Highly specialized Breast Centers did not experience delay of care during COVID-19 pandemic in Italy: the Senonetwork experience

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Abstract

Aim of the study The study aims to evaluate the performance of selected, high-volume, highly specialized, Italian Breast Centers at the time of COVID-19 pandemic (year 2020), compared to pre-pandemic time (year 2019), highlighting differences in terms of clinical presentation of breast cancer (BC) and therapeutic strategies.

Methods Patients’ data were provided by the Senonetwork data warehouse Senonet. In order to examine changes in the surgical and oncological management of BC patients during different phases of COVID-19 pandemic, we took advantage of a selection quality indicators (QIs). We performed the analyses in two time-frames, from July to September (Jul-Sep) (2019 versus 2020) and from October to December (Oct-Dec) (2019 versus 2020).

Results Our analysis did not show any statistically significant difference in terms of diagnosis, surgical, oncological and radiation therapy procedures between the two trimesters 2019 and 2020. Nevertheless, we observed statistically significant differences, favoring 2020, when analyzing time-to surgery and time-to radiotherapy. On the other hand, we observed a significant reduction of neoadjuvant chemotherapy and we did not recollect any data on a major use of neoadjuvant endocrine therapy.

Conclusions In Italian Breast Centers, partners of Senonetwork, we could not observe any treatment delay or change in standard clinical practice for BC care during the 2020 pandemic year, compared to 2019 pre-pandemic year. This finding is in contrast with the globally reported decrease in the performance of the Italian Breast Centers due to the COVID-19 pandemic, and has to be linked to the sharp selection of Senonetwork Breast Centers.

Keywords Covid-19 · Breast cancer · Delay in breast cancer treatment · Breast centers

Introduction

Breast cancer (BC) is a common disease affecting one in eight Western women and is potentially lethal. For the majority of patients with early stage BC, surgery remains the primary treatment and standard guidelines recommend to limit delay from diagnosis to start of treatment, because time-to-surgery, varying from greater than 30–60 days from diagnosis in different studies, has been reported to adversely affect BC prognosis [1–3]. The impact of COVID-19 pandemic on BC oncological surgery worldwide was considerable, and was determined not only by the reduction in surgical procedures, but also by postponement of screening procedures, clinical visits, exams and chemotherapy administration [4]. Early in the COVID-19 pandemic course, both US and European medical societies provided expert opinion regarding how best to manage and prioritize BC patients, issuing recommendations based on individual patient disease risk and hospital resources. For example, surgery delay in clinical stage I, postmenopausal, hormone receptors positive (HR +), HER2 negative tumors, considering neo-adjuvant endocrine therapy, or chemotherapy scheduling modification (switching, when appropriate, from weekly dosing to 2- or 3-weekly dosing) in order to reduce accesses to hospital, was proposed [5].

Aiming to accommodate the many changes brought about by COVID-19, BC care multidisciplinary Italian
associations (composed of oncology, surgery, radiotherapy and radiology experts) collaborated to address recommended treatment strategies. These recommendations had three main goals: (1) to continue safe and effective oncological care for all new and known patients; (2) to decrease the risk of infection for patients and staff; and (3) to ensure the availability of protective materials, staff, and intensive care unit capacity for critically ill patients with COVID-19. Moreover, in line with efforts to prioritize care for COVID-19, national screening programs, including that for BC, were halted from March 2020 to approximately the end of April 2020, with differences in timing and implementational modalities varying across different Italian Regions.

Senonetwork Italia, a non-profit organization devoted to support the quality of multidisciplinary BC care, promoted a national survey to evaluate the impact of COVID-19 pandemic on clinical care of women with BC among Italian Breast Centers [6]. The survey showed how the majority of Italian Breast Centers were operating within hospitals involved in the treatment of COVID-19 patients [6]. Routine activities underwent a major decrease (more than 50%) especially in radiology, surgery, medical oncology and radiotherapy (in 38%, 22%, 11% and 5% of Breast Centers, respectively); in 38% of Breast Centers, the number of weekly procedures was reduced to 38% or more [6]. In addition, a decreased availability of operating room time was reported by the majority of Breast Centers (78%), equally distributed among low- and high-volume centers [6].

