Outcomes of Breast Cancer Patients Treated with Chemotherapy, Biologic Therapy, Endocrine Therapy, or Active Surveillance During the COVID-19 Pandemic

Douglas K. Marks1,2, Nibash Budhathoki3,†, John Kucharczyk3,†, Faisal Fa’ak3,*, Nina D’Abreo1,2, Maryann Kwa1,4, Magdalena Plasilova1,5, Shubhada Dhage1,5, Phyuh Phyuh Soe1, Daniel Becker1, Alexander Hindenburg1,2, Johanna Lee3, Megan Winner1,6, Chinyere Okpara3, Alison Daly3, Darshi Shah3, Angela Ramdhanny3, Marleen Meyers1,4, Ruth Oratz1,4, James Speyer1,4, Yelena Novik1,4, Freya Schnabel1,5, Simon A. Jones7,‡, Sylvia Adams1,4,‡

1Perlmutter Cancer Center, NYU Langone Health, New York, NY, USA
2Department of Medicine, NYU Long Island School of Medicine, Mineola, NY, USA
3NYU Langone Hospital-Long Island, Mineola, NY, USA
4Department of Medicine, NYU Grossman School of Medicine, Manhattan, NY, USA
5Department of Surgery, NYU Grossman School of Medicine, Manhattan, NY, USA
6Department of Medicine, NYU Langone Hospital-Long Island, Mineola, NY, USA
7Department of Population Health, NYU Grossman School of Medicine, Manhattan, NY, USA

*Corresponding author: Douglas K. Marks, Department of Medicine, NYU Long Island School of Medicine, 120 Mineola Blvd, Suite 500 Mineola, NY 11501, USA. Email: douglas.marks@nyulangone.org
†These authors contributed equally to this work.
‡Denotes equal contribution for senior authorship.

Abstract

Purpose: Provide real-world data regarding the risk for SARS-CoV-2 infection and mortality in breast cancer (BC) patients on active cancer treatment.

Methods: Clinical data were abstracted from the 3778 BC patients seen at a multisite cancer center in New York between February 1, 2020 and May 1, 2020, including patient demographics, tumor histology, cancer treatment, and SARS-CoV-2 testing results. Incidence of SARS-CoV-2 infection by treatment type (chemotherapy [CT] vs endocrine and/or HER2 directed therapy [E/H]) was compared by Inverse Probability of Treatment Weighting. In those diagnosed with SARS-CoV-2 infection, Mann–Whitney test was used to assess risk factors for severe disease and mortality.

Results: Three thousand sixty-two patients met study inclusion criteria with 641 patients tested for SARS-COV-2 by RT-PCR or serology. Overall, 64 patients (2.1%) were diagnosed with SARS-CoV-2 infection by either serology, RT-PCR, or documented clinical diagnosis. Comparing matched patients who received chemotherapy (n = 379) with those who received non-cytotoxic therapies (n = 2343) the incidence of SARS-CoV-2 did not differ between treatment groups (weighted risk; 3.5% CT vs 2.7% E/H, P = .523). Twenty-seven patients (0.9%) expired over follow-up, with 10 deaths attributed to SARS-CoV-2 infection. Chemotherapy was not associated with increased risk for death following SARS-CoV-2 infection (weighted risk; 0.7% CT vs 0.1% E/H, P = .246). Advanced disease (stage IV), age, BMI, and Charlson’s Comorbidity Index score were associated with increased mortality following SARS-CoV-2 infection (P ≤ .05).

Conclusion: BC treatment, including chemotherapy, can be safely administered in the context of enhanced infectious precautions, and should not be withheld particularly when given for curative intent.

Key words: breast cancer; COVID-19; SARS-CoV-2; cancer treatment.

Implications for Practice

Worldwide the SARS-CoV-2 pandemic has resulted in delays in the diagnosis and treatment of cancer patients due, in part, to concerns for potential treatment-related immunosuppression. Observational studies published early in the pandemic reported higher morbidity and mortality rates from SARS-CoV-2 infection in cancer patients; however, these studies provide insufficient cancer-related demographic and treatment detail to inform clinical practice. In this mixed urban/suburban study cohort, we observed low rates of SARS-CoV-2 infection and mortality in BC patients on active therapy, including cytotoxic chemotherapy, when administered in the context of enhanced infection precautions. Given the observed efficacy of infection prevention measures in this population, in general, clinicians should exercise caution when considering withholding or substantively modifying evidence-based therapy particularly in the curative setting. Additionally, these findings are informative to physicians when counseling their patients on the safety of receiving BC treatment during the SARS-CoV-2 pandemic.
Background

The SARS-CoV-2 virus has critically impacted the United States’ healthcare system and resulted in significant disruption to the provision of cancer care with one analysis projecting greater than 30 000 excess deaths due to diagnostic delays and treatment interruption.\(^1\)\(^-\)\(^3\) For early-stage high-risk estrogen-receptor positive, HER2-positive, or triple-negative breast cancer (BC), chemotherapy increases the probability of cure when given in neoadjuvant or adjuvant setting.\(^5\) In a survey of patients with BC taken during the SARS-CoV-2 pandemic, approximately 50% reported delays in treatments, with 32% specifically citing delays in infusion therapy.\(^7\)

While initial observational studies reported high mortality rates in cancer patients following SARS-CoV-2 infection, particularly following receipt of chemotherapy, other studies have not consistently confirmed this observation.\(^8\)\(^-\)\(^14\) Until recently, the majority of analyses provided minimal patient-level data, preventing identification of cancer-specific risk factors which may account for the adverse outcomes observed.\(^9\)\(^-\)\(^14\)

