Clinical and Experimental Obstetrics & Gynecology

Clin. Exp. Obstet. Gynecol. **2022**; 49(11): 253
https://doi.org/10.31083/j.ceog4911253

Original Research

Management of Breast Cancer during COVID-19 Pandemic: Trends of the Intervals to Radiotherapy in a Single Center Cohort

Jacopo Di Muzio[1,*], Valeria Chiofalo[1], Cristiano Grossi[1], Francesco Olivero[1], Simona La Sala[1], Anna Mussano[1], Umberto Ricardi[1]

[1]Department of Oncology, University of Torino, 10125 Torino, Italy
*Correspondence: jacopo.dimuzio@gmail.com (Jacopo Di Muzio)
Academic Editor: Giuseppe Carlo Iorio
Submitted: 30 May 2022 Revised: 12 August 2022 Accepted: 16 August 2022 Published: 14 November 2022

Abstract

Background: COVID-19 pandemic led to a drastical rearrangement within healthcare staff and facilities. Due to its high incidence, management of breast cancer (BC) was particularly critical during the COVID-19 pandemic, and the reduction of healthcare staff and facilities influenced the timing in BC care. The aim of the present report was to analyze the timing from diagnosis to surgery, from diagnosis to radiotherapy (RT) start and from surgery to RT start during the COVID-19 pandemic. **Methods**: We retrospectively collected data of women with BC treated with Radiotherapy (RT) after surgery at our Institution (Department of Oncology, Radiation Oncology, S. Anna Hospital, Turin, Italy), during the COVID-19 pandemic. To evaluate patients' data according to the different stages of the pandemic, we identified 4 periods: first wave (FW), first reopening (FR), second wave (SW) and second reopening (SR). Among the 4 periods, we divided patients in 2 groups: patients who underwent adjuvant chemotherapy (CT) before RT (CT-group), and those who received exclusive adjuvant RT (non-CT group). **Results**: from early March 2020 to 31 March 2022, 464 patients were treated. After patients' selection, data from 390 patients were analyzed. Overall, the average interval between biopsy and RT in the non-CT group was 202 days during the FW (101–386), 172 days (85–242) during the FR, 136 days (69–366) during the SW, 159 days (77–455) during the SR. In the CT group, the average interval from biopsy to RT start was 337 days (224–495) during the FW, 277 days (209–496) during FR, 297 days (220–419) during the SW, and 261 days (169–447) during the SR. **Conclusions**: we reported our experience during these two years of the pandemic and how COVID-19 impacted the timing of the management of patients with BC. Overall, during the viral waves there was a remarkable increase in the interval between biopsy/surgery and RT. Nonetheless, we managed to keep optimal BC care and favorable interval trends were observed with reopening phases.

Keywords: breast cancer; radiation therapy; COVID-19; surgery; timing

1. Introduction

On 30 January 2020, World Health Organization (WHO) declared the Coronavirus outbreak in China an International public health emergency. On 11 March 2020, WHO defined the spread of COVID-19 as a pandemic spread throughout the planet. Thereupon, many countries adopted different strategies to contain the spread of the virus. After the first outbreak in Wuhan region, Italy was the second most affected Country with 102,669 cases (10,007 among health workers) and 11,875 deaths [1].

The Italian government declared a lockdown on 9 March 2020. A new phase in Italy, with partial re-openings, started on 4 May 2020. However, due to a second viral wave, restrictions were introduced again from 13 October 2020 with a new lockdown established from 3 December 2020 to 6 April 2021. The Italian government extended the state of emergency until 31 March 2022.

Overall, this situation had a broad impact on healthcare delivery, including cancer care [2–5]. The European Society for Radiotherapy and Oncology (ESTRO) conducted a report in May 2020 that showed how 57% of Radiation Oncologist practices experienced a reduction in staff due to family care (29%), staff illness (26%), and, staff transfer to other areas (13%) [3].

Breast cancer (BC) is the first female cancer worldwide (with more than 2 million new cases and more than 650,000 death per year) [6]. In Italy, about 55,000 new cases of BC were diagnosed in 2020 [7].