The present work aims to evaluate selected, high-volume, highly specialized, Italian Breast Centers performance and clinical presentation of BC at the time of COVID-19 pandemic (year 2020), compared to pre-pandemic time (year 2019), national screening programs, including that for BC, were halted from March 2020 to approximately the end of April 2020, with differences in timing and implementational modalities varying across different Italian Regions.

The present work aims to evaluate selected, high-volume, highly specialized, Italian Breast Centers performance and clinical presentation of BC at the time of COVID-19 pandemic (year 2020), compared to pre-pandemic time (year 2019), taking advantage of the Senonet electronic database, a data warehouse conceived to perform quality assessment and improvement of BC care in Italian Centers.

**Patients and methods**

**Patients’ selection and quality indicators**

Patients’ data were provided by the Senonetwork data warehouse Senonet, which collects data sent by all Centers adhering to the project; Italian Centers involved in the analyses are listed in Table 1. Of note, in order to be part of Senonetwork, Italian Centers should count at least 150 BC cases per year, treated by a dedicated multidisciplinary team of a minimum of one breast surgeon, breast radiologist, breast radiation oncologist, breast medical oncologist and breast pathologist, as per European guidelines [7]. Each single Center provided anonymized patients clinic-pathological data to Senonet, which is protected and managed by a team of dedicated statisticians.

| Table 1 List of Centers participating in Senonet data warehouse |
|---------------------------------------------------------------|
| Breast Centers participating in Senonet                        |
| AOUI Azienda Ospedaliera Universitaria Integrata—Verona       |
| AST Lanciano Vasto Chieti—Ortona                              |
| ASUITS Ospedale Cattinara—Trieste                            |
| Azienda Ospedaliero Universitaria del Policlinico di Modena    |
| Azienda Ospedaliera Universitaria Pisana                      |
| Azienda Ospedaliera S. Giovanni Addolorata—Roma               |
| Breast Unit Multimedica—Milano                                |
| Centro di Senologia Rimini-Sant’Arcangelo di Romagna          |
| Fondazione IRCCS Policlinico San Matteo—Pavia                 |
| Fondazione Poliambulanza—Brescia                              |
| Humanitas Cancer Center Catania                                |
| Humanitas Clinical and Research Center IRCCS, Rozzano—Milan   |
| Istituto Europeo di Oncologia IEO—Milan                       |
| Istituti Clinici Scientifici Maugeri—Pavia                    |
| Nuovo Ospedale di Prato                                       |
| Ospedale Cardinal Massaia di Asti                             |
| Ospedale di Bellaria AUSL di Bologna                          |
| Ospedale di Bolzano                                           |
| Ospedale Mater Sauti Legnago AULSS 9 Veneto—Verona            |
| Policlinico di S. Orsola—Bologna                              |

In order to monitor the quality of breast care, Senonet provided a set of benchmark quality indicators (QIs) [8], a selection of which was used in the present work to examine changes in the surgical and oncological management of patients with BC during the different phases of COVID-19 pandemic. The complete list of the Senonet QIs is shown in Table 2.

With the aim of analyzing specific differences in BC care between the pandemic year 2020 and the pre-pandemic year 2019, highlighting the specific effect of the different COVID-19 waves in Italy, we performed the analyses in two time-frames, considering the third and the fourth trimester of each year, from July to September (Jul–Sep) (2019 versus 2020) and from October to December (Oct–Dec) (2019 versus 2020). The choice of the study periods was based on specific epidemiological data for COVID-19 pandemic waves in Italy during 2019 and 2020 [9, 10].

**Statistical methods**

Quantitative and qualitative variables were described using medians and frequencies/percentages, respectively, as a total and in the four periods. For all the variables, proportion of missing cases was separately documented as proportions and not included in the calculation of distributions.

Differences in the indicators, all defined as proportions, were tested using the chi-squared test for trend in proportions; statistical significance was set at the 0.05 level. For
each indicator, the denominator includes only eligible cases with information available; patients from Centers with more than 25% of missing information were removed from the denominator and the number of units involved in the calculation were documented for each indicator. All the analyses were performed using R version 4.0.5.

