Title

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Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Original article

Factors Associated With Hospitalization Among Breast Cancer Patients With COVID-19: A Diverse Multi-Center Los Angeles Cohort Study

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Abstract

We investigated outcomes of 132 patients with breast cancer and SARS-CoV-2 infection at two Los Angeles health systems. In this study, older age and more comorbidities were associated with COVID-19 hospitalization and death, while Hispanic/Latinx ethnicity was associated with hospitalization. Breast cancer therapies were not associated with hospitalization or death from COVID-19 in our cohort; larger studies are needed to further explore these relationships.

Background: The SARS-CoV-2 virus has infected and killed millions of people worldwide. Breast cancer is the most prevalent cancer in women and few studies have investigated the outcomes of patients with a history of breast cancer and COVID-19. We report the clinical outcomes of patients with invasive breast cancer who tested positive for SARS-CoV-2, including hospitalization and death, and evaluate demographic and cancer-related factors associated with these outcomes.**Patients:** Patients with a history of invasive breast cancer and positive SARS-CoV-2 test from January 1 to December 31, 2020 at two large, academic Los Angeles health systems were included. **Methods:** Retrospective chart review of the electronic medical record was performed. Data for demographic and cancer-related factors were manually abstracted. Relationships between outcomes and clinical variables were evaluated using Fisher's exact test and linear regression analysis. **Results:** Among a total of 132 patients, 40 (30.3%) were hospitalized, while 11 (8.3%) required intensive care support, and 8 patients (6.1%) died. Older age and presence of one or more additional comorbidities were associated with hospitalization and death ($P = .010$, $P = .003$, $P = .034$, $P < .001$). Hispanic/Latinx ethnicity was associated with hospitalization ($P = .047$). Cancer treatment was not associated with hospitalization or death. **Conclusion:** In our diverse, multi-center, breast cancer cohort, Hispanic/Latinx ethnicity, older age and presence of other comorbidities were associated with worse outcomes from COVID-19. Breast cancer treatment, including surgery, radiation, systemic therapy, and endocrine therapy, was not associated with hospitalization in our cohort. Further studies are needed to explore the relationship between breast cancer and COVID-19 outcomes.

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Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus responsible for coronavirus disease 2019 (COVID-19), has caused a global pandemic. Over 258 million people have been infected with SARS-CoV-2 worldwide and over 5.1 million people have died from SARS-CoV-2 related illness.[1] In Los Angeles, over 1.5 million people have been infected and over 27,000 have died from SARS-CoV-2[2]. Older age, men sex, cardiopulmonary disease, obesity, and diabetes mellitus have been extensively studied as risk factors for severe outcomes from COVID-19.[3,4] In contrast, data evaluating cancer as a risk factor has been mixed and may be specific to cancer type. For example, patients with thyroid cancer do not

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appear to have increased mortality with COVID-19, while patients with hematologic malignancies do.[5-15]

Breast cancer is the most common cancer in women, affecting 12.9% of women.[16] Yet studies evaluating outcomes of patients with breast cancer and COVID-19 have been limited in scope, with mixed results.[17-19] Preliminary data from a multi-institutional collaboration reported that 48% of patients with breast cancer, either active or with no evidence of disease (NED), were hospitalized and 9% died, which is significantly higher than the general population.[20] This finding highlights the need for further investigation of COVID-19 outcomes in breast cancer patients and exploration of possible mechanisms driving disease severity in this cohort.[21]

Hormones may influence the pathogenesis of COVID-19, although the exact mechanisms are yet to be determined. Peckham and colleagues reported that among a non-cancer population, men with SARS-CoV-2 infection have 3 times the odds of intensive care unit (ICU) admission and 1.39 times the odds of death compared to women.[22] There are multiple proposed mechanisms for this difference including a common enzyme in the androgen receptor signaling pathway and SARS-CoV-2 replication cycle, estrogen receptor expression by most cells in the immune system, and increased production of interferons in women.[23-25] Estrogens, progesterone, and testosterone also are direct signals for immune cell function.[25] Meanwhile, the impact of HER2 targeted therapies, as well as other systemic agents (CDK4/6, PI3K, PD-L1) on COVID-19 outcomes, remains poorly described in breast cancer patients. Therefore, the influence of cancer therapy on COVID-19 outcomes in breast cancer patients is of particular interest.

In this retrospective, multi-institutional study, we evaluated how breast cancer- and breast cancer treatment-related factors were associated with COVID-19 hospitalization and mortality at two diverse academic health systems. These results can inform optimal clinical care for breast cancer patients with SARS-CoV-2 and can influence future studies of mechanisms of pathogenesis at the intersection of coronavirus infections and malignancy.