Breast cancer management is multidisciplinary and requires coordination of many healthcare professionals as general surgeons, plastic surgeons, radiologists, oncologists, pathologists, anesthesiologists, and primary care. During the pandemic, medical resources have been reorganized and reallocated towards the frontline of pandemic control in responding to the waves of infections and hospitalization, resulting in a sudden temporary suspension of non-urgent activities, including cancer screening services worldwide [8]. Furthermore, postponing BC surgeries helped reallocate healthcare staff to the new COVID departments opened in the hospitals.

Therefore, during the pandemic it has been challenging to maintain an optimal timing within the different stages of BC diagnosis and treatment.

Despite data from randomized trials are missing, in patients not undergoing adjuvant chemotherapy (CT) after surgery, it is recommended to start radiotherapy (RT) after surgical wound are healed and within 8–20 weeks. In patients receiving adjuvant CT after surgery, a sequential schedule is preferred in order to minimize the possible adverse events from the concomitant administration of CT and RT. It is recommended to start RT within 4–6 weeks from the end of CT [9].

Several international scientific societies and experts' consensus published new recommendations for BC patients to keep providing routine oncologic care and limit exposure [10–21].

A selective omission or delay of radiation therapy has been considered a valid strategy to limit the viral spread without compromising oncologic outcomes. All the guidelines agreed on considering the omission of RT for elderly BC patients in the post-operative setting, with particular characteristics such as age >65 or 70, tumor ≤2 or 3 cm in dimension with negative surgical margins, Luminal A (ER+, PgR+, Her2–), negative nodes, and all that cases where endocrine therapy would be indicated [22]. Regarding RT, the use of moderate hypofractionation and ultra-hypofractionation had a certain appeal for selected BC patients during the COVID-19 pandemic.

While moderate hypofractionation was already largely used [14,23], with the latest updates from FAST and FAST forward trials, ultra-hypofractionation started to be routinely adopted during the pandemic [24–26].

Thus, considering this background, we decided to evaluate the timing in BC care at our Institution during the different phases of this pandemic, focusing on RT.

2. Materials and Methods

We retrospectively collected data from patients treated with RT after surgery for BC at our Institution (Department of Oncology, Radiation Oncology, the Health and Science Academic Hospital, S.Anna Hospital, Turin, Italy), during the COVID-19 pandemic.

The aim was to analyze the timing from biopsy to surgery, between biopsy and RT start, and from surgery to RT start. Biopsy was defined as the date when the first histologic sample was taken (for core biopsy, punch biopsy or fine needle aspiration of breast).

From the start of the pandemic (early March 2020) to the end of the state of emergency (31 March 2022), 464 women were treated.

Patients treated for a relapse, palliative cases, and patients who underwent neoadjuvant chemotherapy were excluded.

Therefore, data of 390 patients were analyzed.

We identified, during the pandemic, 4 different periods, according to the restrictions and the waves of viral spread:

- First Wave (FW – from early March 2020 to 31 May 2020);

- First Re-opening (FR – from 1 June to 12 October 2020), with partial ad progressive releasing of restrictions;

- Second Wave (SW – from 13 October 2020 to 6 April 2021) with new progressive restrictions and a second lockdown;

- Second Reopening (SR – from 7 April 2021 to 31 March 2022), characterized by the availability of vaccinations and no new restrictions or lockdown.

Within the 4 periods, we also divided patients into 2 groups: those who underwent adjuvant chemotherapy (CT group), and patients who underwent exclusive adjuvant RT (non-CT group).

Our Institutional Review Board authorized the study.

3. Results

The Median age at the diagnosis was 62 years (28–88). Most of the patients, 354 (90.8%), were treated with breast conservative surgery (BCS – wide resection) and subsequent adjuvant External Beam Radiotherapy (EBRT); 36 women (9.2%) underwent mastectomy followed by adjuvant EBRT.

In 273 cases (70%) the sentinel lymph node was removed, a nodal sampling was performed in only one case, and 53 patients (13.6%) underwent axillary dissection; 63 patients (16.2%) underwent exclusive BCS with no nodal treatment (19/63 due to their comorbidities, and 44/63 had carcinoma *in situ*).