### Results

A total of 6287 invasive lesions were analyzed, median age was 62, most of the patients underwent breast conserving surgery (BCS) (67.4%) and less than a quarter of patients performed neo-adjuvant chemotherapy (12.3%). Most of the patients presented with 1 to 2 cm lesions (pT1c) (38.8%) and had node-negative disease (pN0) (64.3%). The great majority of patients had estrogen and progesterone receptor (ER and PgR) positive disease (88.6% and 77.5%, respectively) and were HER2 negative (score 0–1 + or 2 + and FISH negative; 74.7% and 12.4%, respectively); median Ki-67 was 15%, with around half of the population presenting with Ki-67 < 15% and the other half with Ki-67 ≥ 15% (53.2% and 46.8%, respectively). Patients’ characteristics are depicted in Table 3, together with their subdivision into trimesters from both 2019 and 2020. No statistically significant differences were observed across the different time-frames in terms of disease stage at presentation, considering both the size of the primary tumor and the extent of lymph nodes involvement (data not shown). Analyzing differences in terms of pathological characteristics among the time-frames under investigation, we could observe a statistically significant major ER and PgR positive expression in 2020 compared to 2019 (ER + Trend Test $p$-value = 0.006; PgR + Trend Test $p$-value = 0.006), and higher number of HER2 + cases (HER2 Trend Test $p$-value = 0.038), while no significant differences in terms of Ki-67 percentage (Ki-67 Trend Test $p$-value = 0.999) were observed. Indeed, when looking at BC biological subtypes, triple negative (TN) BC was less prevalent in 2020 compared to 2019, while luminal-A like subtype seemed more prevalent in 2020 compared to 2019 (TNBC Trend Test $p$-value = 0.002; luminal-A like Trend Test $p$-value = < 0.001); no statistically significant differences were observed in the differential prevalence of luminal-B like/luminal-B HER2 + and HER2 enriched-like subtypes between 2019 and 2020 (data not shown). We further analyzed specific differences in terms of diagnosis and surgical treatment timing. Nearly all the surgically treated invasive BC cases had a proper radiological (Birads 5) and/or cytological (C5) confirmed pre-surgical diagnosis, across the two years-time considered (Trend Test $p$-value = 0.836), and a similar proportion of patients underwent a magnetic resonance imaging (MRI) before surgery (Trend Test

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**Table 2** List of Senonet Quality Indicators

| List of Senonet Quality Indicators |
|-----------------------------------|
| Record of histological type, grading, hormonal status, HER2 status, margins, vascular invasion & size for invasive forms |
| Record of histological type, grading, hormonal status, margins & size for non-invasive forms |
| MRI before surgery for invasive cases |
| X-ray of surgical specimen in cases treated with conservative surgery with microcalcification only |
| Surgery within 30 days from indication to treatment |
| Surgery within 42 days from the first diagnostic exam |
| Surgery within 60 days from screening mammography |
| Only one surgical operation for invasive cancer treatment |
| Only one surgical operation for non-invasive cancer treatment |
| At least 10 lymph nodes removed for axillary dissection (sampling excluded) |
| Only sentinel lymph nodes examination in pN0 cases |
| No axillary dissection for non-invasive cases |
| Maximum 3 lymph nodes removed as sentinel lymph nodes |
| Conservative surgery for invasive cases up to 3 cm (non-invasive component included) |
| Conservative surgery for non-invasive cases up to 2 cm |
| Radiotherapy after conservative surgical treatment |
| Post-mastectomy radiotherapy for pN2a cases |
| Radiotherapy within 12 weeks from surgical intervention (if adjuvant chemotherapy not indicated) |
| Endocrine therapy indication for endocrine-sensitive invasive cases |
| Chemotherapy indication for invasive, hormone receptor negative cases if $pT > 1$ cm or $pN+$ |
| Chemotherapy and trastuzumab indication for invasive HER2 + cases |
| Primary chemotherapy indication for inflammatory cancer |
Table 3 Patients’ characteristics

