

SHORT COMMUNICATION

Evaluation of the early adverse effects of radiotherapy in breast cancer patients with COVID-19: Prospective single institutional study

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Abstract

The COVID-19 caused by the SARS-CoV-2 coronavirus is at the origin of a global pandemic. This pandemic has prompted the current health system to reorganize and rethink the care offered by health establishments. We report the early toxicity in patients infected with COVID-19 treated at the same time for early-stage breast cancer (BC). This is a monocentric prospective study of patients treated in our hospital between March 2020 and June 2020 and were diagnosed with COVID-19 infection. The inclusion criteria were to be irradiated for early-stage BC and to have a positive COVID-19 diagnosis on a PCR test and/or a lung computed tomography (CT) scan and/or suggestive clinical symptoms. Radiotherapy (RT) consisted of breast or chest wall irradiation with or without lymph node irradiation, with protocols adapted to pandemic situation. The treatment-related toxicity was graded according to the CTCAE (version 4.03). All 350 patients treated for early-stage BC were studied. Of them, 16 were presented with clinical symptoms of COVID-19 infection and of them, 12 had clinical, CT scan, and PCR confirmation. This entire cohort of 12 pts with median age of 56 (42–72) underwent their RT. During the radiotherapy, there were 9 pts presented radiation dermatitis, 8 (66%) were grade 1 and one was (8%) grade 2. Two patients with lymph nodes irradiation presented esophagitis grade 2. This prospective COVID-19 cohort, treated for early-stage BC demonstrated an acceptable toxicity profile with few low-grade adverse events. Longer follow-up is needed to confirm these findings.

KEYWORDS

adverse effects, breast cancer, cancer, COVID-19, prognosis, radiation therapy, SARS-CoV-2, treatments

1 | INTRODUCTION

COVID-19, caused by the SARS-CoV-2 coronavirus, is responsible for a global pandemic.¹ It was first detected on November 17, 2019, in the city of Wuhan, China, and then spread around the world via the flow of people, especially tourists.² The World Health Organization

(WHO) declared a state of public health emergency in France on January 30, 2020.

SARS-CoV-2 is an RNA virus[5] that mainly infects the respiratory tract. It is usually asymptomatic, but can cause fever (77.4%–98.6%), cough (59.4%–81.8%), asthenia (38.1%–69.6%) and dyspnea (3.2%–55%).² The mean age of patients hospitalized for COVID-19

is 47 years, comprising 42% of females and 58% of males, and the mortality rate varies between 1 and 3% depending on the country.^{1,2}

This pandemic has required reorganization of the current health system and a new approach to the management provided by health care facilities. New guidelines have therefore emerged to limit spread of the virus. Learned societies have issued guidelines for hygiene and barrier measures (COVID-19 arrowed pathways in health care facilities, use of masks, rubbing hands with sanitizer gel, etc.), as well as new practices in each medical or surgical specialty. New guidelines for the management of cancer patients have emerged, with a preference for oral vs. IV chemotherapy, 3-week vs. weekly regimens, home chemotherapy injections, and postponement of nonurgent care. Surgery for carcinoma in situ can therefore be delayed for 3 to 6 months and surgery for invasive ductal carcinoma can be delayed for up to 6 weeks.³ Reorganization of radiotherapy (RT) has required the temporary suspension of time-consuming irradiation techniques, the use of hypofractionated treatment regimens,³ the use of dedicated machines for COVID-19 patients.

Many authors have questioned whether cancer is a risk factor for a severe form of COVID-19. Data in the literature on this subject remain discordant at the present time due to an underrepresentation of cancer patients in published series, preventing identification of cancer as an independent risk factor.⁴ However, the literature tends to agree on a nonstatistically significant association between cancer and severe forms of COVID-19, but the comorbidities of these patients are generally considered to account for the more severe forms of COVID-19 in this population.⁴

To date, no publication has evaluated the short-term effects of radiotherapy in SARS-CoV-2-infected patients treated for nonmetastatic breast cancer during the first wave of the pandemic. In this study, we therefore tried to assess the effects of radiotherapy in a prospective cohort of SARS-CoV-2-infected patients treated for breast cancer in our institution.

2 | MATERIALS AND METHODS

This study, conducted on a prospective, single-center cohort, evaluated all patients treated by radiotherapy for breast cancer between March 2020 and June 2020 in the Radiation Oncology Department, Institut Curie, Paris.

