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COVID-19 in breast cancer patients: a cohort at the Institut Curie hospitals in the Paris area

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Abstract

Background: Cancer patients have been reported to be at higher risk of COVID-19 complications and deaths. We report the characteristics and outcome of patients diagnosed with COVID-19 during breast cancer treatment at Institut Curie hospitals (ICH, Paris area, France).

Methods: An IRB-approved prospective registry was set up at ICH for all breast cancer patients with COVID-19 symptoms or radiologic signs.

Results: Among 15,600 patients actively treated for early or metastatic breast cancer during the last 4 months at ICH, 76 patients with suspected COVID-19 infection were included in the registry and followed. Fifty-nine of these patients were diagnosed with COVID-19 based on viral RNA testing or typical radiologic signs: 37/59 (63%) COVID-19 patients were treated for metastatic breast cancer, and 13/59 (22%) of them were taking corticosteroids daily. Common clinical features mostly consisted of fever and/or cough, while ground-glass opacities were the most common radiologic sign at diagnosis. We found no association between prior radiation therapy fields or extent of radiation therapy sequelae and extent of COVID-19 lung lesions. Twenty-eight of these 59 patients (47%) were hospitalized and 6 (10%) were transferred to an intensive care unit. At the time of analysis, 45/59 (76%) patients were recovering or had been cured, 10/59 (17%) were still followed and 4/59 (7%) had died from COVID-19. All 4 patients who died had significant non-cancer comorbidities. In univariate analysis, hypertension and age (>70) were the two factors associated with a higher risk of intensive care unit admission and/or death.

Conclusions: This prospective registry analysis suggests that the COVID-19 mortality rate in breast cancer patients depends more on comorbidities than prior radiation therapy or current anti-cancer treatment. Special attention must be paid to comorbidities when estimating the risk of severe SARS-CoV-2 infection in breast cancer patients.

Keywords

SARS-CoV-2; COVID-19; breast cancer; outcome; survival

Background

On December 31st, 2019, the World Health Organization was informed about cases of pneumonia of unknown cause in Wuhan, China [1]. A novel coronavirus, named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was identified as the cause of coronavirus disease 2019 (COVID-19)[2]. Over the following months, the viral outbreak shifted from China to the rest of the world and was subsequently recognized as a pandemic [3]. In France, the number of confirmed cases rose during early March: more than 2,800 confirmed cases were officially reported on March 13, 2020, when the French hospital emergency response plan, which coordinates all hospitals, was increased to its maximum readiness level [4]. As of April 24, France is the 6th most severely affected country in the world (in terms of absolute numbers), with approximately 120,000 laboratory-confirmed cases and more than 21,000 official COVID-19-related deaths [4, 5]. With about 6,000 deaths, the Paris area is one of the most severely affected regions in France [6].

The first report on COVID-19 outcome in cancer patients was published on February 14th [7]: in a series of 18 Chinese patients with a history of cancer and a diagnosis of COVID-19, 7 (39%) had to be treated in the intensive care unit (ICU) and/or died. This seminal retrospective study prompted major concerns about the risk of COVID-19 infection in cancer patients. Further studies confirmed that, compared to the Chinese general population, cancer patients are at higher risk of severe COVID-19 symptoms and death [7-10] . Cancer patients with blood, lung or metastatic cancers were reported to have the highest frequency of severe outcome [8, 10]. These retrospective reports, of limited size and restricted to patients hospitalized in Chinese hospitals, may not be fully transposable to Western healthcare systems, as suggested by a preliminary report on New Yorkers admitted to ICU [11].

Our study reports the COVID-19 features and outcomes experienced by inpatients and outpatients actively treated for breast cancer at Institut Curie hospitals (ICH) in the Paris area, France.

Methods

Breast cancer care at IC during the SARS-CoV-2 pandemic

Patient flow. Starting on March 9, 2020, ICH provided information about COVID-19 symptoms and guidelines to patients by means of regular e-mail and text messages. Follow-up consultations were postponed. Consultations not requiring physical examination or detailed explanations were replaced by teleconsultations. Patients were systematically subjected to COVID-19 symptom screening and body temperature checks at the hospital entrances. Those with COVID-19 symptoms were directed to specific emergency room areas and were tested. When necessary, patients with suspected or proven COVID-19 were hospitalized in specific wards or transferred to internal or external intensive care units.

Surgery. The French hospital emergency response plan ("*plan blanc*") required postponement of all non-urgent surgery. ICH surgeons complied with the national guidelines for breast cancer patients issued by learned societies [12], included postponement of surgery for patients at high risk of severe COVID-19, in whom an alternate treatment option was available (eg, neoadjuvant endocrine therapy was proposed in elderly ER+ breast cancer patients). Patients were systematically tested for SARS-CoV-2 RNA (nasopharyngeal swabs) in the two days prior to general anesthesia, even in the absence of symptoms.