|                  | Total  | Jul-Sep 2019 | Oct-Dec 2019 | Jul-Sep 2020 | Oct-Dec 2020 |
|------------------|--------|--------------|--------------|--------------|--------------|
|                  | N      | %            | N            | %            | N            | %            |
| Diagnosis        |        |              |              |              |              |
| In situ          | 745    | 10.6         | 187          | 10.8         | 153          | 9.2          |
| Invasive         | 6287   | 89.4         | 1543         | 89.2         | 1508         | 90.8         |
| Invasive Total   | 6287   | 100%         | 1543         | 100%         | 1508         | 100%         |
| Median age (range) |       |              |              |              |              |
| Missing          | 1406   | 22.4         | 50           | 3.2          | 224          | 14.2         |
| N                | 7032   | 100          | 1730         | 100          | 1791         | 100          |
| Missing          | 1406   | 22.4         | 50           | 3.2          | 224          | 14.2         |
| Total Miss      | 61 (25–100) | 62 (22–95) | 63 (27–98) | 62.5 (22–95) |              |
| N               | 7032   | 100          | 1730         | 100          | 1791         | 100          |
| Neoadj CT        |        |              |              |              |              |
| No               | 4090   | 87.7         | 1046         | 86.4         | 988          | 84.1         |
| Missing          | 1622   | 25.8         | 333          | 21.6         | 405          | 25.6         |
| Total Miss      | 61 (25–100) | 62 (22–95) | 63 (27–98) | 62.5 (22–95) |              |
| N               | 7032   | 100          | 1730         | 100          | 1791         | 100          |
| Surgery type     |        |              |              |              |              |
| Mastectomy       | 1893   | 32.6         | 514          | 35.0         | 469          | 29.7         |
| Missing          | 475    | 7.6          | 73           | 4.7          | 66           | 4.2          |
| Total Miss      | 61 (25–100) | 62 (22–95) | 63 (27–98) | 62.5 (22–95) |              |
| N               | 7032   | 100          | 1730         | 100          | 1791         | 100          |
| pT               |        |              |              |              |              |
| yT0-yTis-yTmic   | 205    | 3.5          | 58           | 4.0          | 47           | 2.9          |
| yT1a-yT1b-yT1c   | 231    | 3.9          | 63           | 4.3          | 79           | 5.3          |
| yT2              | 68     | 1.2          | 24           | 1.7          | 26           | 1.7          |
| yT3-4            | 20     | 0.3          | 9            | 0.6          | 5            | 0.3          |
| T1mic            | 67     | 1.1          | 21           | 1.4          | 13           | 0.9          |
| Missing          | 393    | 6.3          | 94           | 6.1          | 84           | 5.3          |
| Total Miss      | 61 (25–100) | 62 (22–95) | 63 (27–98) | 62.5 (22–95) |              |
| N               | 7032   | 100          | 1730         | 100          | 1791         | 100          |
| pN               |        |              |              |              |              |
| yN0              | 333    | 5.9          | 98           | 7.0          | 110          | 7.7          |
| N0               | 3650   | 64.3         | 898          | 63.9         | 898          | 62.6         |
| Missing          | 610    | 9.7          | 137          | 8.9          | 146          | 9.2          |
| Total Miss      | 61 (25–100) | 62 (22–95) | 63 (27–98) | 62.5 (22–95) |              |
| N               | 7032   | 100          | 1730         | 100          | 1791         | 100          |
| ER               |        |              |              |              |              |
| Negative         | 598    | 11.4         | 175          | 13.2         | 167          | 12.2         |
| Missing          | 1060   | 16.9         | 198          | 12.8         | 206          | 13           |
| Total Miss      | 61 (25–100) | 62 (22–95) | 63 (27–98) | 62.5 (22–95) |              |
| N               | 7032   | 100          | 1730         | 100          | 1791         | 100          |
| PgR              |        |              |              |              |              |
| Negative         | 1173   | 22.5         | 314          | 23.5         | 337          | 24.6         |
| Missing          | 4037   | 77.5         | 1021         | 76.5         | 1031         | 75.4         |
| Total Miss      | 61 (25–100) | 62 (22–95) | 63 (27–98) | 62.5 (22–95) |              |
| N               | 7032   | 100          | 1730         | 100          | 1791         | 100          |
| Her2             |        |              |              |              |              |
| 0/1+             | 4130   | 74.7         | 1037         | 75           | 1031         | 72.5         |
| 2+(FISH -)       | 688    | 12.4         | 159          | 11.5         | 197          | 13.8         |
| 2+(FISH +)       | 193    | 3.5          | 52           | 3.8          | 49           | 3.4          |
| 2+(FISH missing) | 107    | 1.9          | 15           | 1.1          | 31           | 2.2          |
| 3+               | 410    | 7.4          | 120          | 8.7          | 115          | 8.1          |
| Missing          | 759    | 12.1         | 160          | 10.4         | 157          | 9.9          |
| Total Miss      | 61 (25–100) | 62 (22–95) | 63 (27–98) | 62.5 (22–95) |              |
| N               | 7032   | 100          | 1730         | 100          | 1791         | 100          |
| Ki-67            |        |              |              |              |              |
| 0–14%            | 2936   | 53.2         | 740          | 53.4         | 757          | 53.0         |
| ≥ 15%            | 2579   | 46.8         | 645          | 46.6         | 672          | 47.0         |
| Missing          | 772    | 12.3         | 158          | 10.2         | 151          | 9.6          |
| Total Miss      | 61 (25–100) | 62 (22–95) | 63 (27–98) | 62.5 (22–95) |              |
| N               | 7032   | 100          | 1730         | 100          | 1791         | 100          |
Interestingly, in 2020 the time-to-surgery appeared to be shorter than in 2019, with surgery being performed more frequently in ≤ 30 days from clinical indication or in ≤ 42 days from the first test positive for invasive BC (Trend Test p-value = < 0.001 for both QIs) (Fig. 1C, D). Considering surgical indication, there were no statistically significant differences in terms of choice of adequate surgical procedure, with the great majority of patients, across all the time-frames in both 2019 and 2020, undergoing a single surgical procedure for both in situ and invasive lesions (Fig. 2A, B). Nevertheless, we observed a higher preference for BCS for treatment of invasive lesions ≤ 3 cm in 2020 compared to 2019, while no differences were seen in the rate of choice of BCS for non-invasive lesions ≤ 2 cm across the two years considered (Fig. 2C, D). Taking into account the management of the axilla, a statistically significant trend was observed, with more pN0 patients in 2020 treated with sentinel lymph node biopsy (SLNB), without axillary dissection (Trend Test p-value = < 0.001) (Fig. 2E).