Although cytotoxic chemotherapy is potentially immunosuppressive, the clinical relevance may vary between tumor types due to differences in agents, dose administered and immunosuppression due to underlying disease.\(^15\) Furthermore, for some malignancies, optimal cancer treatment may have included concurrent administration of other therapies capable of augmenting the immunosuppressive effect of cytotoxic treatment.\(^16\)\(^,\)\(^17\)

Recently, data derived from newly established COVID-era registries dedicated to assessing the impact of SARS-CoV-2 on cancer specific outcomes have indicated that the pandemic has differentially affected patients with different tumor types.\(^18\)\(^-\)\(^20\) These series support early observations, that patients with hematologic and thoracic malignancy are at particularly high risk for hospitalization and death following SARS-CoV-2 infection.\(^10\)\(^,\)\(^18\)\(^,\)\(^21\) Subsequently several disease-specific patient series, including the TERAVOLT analysis for thoracic malignancies, have provided the greatest resolution on clinical outcomes in this subset of cancer patients.\(^21\)\(^,\)\(^22\) While data remain discordant regarding the additional risk for infection from SARS-CoV-2 with chemotherapy, patients with active metastatic disease appear to be at greatest risk for poor outcomes potentially due to concurrent immune dysfunction which accompanies disease progression.\(^18\)\(^,\)\(^20\)\(^,\)\(^21\)

Despite the high prevalence of BC, few studies have focused specifically on BC patients. Compared with other tumor histologies, historically, patients with BC had low infection and mortality rates with prior viral outbreaks. Between 1998 and 2001 in the United States, patients with prostate cancer and lung cancer had a 5.5-fold and 11-fold higher hospital mortality rate from influenza compared with BC patients.\(^15\) BC patients accounted for only 2% of cancer patients admitted for influenza during the time period. However, BC is a heterogeneous group, and anti-neoplastic therapies have changed significantly over the past decade. Assuming similar outcomes in the context of a pandemic due to a novel virus and new anti-neoplastic therapies may not be accurate.

While limited data are available regarding risk for infection and complication from SARS-CoV-2 in BC patients, one European series suggests BC patients may fare similarly to prior viral outbreaks, reporting only 59 confirmed infections in over 15 000 patients treated during the early pandemic period.\(^24\) While this data set is reassuring, testing rates were very low and cancer-specific data and treatment data were only provided for the small group of BC patients diagnosed with SARS-CoV-2, preventing assessment of clinical risk factors for infection. Despite evidence that supports variable immunity to SARS-CoV-2 within population, nearly all published and presented series which include BC cancer patients focus on risk factors for poor outcomes following infection with SARS-CoV-2, as compared to assessing risk factors for SARS-CoV-2 infection.\(^24\)\(^-\)\(^28\)

With the trajectory and duration of the pandemic uncertain, oncology providers must be prepared to counsel patients on the safety of receiving treatment while SARS-CoV-2 remains an active pathogen. In the absence of randomized trials, real-world data sets are required to inform clinical decision making. This observational study assesses both incidence and complications of SARS-CoV-2 infection in BC patients who received care at an academic cancer center in New York during the peak of the SARS-CoV-2 pandemic. This study endeavors to address the knowledge deficit regarding the risk of anti-cancer therapies in this population by comparing the incidence and complications of SARS-CoV-2 in patients treated with cytotoxic chemotherapy (CT) versus non-cytotoxic therapies (endocrine therapy, HER-2 therapy, targeted therapies, E/H).

Methods

This study is an observational analysis of patients treated for BC at Perlmutter Cancer Center (PCC) at NYU Langone Health. Patients were included in the study if they carried a diagnosis of BC and underwent clinical evaluation, with a telemedicine or in-person encounter on at least one occasion between February 1, 2020 and May 1, 2020 documented in the EMR. All patients were cared for at Manhattan (PCC Manhattan), Brooklyn (PCC Midwood, PCC Sunset Park) or Long Island (PCC Long Island) locations. Hospitalization data were captured from physician documentation and admission records from NYU Langone Health Hospitals (NYU Langone Medical Center, NYU Langone Hospital – Brooklyn, NYU Langone Hospital-Long Island). All patients, seen on-site, underwent symptom assessment and temperature checks prior to entry to cancer center sites, and subsequently were required to wear masks throughout treatment.

Clinical data were abstracted from the electronic health record (Epic Systems, Verona, WI) as well as Perlmutter Cancer Center Data Hub and the NYU Langone Health SARS-CoV-2 Data Mart which includes data from outpatient and inpatient visits in the health system. A physician team (D.M., N.D., N.B., J.K., M.W., A.D., and A.R.) confirmed patient demographics, oncologic treatment history including active treatment course, SARS-CoV-2 status, and clinical status at date of last follow-up. Approximately 800 charts were manually reviewed by the physician team to ensure accuracy, including all SARS-CoV-2 positive patients were reviewed manually. Non-NYU hospitalizations were captured if noted in provider documentation. Patients were classified as positive for SARS-CoV-2 infection if patients either had a positive PCR and/or serology assay or clinician documentation noting symptoms suspicious or consistent with SARS-CoV-2 disease. Staging data were retrieved from the cancer staging field in EMR or
abstracted from notes using Natural Language Processing, when not available. Cause of death was determined by physician review of EMR records. Any patient diagnosed with SARS-CoV-2, who died during the follow up period, was considered a death due to SARS-CoV-2 regardless of proximate cause of death. Other causes of death, such as progression of disease were also noted when possible. In cases where cause of death was unknown, this was annotated.