Methods

Study Design and Participants

This retrospective study enrolled patients based on COVID-19 registries at two major academic health systems in Los Angeles: the University of California Los Angeles (UCLA) Health System and the Los Angeles County-University of Southern California Medical Center (LAC+USC). Patients with a history of invasive breast cancer and a positive SARS-CoV-2 polymerase chain reaction or antibody test from January 1, 2020 to December 31, 2020 were eligible for inclusion. Patients with a history of ductal carcinoma in situ, lobular carcinoma in situ, or Phyllodes tumor without IDC or ILC, as well as those with limited medical records about their cancer, were excluded. The Institutional Review Boards at UCLA (IRB #20-000650) and USC (IRB #HS-20-00401) approved the human subjects research at each institution, respectively.

Data Collection

Clinical data was reviewed and abstracted from the electronic medical record for all patients that met eligibility criteria. Variables collected included demographics, body mass index (BMI greater than or less than 25), smoking status, and history of comorbidities (including diabetes, lung, heart, liver, and kidney disease, immunodeficiency, or other malignancy).[26] Breast cancer-related factors including diagnosis, stage, receptor status, and treatment were also collected. Active cancer was defined by oncology documentation detailing ongoing cancer therapy, including surgery, radiation, or systemic therapy, within 12 months of COVID-19 diagnosis, but not adjuvant endocrine therapy. NED was defined as no evidence of disease per imaging and oncology documentation. Staging was conducted using American Joint Committee on Cancer (AJCC) 8th edition.[27] Systemic regimens were further classified as cytotoxic, HER2 targeted, other targeted therapies (including CDK4/6 inhibitors), or immunotherapy.

COVID-19 related outcomes including hospitalization, ICU admission, thromboembolic disease, need for supplemental oxygen, mechanical ventilation, renal replacement therapy, vasopressor support, extracorporeal membrane oxygenation (ECMO), and death were recorded. Treatments received for COVID-19 were also obtained from the EMR.

Statistical Analysis

Descriptive statistics were used to evaluate demographic factors, cancer-related factors, and COVID-19 outcomes. The pre-specified primary endpoint of interest was hospitalization rate from COVID-19; the secondary endpoint was death from COVID-19. Associations between COVID-19 related hospitalization and other clinical demographic or cancer-related variables were calculated by Fisher's exact test (categorical variables) or linear regression (continuous variables), with alpha of 0.05. Averages were reported as medians with interquartile range (IQR) as measure of variance. Statistical tests were two-sided. Statistical analysis was conducted using Python. Scipy was used for calculations, pandas for data manipulation, and matplotlib for graphical representation.