Medical oncology. Internal guidelines were applied at ICH starting from March 9, in line with national guidelines for breast cancer patients [12]: ongoing chemotherapy was not discontinued. Neoadjuvant chemotherapy was avoided in patients with smaller tumors (< 3 cm), even including triple-negative and HER2-positive subtypes. Adjuvant chemotherapy indications were mostly maintained, but situations associated with a marginal survival benefit had to be discussed with the patients. Dose-dense anthracycline regimens were discouraged. Granulocyte colony-stimulating factor prophylaxis was systematically used for anthracycline-based regimens and docetaxel, with the docetaxel dose reduced to 75 mg/m². In patients experiencing COVID-19 symptoms (proven or unproven), the next chemotherapy cycle was delayed until 14 days after the first day of symptoms, pending the clearance of hyperthermia and dyspnea. Endocrine therapy indications and doses were not modified. Targeted therapy (including CDK4/6 and PARP inhibitors) indications and doses were not modified, except for alpelisib and everolimus. Initiation of a new line of therapy with alpelisib was discouraged, but ongoing treatment was

maintained. Everolimus was discontinued in all patients, except for a handful of patients with prolonged objective response. Atezolizumab indications and doses were not modified, but close monitoring of these patients was recommended. When used as comedication for chemotherapy, corticosteroid doses were systematically reduced by one half and were discontinued whenever possible.

Radiation therapy. Indications and ongoing treatments were not modified, but adjuvant radiotherapy was hypofractionated whenever possible [12, 13]

Palliative care. For patients with advanced metastatic breast cancer and/or severe pre-existing comorbidities, a dedicated COVID-19 videoconference multidisciplinary meeting was held daily to discuss the medical and ethical relevance of antiviral treatments and transfer to ICU. Palliative care for breast cancer patients during the COVID-19 pandemic was conducted according to the guidelines issued by the French society of palliative care [14].

COVID-19 diagnosis: laboratory tests and radiology

SARS-CoV-2 RNA tests. Testing was initially restricted to critically ill patients with COVID-19 symptoms, but subsequently became available to all cancer patients with suspected COVID-19 at the end of March 2020. Nasopharyngeal swabs were analyzed for SARS-CoV-2 RNA by reverse-transcription polymerase chain reaction assays targeting 2 regions of the viral RdRp gene. All assays were validated by the French National Reference Center (Institut Pasteur, Paris, France) [15]

CT scan protocol and image interpretation. Whenever available, CT images were centrally reviewed by two senior radiologists with consensus qualitative and semiquantitative assessment. In accordance with previous reports on COVID-19 imaging [16, 17], the following patterns were sought: ground-glass opacity, crazy paving, focal consolidation and linear consolidation. The predominant pattern was determined for each examination. The severity (%) of lung involvement was evaluated according to the French Society of Radiology guidelines [18]. The presence of lung or pleural metastases was assessed by comparison with previous CT scans. Lung radiation therapy sequelae were evaluated by semiquantitative evaluation of confluent radiologic opacities (grade 3 of the Lent-Soma scoring system [19]) affecting the right, left or middle lobes (0: no involvement; 1: $\leq 10\%$ of lung volumes; 2: 11-25%; 3: $\geq 26\%$ involvement).

Registry

The prospective COVID-19 registry was approved by the ICH institutional review board, which waived documentation of informed consent due to its observational nature. Starting from March 13th, 2020, all proven or suspected COVID-19 cases were prospectively registered, as the registry also allowed for clinical follow-up phone calls scheduled at days 8, 14 and 28. More frequent and/or longer follow-up was provided whenever medically necessary. Patients hospitalized outside IC hospitals were also registered and prospectively followed. For this analysis, data were extracted on April 25th, 2020. This report was written according to the STROBE checklist.

Statistics

Three populations were considered: patients who had biological confirmation of COVID-19 status using RT-PCR (positive RNA test); patients who had a positive RNA test or for whom RT-PCR result was not available (or pending) but suggestive radiologic findings (COVID-19 patients); patients with symptoms only. Main outcome of patients were defined as death or ICU admission. Descriptive and univariate prognostic factor analysis was performed. As a sensitivity analysis, prognostic factor analysis of death only was performed. Due to the highly explorative nature of the report and the small number of events, no adjustment for multiple testing was applied and multivariate analysis was not done. All analyses were performed in SAS v9.4 and R software.

