the total number of EBRT fractions in 2020 and 2021 decreased by 9.3% and 7.3%, respectively, compared to 2019 (Figure 1).

Figure 2 clearly shows the declining trend of the regression line obtained based on the number of weekly EBRT fractions from 2019–2021 (the direction coefficient is negative). The mean weekly number of EBRT fractions delivered in period 0 was 680.5 (SD 67.4), and in period 1 was 617.1 (SD 96.4), which is in accordance with the results of the studies by Martinez et al. [6], Chauhan et al. [9], and Nierengarten [10].

Significant declines in the number of weekly fractions in May 2020 and March 2021 are evident (Figure 2) due to the COVID-19 pandemic, i.e., the transition of other oncology services to the COVID-19 department. This is no different from a study conducted in the United States, where RT centers reported a reduction of treatments from 20% up to 39% (during April 2020) [11]. Switzerland also had a significant reduction in daily activity during April 2020 [12]. A study by Gonnelli et al. [13] for the period March end of May, shows an increase in RT treatments by 5%, which is not in accordance with our results. The Chauhan et al. [9] study agrees with our results for the period from January to the end of May 2020, which were moved two months forward (the pandemic in India started two months earlier than in RS). Amador et al. [14] reported the impact of the COVID-19 pandemic on the care of cancer patients in Spain, comparing the March–June 2019/20 periods, the number of new patients decreased by 20.8%. A study from Brazil [15] noted a 10% reduction in the number of treated patients and a 26% reduction in the number of RT sessions. Finally, the number of patients who received radiotherapy in China also declined by 31.3% during the pandemic period [16].

During the period April–May 2020 (weeks 17–21), the weekly EBRT fractions decreased by 15.8% to 67.9% compared to the same period in 2019, which is in accordance with the results of the study by Vaandering et al. [17] (decline of 45.4% in April 2020). Another significant decrease in the number of weekly patients occurred at the end of 2020 (44–49 weeks, i.e., November–December 2020), from 17.5% to 26.8%. From the 9th to the 14th week of 2021 (March), a new "wave" followed from 20.4 % to 42.4% (Figure 3).

Based on descriptive statistical analysis (Table 2), the mean values of weekly EBRT fractions before the onset of the COVID-19 virus are higher than during the pandemic, while the SD is lower. Parametric one-tailed paired samples *t*-test showed that the occurrence of the COVID-19 pandemic had a statistically significant effect [t (60) = 4.627, $p < 0.05$] on the reduction in the number of weekly EBRT fractions in BL RT Center (comparing 14 months before and during the pandemic).

A greater reduction in EBRT patients between period 0 and period 1 was seen for patients aged 70 years or older compared with those aged younger than 70 years (16.3% vs. 1.6%), which is in accordance with the results of the study by Spencer et al. [4]. Patients older than 70 years accounted for 33.7% and 31.8% of the total number of patients in periods 0 and 1, respectively, which is more than the results of the Chauhan et al. [9] study (about 5% for the first half of period 1).

The largest decrease in the number of EBRT patients older than 70 years by diagnosis is found in GYN (39.6%), breast (29.7%), brain (30.8%), lung (15.4%), prostate (13.1%), bone (15.1%), and skin (84%), which is in accordance with the results of the other study [9, 13,17].

In the group of patients younger than 70 years, we had a decrease in the number of those patients with GYN (21.2%), breast (20.3%), lung (17.9%), and skin (61.5%) cancers, while we had an increase in the number of patients diagnosed with prostate, bone, brain, and bladder cancers (Table 3). The reasons were that surgery and biopsies were stopped or reduced by 50% but also because of health care measures taken nationally and locally to limit the spread of the pandemic.

Brachytherapy

The number of BT applications in 2020 and 2021 is lower by 21.4% and 15.3%, respectively, compared to 2019 (Figure 4).

Figure 5 shows that the regression line has a negative direction coefficient, i.e., it decreased with time from 2019–2021. The total number of BT applications in period 0 (430)

and period 1 (352) indicates a decline in BT applications by 18.1%. The mean monthly number of BT applications delivered in period 0 was 30.7 (SD 9.7), and in period 1 was 25.1 (SD 7.8).

We had the most significant drop in the number of BT applications in April (61.3%) and September (51.9%) 2020 compared to the same period in 2019. Compared to the same period in 2019, there was a 40% decrease in January 2021, and a 95% increase in March 2021 (Figure 6). Based on descriptive statistical analysis (Table 4), the median values of monthly BT applications before the onset of the COVID-19 were higher than during the pandemic (31 vs. 26, respectively).

COVID-19 had a statistically significant effect on reducing the number of monthly BT applications in the BL RT Center according to the nonparametric Wilcoxon signed-rank test (for data of 28 monthly BT applications; Z = -2.42, $p = 0.016$).

Conclusion

A statistically significant decline in EBRT and BT treatments in the BL RT Center was observed in the first 14 months of the COVID-19 pandemic.

The pandemic's "waves" typically "closed" medical departments needed for oncology patient diagnosis and treatment, turning them into COVID-19 wards. Therefore, some oncology patients who would have had indications for RT never reached it.

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Received on October 18, 2021
Accepted on March 8, 2022
Online First March 2022