SARS-CoV-2 testing was performed by the New York City Department of Health and Mental Hygiene, until March 16, 2020 when testing was performed exclusively in NYU Langone Health clinical laboratories either by Roche SARS-CoV-2 assay in Cobas 6800 instruments or by SARS-CoV-2 Xpert Xpress assay with the Cepheid Gene Xpert instruments both under Emergency Use Authorization by the FDA as previously described. Serology testing was performed by Abbott ELISA assay.

The primary endpoint of the study was to define the incidence of SARS-CoV-2 infection by anti-cancer treatment type with either cytotoxic chemotherapy (CT) or non-cytotoxic therapy (E/H). Secondary outcomes included differences in incidence of SARS-CoV-2 infection by specific treatment agent as well as patients not on treatment (NT). Additionally, as a secondary outcome, we compared clinical outcomes (severe illness requiring hospitalization, death) from SARS-CoV-2 disease between groups. Descriptive statistics were used to describe the overall population and subpopulations of different treatment groups. Marginal risk of SARS-CoV-2 infection by treatment group was assessed by Inverse Probability of Treatment Weighting. Associations between cancer-specific factors and previously identified medical comorbidities on the incidence of SARS-CoV-2 infection and death or hospitalization from SARS-CoV-2 disease were assessed by Mann–Whitney test. Anti-neoplastic therapies were defined as either cytotoxic chemotherapy or non-cytotoxic therapy which included endocrine therapy, HER-2 directed therapy, immunotherapy or other targeted therapies. Patients were classified as positive for SARS-CoV-2 if patient either had a positive PCR and/or serology assay or clinician documentation of SARS-CoV-2 disease Patients with congenital or acquired immunodeficiency, who received chemotherapy within 6-month prior to study were excluded given concerns for residual immunosuppression. Patients with inadequate documentation to determine disease or treatment status were also excluded. Study analysis was approved by the NYU School of Medicine Institutional Review Board.

Results

Three thousand seven hundred and seventy-eight BC patients were seen across Perlmutter Cancer Center at NYU Langone Health sites between February 1, 2020 and May 1, 2020, with 3062 patients meeting criteria for inclusion in this study. The cohort comprised 3039 women (99.2%) and 23 men (0.8%) with mean age of 62 (23-104 years). The majority of patients had early-stage disease (stage I-III, 89.3%) versus advanced disease (stage IV, 10.3%). Patient population self-identified as Caucasian (n = 1925, 63%), Black (n = 303, 10%), Asian (n = 198, 6.5%), Hispanic (n = 18, 0.6%), and other/unknown (n = 618, 20%). In terms of anti-cancer therapy, 379 patients were included in CT group, 2343 patients in E/H group and 340 patients in NT group. Patient demographics and oncologic history including cancer stage and receptor subtype are shown by treatment group for CT versus E/H cohorts (Table 1).

Eight hundred and seventy-eight SARS-CoV-2 tests (PCR + Serology) were performed in study cohort during data collection period, with 641 (20.9%) patients tested by either PCR or serology. By treatment group 207, 379, 55 patients were tested in the CT, E/H and NT groups respectively. In the CT group, 194 patients were tested by PCR and 113 patients underwent antibody testing. In the E/H group, 327 patients were tested by PCR and 170 patients underwent antibody testing.

Chemotherapy not Associated With Increased Risk of SARS-CoV-2 Infection as Compared to Endocrine and/or HER2-directed Therapy

In the study cohort, 64 patients were diagnosed with SARS-CoV-2 infection, with 43 patients in the E/H group, 18 patients in the CT group and 3 patients diagnosed while on active surveillance. Of the 64 patients diagnosed with SARS-CoV-2 infection, 62 patients had positive laboratory testing and 2 were diagnosed by clinical diagnosis alone. Patients who received CT during the study period, did not exhibit higher incidence of SARS-CoV-2 infection, as compared with a matched cohort of E/H patients (weighted risk 3.5% CT vs 2.7% E/H, P = .523, Table 2). No difference in test positivity rates was seen between CT versus E/H, with positivity rate of 8.7% in CT group versus 11.3% in E/H group. Of the 18 patients in CT group diagnosed with SARS-CoV-2 infection, 10 patients were treated with single agent and 8 patients with multi-agent regimens. Single-agent paclitaxel was the most common monotherapy regimen, and CMF the most common multi-agent regimen (Supplementary Table 1). No significant difference in risk for SARS-CoV-2 infection was seen by disease stage comparing patients with early stage (Stage I-III) versus advanced stage disease (Stage IV) (P = .98).

Hospitalization and Mortality Following SARS-COV-2 Infection Was Rare in BC Patients Regardless of Treatment

Patients in the CT group had higher rates of all-cause hospitalization versus E/T group (weighted rate 10.1% vs 3.1%, P = .001) and all-cause mortality risk (weighted rate 2.4% vs 0.5%, P = .029). However, COVID-19-specific mortality did not differ between CT versus E/H groups (weighted rate 0.7% vs 0.1%, P = 0.246).

Of the 27 patients expired, 10 patients expired following SARS-CoV-2 infection, including 4 patients on CT, 2 patients on E/H, and 4 patients in NT groups (Supplementary Table 2). In the E/H and CT groups, progression of disease remained the most common cause of death (n = 10), and was 2 times more likely to be the cause of death than SARS-CoV-2 in the CT group.