Results

COVID-19 diagnosis

From March 13th, 2020 to April 25th, 2020 (date of data extraction), 76 patients actively treated for breast cancer were included in the ICH COVID-19 registry. For comparison, 15,600 breast cancer patients had at least one consultation or treatment for breast cancer at one of the IC hospitals in the 4 months before lockdown (11/01/2019 to 02/28/2020). The patient flow-chart for the COVID-19 registry is displayed in **Figure 1A**. RNA testing was performed in 58 patients, while CT scan was performed in 39 patients. A total of 59 patients were diagnosed with COVID-19, based on either a positive SARS-CoV-2 RNA test (N=41 patients) or, in the case of negative or missing RNA test, radiologic findings (N=18 patients). Seventeen

patients only reported symptoms suggestive of COVID-19 that were not confirmed by RNA test and/or lung CT scan. Most patients in the subgroup who underwent both RNA testing and CT scan presented concordant results, as displayed in **Figure 1B**.

Patient history

Breast cancer patient history and comorbidities are shown in **Table 1**. Ten of the 59 COVID-19 patients (17%) were older than 70. Other notable comorbidities among COVID-19 patients included hypertension (36%), obesity (17%), diabetes (17%) and heart disease (14%). The most frequent comedication in this population was corticosteroids (daily intake of more than 20 mg-equivalent dose of prednisolone; 22%). About two-thirds of COVID-19 patients (and all those treated with corticosteroids) were treated for metastatic breast cancer. Ongoing anti-cancer treatments were representative of those currently administered to patients treated for early or metastatic disease, most commonly chemotherapy (49%), followed by endocrine therapy (32%).

Features at diagnosis

Clinical, laboratory and radiologic features at diagnosis are displayed in **Table 2**. Fever and cough were the most common symptoms, observed in 46% and 37% of COVID-19 patients, respectively. Nine of the 59 patients (18%) developed COVID-19 symptoms more than 2 days after being admitted to hospital (IC or elsewhere), corresponding to the interval used to define nosocomial infections. The mean absolute lymphocyte count was normal ($1.5/\text{mm}^3$). Most patients had no or limited extent of COVID-19 lung disease, as 25/28 patients (89%) had less than 25% involvement of their lung volume. The most common radiologic feature was ground-glass opacities, observed in 14/28 (50%) of COVID-19 patients with CT scan at diagnosis. **Figure 2** displays, for each COVID-19 patient, the prior radiation therapy fields, radiation therapy sequelae and extent of COVID-19 lung disease: no significant association was observed between these characteristics or the presence of lung metastases and the extent of COVID-19 lung disease.

Outcome and prognostic factors

All patient outcomes were updated 2 days prior to this analysis. Of the 59 breast cancer patients diagnosed with COVID-19, 28 (47%) were hospitalized, while 31 (53%) returned home. Twenty-three (82%) of the 28 hospitalized patients received antibiotics and 3 (11%) received corticosteroids. No

patients received hydroxychloroquine, antiviral or immunomodulating drugs as frontline treatment at admission, but these putative treatments were available whenever necessary throughout the patient's stay in hospital.

None of the 17 symptom-only patients had to be hospitalized. The flow of COVID-19 patients during the course disease is shown in **Figure 3**. Four patients were transferred to ICU at diagnosis or during hospitalization. As of April 24th, 45 (76%) of the 59 COVID-19 patients were considered to be either recovering or cured. The outcome of 10 (17%) patients remains undetermined (most recent cases with limited follow-up), while 4 (6.7%) patients died: 2 patients were receiving later lines of treatment for metastatic breast cancer (these patients were not transferred to ICU), 1 patient had recently started first-line endocrine therapy combined with palbociclib and 1 patient was receiving neoadjuvant chemotherapy. Noteworthy, this last patient was treated with an anti-CD80/86 antibody (regulating CTLA-4 signaling). Further details on the history of the four deceased patients are available in **Supplementary Table 1**.

An exploratory analysis of factors associated with either ICU admission and/or death in the COVID-19 population showed that only age > 70 years and hypertension were significantly associated with COVID-19 severity (both $p < 0.05$). They remained as prognostic factors in the RNA test-positive patients except that hypertension was of borderline significance.

Discussion

The SARS-CoV-2 outbreak is the first viral pandemic affecting cancer patients and oncology teams. To the best of our knowledge, this is the first report on COVID-19 diagnosis, signs and outcome in breast cancer patients.