Lastly, we sought to analyze possible differences, between the considered time-frames in 2019 and 2020, also in non-surgical procedures, such as radiotherapy and oncological treatments. No statistically significant difference was observed in terms of radiotherapy indication, both after BCS (Trend Test p-value = 0.11) and after mastectomy in pN2a cases (Trend Test p-value = 0.7), while, in accordance

| Table 3 (continued) | Total Jul-Sep 2019 | Oct-Dec 2019 | Jul-Sep 2020 | Oct-Dec 2020 |
|---------------------|-------------------|--------------|--------------|--------------|
|                     | N  | %  | N  | %  | N  | %  | N  | %  |
| Grade               |    |    |    |    |    |    |    |    |
| I                   | 830| 14.6| 200| 14.3| 199| 14.0| 183| 13.5|
| II                  | 3300| 58.1| 784| 56.2| 822| 57.7| 791| 58.3|
| III                 | 1552| 27.3| 411| 29.5| 403| 28.3| 382| 28.2|
| Missing             | 605| 9.6| 148| 9.6| 156| 9.9| 152| 10.1|

Fig. 1  A Radiological and/or cytological confirmed pre-surgical diagnosis.  B MRI before surgery.  C Time-to-surgery in ≤30 days from clinical indication.  D Time-to-surgery in ≤42 days from the first test positive for invasive BC
to what was observed for time-to-surgery, we observed a better outcome in 2020 compared to 2019 in terms of time-to-radiotherapy, when the latter was clinically indicated (Trend Test \( p \)-value = \(<0.001\)) (Fig. 3A–C). When analyzing oncological treatment indication, we could not find any statistically significant difference in terms of adjuvant treatments decision between the two years-time considered (Trend Test \( p \)-value = 0.478, 0.392 and 0.162 for endocrine therapy in hormone receptor positive case, chemotherapy for high risk hormone receptor negative cases and trastuzumab for HER2 + cases, respectively) (Fig. 3D–F). On the other hand, we observed a statistically significant reduction in neoadjuvant chemotherapy indication in 2020 compared to 2019 (Trend Test \( p \)-value = \(<0.001\)).