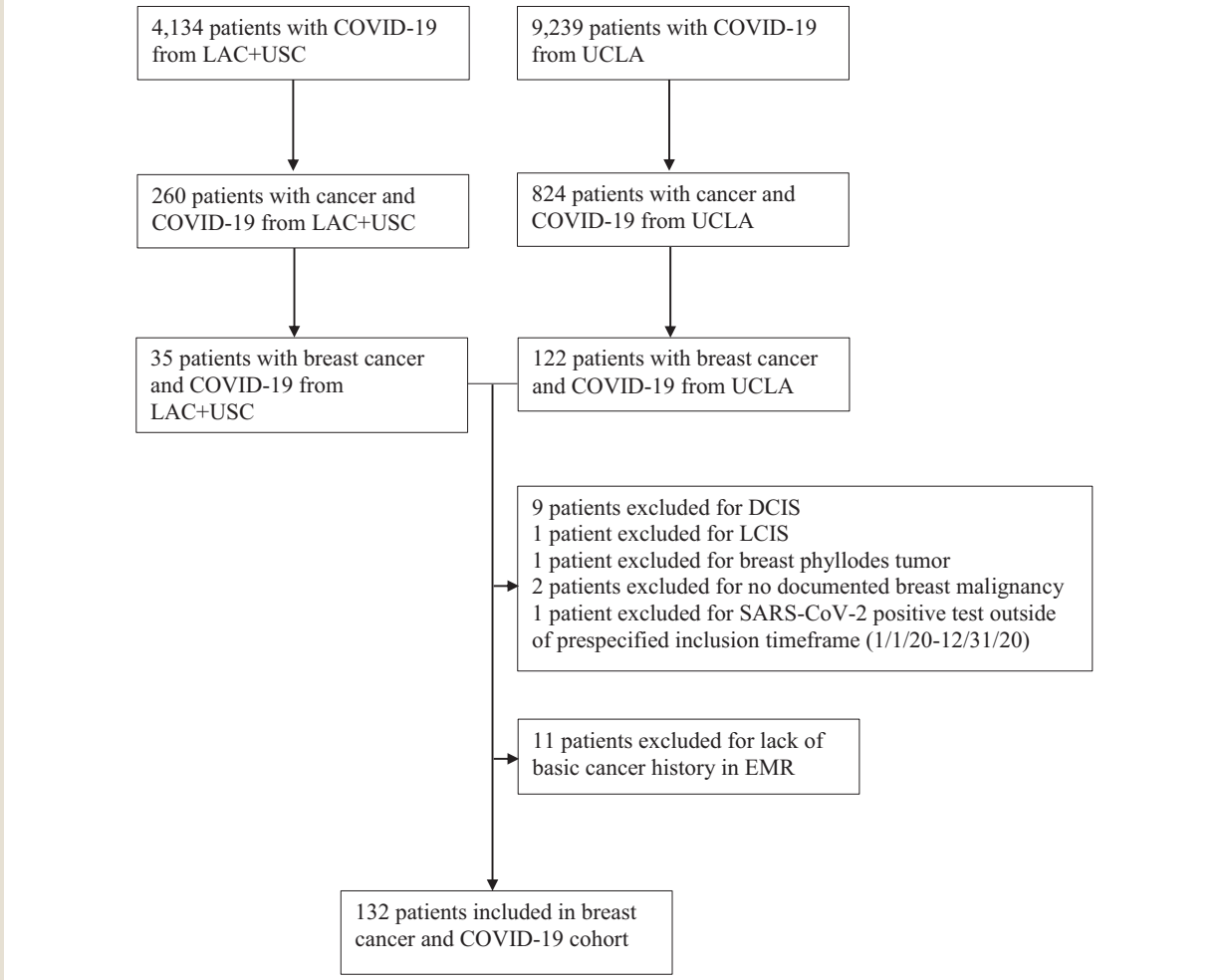
Results

Study Population

Of 13,373 patients with a positive SARS-CoV-2 test at the UCLA and LAC+USC medical centers in 2020, 1,084 had a diagnosis of cancer (8.1%). Of these, 157 patients were coded in the database as having a history of breast cancer (1.17% of total patients, 14.5% of cancer patients), of which 25 patients were excluded based on no history of IDC or ILC, a SARS-CoV-2 positive test outside of prespecified inclusion timeframe, or inadequate information about their cancer diagnosis. Ultimately, 132 patients were included in the study population (**Figure 1**). The median age of our cohort was 60 years (IQR 50-72 years); 62 patients (47.0%) were White/Caucasian and 47 (35.6%) Hispanic/Latinx (**Table 1**). Most patients (74, 56.1%) had at least one comorbidity, in addition to breast cancer. The most prevalent comorbidities were diabetes (32, 24.2%), lung (32, 24.2%), heart (16, 12.1%), and renal disease (16, 12.1%). In addition, 17 patients (12.9%) had a history of a second primary cancer besides breast cancer. A total of 37 patients (28.1%) reported current or former tobacco use. Other demographics are reported in **Table 1**.

Cancer related variables are listed in **Table 2** . Most patients had NED (105, 79.5%), while 27 patients had active cancer (20.5%).

Figure 1 Patient inclusion/exclusion diagram.



Among all included patients, 15 (11.4%) had HR+ HER2+ cancer, 83 (62.9%) HR+ HER2-, 13 (9.8%) HR- HER2+, and 17 (12.9%) had triple negative breast cancer. The most common histology subtype (108, 81.8%) was invasive ductal carcinoma (IDC). Most patients (74, 56.1%) presented with localized disease, while 43 patients (32.6%) had regional disease, and 12 patients (9.1%) distant metastatic disease.