While 15,600 patients were actively treated for breast cancer at Institut Curie Hospitals over the 4 months prior to the pandemic, only 59 were diagnosed with COVID-19 by either RNA test or CT scan. A recent study estimated that more than 10% of inhabitants of the greater Paris area have been infected by the SARS-CoV-2 virus [20]. While our study cannot determine the incidence of COVID-19 infection among breast cancer patients, the small number of diagnosed cases suggests that breast cancer patients, as a whole, are not at high risk of symptomatic COVID-19 infection. This apparent low incidence could possibly be attributed to much stricter application of social distancing procedures by cancer patients, who had been

informed that they may be at higher risk of severe COVID-19 infection. Prophylactic changes implemented in breast cancer care (e.g., postponement of all non-mandatory visits to ICH, changes in medical treatments, etc.) may also have contributed to further reduce the risk of SARS-CoV-2 infection. A limitation of our study is that some patients may have been treated by their family physicians or referred to local hospitals, without any notification to ICH. Rates of high BMI and hypertension in our COVID-19 patient cohort were very similar to those reported in a recent prospective large-scale report on French breast cancer patients [21], suggesting that these comorbidities do not increase the risk of COVID-19. Our analyses showed that breast cancer patients have similar clinical and radiologic features of COVID-19 to those previously described in other reports on non-cancer COVID-19 patients. Importantly, we found no trend in favor of a relationship between a history of breast and lymph node radiation therapy, radiation therapy sequela and radiologic extent of disease or outcome.

In terms of COVID-19 outcome, we observed a non-negligible mortality rate of 6.7% (4/59) among breast cancer patients diagnosed with COVID-19, with a higher mortality rate of 9.7% (4/41) in the subgroup with positive RNA tests. As of April 26th, the reported mortality rate among RNA-positive patients in the general population ranges from 18.2% in France to 5.6% in the USA and 3.7% in Germany [4]. However, these percentages reflect more testing policy more than true differences in mortality rates. As in the general population, the true infection and mortality rates could subsequently be determined by serology tests detecting an immune response to SARS-CoV-2. Nevertheless, on univariate analysis, age and hypertension were associated with disease severity rather than the extent of disease or ongoing cancer therapy, suggesting that breast cancer patients share the same risk factors for severe COVID-19 as the general population. Strikingly, the only early breast cancer patient who died was concomitantly treated for a systemic disease by a CTLA-4 signalling modulator, suggesting that breast cancer *per se* is not a major contributor to COVID-19 mortality.

Conclusions

While lockdown lifting procedures are being discussed in most Western countries, this first report on breast cancer patients suggests that comorbidities (apart from breast cancer) should be the primary focus of attention to define patients at high risk. Further studies devoted to breast cancer patients will help to

define breast cancer care for the following months, until preventive treatments, such as a vaccine, have been found.

Declarations

Ethics approval

The COVID-19 registry was approved by the Institut Curie institutional review board, which waived documentation of informed consent due to the observational nature of the registry.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated and analyzed during this study are not publicly available due to French HIPAA (birthdate, admission date, discharge date, date of death), but are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

MF, TR, CB, SD, AN, AB, VS, YK, LC and JYP contributed to data collection and interpretation. LB and PC set up the registry and contributed to data interpretation. LC contributed to manuscript writing. PV and FCB collected the data, contributed to the analysis and wrote the manuscript. XP set up the registry, performed statistical analyses and contributed to writing of the manuscript. All authors have read and approved the final manuscript.

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Table 1: Patients' medical history