**Discussion**

The present study, conducted among Senonet Italian Breast Centers, focused on the management of BC care during 2020 COVID-19 pandemic. Comparing patients’ clinicopathological characteristics, diagnosis, surgical and medical treatment variables between 2019 and 2020 time-frames, we sought to investigate if, in this selected, high-volume network of Breast Centers, any change in standard practice occurred due to the onset of the pandemic. To do so, we took advantage of data collected in Senonet, the Senonet data warehouse, and used a set of QIs, configured to monitor quality and commitment of Breast Centers in BC care, to describe changes in specific BC treatment areas.

Our analysis did not show any statistically significant difference in terms of diagnosis, surgical, oncological and radiation therapy procedures when comparing the two trimesters of the years considered. Nevertheless, we observed statistically significant differences, favoring the 2020 pandemic year, when analyzing time-to surgery and time-to radiotherapy (when indicated). This could be explained by an improvement in treatment strategies and even more strict collaboration between different Breast Centers. Indeed, since the first onset of the pandemic, Italian Breast Centers’ activities have been promptly reorganized, in response to the need of balancing the emergency of COVID-19 patients with the urgency of continuum of care for oncological patients, bearing in mind the potential exposure to SARS-CoV-2 infection of these frail patients. As cited before, many international guidelines

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**Fig. 2** A Single surgery procedure for invasive tumors. B Single surgery procedure for in situ tumors. C BCS for treatment of invasive lesions \( \leq 3 \) cm. D BCS for treatment of non-invasive lesions \( \leq 2 \) cm. E pN0 patients treated with sentinel lymph node biopsy

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| A | B | C |
|---|---|---|
| **Single surgery procedure for invasive tumors** | **Single surgery procedure for in situ tumors** | **BCS for treatment of invasive lesions \( \leq 3 \) cm** |
| **Jul19** | **Oct19** | **Jul20** | **Oct20** | **Jul19** | **Oct19** | **Jul20** | **Oct20** | **Jul19** | **Oct19** | **Jul20** | **Oct20** |
| 96.5% | 96.7% | 96.1% | 96.7% | 93.2% | 93.4% | 90.4% | 90.3% | 82.8% | 85.9% | 86.1% | 86.9% |
| \( p = 0.938 \) | \( p = 0.208 \) | \( p = 0.019 \) |
| (15 units, median missing 1%) | (15 units, median missing 1%) | (14 units, median missing 1%) |

| D | E |
|---|---|
| **BCS for treatment of non-invasive lesions \( \leq 2 \) cm** | **pN0 patients treated with sentinel lymph node biopsy** |
| **Jul19** | **Oct19** | **Jul20** | **Oct20** | **Jul19** | **Oct19** | **Jul20** | **Oct20** |
| 86.6% | 86.7% | 87.5% | 92.6% | 96.8% | 98.5% | 98.5% | 99.2% |
| \( p = 0.183 \) | \( p = <0.001 \) |
| (14 units, median missing 2%) | (15 units, median missing 0%) |
recommended postponing surgery in low to medium risk BC patients, favoring neoadjuvant approaches, with many studies reporting a five-fold increment in the choice for neoadjuvant endocrine therapy in HR positive, HER2 negative tumors [11, 12]. In our dataset, we observed a significant reduction in the use of neoadjuvant chemotherapy and we did not recollect any data on a major use of neoadjuvant endocrine therapy. This might be due to the fact that our high-volume, highly selected, Breast Centers were restructured to serve as BC care hubs for other low volume Hospitals and were organized to be able to perform upfront surgery (mainly BCS, as encouraged by International Guidelines) to the majority of ≤ 3 cm, HR positive, HER2 negative patients.