In terms of staging, data were heterogenous. In most cases (133; 34.1%) there was a single lesion with a size ranging between 1 and 2 cm (T1c); 87 (22.31%) cases had a lesion size between 0.5–1 cm (T1b) one of which was multifocal; in 16 (4.1%) cases the size was <0.5 cm (T1a) and 6 (1.54%) patients had a T1mi stage; 82 (21.03%) women had a lesion >2 cm (T2) and 14 of them had a multifocal lesion; 11 (2.82%) patients had a lesion >5 cm (T3), 4 of which multifocal.

Skin involvement (T4) was recorded only in one case. Two patients had a Tx but underwent axillary dissection because of multiple pathologic lymph nodes seen at the imaging.

As for the histology, most of the patients (338, 86.7%) had a non-special histotype (NST). A small number 52 women (13.3%) had a lobular carcinoma. Surgical margins were negative in 348 (89.5%) patients, and in 41 (10.5%) margins were positive. The decision on adjuvant treatment was taken after discussing each case in a multidisciplinary tumor board.

Adjuvant Chemotherapy (CT) was administered in 80 patients (20.51%) with Epirubicine and Ciclofosfamide (EC) for 4 cycles, followed by 12 cycles with Taxol.

Most patients were treated with a schedule with a total dose of 40.05 in 15 fractions; when needed a boost on surgical bed was administered with a total dose of 48 Gy in 15 fractions.

Table 1. Timing in BC care for CT and non-CT group during pandemic's different period.

	Non-CT group	CT group
First Wave (early March 2020–31 May 2020)		
N° patients	46	20
Average time biopsy - surgery	70 days (13–194)	69 days (41–113)
Average time surgery – RT	132 days (71–255)	268 days (163–437)
Average time biopsy – RT	202 days (101–386)	337 days (224–495)
First Re-openings (1 June 1 2020–12 October 2020)		
N° patients	61	13
Average time biopsy - surgery	69 days (23–166)	69 days (28–116)
Average time surgery – RT	103 days (23–186)	208 days (119–406)
Average time biopsy – RT	172 days (85–242)	277 days (209–496)
Second Wave (13 October 2020–6 April 2021)		
N° patients	56	12
Average time biopsy - surgery	61 days (3–189)	65 days (35–157)
Average time surgery – RT	75 days (37–190)	232 days (168–330)
Average time biopsy – RT	136 days (69–366)	297 days (220–419)
Second Re-openings (7 April 2021–31 March 2022)		
N° patients	147	35
Average time biopsy - surgery	74 days (6–224)	50 days (19–93)
Average time surgery – RT	85 days (40–261)	202 days (126–390)
Average time biopsy – RT	159 days (77–455)	261 days (169–447)

BC, breast cancer; RT, Radiotherapy; CT, Chemotherapy.

Ultra-hypofractionated schedules were also used: 3 patients (0.76%) received 26 Gy in 5 fractions (daily), and 11 patients (2.82%) were treated with 28 Gy in 5 fractions, one fraction per week.

Only 12 patients (3.1%) tested positive for COVID-19 during the treatment period (surgery, CT or RT). A median of 9 lost days (5–19) for each patient tested positive during RT was observed.

During the FW 66/390 women (16.9%) were treated. Among these patients, 20 were in the CT-group and 46 in the non-CT group. In the FR period 74/390 patients (19%) were treated, 61 in non-CT group, 13 in CT group.

During the SW 68/390 women (17.4%) were treated, 12 in the CT-group and 56 in the non-CT group.

We treated 182/390 patients (46.7%) in the SR period, 35 in the CT-group and 147 in the non-CT-group.

Data showing the intervals between the different periods (biopsy to surgery, surgery to RT start, and biopsy to RT start) are shown in Table 1.

Trends of the intervals among the 4 periods of observation are shown in Figs. 1,2,3.

During RT, 7/12 patients tested positive for COVID-19. During the FW, 2 patients tested positive for COVID-19 and lost 11 and 19 days of RT. In the SW, only one patient lost 10 days of RT. The remaining four patients developed Sars-COV2 infection during the SR period, and none of them lost more than 9 RT sessions.