	Positive RNA test N pts / N evaluable (%)	COVID-19 patients N pts / N evaluable (%)	Symptoms only N pts / N evaluable (%)
Patient characteristics			
Median age (IQR)	57 (48–68)	58 (48–68)	60 (46–67)
Median BMI (IQR)	26 (22–29)	26 (22–30)	27 (22–31)
Comorbidities			
Age > 70 yo	8/41 (20%)	10/59 (17%)	4/17 (24%)
Obesity (BMI>30)	7/41 (17%)	10/59 (17%)	7/17 (41%)
Active smokers	3/41 (7%)	4/59 (7%)	1/17 (6%)
Chronic lung disease	1/41 (2%)	2/59 (3%)	0/17 (0%)
Diabetes	9/41 (22%)	10/59 (17%)	0/17 (0%)
Hypertension	17/41 (42%)	21/59 (36%)	3/17 (18%)
Heart disease	8/41 (20%)	8/59 (14%)	0 /17 (0%)
Systemic disease	3/41 (7%)	3/59 (5%)	0/17 (0%)
Any of the above	13/41 (32%)	20/59 (34%)	7/17 (41%)
Comedications			
Corticosteroids	9/41 (22%)	13/59 (22%)	1/17 (6%)
NSAID	0/41 (0%)	0/59 (0%)	0/17 (0%)
ACE inhibitor / ARB	13/41 (32%)	15/59 (25%)	1/17 (6%)
Anticoagulants	5/41 (12%)	8/59 (14%)	1/17 (6%)
Immunosuppressives	1/41 (2%)	1/59 (2%)	0/17 (0%)
Breast cancer			
Subtype			
HR+	29/41 (70%)	39/59 (66%)	10/17 (59%)
Triple-negative	6/41 (15%)	10/59 (17%)	4/17 (23%)
HER2+	6/41 (15%)	10/59 (17%)	3/17 (18%)
Clinical setting			
Neoadjuvant	7/41 (17%)	7/59 (12%)	4/17 (24%)
Adjuvant	15/41 (37%)	15/59 (25%)	8/17 (47%)
Metastatic, <3 prior lines	11/41 (27%)	20/59 (34%)	3/17 (18%)
Metastatic, ≥3 prior lines	8/41 (20%)	17/59 (29%)	2/17 (12%)
History of radiation therapy			
Breast / chest wall irradiation	19/41 (46%)	36/59 (61%)	8/17 (47%)
SCLN irradiation	14/41 (34%)	29/59 (49%)	7/17 (41%)
IMN irradiation	11/41 (27%)	23/59 (39%)	6/17 (35%)
None	22/41 (54%)	23/59 (39%)	8/17 (47%)
Metastatic sites (in metastatic pts)			
<3 sites	14/19 (74%)	22/37 (60%)	3/5 (60%)
≥3 sites	5/19 (26%)	15/37 (41%)	2/5 (40%)
Lung/pleural metastases	5/19 (26%)	16/37 (43%)	2/5 (40%)
Bone metastases	17/19 (90%)	24/37 (65%)	5/5 (100%)
Liver metastases	5/19 (26%)	11/37 (30%)	1/5 (20%)
CNS metastases	3/19 (16%)	7/37 (19%)	0/5 (0%)
Other sites	7/19 (37%)	16/37 (43%)	1/5 (20%)
Ongoing therapy			
Surgery	3/41 (7%)	3/59 (5%)	2/17 (12%)
Chemotherapy	18/41 (44%)	29/59 (49%)	9/17 (53%)
Radiation therapy	4/41 (10%)	4/59 (7%)	4/17 (24%)
Endocrine therapy	11/41 (27%)	19/59 (32%)	5/17 (29%)
Targeted therapy	7/41 (17%)	13/59 (22%)	3/17 (18%)
Immunotherapy	0/41 (0%)	0/59 (0%)	0/17 (0%)
Total	N=41	N=59	N=17

BMI: body mass index; Corticosteroids refer to a chronic daily dose equivalent to ≥ 20 mg of prednisolone (chemotherapy premedication not taken into account). NSAID: non-steroidal anti-inflammatory drugs; ACE: angiotensin-converting enzyme; ARB: angiotensin II receptor blockers; HR+: hormone receptor-positive; Triple-negative: HER2- and hormone receptor-negative; HER2+: HER2-positive; CNS: central nervous system; SCLN: supraclavicular lymph nodes; IMN: internal mammary nodes

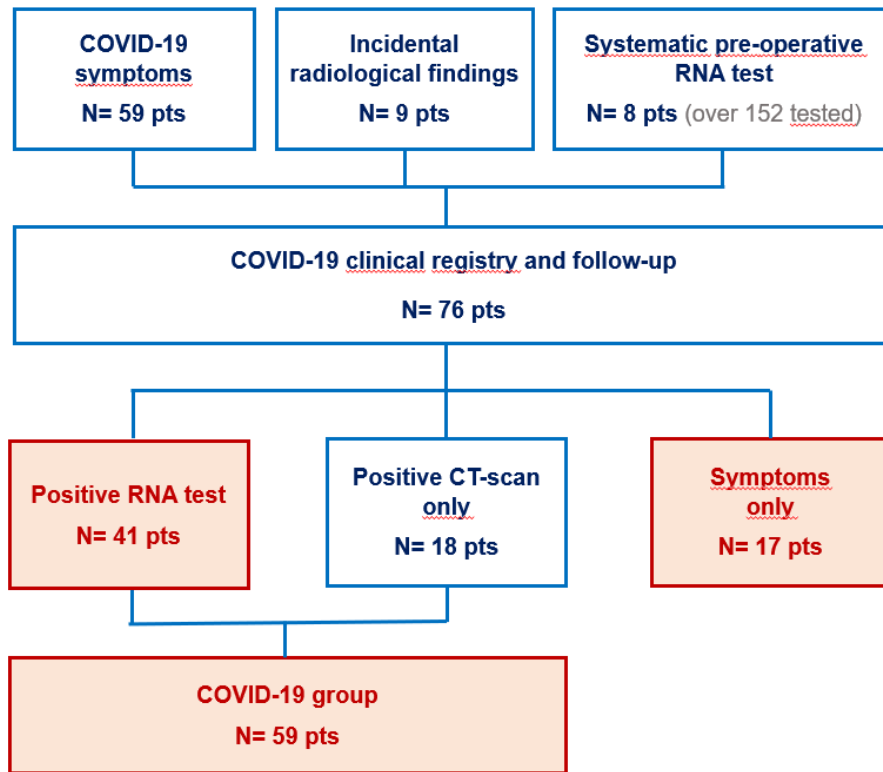
Table 2: Clinical, laboratory and radiologic features at first examination