Advanced Stage (stage IV) Disease and Established Nononcologic Risk Factors Are Associated With Increased Risk for Death Following SARS-CoV-2 Infection

While receipt of CT versus E/H treatment and disease stage does not appear to increase risk for SARS-CoV-2, metastatic disease was associated with mortality following SARS-CoV-2 infection (P = .019). Additionally, advanced age (mean 73 vs 58, P = .001), higher Charlson Comorbidity Index (6.1 vs
3.37, \( P = .014 \)) and greater BMI (33.5 vs 29.2, \( P = 0.05 \)) were associated with death following SARS-CoV-2 infection in this BC cohort (Table 3).

**Discussion**

In response to the SARS-CoV-2 pandemic, numerous "expert-opinion" guidelines have been released by healthcare systems and oncologic societies which propose modifications to evidence based practice. These guidelines intend to balance an individual patient's risk of progression or recurrence with risk for complications of SARS-CoV-2.7,10,29-36 However, significant concerns exist regarding these guidelines, as substantial delays in cancer care delivery have been reported, with 44% of patients in one series, which included high-risk, reporting delays in care.7 Initially, these guidelines were developed in

---

**Table 1. Patient demographics by treatment group.**

| Demographics                      | Treatment group (unweighted) | SMD^a       |
|-----------------------------------|-----------------------------|-------------|
|                                   | CT                          | E/H         |               |
| N                                 | 379                         | 2343        |               |
| Mean SD/%                         | Mean SD/%                   | Mean SD/%   |               |
| Age (mean [SD])                   | 58.8 12.84                  | 61.9 12.73  | 0.059        |
| Male Gender                       | 3 0.8                       | 19 0.8      | 0.056        |
| Race (%)                          | 0.159                       |             |              |
| Asian                             | 20 5.3                      | 178 7.6     | 7.6          |
| Black                             | 78 20.6                     | 225 9.6     | 9.6          |
| Hispanic                          | 2 0.5                       | 16 0.7      | 0.7          |
| Native American                   | 1 0.3                       | 5 0.2       | 0.2          |
| Native Hawaiian or Other Pacific Islander | 1 0.3    | 4 0.2      | 0.2          |
| Other                             | 40 10.6                     | 192 8.2     | 8.2          |
| Patient Refused                   | 0 0                         | 7 0.3       | 0.3          |
| Unknown                           | 6 1.6                       | 22 0.9      | 0.9          |
| White                             | 231 60.9                    | 1694 72.3   | 72.3         |
| Location (%)                      |                             |             | 0.044        |
| Brooklyn                          | 37 9.8                      | 91 3.9      | 3.9          |
| Manhattan                         | 244 64.4                    | 1664 71     | 71           |
| Long Island                       | 96 25.9                     | 588 25.1    | 25.1         |
| BMI (mean [SD])                   | 27.44 6.49                  | 23.09 11.61 | 0.189        |
| CCI (mean [SD])                   | 5 3.39                      | 3.13 2.58   | 0.056        |
| BC Subtype (%)                    |                             |             | 0.126        |
| ER-/HER2-                         | 28.6 0.3                    | 0.3         |              |
| ER-/HER2+                         | 6.6 3.2                     | 3.2         |              |
| ER+/HER2-                         | 46.4 78.4                   | 78.4        |              |
| ER+/HER2+                         | 18.4 18.1                   | 18.1        |              |

Table includes all patients (unweighted). Weighted/matched analysis performed with Inverse Probability of Treatment Weighting (IPTW).

^aSMD from post-weighting cohort analyses.

Abbreviations: CT, chemotherapy; E/H, non-cytotoxic/Endocrine/HER2-directed therapy; SMD, standardized mean difference.

**Table 2. COVID-19 infection and mortality by treatment group.**

| N   | SARS-CoV-2 infection | Rate | Weighted rates | Risk difference | 95% LCI | 95% UCI | P value |
|-----|----------------------|------|----------------|-----------------|---------|---------|---------|
| CT  | 379                  | 18   | 4.7% 3.5%      | 0.8%            | −1.7%   | 3.4%    | .523    |
| E/H | 2343                 | 43   | 1.8% 2.7%      |                 |         |         |         |
| N   | Overall mortality^a  |      |                |                 |         |         |         |
| CT  | 379                  | 13   | 3.4% 2.4%      | 1.9%            | 0.2%    | 3.6%    | .029    |
| E/H | 2343                 | 10   | 0.4% 0.5%      |                 |         |         |         |
| N   | COVID-19-specific mortality | | | | | | |
| CT  | 379                  | 4    | 1.1% 0.7%      | 0.6%            | −0.4%   | 1.6%    | .246    |
| E/H | 2343                 | 2    | 0.1% 0.1%      |                 |         |         |         |

Chemotherapy (CT), Non-cytotoxic therapy (E/H).

^aOverall mortality includes patients who expired from progression of disease, nononcologic/non-COVID-19 illness, COVID-19, and from unknown cause.
The context of limited data and scarce healthcare resources; however, now should be updated to reflect emerging data indicating significant heterogeneity in clinical outcomes following SARS-CoV-2 infection among patients with cancer.19

Unfortunately, 6 months after the World Health Organization assigned pandemic status to SARS-CoV-2 disaster, the overwhelming majority of publications, across all cancer types, have focused on patient outcomes post-infection.12,18-21,37-44 This approach has limited identification of the cancer-specific risk factors for SARS-CoV-2 infection and complications.