Overall, the average interval between biopsy and RT in the non-CT group was 202 days during the FW (101–386), 172 days (85–242) during the FR, 136 days (69–366) during the SW, 159 days (77–455) during the SR.

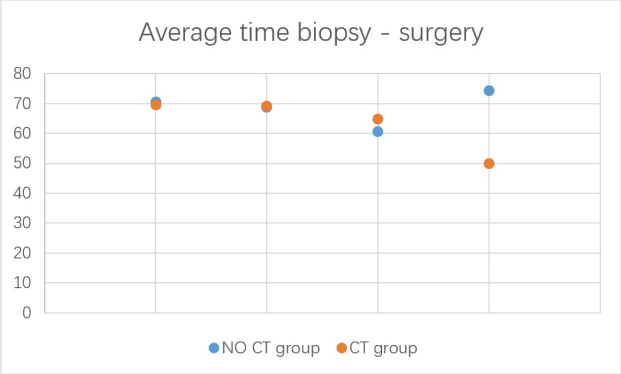

Fig. 1. Trends of average intervals (days) from biopsy to surgery during the 4 periods (from left to right: FW, FR, SW and SR), in non-CT group (blue spots) and in CT group (orange spots). FW, first wave; FR, first reopening, SW, second wave; SR, second reopening; CT, Chemotherapy.

In the CT group, the average interval from biopsy to RT start was 337 days (224–495) during the FW, 277 days (209–496) during FR, 297 days (220–419) during the SW, and 261 days (169–447) during the SR.

4. Discussion

During our observation period, there has been a significant increase of COVID-19 cases in the Region of our institution (Piemonte, Italy), with a total of 1,050,370 cases overall. Considering the four different periods we analyzed,

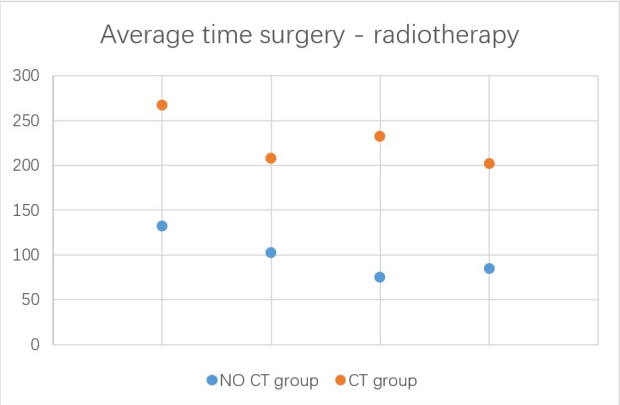

Fig. 2. Trends of average time (days) from surgery to RT start during the 4 periods (from left to right: FW, FR, SW and SR), in non-CT group (blue spots) and in CT group (orange spots). RT, Radiotherapy; FW, first wave; FR, first reopening, SW, second wave; SR, second reopening; CT, Chemotherapy.

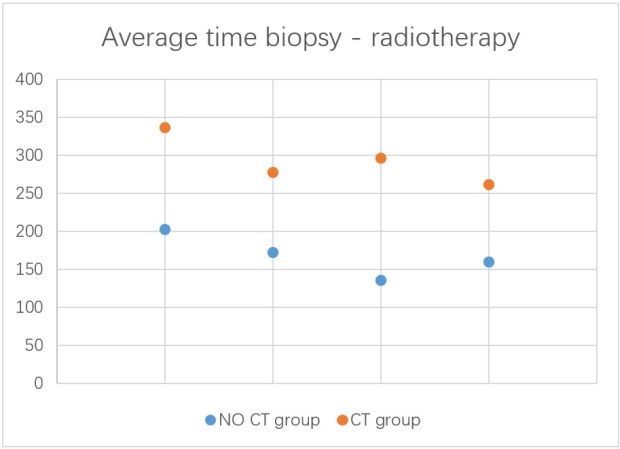

Fig. 3. Trends of average time (days) from biopsy to RT start during the 4 periods (from left to right: FW, FR, SW and SR), in non-CT group (blue spots) and in CT group (orange spots). RT, Radiotherapy; FW, first wave; FR, first reopening, SW, second wave; SR, second reopening; CT, Chemotherapy.

there were, respectively: 9301 cases during the FW, 29,656 during the FR, 279,205 during the SW and 732,208 during the SR [27].