	Positive RNA test N pts / N evaluable (%)	COVID-19 patients N pts / N evaluable (%)	Symptoms only N pts / N evaluable (%)
Clinical examination			
Fever ($\geq 38.0^\circ$)	21/41 (51%)	27/59 (46%)	10/17 (59%)
Cough	18/41 (44%)	22/59 (37%)	8/17 (47%)
Dyspnea	10/41 (24%)	17/59 (29%)	6/17 (35%)
Decreased saturation ($< 96\%$)	5/41 (12%)	7/59 (12%)	0/17 (0%)
GI disorders	5/41 (12%)	6/59 (10%)	2/17 (12%)
Headache	3/41 (7%)	3/59 (5%)	6/17 (35%)
Anosmia/Dysgeusia	4/41 (10%)	5/59 (8%)	2/17 (12%)
Possible nosocomial infection	8/41 (20%)	9/59 (15%)	0/17 (0%)
Laboratory parameters			
Neutrophil count: mean (IQR) (/mm ³)	4.3 (2.0–5.0) N=31	4.0 (2.0–5.1) N=49	4.0 (1.8–5.4) N=9
Lymphocyte count: mean (IQR) (/mm ³)	1.5 (1.3–3.9) N = 31	1.5 (0.8–1.9) N = 49	1.2 (0.7–1.5) N=9
LDH > ULN	4/4 (100%)	11/12 (92%)	0/3 (0%)
CT scan (central review)			
Extent of lesions (% of lung volume)			
No lesion	2/14 (14%)	3/28 (11%)	5/5 (100%)
< 10%	2/14 (14%)	10/28 (36%)	0/5 (0%)
10-25%	8/14 (57%)	12/28 (42%)	0/5 (0%)
26-50%	1/14 (7%)	2/28 (7%)	0/5 (0%)
51-75%	1/14 (7%)	1/28 (4%)	0/5 (0%)
> 75%	0/14 (0%)	0/28 (0%)	0/5 (0%)
Predominant type of lesion			
No lesion	2/14 (14%)	2/28 (7%)	5/5 (100%)
Ground-glass opacities	7/14 (50%)	14/28 (50%)	0/5 (0%)
Crazy paving	1/14 (7%)	4/28 (14%)	0/5 (0%)
Focal consolidation	3/14 (22%)	7/28 (25%)	0/5 (0%)
Linear consolidation	1/14 (7%)	1/28 (0%)	0/5 (0%)

GI: gastrointestinal; nosocomial infection refers to a new infection diagnosed >2 days after admission to hospital; ULN: upper limit of normal.

Figure 1: Patient flow and COVID-19 testing

1A: Patient flow



1B: Relationship between clinical, laboratory and radiologic features

Venn diagram focusing on the 30 patients with symptoms and available CT scan and RNA test results.

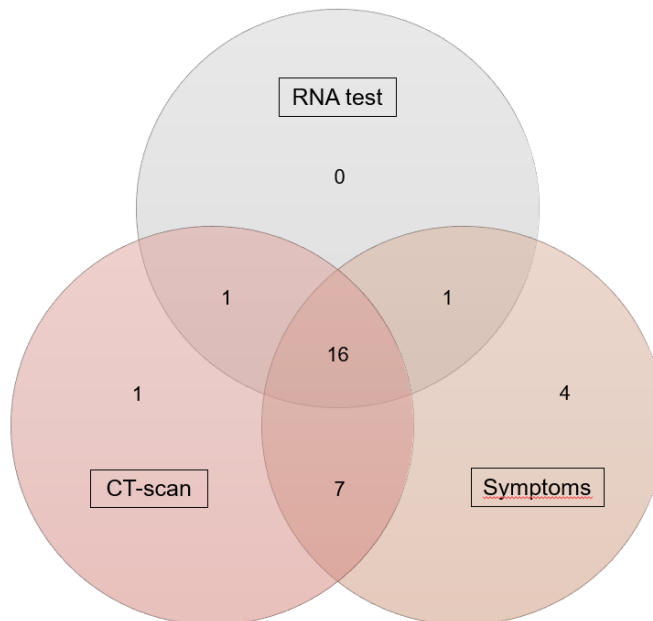


Figure 2: Radiation therapy and COVID-19 features

Presence of pleural or lung metastases (inner circle), radiation therapy sequelae (semiquantitative estimates, green circle) and extent of COVID-19 lung disease (semiquantitative estimates, red circle) are displayed by irradiation fields (blue circle) for each of the 59 COVID-19 patients. Patients who died are surrounded in black. CT scans not available for central review are not displayed on the graph (marked as 'not done').