Several studies observed worse outcomes in cancer patients when diagnosed with SARS-CoV-2 infection, particularly following receipt of antineoplastic therapy, however, until recently, these studies were either small series or present aggregated outcomes from variety of cancer types and treatment history.8,10,41-49 For high-risk estrogen-receptor positive, HER2-positive, or triple-negative BC, chemotherapy significantly increases the probability of cure when given in neoadjuvant or adjuvant setting.6 In addition to directly impacting cancer-specific outcomes, the pandemic has led to an increase in psychological complaints including fear and anxiety in patients on active treatment.3,18-21,37-44 This approach has limited identification of the cancer-specific risk factors for SARS-CoV-2 infection and complications.

Several studies observed worse outcomes in cancer patients when diagnosed with SARS-CoV-2 infection, particularly following receipt of antineoplastic therapy, however, until recently, these studies were either small series or present aggregated outcomes from variety of cancer types and treatment history.8,10,41-49 For high-risk estrogen-receptor positive, HER2-positive, or triple-negative BC, chemotherapy significantly increases the probability of cure when given in neoadjuvant or adjuvant setting.6 In addition to directly impacting cancer-specific outcomes, the pandemic has led to an increase in psychological complaints including fear and anxiety in patients on active treatment.3,18-21,37-44 This approach has limited identification of the cancer-specific risk factors for SARS-CoV-2 infection and complications.

Studies designed to assess the associations of specific therapies and SARS-CoV-2-infection and complications are required for clinicians to make informed clinical decisions and accurately counsel patients during this pandemic.

In our cohort of 3062 patients with BC treated at an academic cancer center in the locus of the outbreak in the United States, we observed a low rate of SARS-CoV-2 infection. Our findings, are consistent with previously published studies where a very low incidence of SARS-CoV-2 was observed in BC patient cohorts in France and South Korea.24,56 In France, only 76 of 15 600 BC patients within the Institute Curie Hospital system tested positive for the SARS-CoV-2 virus during a four month time period surrounding the March 2020 lockdown. However, very limited data are provided regarding extent of clinical evaluation, testing, and oncologic treatment history of the patients in these reported series.24,56

All 379 patients treated with CT during study period were clinically evaluated for signs and symptoms of SARS-CoV-2 and 55% of patients underwent either PCR and/or serologic testing for SARS-CoV-2. Despite this, we did not observe a statistically significant increase risk for infection or mortality from SARS-CoV-2 in patients treated with CT versus E/T. Additionally, in the patients that were subsequently diagnosed with SARS-CoV-2, there was no detectable association with having previously received multagent versus single-agent chemotherapy. The low infection rate we observed in this BC cohort underscores the heterogeneity of cancer patients with regards to the degree of immunosuppression associated with their specific underlying disease and treatment history. While testing performed early in the pandemic was primarily for diagnostic purposes and therefore inherently underestimates the incidence of asymptomatic infection, in this cohort, 40% of patients were diagnosed with asymptomatic infection which is similar to rates reported in the general population during this period.57,38 Although testing was available to cancer center patients throughout the study window, to account for potential underdiagnosis, we confirmed survival status of all study patients with death registry. Including patients who died of unknown cause, the probability of dying
was <2% by close of data collection with no increased risk observed between CT versus E/H groups \((P = .533)\).

Despite concerns that functional immunosuppression associated with metastatic disease might increase the risk for SARS-CoV-2 infection, patients with early stage breast cancer (stage I-III) and advanced breast cancer (stage IV) exhibited similar test positivity rates for SARS-CoV-2, which were in line with those reported in the New York City-metro area at the time (10% in the present cohort vs 19.9% in New York City and 11.4% on Long Island).59 These findings should empower breast oncology providers to reassure their patients that BC does not appear to be a risk factor for contraction of SARS-CoV-2 and that infectious precautions are expected to be equally beneficial and adequate for this patient subgroup.44,60

While the numbers were small, following SARS-CoV-2 infection, a greater proportion of patients with advanced disease (stage IV) expired, underscoring the importance of vigilant infection prevention strategies. However, despite this, the metastatic BC subset remained more likely to die from progression of disease rather than SARS-CoV-2, indicating the importance of maintaining active cancer therapy.

We additionally confirmed expected associations between known non-oncologic risk factors, including age, Charlson Comorbidity Index, and BMI and mortality following SARS-CoV-2 infection in this BC population. These results highlight the importance of oncology providers educating elderly patients, particularly those with diabetes, cardiovascular disease, chronic kidney disease, and underlying lung disease on the importance of vigilance with regards to infection prevention.

**Study Limitations**

Given the retrospective design of the study, we are unable to exclude the possibility that bias may exist due to patient treatment selection for chemotherapy during the context of the pandemic although our analysis does include a substantial number of patients treated with chemotherapy, including multiagent regimens. Similarly, we cannot exclude that a prospective analysis may identify a specific treatment or patient-related risk factor associated with increased risk for infection and/or complication from SARS-CoV-2. While the very low mortality rate we observed is highly reassuring regarding the safety of BC treatment during the pandemic, it does limit our ability to exclude the presence of a minor impact of any specific therapy on SARS-CoV-2 specific mortality. That said, the low event rate observed in this cohort suggests that the magnitude of any identified risk factor would be modest. Additionally, due to low event rate, secondary analyses are largely univariate analyses and confounding variables cannot be excluded. Of note, patients were instructed to follow enhanced infection precaution measures such as mask-wearing and social distancing and similar outcomes should not be assumed in the absence of these measures. Patient data was extracted from electronic medical record which included clinical documentation and laboratory testing data from NYU Langone Health. As such, patients diagnosed outside NYU Langone Health, without clinical or laboratory documentation within the EMR were not captured.