Overall, the interval between biopsy/surgery and RT start in the non-CT group was longer during the first wave, then decreased during the first reopening and the second wave. However, it increased again during the second reopening. During the SR, despite the bigger number of COVID cases, thanks to a massive vaccination campaign, patients have been able to access treatment more efficiently, and healthcare professionals were also more protected. Therefore, this trend could be explained considering the progressive re-openings and operating rooms saturation.

On the other hand, in the CT group, the interval between biopsy/surgery and RT directly depended on reopening phases, with shorter intervals during FR and SR.

To explain the difference between the average time from biopsy to surgery between non-CT group (65 days) and CT group (50 days) during the SW, we hypothesized that patients with more aggressive disease at diagnosis or with a more extensive disease at the staging exams (thus, where adjuvant CT was indicated), took precedence.

Several experiences reporting on BC management during the Pandemic were published [2,22,28].

A retrospective Canadian study analyzed the time interval from biopsy to surgery and from surgery to oncology consultation (medical oncology or radiation oncology), in 2 cohorts of patients treated for BC in 2019 (99 patients) and 2020 (162 patients). Overall, wait from core biopsy to surgery was 40 days in 2019 vs 45 days in 2020 (p = 0.18). The wait time from biopsy to BC oncology consultation (medical oncology or radiation oncology) was 77 days in 2019 and 75 days in 2020 [29]. This is consistent with our result. The authors divided the 2020 cohort in 3 time groups, reflecting the changing hospital policies during the pandemic. The interval from biopsy to surgery decreased during the pandemic. This trend was explained by a strong co-operation between healthcare providers, administration of neoadjuvant therapy when needed, and reorganization of the operating room waiting list according to the BC risk-group. In this cohort, authors also reported also an increase in the use of local anaesthesia to avoid intubation when not necessary, due to the reduced anaesthesiologists availability.

During the lockdown few studies reported that adjuvant RT con be delayed up to 3 moths after surgery [13,30–32].

A retrospective study of patients with early-stage breast cancer evaluated time to treatment initiation (TTI) between a cohort of patients diagnosed between 1 January 2020, and 15 May 2020 (164 patients) and an unaffected cohort diagnosed between 1 January 2018 and 15 May 2018 (202 patients) [33]. The mean unadjusted TTI in 2018 was 45 days (median 41, Interquartile Range (IQR) 29–55) versus 44 days (median 36, IQR 27–52) in 2020 cohort. In the 2020 cohort, the mean time from presentation to histologic diagnosis was 38 days (median 23, IQR 13–48), from histologic diagnosis to initial appointment 17 days (median 14, IQR 8–21), and from initial appointment to first treatment start 27 days (median 22, IQR 15–33). Histologic diagnosis was defined as the date of the histologic result and initial treatment was the recorded date when a patient received their first step in treatment (surgery, chemotherapy, hormonal therapy, or radiation therapy). In the 2020 cohort, initial therapy included upfront hormonal therapy in 23.2% of patients. Overall, there was no difference in TTI among patients diagnosed in 2020 compared with 2018. This has been explained with the increasing use of upfront hormonal therapy for early-stage patients with HR1, HER2 disease.

Authors pointed out that despite a care delay in 44.4% of patients in the COVID-19 cohort, most of this reflected a delay in surgery that is not captured in the TTI end point. In our cohort no upfront hormonal therapy was administred. Therefore, our data reflect the real-life delay in surgical BC first treatment. Nevertheless, overall the time from histologic diagnosis to initial treatment was 44 days in the 2020 cohort, which is less than our timing between biopsy and surgery, since we calculated it from the date of the sampling, taking into account also the pathology timing needed to have the result.