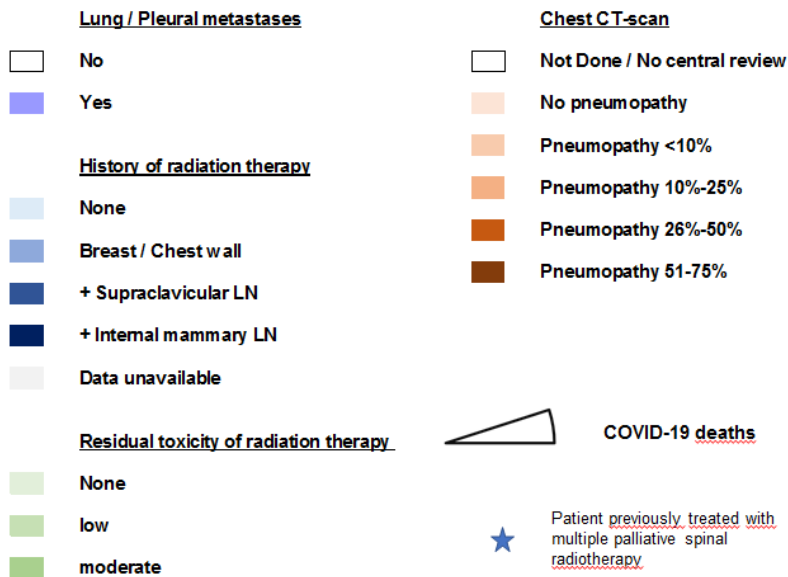
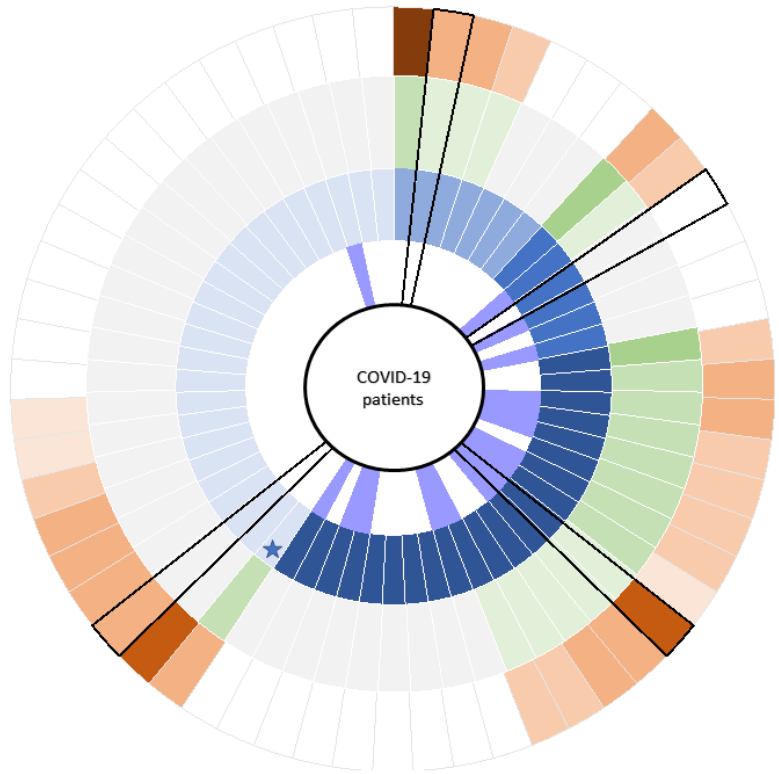
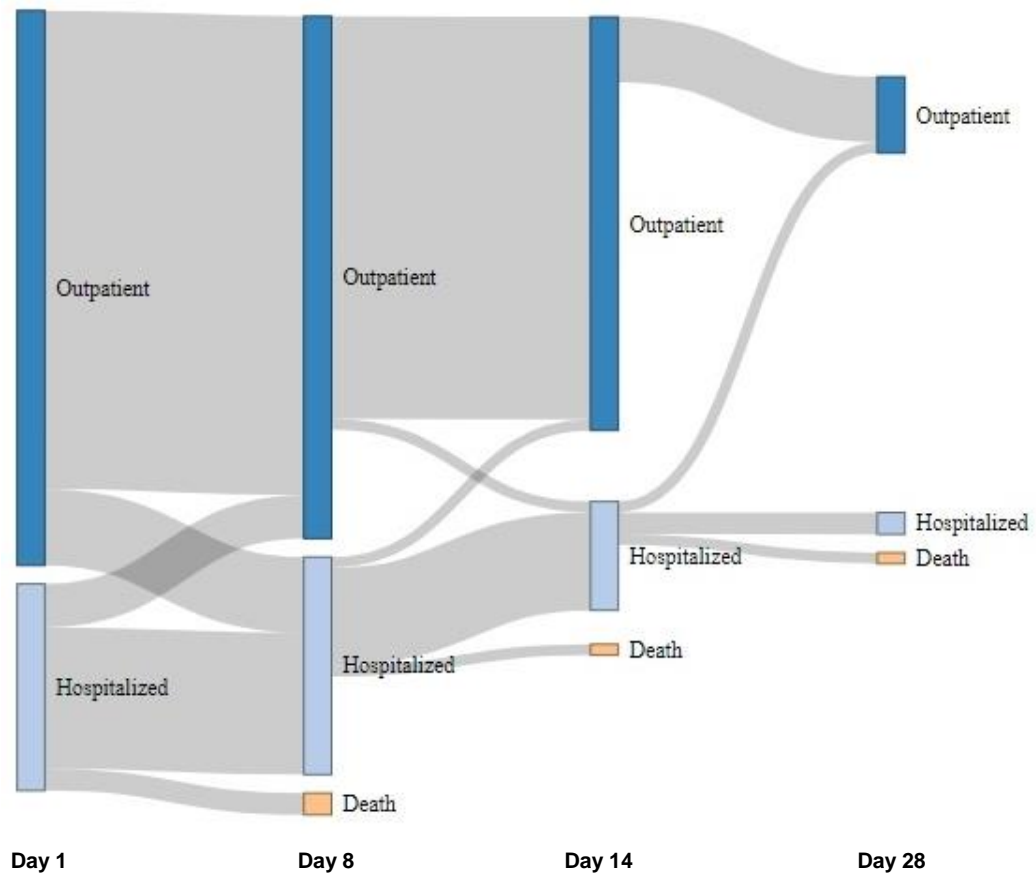