Starting in March 2020, in agreement with the Institut Curie Paris Institutional Review Board, all confirmed or suspected cases of COVID-19 were prospectively registered in an institutional data base. Notification of all confirmed or suspected cases of COVID-19 was made compulsory by the Director of the Institut Curie Paris. All notified patients were included in the registry on the day of notification. We consecutively registered all patients presenting symptoms suggestive of COVID-19 and/or COVID-19 confirmed by reverse transcription polymerase chain reaction (RT-PCR) on nasopharyngeal swabs and/or chest CT images suggestive of COVID-19. The multi-disciplinary COVID-19 patient registration group was set up to centralize and coordinate all decisions and strategies related to the COVID-19 pandemic. This study

was submitted to the COVID-19 group and was approved as a prospective study to be conducted on this data base. All patients provided their oral consent for inclusion in this study.

Study inclusion criteria were patients treated for nonmetastatic breast cancer at the Institut Curie Paris with a positive diagnosis of COVID-19 on RT-PCR test and/or chest CT and/or clinical symptoms (fever, dyspnea, ageusia, anosmia, etc.).

The study, designed to assess radiation-related toxicity in a population of breast cancer patients treated by local-regional radiotherapy with a concomitant diagnosis of COVID-19 diagnosed during the radiotherapy, was proposed to and approved by the Institut Curie COVID-19 group scientific and ethics committee. We used dedicated machine with special measures for the protection of the medical and paramedical staff.

Routine screening including a questionnaire and a systematic body temperature was implemented at the entrance to the Institut Curie at the beginning of the epidemic. According to French national guidelines, the SARS-CoV-2 RNA test on nasopharyngeal swabs was initially limited to health care workers and critically ill patients. Subsequently, RT-PCR tests became more widely available for patients with symptoms of COVID-19 and were performed whenever possible. Most of the patients included in this study presenting symptoms suggestive of COVID-19 were therefore screened by RT-PCR or diagnostic chest CT. Weekly review in the outpatient department or by teleconsultation was set up to monitor the course of the infection and COVID-19 symptoms and to assess any acute adverse effects of radiotherapy.

A 6-month evaluation of COVID-19 after completion of radiotherapy was planned from the time of inclusion of the patients in the study and consisted of a 6-month follow-up visit comprising clinical examination assessing the initial symptoms associated with SARS-CoV-2 infection, and the late toxicities of radiotherapy. A 6-month follow-up chest CT scan was also planned at the time of inclusion with centralized review by the same expert radiologist who interpreted the initial chest CT scans.