Lastly, as the pandemic continues, new variants in the virus have emerged which may differ in contagious risk, and therefore we anticipate these types of studies will need to be repeated over the course of the pandemic.

**Summary**

Worldwide the SARS-CoV-2 pandemic has resulted in delays in diagnosis and treatment of cancer. Although chemotherapy is associated with survival benefit in a large group of patients with BC, concerns exist regarding administration of potentially immunosuppressive medications in the context of the SARS-CoV-2 pandemic. While several observational studies have reported increased morbidity and mortality from SARS-CoV-2 infection in cancer patients, these studies provide insufficient cancer-related demographic and treatment detail to inform clinical practice. As risk for infection and complications from SARS-CoV-2 may vary by tumor type and treatment, these factors must be incorporated into analyses of cancer patient outcomes. Our study provides SARS-CoV-2 outcome data specific to BC, from a large cohort of patients with known treatment history. In this BC cohort, we observed a very low infection rate regardless of treatment administered and did not identify any increased risk for SARS-CoV-2 infection in patients treated with chemotherapy. We did however confirm associations with several nononcologic risk factors including advanced age and greater Charlson Comorbidity Index score with SARS-CoV-2 mortality. This study demonstrates that evidence-based cancer therapy, including chemotherapy, can be administered safely to patients with BC in the context of enhanced infection precautions, clinical monitoring, and recently efficacious vaccines. Our findings additionally support clinicians when counseling patients on the safety of receiving treatment during the SARS-CoV-2 pandemic.

**Acknowledgments**

This study is dedicated to our patients who inspire us every day. While navigating a cancer diagnosis is never easy, doing so during a pandemic requires heroic personal strength. We also would like to acknowledge the entire medical staff who help keep our patients safe, and Perlmutter Cancer Center leadership for their support of this study.

**Funding**

This study was supported with departmental funds. D.M. has research and salary support from Manhasset Women’s Coalition Against Breast Cancer and the Shifrin Myers Breast Cancer Discovery Fund.

**Conflict of Interest**

The authors indicated no financial relationships.

**Author Contributions**

Conception/design: D.K.M., S.A., and S.A.J. Provision of study material or patients: D.K.M., N.D., M.K., M.P., S.D., P.P.S., D.B., A.H., J.L., M.W., M.M., R.O., J.S., Y.N., F.S., and S.A. Collection and/or assembly of data: N.B., J.K., A.D., and A.R. Data analysis and interpretation: D.K.M., C.O., D.S., and P.P.S. Manuscript writing: D.K.M., S.A., S.A.J., M.K., N.D., and FF. Final approval of manuscript: All authors.
Data Availability
The data underlying this article will be shared on reasonable request to the corresponding author.

Supplementary Material
Supplementary material is available at The Oncologist online.