A retrospective Canadian study analyzed the delay in RT during COVID-19 pandemic between March 2020 and August 2020. Delay was calculated from the date when the patient is "ready to start" treatment to the date when the first radiation treatment is delivered. This is the methodology required locally for government reporting. Authors reported an average delay in BC of 30 days. It was also reported an increase in moderate hypofractionated schedules for BC RT (+287%) [28].

A retrospective Italian study analyzed the delay on BC treatments during the first wave comparing 2 groups: patients treated during the lockdown and patients treated in pre-lockdown. The average time between biopsy and surgery was 56 days (range 6–134) [2]. Considering the delay period between diagnosis and surgery our results are only slightly different from once presented in this article.

Another series from Yale School of Medicine reported an acceptable delay of RT stratifying the patient in 5 categories characterized by clinical and histological parameters. Depending on risk factors, a delay from 6 to 12 weeks is acceptable for patients with positive lymph nodes, positive margins, young age; a delay between 16–20 weeks could be acceptable for early-stage BC with negative margins, hormone receptor + and age >50. Only patients with inflammatory BC and progression during neoadjuvant CT should begin RT before 6–8 weeks [22].

According to these considerations, the non-CT group in our cohort had an average acceptable delay. As for the delay of RT in our CT group, there are many confounding factors due to the administration of systemic therapy, but, according to the standard of our department, as mentioned before, RT should begin within 6 weeks from the end of CT.

Our study has several limitations. One of these is the relatively small sample size and the single-institution cohort design. We aknowledge the lack of a control group and the lack of statistical analysis. Nonetheless, our aim was to describe the real-life practice during the pandemic.

Lastly, it's necessary to point out that only few patients of our series tested positive for COVID-19 during treatment (12/390) and only 7 out of 12 patients became positive during RT and had to lose treatment days. However, the major cause of delay, as already mentioned, was due to the shifting of resources (mainly nurses and anaesthesiologists) to COVID departments.

5. Conclusions

We reported our experience during these two years of the pandemic and how COVID-19 impacted the timing of the management of patients with BC.

Many aspects influenced the timing such as the reduction of healthcare staff and the lack of operating rooms. Overall, during the viral waves there was a remarkable increase in the interval between biopsy/surgery and RT. Nonetheless, we managed to keep optimal BC care and favorable interval trends were observed with reopening phases.

Despite the several limitations of this analysis, we believe that a descriptive report of the real-life clinical practice during the pandemic could reveal the critical points in cancer care and, subsequently, reflect on the possible improvements to face a worldwide emergency situation.

Abbreviations

BC, Breast Cancer; BCS, Breast Conservative Surgery; CT, ChemoTheray; EBRT, External Beam RadioTherapy; FR, First Reopening; FW, First Wave; ICU, intensive care unit; RT, RadioTherapy; SR, Second Reopening; SW, Second Wave.

Author Contributions

All authors significantly contributed to the present manuscript. CG, FO, AM and SLS collected the clinical data. JDM, VC, FO and UR wrote the manuscript. JDM, AM, VC and UR reviewed the manuscript. SLS and CG performed the descriptive analysis and designed the graphs. All authors read and approved the final manuscript.

Ethics Approval and Consent to Participate

Given the characteristics of the report, the Internal Review Board of the Department of Oncology of the University of Turin (Turin, Italy) approved the study was not required approval. All subjects gave their informed consent for inclusion before they participated in the study.

Acknowledgment

Thanks to all the secretarial staff for their help in reviewing the patients' records.

Funding

This research received no external funding.

Conflict of Interest

The authors declare no conflict of interest.

References

[1] Casella D, Fusario D, Cassetti D, Miccoli S, Pesce AL, Bernini A, *et al*. The patient's pathway for breast cancer in the COVID-19 era: an Italian single-center experience. The Breast Journal. 2020; 26: 1589–1592.