With regards to prior cancer therapy, the vast majority of patients had undergone surgical intervention [either lumpectomy (66, 50.0%) or mastectomy (62, 47.0%)], at any time point in their care, while 91 patients (68.9%) received radiation and 77 (56.8%) received systemic therapy (Table 2). Systemic therapies administered included cytotoxic chemotherapy for 68 patients (90.7%), and HER2 therapy for 13 (17.3%); only 2 patients (2.7%) received immunotherapy. Of the 132 patients with breast cancer, 94 (71.2%) received endocrine therapy from which, 40 (42.5%) received selective estrogen receptor modulators (SERM), 68 (72.3%) aromatase inhibitors (AI), 9 (9.6%) gonadotropin-release hormone/luteinizing hormone releasing hormone (GnRH/LHRH) agonists, and 1 (1.1%) received a selective estrogen receptor degrader (SERD). When assessing cancer therapy at the time of COVID-19 diagnosis, 27 (20.5%) of all breast cancer patients underwent any form of treatment (surgery, radiation or systemic therapy) within 90 days of COVID-19 diagnosis. Additionally, among all 132 breast cancer patients, 50 (37.9%) were on hormonal therapy at the time of COVID-19 diagnosis, including 11 patients (20.8%) taking a SERM, 35 (66.0%) AI, and 7 (13.2%) GnRH/LHRH agonist; none were taking SERD. Additional cancer-related factors are reported in Table 2.

Clinical Outcomes in Breast Cancer Patients with COVID-19

COVID-19 outcomes are listed in Table 3. Among all patients, 40 (30.3%) were hospitalized for SARS-CoV-2 infection, and 31 (23.5%) required supplemental oxygen. Eleven patients (8.3%) required ICU admission, 3 (2.3%) required invasive mechanical ventilation, 2 (1.5%) renal replacement therapy, 2 (3.0%) vasopressor therapy, and 1 patient (0.8%) required ECMO.

Table 1 Demographic Characteristics and Comorbidities of Breast Cancer Patients With COVID-19

Characteristic Total		Total (%) N = 132	Hospitalized N = 40	Not Hospitalized N = 92
Age (years)	15-44 y old	14 (10.6%)	4 (28.6%)	10 (71.4%)
	45-54 y old	35 (26.5%)	6 (17.1%)	29 (82.9%)
	55-64 y old	31 (23.5%)	10 (32.3%)	21 (67.7%)
	65+ y old	52 (39.4%)	20 (38.5%)	32 (61.5%)
Sex	Women	132 (100%)	40 (30.3%)	92 (69.7%)
Race/Ethnicity	White/Caucasian	62 (47.0%)	18 (29.0%)	44 (71.0%)
	Hispanic/Latino	47 (35.6%)	19 (40.4%)	28 (59.6%)
	Black/African	10 (7.6%)	2 (20.0%)	8 (80.0%)
	American	7 (5.3%)	0 (0%)	7 (100%)
	Asian	6 (4.5%)	1 (16.7%)	5 (83.3%)
	Other Race			
Body Mass Index	<25.0	43 (32.6%)	15 (34.9%)	28 (65.1%)
	25.0-29.9	32 (24.2%)	9 (28.1%)	23 (71.9%)
	>30.0	57 (43.2%)	16 (28.1%)	41 (71.9%)
Co-morbidities	Type 2 Diabetes Mellitus	32 (24.2%)	14 (43.8%)	18 (56.3%)
	Lung disease	32 (24.2%)	14 (43.8%)	18 (56.3%)
	Heart disease	16 (12.1%)	9 (56.3%)	7 (43.8%)
	Renal disease	16 (12.1%)	10 (62.5%)	6 (37.5%)
	Immunodeficiency	7 (5.3%)	4 (57.1%)	3 (42.9%)
	Liver disease	2 (1.5%)	1 (50%)	1 (50%)
	Other primary cancer	17 (12.9%)	5 (29.4%)	12 (70.6%)
	Current/Former smoker	37 (28.1%)	14 (37.8%)	23 (62.2%)
Number of Comorbidities	0	58 (43.9%)	10 (17.2%)	48 (82.8%)
	1	42 (31.8%)	12 (28.6%)	30 (71.4%)
	2	17 (12.9%)	9 (52.9%)	8 (47.1%)
	3	11 (8.3%)	6 (54.5%)	5 (45.5%)
	4+	4 (3.0%)	3 (75.0%)	1 (25.0%)

Forty-six (34.8%) received some pharmacologic COVID treatment, including remdesivir, dexamethasone, hydroxychloroquine, azithromycin, convalescent plasma, leronlimab, bamlinivimab, baracitinib, tocilizumab, molnupiravir, or other antibiotics. Among all 132 breast cancer patients, a total of 8 patients (6.1%) died from COVID-19 infection.