Figure 3: COVID-19 patients' trajectory

Follow up consisted in clinical evaluation by phone calls scheduled at days 8, 14 and 28.



Supplementary Table 1: Description of COVID-19-related deaths.

<p>Patient #1 was a 69-year-old woman with a history of diabetes, hypertension, hypertrophic cardiomyopathy and rheumatoid arthritis treated by abatacept (a CTLA-4 immunoglobulin). She was diagnosed with stage IIB triple-negative breast cancer in February 2020 and started neoadjuvant chemotherapy (epirubicin and cyclophosphamide) in March. Three days after the first cycle, she was referred to the emergency room (ER) with chest pain, fever and lung infection. SARS-CoV-2 infection was diagnosed based on positive RNA PCR and chest CT scan. She was admitted to ICU for acute respiratory distress on day 3, treated with antibiotics and endotracheal intubation and ventilation. She died 16 days later.</p>
<p>Patient #2 was a 44-year-old patient with no relevant medical history, diagnosed with <i>de novo</i> stage IV hormone-sensitive breast cancer (node, bone and hepatic metastases, with 4N cytotoxicity) in February 2020. She received a first-line combination of CDK4/6 inhibitor, aromatase inhibitor and complete ovarian function suppression. On day 17 of her first month of treatment, she was referred to the ER for asthenia, dyspnea, thrombocytopenia ($14,000/\text{mm}^3$) and neutropenia ($200/\text{mm}^3$). She was diagnosed with SARS-CoV-2 lung infection complicated by thrombotic microangiopathy, based on positive RNA test, chest CT scan and laboratory data. She was treated symptomatically, including antibiotics, and was not transferred to the intensive care unit due to her metastatic disease. She died 8 days after ER admission.</p>
<p>Patient #3 was a 78-year-old woman with a history of hypertension. She had been treated since November 2013 for stage IV hormone-sensitive breast cancer (lung and bone metastases). In March 2020, she received two cycles of weekly paclitaxel as second-line chemotherapy. Five days after the last injection, she was referred to the ER with dyspnea and hypoxia. SARS-CoV-2 infection was diagnosed based on a typical chest CT scan with extensive consolidation involving approximately 50% of the lungs. PCR RNA test was negative. Hydroxychloroquine and antibiotics were rapidly initiated on day 1, but the patient was not transferred to the intensive care unit due to her metastatic disease. She died on day 4.</p>
<p>Patient #4 was a 80-year-old woman treated for metastatic hormone-sensitive breast cancer (bone metastasis only) since February 2016. Since January 2020, after tumor progression, systemic therapy were stopped in favor of best supportive care. She had been hospitalized for tumor-related symptoms since February 2020. In late March, she presented signs of lung infection, followed by acute respiratory distress. Nosocomial SARS-CoV-2 infection was diagnosed based on positive RNA PCR and chest CT scan with ground-glass opacities involving approximately 20% of the lungs. Palliative symptomatic treatments with nasal oxygen therapy were initiated and the patient died 12 days after onset of the first symptoms.</p>