[2] Vanni G, Tazzioli G, Pellicciaro M, Materazzo M, Paolo O, Cattadori F, *et al*. Delay in Breast Cancer Treatments During the First COVID-19 Lockdown. A Multicentric Analysis of 432 Patients. Anticancer Research. 2020; 40: 7119–7125.
[3] Slotman BJ, Lievens Y, Poortmans P, Cremades V, Eichler T, Wakefield DV, *et al*. Effect of COVID-19 pandemic on practice in European radiation oncology centers. Radiotherapy and Oncology. 2020; 150: 40–42.
[4] ASTRO: COVID-19's impact on radiation. 2020. Available at: https://www.astro.org/ASTRO/media/ASTRO/News%20and%20Publications/PDFs/ASTROCOVID19Survey1-ExecSummary.pdf (Accessed: 3 May 2022).
[5] Buonomo OC, Materazzo M, Pellicciaro M, Caspi J, Piccione E, Vanni G. Tor Vergata University-Hospital in the Beginning of COVID-19-Era: Experience and Recommendation for Breast Cancer Patients. In Vivo. 2020; 34: 1661–1665.
[6] Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, *et al*. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA: A Cancer Journal for Clinicians. 2021; 71: 209–249.
[7] AIOM-Airtum. I Numeri del Cancro in Italia 2020. AIOM-AIRTUM-Siapec-Iap. 2020. Available at: https://www.aiom.it/wp-content/uploads/2020/10/2020_Numeri_Cancro-operatori_web.pdf (Accessed: 3 May 2022).
[8] Hamilton W. Cancer diagnostic delay in the COVID-19 era: what happens next? The Lancet Oncology. 2020; 21: 1000–1002.
[9] Linee Guida AIOM Neoplasie della Mammella 2021. 2021. Available at: https://www.aiom.it/wp-content/uploads/2021/11/2021_LG_AIOM_Neoplasie_Mammella_11112021.pdf.pdf (Accessed: 3 May 2022).
[10] Daraï E, Mathelin C, Gligorov J. Breast Cancer Management during the COVID 19 Pandemic: French Guidelines. European Journal of Breast Health. 2020; 16: 160–161.
[11] Soran A, Gimbel M, Diego E. Breast Cancer Diagnosis, Treatment and Follow-Up During COVID-19 Pandemic. European Journal of Breast Health. 2020; 16: 86–88.
[12] Çakmak GK, Özmen V. Sars-CoV-2 (COVID-19) Outbreak and Breast Cancer Surgery in Turkey. European Journal of Breast Health. 2020; 16: 83–85.
[13] Coles CE, Aristei C, Bliss J, Boersma L, Brunt AM, Chatterjee S, *et al*. International Guidelines on Radiation Therapy for Breast Cancer during the COVID-19 Pandemic. Clinical Oncology. 2020; 32: 279–281.
[14] Curigliano G, Cardoso MJ, Poortmans P, Gentilini O, Pravettoni G, Mazzocco K, *et al*. Recommendations for triage, prioritization and treatment of breast cancer patients during the COVID-19 pandemic. The Breast. 2020; 52: 8–16.
[15] de Azambuja E, Trapani D, Loibl S, Delaloge S, Senkus E, Criscitiello C, *et al*. ESMO Management and treatment adapted recommendations in the COVID-19 era: Breast Cancer. ESMO Open. 2020; 5: e000793.
[16] Dietz JR, Moran MS, Isakoff SJ, Kurtzman SH, Willey SC, Burstein HJ, *et al*. Recommendations for prioritization, treatment, and triage of breast cancer patients during the COVID-19 pandemic. the COVID-19 pandemic breast cancer consortium. Breast Cancer Research and Treatment. 2020; 181: 487–497.
[17] Ontario Health. Pandemic planning clinical guideline for patients with cancer. 2020. Available at: https://www.cancercareontario.ca/sites/ccocancercare/files/guidelines/full/PandemicPlanningClinicalGuidelines-Cancer.pdf (Accessed: 10 May 2022).
[18] Wright JL, Alcorn SR, McNutt T, Han-Oh S, Gonzales R, Lan L *et al.* An integrated program in a pandemic: Johns Hopkins Radiation Oncology Department. Advances in Radiation Oncology. 2020; 5: 666–672.