Associations Between Patient Demographics and Breast Cancer Characteristics with COVID-19 Outcomes

Statistical analysis revealed that breast cancer patients hospitalized for COVID-19 were older than patients who did not require hospitalization [median age 64.5 years (IQR 53.5-79 years) vs. 58 years (IQR 49-67.5 years), $P = .010$]. In addition, Hispanic/Latinx patients were more likely to be hospitalized for COVID-19 than non-Hispanic/Latinx [19/47 (40.4%) vs. 21/85 (24.7%), $P = .047$]. There was no association between the other minority racial groups (Black/African American, Asian, and other) and hospitalization; when the Hispanic/Latinx cohort was combined with other minority groups, the association with increased hospitalization was no longer apparent. Patients with one or more additional comorbidities were more likely to be hospitalized for COVID-19, compared to those without additional comorbidities [30/74 (40.5%) vs. 10/58 (17.2%), $P = .003$].

Hospitalization rates were higher among patients with lobular subtype compared to ductal subtype ($P = .034$), despite small numbers of patients with lobular histology. There were no other demographic or cancer-related variables that were significantly associated with hospitalization due to COVID-19 (**Figure 2**). Patients with breast cancer who died from COVID-19 were significantly older than patients who did not die from COVID-19 [83.5 years (IQR 69.5-94 years) vs. median age 59 years (IQR 49-71 years), $P = .034$]. Patients who died from COVID-19 were also more likely to have one or more comorbidities compared to patients who did not die [8/8 (100%) vs. 66/124 (53.2%), $P < .001$]. No other significant associations were found between death from COVID-19 and other clinical variables.

Discussion

We report the outcomes of patients with a history of breast cancer who tested positive for SARS-CoV-2 at two academic medical centers in Los Angeles. In contrast to other previously reported studies of clinical outcomes among cancer patients with SARS-

Table 2 Breast Cancer Characteristics of Patients With COVID-19

Cancer Status	Active	27 (20.5%)	8 (29.6%)	19 (70.4%)
	No Evidence of Disease (NED)	105 (79.5%)	32 (30.5%)	73 (69.5%)
Years Since Cancer Diagnosis	<5 years before COVID	63 (47.7%)	19 (30.2%)	44 (69.8%)
	>5 years before COVID	67 (50.8%)	21 (31.3%)	46 (68.7%)
	Unknown	2 (1.5%)	0 (0%)	2 (100%)
Hormone Receptor (HR) Status	HR+, HER2+	15 (11.4%)	4 (26.7%)	11 (73.3%)
	HR+, HER2-	83 (62.9%)	23 (27.7%)	60 (72.3%)
	HR-, HER2+	13 (9.8%)	4 (30.8%)	9 (69.2%)
	Triple negative	17 (12.9%)	6 (35.3%)	11 (64.7%)
	Unknown	4 (3.0%)	3 (75.0%)	1 (25.0%)
Histology Type	Invasive ductal carcinoma	108 (81.8%)	28 (25.9%)	80 (74.1%)
	Invasive lobular carcinoma	12 (9.1%)	7 (58.3%)	5 (41.7%)
	Unknown	12 (9.1%)	5 (41.7%)	7 (58.3%)
Stage	Stage I	49 (37.1%)	13 (26.5%)	36 (73.5%)
	Stage II	44 (33.3%)	14 (31.8%)	30 (68.2%)
	Stage III	22 (16.7%)	5 (22.7%)	17 (77.3%)
	Stage IV	12 (9.1%)	4 (33.3%)	8 (66.7%)
	Unknown	5 (3.8%)	4 (80.0%)	1 (20.0%)
Extent of Disease	Local disease	74 (56.1%)	24 (32.4%)	50 (67.6%)
	Regional disease	43 (32.6%)	10 (23.3%)	33 (68.2%)
	Distant disease	12 (9.1%)	4 (33.3%)	8 (66.7%)
	Unknown	3 (2.3%)	2 (66.7%)	1 (33.3%)
Tumor Size (mm)	0-20	59 (44.7%)	14 (23.7%)	45 (76.3%)
	21-50	45 (34.1%)	15 (33.3%)	30 (66.7%)
	>50	14 (10.6%)	4 (28.6%)	10 (71.4%)
	Unknown	14 (10.6%)	7 (50.0%)	7 (50.0%)
Lymph Node Metastasis	None	71 (53.8%)	22 (31.0%)	49 (69.0%)
	1-3 lymph nodes	31 (23.5%)	6 (19.4%)	25 (80.6%)
	4-9 lymph nodes	14 (10.6%)	7 (50.0%)	7 (50.0%)
	10+ Lymph nodes	5 (3.8%)	0 (0%)	5 (100%)
	Unknown	11 (8.3%)	5 (45.5%)	6 (54.5%)
Distant Metastasis	No distant metastasis	117 (88.6%)	34 (29.1%)	83 (70.9%)
	Distant metastasis	12 (9.1%)	4 (33.3%)	8 (66.7%)
	Unknown	3 (2.3%)	2 (66.7%)	1 (33.3%)
Surgery	Lumpectomy	66 (50.0%)	20 (30.3%)	46 (69.7%)
	Mastectomy	62 (47.0%)	20 (32.3%)	42 (67.7%)
	Unknown	2 (1.5%)	0 (0%)	2 (100%)
	After COVID-19	2 (1.5%)	0 (0%)	2 (100%)
Radiation Therapy	Yes	91 (68.9%)	28 (30.8%)	63 (69.2%)
	No	41 (31.1%)	12 (29.2%)	29 (70.7%)
		N = 132		
Systemic Therapy	Yes	75 (56.8%)	24 (30.7%)	52 (69.3%)
	No	56 (42.4%)	16 (28.6%)	40 (71.4%)
	Unknown	1 (0.8%)	1 (100%)	0 (0%)
		N = 75		