References
1. Maringe C, Spicer J, Morris M, et al. The impact of the COVID-19 pandemic on cancer deaths due to delays in diagnosis in England, UK: a national, population-based, modelling study. Lancet Oncol. 2020;21(8):1023-1034.
2. Sud A, Torr B, Jones ME, et al. Effect of delays in the 2-week-wait cancer referral pathway during the COVID-19 pandemic on cancer survival in the UK: a modelling study. Lancet Oncol. 2020;21(8):1035-1044.
3. Lai AG, Pasea L, Banerjee A, et al. Estimated impact of the COVID-19 pandemic on cancer services and excess 1-year mortality in people with cancer and multimorbidity: near real-time data on cancer care, cancer deaths and a population-based cohort study. BMJ Open. 2020;10:e043828. doi:10.1136/bmjopen-2020-043828.
4. Misskowksi C, Paul SM, Snowberg K, et al. Stress and symptom burden in oncology patients during the COVID-19 pandemic. J Pain Symptom Manage. 2020;60(5):e25-e34.
5. Choi JH, Simone CB, II. Caring for patients with cancer in the face of self-vulnerability during the covid-19 pandemic. JAMA Oncology. 2020;6(10):1639-1640.
6. Blum JF, Flynn PJ, Yothers G, et al. Anthracyclines in early breast cancer: The abc trials—us06-090, nsabp b-46/us07132, and nsabp b-49 (mrg oncology). J Clin Oncol. 2017;35:2647-2655.
7. Papautsky EL, Hamlish T. Patient-reported treatment delays in breast cancer care during the covid-19 pandemic. Breast Cancer Res Treat 2020;184:1-6.
8. Iftimie S, López-Azcona AF, Vicente-Miralles M, et al. Risk factors associated with mortality in hospitalized patients with SARS-CoV-2 infection. A prospective, longitudinal, unicenter study in Reus, Spain. PLoS One. 2020;15(9):e0234452.
9. Dai M, Liu D, Liu M, et al. Patients with cancer appear more vulnerable to SARS-CoV-2: a multicenter study during the COVID-19 outbreak. Cancer Discov. 2020;10(6):783-791.
10. Liang W, Guan W, Chen R, et al. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. Lancet Oncol. 2020;21(3):335-337.
11. Barlesi F, FS, Bayle A, et al. Outcome of cancer patients infected with COVID-19, including toxicity of cancer treatments. Presented at: American Association for Cancer Research (AACR) Virtual Annual Meeting I and April 27-28 Ps. Virtual Annual Meeting, April 27–28, 2020.
12. Mehta V, Goel S, Kabarriri R, et al. case fatality rate of cancer patients with COVID-19 in a New York Hospital System. Cancer Discov. 2020;10(7):935-941.
13. Petrilll CM, Jones SA, Yang J, et al. Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: prospective cohort study. BMJ. 2020;369:m1966.
14. Lee LY, Cazier JB, Angelis V, et al.; UK Coronavirus Monitoring Project Team. COVID-19 mortality in patients with cancer on chemotherapy or other anticancer treatments: a prospective cohort study. Lancet. 2020;395(10241):1919-1926.
15. Cooksley CD, Avritscher EB, Bekele BN, Rolston KV, Geraci JM, Elting LS. Epidemiology and outcomes of serious influenza-related infections in the cancer population. Cancer. 2005;104(3):618-628.
16. Rafailidis PI, Kakisi OK, Vardakas K, Falagas ME. Infectious complications of monoclonal antibodies used in cancer therapy: a systematic review of the evidence from randomized controlled trials. Cancer. 2007;109(11):2182-2189.
17. Aksoy S, Dizdar O, Hayran M, Harputluoglu H. Infectious complications of rituximab in patients with lymphoma during maintenance therapy: a systematic review and meta-analysis. Leuk Lymphoma. 2009;50(3):357-365.
18. Kuderer N, Choueiri TK, Shah DP, et al.; COVID-19 and Cancer Consortium. Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study, Lancet. 2020;395(10241):1907-1918.
19. Lee LY, Cazier JB, Starkey T, et al.; UK Coronavirus Cancer Monitoring Project Team. COVID-19 prevalence and mortality in patients with cancer and the effect of primary tumour subtype and patient demographics: a prospective cohort study. Lancet Oncol. 2020;21(10):1309-1316.
20. Robilotti EV, Babady NE, Mead PA, et al. Determinants of COVID-19 disease severity in patients with cancer. Nat Med. 2020;26(8):1218-1223.
21. Garassino MC, Whisnant JG, Huang LC, et al.; TERAVOLT investigators. COVID-19 in patients with thoracic malignancies (TERAVOLT): first results of an international, registry-based, cohort study. Lancet Oncol. 2020;21(7):914-922.
22. Lee J, Foote MB, Lumish M, et al. Chemotherapy and covid-19 outcomes in patients with cancer. J Clin Oncol. 2020;38(30):3538-3546.
23. Mato AR, Roeker LE, Lamanna N, et al. Outcomes of COVID-19 in patients with CLL: a multicenter international experience. Blood. 2020;136(10):1134-1143.
24. Vuagnat P, Frelaut M, Ramtohul T, et al.; Institut Curie Breast Cancer and COVID Group. COVID-19 in breast cancer patients: a cohort at the Institut Curie hospitals in the Paris area. Breast Cancer Res. 2020;22(1):55.
25. Braun J, Loyal L, Frentsich M, et al. SARS-CoV-2-reactive T cells in healthy donors and patients with COVID-19. Nature. 2020;587(7833):270-274.
26. Zhang B, Xie R, Hubert SM, et al. Characteristics and outcomes of 35 breast cancer patients infected with Covid-19. Front Oncol. 2020;10:570130.
27. Khaki AR, Shah DP, Lustberg MB, et al. Characteristics and outcomes of sars-cov-2 infection in patients with invasive breast cancer (bc) from the covid-19 and cancer consortium (ccc19) cohort study. Presented at Presented at the 2020 San Antonio Breast Cancer Symposium (SABCS). Virtual presentation, December 8–11, 2020.
28. Kalinsky K, Accordino MK, Hosi K, et al. Characteristics and outcomes of patients with breast cancer diagnosed with SARS-CoV-2 infection at an academic center in New York City. Breast Cancer Res Treat. 2020;182(1):239-242.
29. Al-Shamsi HO, Alhazzani W, Alhuraiji A, et al. A practical approach to the management of cancer patients during the novel Coronavirus disease 2019 (COVID-19) pandemic: an international collaborative group. Oncologist. 2020;25(6):e936-e945.
30. Chan JJ, Sim Y, Ow SGW, et al. The impact of COVID-19 on and recommendations for breast cancer care: the Singapore experience. Endocr Relat Cancer. 2020;27(9):R307-R327.
31. Gasparri ML, Gentilini OD, Lueftner D, Kuehn T, Kaidar-Person O, Poortmans P. Changes in breast cancer management during the Corona Virus Disease 19 pandemic: an international survey of the European Breast Cancer Research Association of Surgical Trialists (EBREAST). Breast. 2020;52:110-115.
32. Soreide K, Hallet J, Matthews JB, et al. Immediate and long-term impact of the COVID-19 pandemic on delivery of surgical services. Br J Surg. 2020;107(10):1250-1261.
33. Viale G, Licata L, Sica L, et al. Personalized Risk-Benefit Ratio Adaptation of Breast Cancer Care at the Epicenter of COVID-19 Outbreak. Oncologist. 2020;25(7):e1013-e1020.
34. Curigliano G, Banerjee S, Cervantes A, et al. Managing cancer patients during the covid-19 pandemic: An esmo interdisciplinary expert consensus. Ann Oncol. 2020;31:1320-1335.
35. Dietz JR, Moran MS, Isakoff SJ, 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 Res Treat.* 2020;181(3):487-497.