[19] Braunstein LZ, Gillespie EF, Hong L, Xu A, Bakhoum SF, Cuaron J, *et al*. Breast Radiation Therapy under COVID-19 Pandemic Resource Constraints—Approaches to Defer or Shorten Treatment from a Comprehensive Cancer Center in the United States. Advances in Radiation Oncology. 2020; 5: 582–588.
[20] Yu, JB. COVID Yale radiation oncology flowchart. ROhub. 2020. Available at: https://rohub.astro.org/communities/community-home/digestviewer/viewthread?MessageKey=9ac16312-3905-4303-bd5b-22549c0be6e6&CommunityKey=881f9cc8-10ec-45b6-ad5f-5ff678d86fdd&tab=digestviewer#bm61dc0ea1-9fd7-4b65-a73c-65e6568fbbf9 (Accessed: 12 May 2022).
[21] Wakefield DV, Sanders T, Wilson E, Hubler A, DeWeese T, Smith BD, *et al*. Initial Impact and Operational Responses to the COVID-19 Pandemic by American Radiation Oncology Practices. International Journal of Radiation Oncology Biology Physics. 2020; 108: 356–361.
[22] Knowlton CA. Breast Cancer Management during the COVID-19 Pandemic: the Radiation Oncology Perspective. Current Breast Cancer Reports. 2022; 14: 8–16.
[23] Smith BD, Bellon JR, Blitzblau R, Freedman G, Haffty B, Hahn C, *et al*. Radiation therapy for the whole breast: Executive summary of an American Society for Radiation Oncology (ASTRO) evidence-based guideline. Practical Radiation Oncology. 2018; 8: 145–152.
[24] Brunt AM, Haviland JS, Sydenham M, Agrawal RK, Algurafi H, Alhasso A, *et al*. Ten-Year Results of FAST: a Randomized Controlled Trial of 5-Fraction whole-Breast Radiotherapy for Early Breast Cancer. Journal of Clinical Oncology. 2020; 38: 3261–3272.
[25] Murray Brunt A, Haviland JS, Wheatley DA, Sydenham MA, Alhasso A, Bloomfield DJ, *et al*. Hypofractionated breast radiotherapy for 1 week versus 3 weeks (FAST-Forward): 5-year efficacy and late normal tissue effects results from a multicentre, non-inferiority, randomised, phase 3 trial. Lancet. 2020; 395: 1613–1626.
[26] Hanumanthappa N, Goldsmith C, Sawyer E, Tutt A, Castell F, Azad G, *et al*. Adjuvant Breast Radiotherapy at an Academic Centre during the COVID-19 Pandemic: Reassuringly Safe. Clinical Oncology. 2021; 33: e221.
[27] Ministero della Salute. Avilable at: https://www.salute.gov.it/portale/nuovocoronavirus/homeNuovoCoronavirus.html (Accessed: 12 May 2022).
[28] Roberge D, Delouya G, Bohigas A, Michalowski S. Catching the Wave: Quantifying the Impact of COVID on Radiotherapy Delivery. Current Oncology. 2020; 28: 152–158.
[29] Cadili L, DeGirolamo K, McKevitt E, Brown CJ, Prabhakar C, Pao JS, *et al*. COVID-19 and breast cancer at a Regional Breast Centre: our flexible approach during the pandemic. Breast Cancer Research and Treatment. 2021; 186: 519–525.
[30] Ng CWQ, Tseng M, Lim JSJ, Chan CW. Maintaining breast cancer care in the face of COVID-19. The British Journal of Surgery. 2020; 107: 1245–1249.
[31] Flores-Balcázar CH, Flores-Luna L, Villarreal-Garza C, Mota-García A, Bargalló-Rocha E. Impact of Delayed Adjuvant Radiotherapy in the Survival of Women with Breast Cancer. Cureus. 2018; 10: e3071.
[32] Simcock R, Thomas TV, Estes C, Filippi AR, Katz MS, Pereira IJ, *et al*. COVID-19: Global radiation oncology's targeted response for pandemic preparedness. Clinical and Translational Radiation Oncology. 2020; 22: 55–68.
[33] Hawrot K, Shulman LN, Bleiweiss IJ, Wilkie EJ, Frosch ZAK, Jankowitz RC, *et al*. Time to Treatment Initiation for Breast Cancer During the 2020 COVID-19 Pandemic. JCO Oncology Practice. 2021; 17: 534–540.