(*continued on next page*)

Table 2 (*continued*)

Cancer Status	Active	27 (20.5%)	8 (29.6%)	19 (70.4%)
Type of Systemic Therapy	Cytotoxic chemotherapy	68 (90.7%)	20 (29.4%)	48 (70.6%)
	HER2 targeted	13 (17.3%)	5 (38.5%)	8 (61.5%)
	Other targeted (not Her2 targeted)	20 (26,7%)	6 (30.0%)	14 (70.0%)
	Immunotherapy	2 (2.7%)	0 (0%)	2 (100%)
		N = 68		
Timing of Cytotoxic Chemotherapy	<12 mo before COVID	12 (17.6%)	4 (33.3%)	8 (66.7%)
	>12 mo before COVID	56 (82.4%)	16 (28.6%)	40 (71.4%)
		N = 132		
Endocrine Therapy Ever	Yes	94 (71.2%)	27 (28.7%)	67 (71.3%)
	No	37 (28.0%)	12 (32.4%)	25 (67.6%)
	Unknown	1 (0.8%)	1 (100%)	0 (0%)
		N = 94		
Type of Endocrine Therapy Ever	Selective Estrogen Receptor Modulator (SERM)	40 (42.5%)	11 (27.5%)	29 (72.5%)
	Aromatase inhibitor	68 (72.3%)	20 (29.4%)	48 (70.6%)
	GnRH/LHRH Agonist	9 (9.6%)	3 (33.3%)	6 (66.7%)
	Selective Estrogen Receptor Degrader (SERD)	1 (1.1%)	0 (0%)	1 (100%)
Endocrine Therapy During COVID-19 Diagnosis	Yes	50 (37.9%)	15 (30.0%)	35 (70.0%)
	No	82 (62.1%)	25 (30.5%)	57 (69.5%)
Type of Endocrine Therapy During COVID-19 Diagnosis	SERM	11 (20.8%)	2 (18.2%)	9 (81.8%)
	Aromatase inhibitor	35 (66.0%)	12 (34.3%)	23 (65.7%)
	GnRH/LHRH Agonist	7 (13.2%)	2 (28.6%)	5 (71.4%)
	SERD	0 (0%)	0 (0%)	0 (0%)
Surgery, Radiation, or Systemic Therapy within 90 days of COVID-19 Diagnosis	Yes	27 (20.5%)	9 (33.3%)	18 (66.7%)
	No	103 (78.0%)	29 (28.2%)	74 (71.8%)
	Unknown	2 (1.5%)	2 (100%)	0 (0%)