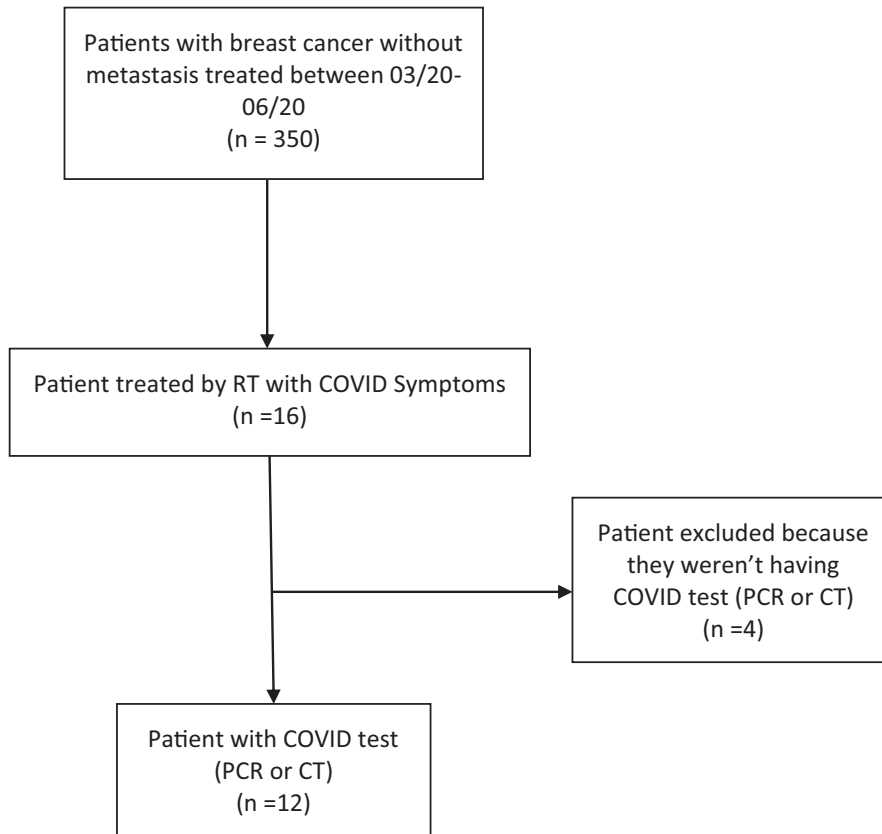
3 | RESULTS

This prospective single-center study evaluated 350 patients treated for early-stage breast cancer in our department between March 2020 and June 2020 (Figure 1). A very detailed analysis was performed on 12 patients to address a previously unanswered question: "Does radiotherapy used in the treatment of breast cancer increase the risk of side effects, including lung sequelae, in patients irradiated during the course of COVID-19?"

3.1 | Primary outcome

SARS-CoV-2 RT-PCR and/or chest CT were performed in 12 of these patients. Six patients had a positive PCR test, and 4 patients had chest CT signs compatible with COVID-19.

FIGURE 1 Flow Chart of the study



Six of the 12 patients had images indicating initial lung involvement. Chest CT scan to screen for COVID-19 was performed in 50% of this population and, in 4 out of 6 patients, chest CT demonstrated minimal to moderate signs of COVID-19. Two patients presented signs of lung involvement considered to be minimal (<10%) and two other patients presented moderate involvement (10%–25%).

In this study population, 36% of patients were treated by hypofractionation with a dose of 40 Gy in 15 fractions and 63% were treated according to conventional fractionation with a dose of 50 Gy in 25 fractions. The following techniques were used 9 patients were treated by Vmat IMRT, 2 patients were treated by 3D isocentric lateral decubitus technique, and one patient received electron beam radiotherapy to the chest wall.

3.2 | Toxicities

Adverse effects experienced by patients during treatment were assessed at treatment visits by the CTCAE criteria (version 4.03).

Analysis of acute toxicities according to the CTCAE criteria found: 66% of grade 1 radiation dermatitis, 8% of grade 2 radiation dermatitis, 25% of grade 1 esophagitis/dysphagia and 17% of grade 1 asthenia. These results are in line with the toxicities classically reported in the literature on this subject.

4 | DISCUSSION

This is the first prospective study and currently the largest series evaluating the long-term lung toxicities by CT scan in COVID-19 patients irradiated for breast cancer. The current literature on COVID-19 in cancer patients mainly adopts the various management guidelines for these patients during the epidemic, as well as new guidelines (3). Some studies have tried to analyze risk factors for severe forms of COVID-19 in cancer patients (4), and tend to suggest that cancer is not an independent risk factor for excess mortality in SARS-CoV-2-infected patients.⁴ This study, based on a prospective, single-center cohort in the Institut Curie Paris department of radiotherapy assessed the early and late (6 months) adverse effects of radiotherapy in breast cancer patients with concomitant COVID-19. Of the 350 patients treated for breast cancer during the inclusion period, only 12 had confirmed COVID-19. Baseline and 6-month follow-up chest CT scans were reviewed centrally by an expert radiologist to assess the course of COVID-19-related lung lesions prior to and 6 months after radiotherapy. This CT analysis did not reveal any sequelae of COVID-19 or radiation-induced lesions in the patients studied. Analysis of acute toxicities did not reveal any increase in clinical adverse effects (respiratory, skin, etc) compared with data of the literature.

COVID-19 therefore does not appear to increase the early adverse effects of radiotherapy.

However, these results need to be confirmed by studies based on larger patient cohorts, with longer follow-up. All these patients were diagnosed during the radiotherapy and it was difficult to stop their treatment especially in patients without symptoms because the risk of recurrence.

This study highlights the value of treating each patient with a technique adapted to anatomy and comorbidities. Hypofractionation protocols must also be adapted to the volumes irradiated.

This study therefore tends to show that the initial lesions or lung sequelae associated with COVID-19 are not more severe or more prolonged after radiotherapy, in patients treated for breast cancer with proven COVID-19. Radiotherapy should therefore not be delayed in patients requiring radiation, despite the presence of COVID-19.

In conclusion, radiotherapy for breast cancer patients with COVID 19 is feasible and well tolerated in minimally symptomatic patients treated by techniques adapted to their anatomy. These data need to be confirmed by longer follow-up in this population of patients.

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CONFLICT OF INTEREST

No conflict of interest.

DATA AVAILABILITY STATEMENT

Data are stored in an institutional data base and are accessible upon request.

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