36. Ueda M, Martins R, Hendrie PC, et al. Managing cancer care during the COVID-19 pandemic: Agility and collaboration toward a common goal. *Journal of the National Comprehensive Cancer Network.* 2020;18:366-369.

37. Assaad S, Avrillon V, Fournier ML, et al. High mortality rate in cancer patients with symptoms of COVID-19 with or without detectable SARS-COV-2 on RT-PCR. *Eur J Cancer.* 2020;135:251-259.

38. Baud D, Qi X, Nielsen-Saines K, Musso D, Pomar L, Favre G. Real estimates of mortality following COVID-19 infection. *Lancet Infect Dis.* 2020;20(7):773.

39. Juanjuan L, Santa-Maria CA, Hongfang F, et al. Patient-reported outcomes of patients with breast cancer during the COVID-19 outbreak in the epicenter of China: a cross-sectional survey study. *Clin Breast Cancer.* 2020;20(5):e651-e662.

40. Luo J, Rizvi H, Preeshagul IR, et al. COVID-19 in patients with lung cancer. *Ann Oncol.* 2020;31(10):1386-1396.

41. Miyashita H, Mikami T, Chopra N, et al. Do patients with cancer have a poorer prognosis of COVID-19? An experience in New York City. *Ann Oncol.* 2020;31(8):1088-1089.

42. Yang K, Sheng Y, Huang C, et al. Clinical characteristics, outcomes, and risk factors for mortality in patients with cancer and COVID-19 in Hubei, China: a multicentre, retrospective, cohort study. *Lancet Oncol.* 2020;21(7):904-913.

43. Zhang H, Wang L, Chen Y, et al. Outcomes of novel coronavirus disease 2019 (COVID-19) infection in 107 patients with cancer from Wuhan, China. *Cancer* 2020;126:4023-4031.

44. Zhang L, Zhu F, Xie L, et al. Clinical characteristics of COVID-19-infected cancer patients: a retrospective case study in three hospitals within Wuhan, China. *Ann Oncol.* 2020;31(7):894-901.

45. Desai A, Sachdeva S, Parekh T, Desai R. COVID-19 and Cancer: Lessons From a Pooled Meta-Analysis. *JCO Glob Oncol.* 2020;6:557-559.

46. Mahase E. Covid-19: Outbreak could last until spring 2021 and see 7.9 million hospitalised in the UK. *BMJ.* 2020;368:m1071.

47. Onder G, Rezza G, Brusaferro S. Case-fatality rate and characteristics of patients dying in relation to COVID-19 in Italy. *JAMA.* 2020;323(18):1775-1776.

48. Cheng W-T, Ke Y-H, Yang G-Y, et al. Analysis of clinical features of COVID-19 in cancer patients. *Acta Oncologica* 2020;59:1-4.

49. Liu C, Li L, Song K, et al. A nomogram for predicting mortality in patients with COVID-19 and solid tumors: A multicenter retrospective cohort study. *J Immunother Cancer.* 2020;8:1-9.

50. Kokou-Kpolou CK, Megalakaki O, Laimou D, Kousouri M. Insomnia during COVID-19 pandemic and lockdown: Prevalence, severity, and associated risk factors in French population. *Psychiatry Res.* 2020;290:113128.

51. Karacin C, Bilgetekin I, Basal F, Oksuzoglu OB. How does COVID-19 fear and anxiety affect chemotherapy adherence in patients with cancer. *Future Oncol.* 2020;16(29):2283-2293.

52. Swainston J, Chapman B, Grunfeld EA, Derakshan N. COVID-19 lockdown and its adverse impact on psychological health in breast cancer. *Front Psychol.* 2020;11:2033.

53. Poggio F, Tagliamento M, Di Maio M, et al. Assessing the impact of the COVID-19 outbreak on the attitudes and practice of Italian oncologists toward breast cancer care and related research activities. *JCO Oncol Pract.* 2020;16(11):e1304-e1314.

54. Fedele P, Ferro A, Sanna V, et al. Exploring metastatic breast cancer treatment changes during COVID-19 pandemic. *J Chemother.* 2020;33:1-6.

55. Teckie S, Andrews JZ, Chen WC-Y, et al. Impact of the COVID-19 pandemic surge on radiation treatment: Report from a multicenter new york area institution. *JCO Oncol Pract.* 2021;17:1270-1277.

56. Lee SJ, Kim J, Chae YS. Clinical outcome of breast cancer patients on chemotherapy during the COVID-19 Pandemic in South Korea. *Clin Oncol (R Coll Radiol).* 2021;33(1):e85-e86.

57. Prevalence of asymptomatic SARS-CoV-2 infection. *Annals of Internal Medicine* 2020;173:362-367.

58. Covid-19 pandemic planning scenarios. CDC: Centers for Disease Control, 2020. Available at https://www.cdc.gov/coronavirus/2019-ncov/hcp/planning-scenarios.html Accessed November 1, 2020.

59. New York State. Amid ongoing COVID-19 pandemic, governor Cuomo announces results of completed antibody testing study of 15,000 people showing 12.3 percent of population has COVID-19 antibodies. 2020. Available at: https://www.governor.ny.gov/news/amid-ongoing-covid-19-pandemic-governor-cuomo-announces-results-completed-antibody-testing. Accessed January 1, 2022.

60. Angelis V, Tippu Z, Joshi K, et al. Defining the true impact of coronavirus disease 2019 in the at-risk population of patients with cancer. *Eur J Cancer.* 2020;136:99-106.