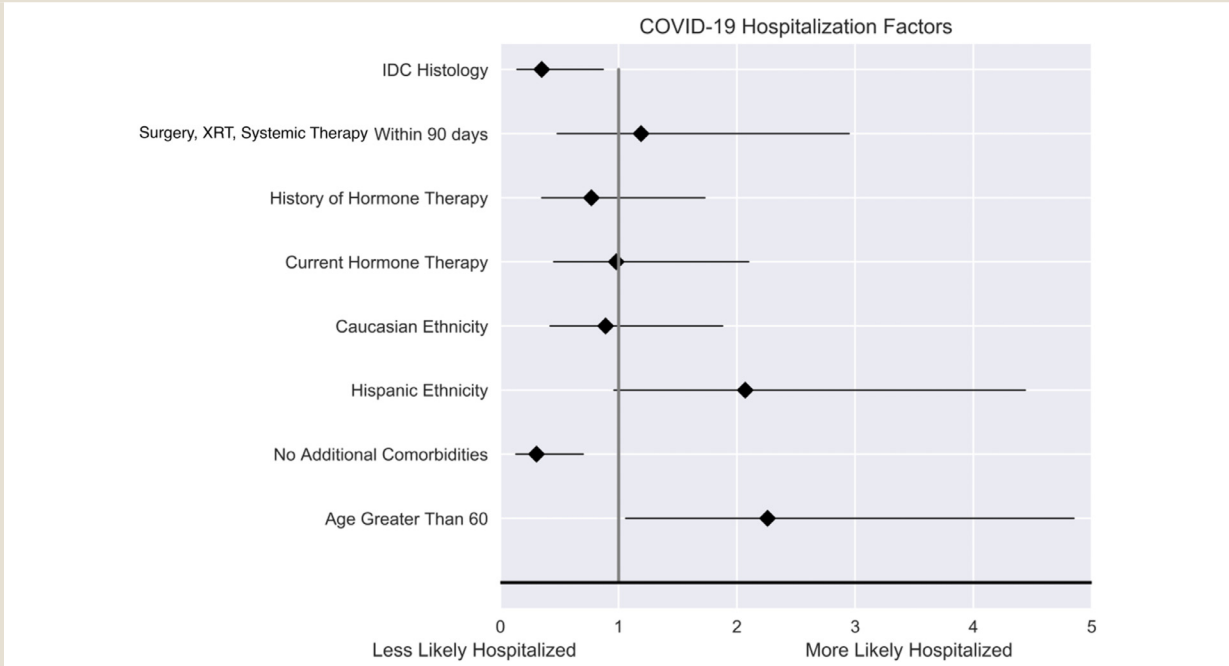
Table 3 COVID-19 Related Outcomes

COVID-19 Outcomes	Number (%)
Hospitalization	40 (30.3%)
Supplemental oxygen during hospitalization	31 (23.5%)
COVID-related thrombosis	3 (2.3%)
ICU admission	11 (8.3%)
Mechanical ventilation	3 (2.3%)
Need for renal replacement therapy	2 (1.5%)
Need for vasopressor therapy	4 (3.0%)
Required ECMO	1 (0.8%)
Death	8 (6.1%)
Received some COVID treatment	46 (34.8%)

CoV-2 infection, our study is highlighted by two strengths. First, our study population reflects outcomes from Los Angeles, California, which became the second major epicenter for the COVID-19 pandemic in late 2020, several months after the first epicenter struck New York City.[2, 28-30] This is important to note, as many important COVID-19 therapeutics had been well described and were available to our hospitalized patients at this time. Second, the uniquely diverse racial-ethnic make-up in Los Angeles allows us to comment on the impact of COVID-19 among a large Hispanic/Latinx demographic.[13, 31-33] As such, our motive was to evaluate for associations between demographic and cancer-related variables in connection with hospitalization and death as critical outcomes of COVID-19 in this population.

In this analysis, older age and multiple comorbidities were significantly associated with both hospitalization and death from COVID-19; this is consistent with two other studies of breast cancer patients with COVID-19 infection.[18,21] Unlike other studies among non-cancer patients which reported an association between obese BMI (>30) and worse outcomes from SARS-CoV-2 (including mortality and hospitalization), our cohort did not reflect this, although this may be because our methodology was not designed to address this (BMI was considered a binary variable, greater than or less than 25).[34-36] However, our study did allow us to query the impact of ethnic diversity; here we found that Hispanic/Latinx ethnicity was significantly associated with hospitalization for COVID-19 in breast cancer patients compared to non-Hispanic/Latinx patients. This trend has also been shown among non-cancer patients, as well as among a cohort of all cancer patients, which found that

Figure 2 Forest plot of odds ratios for COVID-19 hospitalization by demographic and cancer-related variables.



Hispanic/Latinx persons were 4 times more likely to have COVID-19 compared to White/Caucasian patients.[37-40] To our knowledge, this study is the first to report this association in the breast cancer population. Consistent with other studies of ethnic disparities in COVID-19 outcomes among the general population, we suspect this association may be multifactorial in nature, and warrants further investigation.[34,38] In contrast to other studies showing increased rates of hospitalization from COVID-19 in Black/African American patients, we did not see this association, likely because of our small population of Black/African Americans, whereas our Hispanic/Latinx population was much larger.[9,41] Of note, we did not find an association between Hispanic/Latinx (or any race) and death due to COVID-19, although there were only a small number of deaths in our cohort, thus limiting our ability to comment on this specifically. Still, these findings overall suggest the need for continued attention to the ongoing health disparities experienced by Hispanic/Latinx persons.