Moreover, a major implement of SLNB, without axillary lymph node dissection (ALND), was observed in our case series in 2020 compared to 2019. This might be explained by the elevated number of small, cN0 tumors selected for upfront surgery, as previously explained, but it might also reflect the gradual paradigm shift that the surgical management of the axilla have been encompassing through the last years, due to the wide acceptance of Z0011 trial findings on the possibility of omitting ALND in selected low-risk tumors [13].

Regarding radiation therapy, moderate-hypofractionated schedules were strongly recommended during the COVID-19 pandemic, reducing treatment duration and patients’ risk exposure [14], and in case of clinical indication for a boost, a further dose to the tumor bed, was preferably a simultaneous integrated one [15]. These management indications, together with the possibility of addressing BC patients to dedicated Breast Centers hubs for adjuvant radiotherapy and the lowering of indications for palliative radiation treatments, might explain the shorter time-to radiotherapy observed in our case series in 2020 compared to 2019.

Immediate breast reconstruction was offered also during COVID-19 pandemic in order to maintain therapeutic standards, nevertheless some degree of variation in the clinical protocol was adopted by many centers to face the pandemic outbreak [16].

In conclusion, even if we globally observed a decrease in the performance of the Italian Breast Centers due to the COVID-19 pandemic, with major issues regarding an adequate and prompt access to treatment [6], in our study, providing data from a highly selected network of high-volume Breast Centers, we could not notice any treatment delay or radical change in standard clinical practice. These findings probably reflect the Senonetwork selection

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### Fig. 3

A Radiotherapy after BCS

|          | Jul19 | Oct19 | Jul20 | Oct20 |
|----------|-------|-------|-------|-------|
| Radiotherapy | 88.7% | 90.1% | 90.9% | 90.7% |

\[ p = 0.11 \]

(14 units, median missing 5%)

B Radiotherapy after mastectomy in pN2a

|          | Jul19 | Oct19 | Jul20 | Oct20 |
|----------|-------|-------|-------|-------|
| Radiotherapy | 75.4% | 80.4% | 70.2% | 75.6% |

\[ p = 0.7 \]

(11 units, median missing 6%)

C Time-to-radiotherapy ≤ 12 weeks

|          | Jul19 | Oct19 | Jul20 | Oct20 |
|----------|-------|-------|-------|-------|
| Time-to-radiotherapy | 43.9% | 53.5% | 73.7% | 62.8% |

\[ p = <0.001 \]

(9 units, median missing 6%)

D Endocrine therapy in HR+ cases

|          | Jul19 | Oct19 | Jul20 | Oct20 |
|----------|-------|-------|-------|-------|
| Endocrine therapy | 92.1% | 91.6% | 94.2% | 90.5% |

\[ p = 0.478 \]

(14 units, median missing 3%)

E Chemotherapy for high risk (T > 1 cm or N+) HR- cases

|          | Jul19 | Oct19 | Jul20 | Oct20 |
|----------|-------|-------|-------|-------|
| Chemotherapy | 84.5% | 85.7% | 88.7% | 77.6% |

\[ p = 0.392 \]

(14 units, median missing 6%)

F Trastuzumab for HER2+ cases

|          | Jul19 | Oct19 | Jul20 | Oct20 |
|----------|-------|-------|-------|-------|
| Trastuzumab | 98.7% | 97% | 93% | 95.5% |

\[ p = 0.162 \]

(15 units, median missing 7%)
of Breast Centers fulfilling high-standard requirements of multidisciplinary organization and the capability of this network of Breast Centers to cooperate, joining forces also to serve as surgical and radiation therapy hubs for the nearest territorial area.

Due to the persistence of pandemic waves after 2020 and the unceasing need for COVID-19 inpatient care, which might lead to an increased number of women with advanced BC at diagnosis in the future, we still need to accurately monitor the performance of Italian Breast Centers through the years and take in place appropriate actions to prevent disfunction in the health care of oncologic patients.

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