Among the many clinical challenges facing cancer patients with COVID-19, one is the timing of cancer therapy. While there is now improved understanding of the complex pathophysiology of severe SARS-CoV-2 infection amongst non-cancer patients, and thus leading to the development of critical therapeutic strategies, the mechanisms of how SARS-CoV-2 infection interplay with underlying cancer and cancer therapies remain poorly understood. Furthermore, the impact of multiple delays in cancer care has led to concerns that untreated malignancy may go unfettered, resulting in progression with advanced disease, or development of resistant malignant clones.[42] In the current study, we did not see any association between any breast cancer therapy (including systemic therapy, surgery, or radiation) within 90 days and increased risk of hospitalization for COVID-19.[18,19] Again, we are limited by our sample size, and note that only 40 patients in total were hospitalized for COVID-19. Still, this is somewhat counterintuitive, as cytotoxic chemotherapy and radiation are known to be myelosuppressive and surgery as well may predispose to infectious risk.[43] At the same time, we also speculate that many clinicians, when understanding the risk of SARS-CoV-2 infection, were already more careful in only selecting robust patients for cancer therapy and excluding higher risk patients.[44] Given the role of estrogen in enhancing adaptive and humoral immunity, we had hypothesized that patients receiving endocrine therapy would have worse outcomes from COVID-19.[24,25] However, we did not detect any association between endocrine therapy and either hospitalization or death from COVID-19 infection. In at least one other study, Montopoli et al, also found no association between antiestrogen therapy and COVID-19 outcomes in estrogen-responsive malignancies.[45] Further studies are needed to clarify the interaction between active SARS-CoV-2 infection and breast cancer therapy, to help guide clinicians facing this situation. Until then we advocate that each breast cancer patient should still undergo careful decision-making to assess the risks and benefits with their provider in a personalized approach when infected with SARS-CoV-2.

Despite the low number in our cohort, we found that death from COVID-19 was associated with older age and the presence of additional comorbidities in our cohort of breast cancer patients, which has consistently been reported by many COVID-19 studies, as noted above.[3,4,14] Among our small sample size, 4 of 8 patients (50.0%) who died had advanced dementia at time of hospital-

ization, which may have contributed to decisions about goals of care and thereby impacted outcomes; this reflects the challenge of decision-making for frail or high-risk patients in the era of COVID-19 and the debate about how to best utilize health care resources. In addition, all patients who died were noted to be HER2-receptor negative, although we strongly caution against over-interpretation of this finding, again, given the extremely low numbers. Going forward, closer study of the specific variables which may predispose to death from COVID-19 should be more closely examined.

Our study has several limitations, including its small sample size and its retrospective nature. As mentioned above, we had a low death rate in our cohort, thus limiting our ability to comment on variables associated with death. Accordingly, there were few patients with metastatic disease, and very few patients who received novel systemic agents, such as PD-L1 based immunotherapy or other targeted agents. Nevertheless, our cohort comprises a relatively homogenous cohort in terms of breast cancer therapy, as nearly all patients were treated with standard approaches for localized or regionally advanced disease, including surgery, radiation, systemic therapy, and endocrine therapy, and thus may provide some clues as to how to view SARS-CoV-2 infection in the context of breast cancer. Furthermore, this multi-institutional cohort also provides an informative perspective with respect to the Hispanic/Latinx breast cancer population, in particular. We recommend larger studies to further investigate these reported relationships.

Conclusion

In conclusion, we describe the clinical outcomes of patients with a history of breast cancer from a diverse, multicenter cohort from Los Angeles. Age and the presence of at least one additional comorbidity were significantly associated with hospitalization and death. Hispanic/Latinx ethnicity was associated with hospitalization, but not death. Breast cancer treatments were not associated with hospitalization or death in our cohort.

Clinical Practice Points

- In a diverse, multicenter cohort of patients with breast cancer who tested positive for SARS-CoV-2, older patients and patients with one or more additional comorbidities were more likely to be hospitalized and die from COVID-19
- Patients of Hispanic/Latinx ethnicity were more likely to be hospitalized, suggesting continued attention to health disparities faced by Hispanic/Latinx populations
- Patients receiving endocrine therapy were not more likely to have worse outcomes from COVID-19 infection in our cohort
- These findings can help guide providers and patients through the ongoing COVID-19 pandemic

Disclosure

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